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Review

Colonoscopy for Colorectal Cancer Screening

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Abstract

Colorectal cancer (CRC) is the second leading cause of cancer death in the United States. Many, if not most, cases arise from premalignant lesions (adenomas) which may be identified and removed prior to becoming frankly malignant. For over a decade, colonoscopy has been the preferred modality for both CRC screening and prevention in the US. Early reports suggested that colonoscopic screening imparted a 90% risk reduction for colorectal cancer. Subsequent studies showed that estimate to be overly optimistic. While still an outstanding CRC screening and detection tool, colonoscopy has several important limitations. Some of these limitations relate to the mechanics of the procedure such as the risk of colonic perforation, bleeding, adverse consequences of sedation, and the inability to detect all colonic polyps. Other limitations reflect issues with patient perception regarding colonoscopy which, at least in part, drive patient non-adherence to recommended testing. This review examines the literature to address several important issues. First, we analyze the effect of colonoscopy on CRC incidence and mortality. Second, we consider the patient-based, periprocedural, and intraprocedural factors which may limit colonoscopy as a screening modality. Third, we explore new techniques and technologies which may enhance the efficacy of colonoscopy for adenoma detection. Finally, we discuss the short and long-term future of colonoscopy for CRC screening and the factors which may affect this future.

Key words: Colonoscopy, colon cancer, screening, adenocarcinoma

1. Introduction

Colorectal cancer (CRC) is the second leading cause of cancer death in the United States (1). In 2008, the most recent year for which there are reliable statistics, 142,950 people were diagnosed with colorectal cancer and 52,857 people died from the disease. This is despite the fact that the incidence has dropped from 59.5 per 100000 people in 1975 to 44.7 per 100000 people in 2007 while mortality has decreased from 28.6 per 100000 people in 1976 to 16.7 per 100000 people in 2007.(2) Unfortunately, most early cancers are clinically silent making screening for frank malignancy as well as premalignant lesions an attractive option. While there are many potential screening modalities, the major clinical guidelines all recommend colonoscopy as the preferred test as it detects both cancers as well as precancerous lesions with high reliability. Moreover, the literature suggests a reduction in cancer incidence and mortality for those who undergo colorectal cancer screening via colonoscopy. From a population health standpoint, colonoscopy is also cost effective with cost-benefit analysis showing screening colonoscopy well within the acceptable rates of 20000$/year life saved. (3)

Screening colonoscopy is of potential benefit to patients in two ways. First and most commonly, it can detect and facilitate removal of precancerous polyps.

Several studies have shown that colonoscopy with polypectomy is effective at decreasing CRC (see section II). In addition, a negative colonoscopy, if of sufficient quality, has a high negative predictor value for CRC development which is some studies extends to 20 years. (4) Second, colonoscopy may detect cancers at an early stage where there is a higher chance for cure than in those discovered in a more advanced stage.

While a highly effective screening and prevention tool, colonoscopy is imperfect. Numerous studies have shown that there is a substantial, though variable, polyp miss rate even among expert examiners who know that they are being scrutinized. There are multiple factors which contribute to this miss rate, and it is likely that not all the reasons are yet known. This article will discuss the various factors – systemic, patient –based, and endoscopist-based, which play a role in adenoma detection. We will also discuss the current methods, both systemic and technical, of improving colonoscopy as a screening tool. Finally, we will discuss the future of colonoscopy for CRC screening.

