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GI ONCOLOGY (R BRESALIER, SECTION EDITOR)

Does Increased Adenoma Detection Reduce the Risk of Colorectal Cancer, and How Good Do We Need to Be?

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Abstract

Purpose of Review Colorectal cancer (CRC) is largely preventable with colonoscopy and other screening modalities. However, the effectiveness of screening and surveillance depends on the quality of the colonoscopy exam. Adenoma detection rate (ADR) is the best-validated metric by which we measure individual physicians' performance.

Recent Findings Recent evidence suggests that ADR benchmarks may be inappropriately low. There is proof that improving ADR leads to significant reductions in post-colonoscopy CRC (PCCRC). Two studies have demonstrated that when a colonoscopy is performed by physicians with higher ADRs, patients are less likely to have advanced adenomas on surveillance and less likely to develop or die from PCCRC. Finally, there is at least some evidence that higher ADRs do not lead to more cumulative surveillance exams.

Summary The ADR is a useful outcome measure that can provide individual endoscopists and their patients with information about the likelihood of developing PCCRC. To achieve the lowest possible PCCRC rate, we should be striving for higher ADRs. While strategies and innovations may help a bit in improving ADRs, our efforts should focus on ensuring a complete mucosal exam for each patient. Behavioral psychology theories may provide useful frameworks for studying motivating factors that drive a careful exam.

Keywords Screening; colonoscopy · Quality · Colorectal neoplasms

Introduction

Colonoscopy is performed not just to detect, but to prevent CRC [1]. Adenomas are precursors to CRC, and the goal of primary prevention is to remove them before they progress to invasive cancer. Colonoscopy with polypectomy was initially thought to be associated with about 80% reduction in CRC incidence; however, subsequent adenoma cohort studies have shown less impressive results [2]. Patients agree to undergo colonoscopy, an invasive procedure, because they trust that it will protect them from cancer. However, some physicians are more skilled than others at detecting and removing polyps, meaning patients are not equally protected against CRC. Measuring our outcomes can help us estimate the level of protection we provide and can motivate us to improve. The "ultimate" outcome is CRC mortality; fortunately, few endoscopists have enough patients in surveillance programs with this outcome for CRC mortality to be a useful measure of effectiveness, or a quality metric suitable for interventions. We therefore must use surrogate measures that provide us with more immediate data but that correlate with the ultimate outcome of CRC mortality.

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The Adenoma Detection Rate

The best-established surrogate outcome measure is the adenoma detection rate (ADR). The ADR is "the proportion of screening colonoscopies performed by a physician that detect at least one histologically confirmed colorectal adenoma or adenocarcinoma." [3] Initially, only screening exams were used to calculate ADR, partly because of concerns about "contaminating" the

measurement with that of surveillance and diagnostic exams. Recent evidence shows that ADRs calculated in mixed screening/surveillance populations are similar to the traditional screening-only ADR. There was concern that "indication gaming" might tempt some endoscopists to select the procedure indication as "screening" whenever he or she was confident that an adenoma had been removed, while using another indication if it was present and an adenoma had not been removed. However, when Rex and colleagues measured ADR using indication gaming and true indications, the ADR was similar in both measurement methods [4].

The ADR is useful because it correlates with the post-colonoscopy colorectal cancer (PCCRC) rate [5]. A PCCRC is an interval cancer, diagnosed after a screening or surveillance colonoscopy in which no cancer is detected, and before the next recommended examination [6]. In a landmark study, Corley and colleagues examined the correlation between ADR and risk of PCCRC death. They found that "physicians who increase their ADR from <19% to >34% might prevent 1 additional interval cancer over the next 10 years for every 213 colonoscopies performed," and that "each 1% increase in ADR was associated with a 5% decrease in the risk of a fatal interval CRC within the observed range of ADRs." [3]

Samadder and colleagues found that 6% of colon cancers detected were in patients who had had a colonoscopy at least 6 months but fewer than 5 years prior to the cancer diagnosis, which suggests that 6% of cancers detected were interval cancers [7]. Le Clerq and colleagues found that 86.4% of 147 PCCRCs were related to procedural factors (incomplete resection, missed lesions, inadequate exam/surveillance), while only 13% were truly de novo aggressive cancers [8]. Robertson and colleagues found that 71% of 58 PCCRCs were related to procedural factors, while 24% were aggressive rapidly growing cancers [9••]. Taken together, these data imply that improving procedural quality could bring the PCCRC rate closer to a theoretical minimum of 0.78–1.4% of CRC .