2. Benefits of Colonoscopy for CRC Screening

In patients who do not have inflammatory bowel disease, most primary colorectal cancers are thought to derive from precancerous polyps. (5) The majority of these polyps arise over the course of a decade or more via a well described series of mutations. For years, our understanding of adenoma prevalence was that 25% of males and 15% of females will have adenomatous polyps by the time they reach age 50. Recent studies conducted in both academic and community practice settings suggest that the true rate may be higher. (6) Moreover, the vast majority of these polyps, and even early cancers, are asymptomatic. (5) Since colonoscopy allows for the detection and removal of these polyps prior to the progression to cancer, it would seem to be an ideal screening tool. Several critical questions needed to be answered, however, before colonoscopy could be considered a valid (and valuable) screening tool. For example, it has to be superior to other available screening modalities. In particular, it must be compared to flexible sigmoidoscopy (FS), a less invasive screening method which does not require sedation and which had been shown to reduce colorectal cancer incidence and mortality.(7) Several trials address the safety and efficacy of colonoscopy as a primary screening test in asymptomatic individuals. The first was the VA Cooperative Study-380 published by Lieberman and colleagues in 2000. (8) This cohort study examined 3196 subjects, 3121 of whom underwent a complete colonoscopy. While patients with adenomas in the distal colon were statistically more likely to have adenomas in the proximal colon than those without such lesions, 52 percent of those with advanced proximal neoplasia had no distal adenomas. Thus, advanced proximal lesions would have been missed in more than half the patients in an FS based screening program. One significant limitation of this study is the fact that nearly 97 percent of the subjects were male. To determine the efficacy of primary screening colonoscopy in asymptomatic woman, Schoenfeld and colleagues conducted the CONCeRN trial. (9) This prospective cohort study of 1463 women undergoing complete colonoscopy found that only 35% of women with proximal neoplasia would have had their lesions detected by flexible sigmoidoscopy. The authors concluded that colonoscopy may be the preferred CRC screening tool for women. From these studies, it is clear that colonoscopy detects more adenomas than flexible sigmoidoscopy. A more vital concern, perhaps, is the effect of adenoma removal (i.e. polypectomy) on colorectal cancer incidence and mortality.

Effect on Colon Cancer Incidence

There are reasonably good data to support a decrease in colorectal cancer in those undergoing colonoscopy with polypectomy. The first study to suggest this benefit was the National Polyp Study which was published in 1993. (10) While this study had some significant limitations, such the use of historical controls, its conclusion that colonoscopic polypectomy could prevent between seventy six and ninety percent of colorectal cancers. A similar study conducted in Italy by Citarda and colleagues showed a reduction in colon cancer incidence of sixty-six percent. (11) Again, this study was limited in that controls were not taken from a matched cohort, but rather a mathematical model was used to calculate the expected CRC incidence in a hypothetical group.

Effect on Colon Cancer Mortality

As for all outcomes of screening colonoscopy, the evidence for a reduction in CRC mortality is indirect. Nonetheless, the consistency of the data reassures us that a significant benefit is derived from colonoscopic screening, even if the magnitude of that benefit is not perfectly defined. Thus far, two primary study designs have been used to address the question: retrospective case-control studies and prospective cohort studies. While neither method has the strength of a randomized controlled trial, most study authors' have worked diligently to shore up the statistical limitations inherent in the studies' designs and these

studies represent the best available science on which clinicians must base patient care decisions. These studies are listed in table 1 below. (12-15)

In 2009, Baxter and colleagues published a population based, case-control study examining subjects who received a CRC diagnosis between 1996 and 2001 and who died of CRC by 2003. They matched each case 1:5 with a control. The authors noted an impressive 67% reduction in left sided colorectal cancer but none in right sided diseases. This study has several important limitations worth noting. The cecal intubation rate of 79-83% is substantially below the 95% rate which would be expected for screening examinations and 90% for all examinations. (16,17) While the authors rightly controlled for this by performing a sub-analysis on "complete" colonoscopies, the low rate of cecal intubation may reflect overall poor colonoscopic technique (including inspection for adenomas) which such adjustments will not mitigate. Additional support for this theory is found in the low polyp detection rate of 26% in case patients. Current standards dictate a 25% adenoma detection rate in men and a 15% adenoma detection rate in women. (18) Given that a number of the polyps detected in the study were likely hyperplastic, one would expect a total polyp detection rate (adenomas + hyperplastic) to be in the 30-40% range. Another limitation is the fact that not all of the colonoscopies included were performed for screening. Patients with symptomatic cancers which prompted the examination would be cases based on the design, but would have more likelihood of having advanced disease, and thus less chance of benefitting from the screening test. Despite these limits, the difference in right and left sided benefit in this study is impressive and should not be lightly dismissed.