Kim and colleagues found that in patients with one or two adenomas, a low ADR for the endoscopist performing the baseline screening was as significant a risk factor for metachronous cancer as the number, size, and histology of adenomas at baseline [10•]. However, patients with no adenomas at screening had such a low risk of metachronous cancer that the endoscopist's ADR did not matter. This supports the findings by Robertson and colleagues that most of the risk of PCCRC comes from missed lesions, incomplete polypectomy, and improper surveillance intervals [11].

What Is an Adequate ADR?

Older American guidelines suggested that the ADR should be at least 15% in women and 25% in men [12]. These have been revised upwards to 20% and 30% in women and men, respectively [13]; however, the possibility that even this new benchmark may be too low is a frequent subject of debate. As high-definition colonoscopes and multiple technological advances have come into use, along with more awareness about the importance of colonoscopy quality, much higher ADRs have consistently been reported in the recent literature. Kaminski and colleagues in 2017 divided their endoscopists into quartiles; the highest had a mean ADR of 31.3%, and the lowest had mean of 10.8% [14•]. Their study population developed 168 interval cancers in 895,916 person-years of follow-up, representing 10.1% of all cancers detected during a 5-year follow-up. They found that those endoscopists who increased their ADR from the lowest to the highest quartile decreased their interval cancer rate from 25.3 cases/100,000 patient-years to 7.1 cases/100,000 patient-years [14••]. They showed that a benchmark of 24.6% was the threshold needed to reach a "profound and statistically significant reduction in the risk of interval colorectal cancer."

European performance measures also indicate a minimum ADR of ≥ 25% when looking at all colonoscopies in patients 50 years and older, excluding emergencies and therapeutic indications; screening and surveillance exams are included together [15]. Multiple studies have demonstrated that the ADR is higher in women physicians, gastroenterologists, and those with 9 or fewer years since residency training [16•]. The total ADR may not tell the whole story, as James and colleagues measured distal and proximal ADR for endoscopists and found that they are only modestly correlated [17•].

So far, no study has found a "ceiling" for ADR, although there is a steady decrease in interval cancer rate as ADR increases. Shaukat and colleagues developed a nonlinear Poisson regression model plotting the relationship between physicians' ADRs and the incidence of PCCRC [18]. This study suggests that a plateau for ADR is between 50 and 60%; at this level, the incidence of PCCRC appears to be less than one cancer per 10,000 person-years. This appears to be significantly lower than what would be estimated based on CRC incidence data. The incidence of CRC was 40.7/100,000 person-years between 2009 and 2013 [19]. Using estimates that 13–24% of interval cancers are aggressive and not due to procedural factors, we would expect that an endoscopist who performs 500 colonoscopies per year for 10 years might see 0.3–0.56 PCCRCs that he or she could not have prevented. Because an ADR of 50% seems to correlate with a PCCRC rate lower than this estimated minimum, then 50% is probably a good estimate of an "ideal", "aspirational", or "ceiling" ADR. Clearly, more studies are needed to assess whether a ceiling ADR should exist, and what its value should be.

How Does ADR Affect the Surveillance Interval?

It is likely that endoscopists with very high ADRs are detecting more diminutive adenomas that are not necessarily

clinically significant. In other words, attaining ADRs higher than aspirational levels, almost at the level of the true population prevalence of adenomas, could reflect the law of diminishing returns rather than improved prevention for patients. This could lead to more frequent surveillance exams where little pathology is detected, increasing costs and risks without clear clinical benefit. Conversely, finding diminutive polyps and taking the time to remove them can be considered a marker of a more thorough exam.

The colonoscopist's ADR affects the yield of future colonoscopies. Mangas-Sanjuan and colleagues studied a higher-risk group, which was a cohort of patients who had an advanced adenoma detected on index exam. They found that the ADR of the colonoscopist who performed the baseline exam predicted finding advanced neoplasia at surveillance colonoscopy [20••]. Kim and colleagues studied a lower-risk group, which was patients who had no or only 1 or 2 non-advanced adenomas at a baseline exam [10•]. They showed that when compared to physicians with a low ADR, if the physician performing an initial screening exam has a moderate or high ADR, and at least one adenoma was found at baseline, it was about 2/3 less likely that any neoplasia or an advanced adenoma would be found at the next surveillance exam. This effect did not reach statistical significance if no adenomas were found during the baseline exam. This study defined a "hidden risk" group with the highest risk of advanced neoplasia at follow-up exam and two adenomas at baseline and had their initial exam performed by a physician with a low ADR. Taken together, these studies suggest that the ADR of the endoscopist performing the baseline colonoscopy should impact surveillance recommendations, particularly for patients with adenomas and low physician ADR. Conversely, if an exam is performed by a physician who has a high ADR, lengthening the surveillance interval may be considered [21].

When a colonoscopy is performed by a physician with a high ADR, there are two implications. First, it is more likely that one or more polyps will be found, which will shorten the surveillance interval from 10 to 5 or even 3 years. Second, it is less likely that a polyp will be left behind, which implies that the yield of the next exam will be lower. These patients are doubly protected; physicians with a high ADR protect their patients both by removing all pathology and by recommending shorter surveillance intervals. Physicians with a low ADR do their patients a double disservice, by missing pathology and by recommending inappropriately longer surveillance intervals. Conversely, some physicians seem to be aware that they are at risk of missing pathology and recommend shorter surveillance intervals than guidelines would recommend after a negative exam. It is not clear what effect these practice patterns have on PCCRC risk. Current guidelines do not incorporate endoscopist ADR among factors determining appropriate surveillance intervals, but assume a "high quality" colonoscopy at baseline, meaning that minimum benchmarks have been met. .

Other Measures of Colonoscopy Quality

In addition to the ADR and the PCCRC rate, other measures have been proposed or used as markers of colonoscopy quality. "Adenomas per colonoscopy" (APC) has been suggested by an ACG/ASGE joint task force [13]. When ADR is measured, some physicians will search less aggressively for polyps after the first adenoma is found [22], as removing additional polyps will lengthen the procedure without improving the ADR. The APC would reduce this tendency. However, to measure APC accurately, each polyp would need to be examined separately to confirm that it is an adenoma. This could generate increased costs for photography software and pathology. Hilsden and colleagues found that the ADR and APC were complementary; APC did a better job of discriminating between the lowest- and highest-performing endoscopists, but some endoscopists achieved minimum benchmarks on one measure but not the other [23]. Routinely reporting both measures may act as a motivating factor for physicians who are above the ADR benchmark but have room for improvement.

In the USA, withdrawal time (WT) is frequently tracked. WT is the amount of time a physician spends examining the colonic mucosa after intubation and identification and photo documentation of the cecum landmarks of appendicular orifice and ileocecal valve, until the endoscope is withdrawn from the anus [24•]. Currently, WT is best used as a target for intervention for endoscopists who have low ADRs and short WTs. European performance measures include numerous pre- and post-procedure factors, such as bowel preparation, time slot for colonoscopy, polyp detection rate, appropriate polypectomy technique, polyp retrieval rate, tattooing resection sites, complication rate, patient experience, and appropriate post-polypectomy surveillance [15]. The advanced adenoma detection rate has been suggested, with the rationale that these are more clinically meaningful lesions. However, size measurements are somewhat subjective [4]. "Polyp detection rate" can be used, but this measurement can be gamed by removing clinically insignificant polyps [4]. The serrated polyp detection rate has also been considered, as serrated lesions are more difficult to detect and contribute significantly to PCCRC. This measurement is problematic, however, because serrated neoplasia detection tends to correlate with that of adenomas especially for high-level detectors, and because of the significant inter-observer variability among pathologists in the interpretation of subtypes of serrated polyps.

How Can a Physician Improve His or Her ADR?

Some factors associated with a higher ADR are immutable, such as being female, being a gastroenterologist, and being in practice for less than 9 years [16•]. However, other factors can be changed. A combination of feedback, benchmarking, and training has been most effective in improving ADRs. Many

physicians improve gradually over time when they know they are being monitored. For example, multiple studies using performance feedback have shown that ADR improves steadily throughout the duration of the tracking period [21, 25]. A meticulous and compulsive mucosal inspection technique is critical. Interestingly, attempts at re-training after entering practice have been met with mixed results. Interventions that have been studied to determine the effect on improving ADR are summarized in Table 1. A network meta-analysis found that low-cost interventions (dynamic position changes, second observer, water-immersion colonoscopy) were just as effective as add-on devices (cap, G-EYE, Endocuff, Endorings), image enhancement (chromoendoscopy, narrow band imaging, flexible spectral imaging color enhancement, blue laser imaging), or newer scopes (FUSE, extra-wide-angle-view colonoscopy, Dual Focus) [40]. There is insufficient evidence to recommend for or against the use of specific bowel preparations, CO_2 insufflation, Propofol sedation, antispasmodics, or position changes for the purpose of improving ADR.