Singh *et al.* found a similar disparity in the protective benefit of colonoscopy. In his retrospective cohort study, Singh used Manitoba's claims database to compare CRC mortality between patients who had colonoscopic CRC screening versus the standardized CRC mortality rate for the general population. In examining 54,803 subjects, he noted a 29% overall reduction in CRC mortality, all of which was derived from a decrement in left-sided cancer deaths. Interestingly, when the authors stratified the data according to the specialty of the endoscopists, gastroenterologist conferred a reduction in right sided CRC of 59%. This strongly suggests that the type of examiner (and by extension their training and experience) matter greatly in optimizing the performance characteristics of colonoscopy as a CRC screening tool.

Rabeneck and colleagues performed a cohort study on all adults 50-90 years old living in Ontario on 1 January 1993 in which they followed subjects for 14 years and stratified them by the "intensity of colonoscopy use" in their region. They performed multivariable analysis adjusting for age, gender, comorbidity, income, and residence (urban vs. rural). Rabeneck found that for every 1% Increase in the complete colonoscopy rate, the hazard rate of death decreased by 3%. While there are a number of limitations to this study, including an inability to attribute causality, the magnitude of the effect, the size of the sample study, and the biologic plausibility of the finding offer food for thought.

The most recent study to address the effect of screening colonoscopy on CRC mortality was from the National Polyp study. The authors examined 2602 patient who had had adenomas removed via colonoscopic polypectomy and then were followed for a mean of 15.8 years. Compared to historical controls, this group enjoyed a 53% reduction in CRC. While this study is limited by the fact that endoscopists were all in expert centers, the results are nonetheless compelling, particularly because they are in keeping with prior studies in showing a clear reduction in mortality in association with screening.

Table 1: Major trials addressing a reduction in CRC mortality.

Author	Year	Design	N	CRC Mortality Reduction
Baxter[12]	2009	Case-Control	10,292 (Case) 51,460 (Control)	67% - left sided 1% (NS) -right-sided
Singh [13]	2010	Cohort	54,803	29% overall 47% left-sided 0% right-sided
Rabeneck[14]	2010	Cohort	2,412,077	3% decrease/1% increase in colonoscopy
Zauber [15]	2012	Cohort	2602	53% overall

3. Limitations to Colonoscopy for CRC screening

Adherence to Screening

Despite the impressive statistics cited above, CRC remains the number two cause of cancer-related death among Americans, largely because only one in three eligible patients over 50 is screened. There are multiple barriers that diminish adherence to CRC screening. Overcoming these obstacles may yield further declines in CRC incidence and mortality.

Barriers to CRC screening include lack of health insurance limiting access to care, aversion to bowel preparations, and fear of invasive procedures. Psychosocial barriers identified as "parasexual" sensitivities affecting adherence include homophobia or prior sexual trauma, fatalism, negative prior experiences with testing, and financial skepticism about screening recommendations. (19) A recent telephone survey of 454 ethnically diverse adults ≥ 50 showed fear of embarrassment, fear of getting AIDs, fear of procedural pain, and older age were all positive markers of avoiding CRC screening. (20) Fear of cancer and medical mistrust were shown to be positive markers for willingness to undergo CRC screening. An effective, patient-centered approach to CRC screening which addresses the particular barriers found in a given patient population may overcome these hurdles