Negative Effects of Increasing ADR

While the GI field is focused on improving the ADR, there are some potential downsides to this goal. Modeling has projected an increased burden of surveillance endoscopies that are recommended after adenoma removal [14••]. However, in the study by Mangas-Sanjuan and colleagues, a high ADR was not associated with more frequent surveillance [20••]. Procedure times may be longer due to time spent on careful mucosal inspection and on removing pathology. The clinical benefit of removing diminutive polyps is not clear, since the vast majority of these will not progress to invasive cancer. Patients may experience anxiety after being labeled "high-risk" when more than two adenomas are found, as current guidelines recommend the same surveillance interval for patients with a few diminutive adenomas as for those with a histologically advanced adenoma. Finally, there is the concern about increased complication rates due to more frequent surveillance exams; however, in multiple studies, the perforation rate was the same for those who improved ADR and those who did not (0.02% for both groups) [14••]. Furthermore, Brenner and colleagues found that as ADR improved, bleeding and perforation rates were stable over 10 years [21].

Why Do Some Physicians Lack Motivation to Improve?

If there are so many methods available that help improve the ADR, why do some individual physicians not adopt them? A number of factors might be at play. Michie and colleagues studied psychological theories that influence behavior change when implementing evidence-based medicine guidelines. They developed a list of 12 domains that could be studied to learn more about behavior change [41]. This study illustrates that informing physicians about the importance of a practice and ensuring that they have the skills to change their behavior are only part of the process; many additional factors determine whether they will implement the change. For example, if physicians lack the self-efficacy to believe that they are capable of achieving an ADR of 50%, it is unlikely that they will make significant efforts toward achieving that goal. If the endoscopy unit environment is not designed to allow for ample withdrawal times, then competing pressures will outweigh physicians' motivation to spend more time examining. If group norms in the environment stress productivity over ADR and other metrics, physicians will strive for higher productivity. It has also been proposed that obsessive-compulsive or other personality traits may be more prominent in endoscopists with a high ADR, and these traits are more difficult to impact.

For those who are not receiving feedback in the form of ADR, withdrawal times, or interval cancer rates, the Dunning-Kruger effect might be playing a role [42]. In the studies conducted by Dunning and Kruger, subjects assessed their own skills as being about average when they were significantly below average. This finding suggests that endoscopists who have a below-average ADR may not believe their skills are inferior to their colleagues' skills.

For those who are aware that their ADR is below average but choose not to adopt new methods or technology to improve their skills, it may be difficult to see the benefit of improving the ADR. For example, Kaminski and colleagues found that endoscopists who increased their ADR from the lowest (10.8%) to the highest quartile (31.1%) decreased their interval cancer rate from 25.3 cases/100,000 patient-years to 7.1 cases/100,000 patient-years [14••]. The event of an interval cancer is so rare that an individual endoscopist is very unlikely to notice a difference after improving his/her ADR. The benefit is seen at the population level, when the pool of physicians improves its collective ADR. When weighing the cost of additional training, additional equipment, and the additional time they would spend on each exam doing a more thorough mucosal examination, many physicians cannot perceive the benefit of possibly seeing a fewer interval cancers as justifying those costs. Furthermore, the cost of treating invasive cancer would be borne by the patient/insurance company, not by the endoscopist. In his landmark work on game theory, Thomas Schelling wrote of the difficulty convincing people to act to benefit the greater good when they are motivated by personal reward [43]. Daniel Kanneman's theory of loss aversion also partially explains this. He argues that it is difficult for people to choose to act when the outcome being prevented is in the future, the effects are uncertain, and the action involves personal cost [44]. Certainly, the outcome of a PCCRC would fit these criteria.

Table 1 Interventions aimed at improving ADR (original)