The psychology literature suggests that too much choice can in itself be a deterrent to action. (21) While each screening modality has its own strengths and weaknesses, the array of options may confuse patients and lead to screening inertia. What is lost in that confusion is that adherence to *any* CRC screening is superior to no screening at all. (22) A patient-centered approach focusing on their preference in the decision process is crucial for successful CRC screening. For example, when test sensitivity was rated highest among the patient's concerns, colonoscopy was the preferred test. (23-26) This data must be interpreted with caution, however, as a large percentage of patients in these studies were white males with previous exposure to colonoscopy potentially biasing their choice. Supporting this notion are other studies showing that when patients of different genders and ethnicity who were, screening-naïve patients were questioned, colonoscopy was not the preferred choice. (27-28) Inadomi and colleagues tested this patient-centered approach in a study of 1000 patients who were randomized into three arms, FOBT only, colonoscopy only, or a choice of either test. (29) Those offered either FOBT only or a choice of either test were twice as likely to undergo screening versus those only offered colonoscopy. This study showed variance along racial/ethnic and gender lines, but it did not support previous conclusions that offering a choice resulted in lower screening rates. One major difference was that patients were only given two options which implies that giving some options is beneficial for adherence compared to discussing all available options. Several studies support the notion that, among lower socioeconomic groups, the cost of the screening test exerts a major influence on test preference and screening adherence. (30-31) A British study with free CRC screening showed that higher cancer fatalism, lower socioeconomic status, and lower self-rated health were more of an influence to not undergo screening than cost. (32) Clearly, patient preference plays an important part in the adherence to CRC screening recommendations. Addressing patient-specific concerns, particularly at the primary care level, should enhance screening adherence.

Periprocedural Factors

A thorough colonoscopic purge is crucial to successful colonoscopic CRC screening. Unfortunately, up to 25% of all patients have an inadequate bowel preparation at the time of their examination. A significant amount of interest has been centered on the quality of the bowel preparation and its effect on one's ability to detect polyps <10 mm. A recent study by Sherer *et al.* in 2012 investigated ADR in 3638 subjects undergoing colonoscopy, separating them into poor and fair versus good and excellent bowel preps. (33) Only a poor prep led to a significant decline in ADR, suggesting that a patient with a fair prep could follow standard post-procedure guidelines. Another recent study, however, came to a very different conclusion. Chokshi and colleagues performed a retrospective chart review on 373 patients with inadequate bowel preps to see what was detected at their follow up colonoscopy. (34) The mean interval between colonoscopies was 340 days for low risk patients and 271 for high risk patients. On repeat examination, the per adenoma miss rate was 47.9 percent. Even more concerning is that in patients with no adenomas detected on index colonoscopy, 33.8% had an adenoma on repeat examination and 18% had advanced adenomas, placing them at high risk for subsequent malignancy if undetected.

Intraprocedural factors

The intraprocedural limitations of screening colonoscopy may be divided into three categories: endoscopist factors, equipment factors, and anatomic/physiologic factors. The recommendations on minimizing endoscopist-related factors focus on ad-

herence to an accepted group of quality indicators. (18) Ultimately, these indicators are designed to ensure adequate and careful visualization of the colonic mucosa which should lead to enhanced polyp detection, which seems to correlate with enhanced adenoma detection. (35) The indicators consist of a cecal intubation rate within accepted standards (including photo documentation of the cecum), a withdrawal time of ≥ 6 minutes, and documentation of the adequacy of bowel prep. Achieving these benchmarks should help endoscopists achieve adenoma detection rates (ADR's) of ≥25% for men and ≥15% for women in asymptomatic patients older than 50 undergoing routine screening. The American College of Gastroenterology Task Force recommends that all endoscopy centers employ these indicators as part of a continuous quality improvement process with the goal of reducing variation in sensitivity among endoscopists. (18)

Cecal intubation with photodocumentation and adequate withdrawal time are both markers of complete and careful examination of the entire colon. Complete colonoscopies with cecal intubation helps avoid excessive costs from repeat procedures and additional follow-up radiologic studies. Withdrawal times of ≥ 6 minutes have been suggested as quality indicator to meet benchmark adenoma detection rates. (36) However a recent study has questioned whether endoscopic interventions that target this and other quality indicators are successful. (37) This meta-analysis reviewed 7 studies and 10 abstracts which examined the effects of performance improvement measures on various outcomes. Only one study intervention led to any improvement in ADR -- using a combination of an audible timer to ensure adequate withdrawal time and training on enhanced inspection techniques. Thus, there is little current evidence that interventions targeting these quality indicators have any beneficial effect on polyp or adenoma detection rates. It may be that benchmarks such as the 6 minute withdrawal time are simply surrogate markers for a careful and attentive endoscopist. Thus, targeting the marker rather than the performance trait may not lead to improved performance.