Method	Population studied	Effect on ADR	Limitations
Training in withdrawal technique and lesion identification	EQUIP 1 & 2 - Average ADR 36%	ADR improved to 47% [26] and remained improved after 5 months [27].	
	EQUIP-3 – Average ADR 31% in the intervention group, 36% in the control group	ADR improved by 12% in the intervention group, but endoscopists receiving passive monitoring improved by 4% [28•].	
Mandating a minimum withdrawal time for each of four segments	Single-center study, physicians were asked to spend at least 2 min per colon segment	Mean ADR improved from 23.5% before to 34.7% after the intervention [29].	Mandating a withdrawal time for the whole exam has not led to improvements in ADR. Instead, endoscopists should focus on mastering the technique of effective mucosal exposure, as this will naturally lead to longer withdrawal times [30•].
Switching to high-definition endoscopes	Meta-analysis; mixed population	incremental yield of 3.5% for small adenomas but not for larger or more advanced neoplasia. [24•]	
Use of narrow band imaging	Control ADR of 34.4%	ADR improved to 48.3% in 190-NBI group. Polyp detection also increased, without a difference in adenoma miss rate [31].	NBI on older scopes was darker and not as effective
Dye-based Chromoendoscopy	Meta-analysis (mixed population)	increase of 30% (0.33 lesions) in adenoma detection, but with increased cost and procedure duration [32]	Only one study used high-definition colonoscopes as controls
Water exchange colonoscopy	Baseline ADR not reported	Higher ADR with water immersion/exchange vs. air (36.3% vs. 31.4%) [33]	
Second examination of the right colon (either retroflexed or in forward view)	30.2–34% on first pass	7.5% had an additional adenoma in retroflexion, 10.5% had an additional adenoma on 2nd forward view exam; there was no difference between techniques [34]	mean withdrawal time in these studies was 12.5 min, so it is possible that the increased ADR is related to a longer withdrawal time and not necessarily to the method of examination
Reporting ADR to physicians	Tertiary-care VA with six physicians	Mean ADR increased from 44.7% before to 53.9% after implementing quarterly report cards [25].	
Leadership training	Polish study where center leaders underwent intensive training	ADR for not just the participant leaders, but for the facilities led by participants improved from a mean of 18.4% to 24.1% [35].	
Cap-assisted colonoscopy	Board-certified gastroenterologists at two centers (one VA), using 180 scopes	No difference in ADR between cap-assisted or standard exam (60% vs. 57%) [36]	
Endocuff	Meta-analysis of studies from multiple international sites, but mostly academic hospitals	ADR in Endocuff group was 50.4%, compared to 43.3% in standard colonoscopy group [37].	It appears that the Endocuff was more useful in groups where the control ADR was lower. The device has subsequently been replaced by the Endocuff Vision, which has not been extensively studied.
	Single-center RCT in the UK	No significant difference between ADR in Endocuff group (60.9%) and standard group (63.0%) [38].	
FUSE	Regional screening program of FIT-positive patients	No significant difference in ADR between FUSE (43.6%) and standard forward view (45.5%) [39].	Several other devices are available (mostly outside the US) to improve the field of view, and these generally result in an improvement in ADR by about 7%, but the cost of these devices precludes routine use [30•].

Because the outcome of interval cancer is so rare, and because physicians may not even learn of an interval cancer found in their patients, surrogate outcomes such as ADR and withdrawal time are used for more immediate feedback. However, if physicians do not appreciate the correlation between these surrogate markers and PCCRCs, they may place less importance on improving these measures. Indeed, there are "ADR deniers" who may be skeptical that it is a useful metric, consider it a passing medical trend, and disregard their audit data. This can likely be explained using some of the behavioral psychology theories described above, but further study of this might help inform future interventions.

Conclusion—the Future of Screening

In the ideal situation, the ADR would inform screening and surveillance recommendations, in addition to patient risk factors and colonoscopy findings. A screening colonoscopy done by a physician who has an aspirational ADR imparts a high degree of protection against CRC. If no adenomas are found, the patient can avoid another exam for at least 10 years, and if adenomas are found, then surveillance intervals longer than the conventional 3 or 5 years can be considered, based on details of adenoma findings. If the initial exam is performed by a physician with an ADR just above established benchmarks, then established screening and surveillance intervals would need to be followed. More research is needed before recommendations could be provided if the initial exam is performed by a physician who does not meet minimum benchmarks.

Future studies might explore the best surveillance interval after a colonoscopy is performed by a physician with an aspirational ADR. It would also be valuable to apply behavioral psychology theories to the practice of colonoscopy; learning how to motivate physicians to perform a complete mucosal exam could have a major impact on the PCCRC rate.

Key points

• The adenoma detection rate (ADR) is now well-established as a marker of risk for post-colonoscopy colorectal cancer (PCCRC).
• Improving one's ADR is correlated with a reduction in the PCCRC rate.
• Existing benchmarks for adequate ADRs may be too low to provide adequate protection from PCCRC.
• While techniques and technology are available that make minor contributions to improving ADR, the most important factor is a complete mucosal exam.
• Behavioral psychology theories may provide useful frameworks for studying factors that motivate endoscopists to perform a careful exam.

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Compliance with Ethical Standards

Conflict of Interest Christen Dilly and Charles Kahi declare no conflict of interest.

Human and Animal Rights This article does not contain any studies with human or animal subjects performed by any of the authors.

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