The inability to identify and remove precancerous and early cancerous lesions of the colon is the main factor associated with a suboptimal reduction in CRC incidence and mortality, particularly within the right colon. The current evidence supporting our understanding of the colonoscopic miss rate was outlined by Rex et al. (18) Originally, the National Polyp Study showed a risk reduction of 76 to 90% for CRC in patients with adenomas. (10) Subsequent studies, however, using techniques like tandem colonoscopy/sigmoidoscopy and computed tomography (CT) colonography showed miss rates for large adenomas from 6 to 17% and up to 27% for diminutive polyps. (38-42) Additionally, and even more concerning, were two large studies showing miss rates for CRC in the 4-6% range.(43-45) One conclusion which came out of these studies was that miss rates were variable between gastroenterologists and non-gastroenterologists thus supporting operator performance as a key factor in the ability of colonoscopy to detect and prevent CRC.(40, 46) While ongoing process improvement efforts target enhancing the ADR among endoscopists, recent evidence suggests that the protective effect of colonoscopy is not the same for the proximal and distal colon. Multiple studies offer competing views on the protective effects of colonoscopy on CRC in the right versus left colon. (12, 47-49) Lakoff et al. showed no protective effect in the right colon until ~year 7 of the study which suggested that screening sigmoidoscopy would be just as beneficial as a colonoscopy with lower costs and less risk. (49) Several factors have been addressed as possible explanations for the lack of improvement in right-sided CRC such as poor prep, endoscopic technique, and different polyp characteristics. Based on several recent studies, ADR is highly operator dependent, and thus is, in theory, correctable. (13, 50-51).

Risks of Colonoscopy

Finally, as with any screening procedure where asymptomatic patients are examined for pre-malignant conditions, the risks of the procedure should not outweigh the benefit. Previous meta-analysis has shown an overall low rate of serious complications of 2.8 per 1000 procedures with 85% of those occurring in patients with polypectomy. (52) A more recent study in 2012 showed higher rates of serious adverse events of 4.7 per 1000 and 6.8 per 1000 for screening and follow-up colonoscopies, respectively. (53) The more serious complications in those select patients undergoing screening/surveillance colonoscopies included cardiopulmonary deterioration, bowel perforation, hemorrhage, infection, and post-polypectomy syndrome. The rate of cardiopulmonary complications in one review of the CORI database was 0.9% for all procedures but made up 67% of the unplanned events in the peri-procedural period. Perforation rates are typically less than 0.1%. (54, 55) Bleeding is almost always related to polypectomy with an overall risk of 0.1 to 0.6% and a post-polypectomy risk of 0.5 to 2.2% and can occur immediately or after 7-10 days. (56-60). Risk factors for post-polypectomy bleeding include polyp size,

histology, number removed, location in the right hemi-colon, and current anti-coagulation use. (56-58, 61-69) Aspirin use alone was not associated with higher bleeding rates but dual therapy with either aspirin or NSAIDs and clopidogrel was. (57-59, 67) Post-polypectomy syndrome is a full-thickness burn from electrocautery resulting in local peritonitis and occurs in the range of .003 to 0.1%. (70) Transient bacteremia has been reported in up to 4% of patients with a range of 0-25% however no definite causal relationship between colonoscopy and infection have been made. (60, 71) It is worth noting that other activities of daily living including eating, flossing one's teeth, and defecation are associated with similar bacteremia rates. Overall risk of death with or without polypectomy was reported as 0.03% in over 370,000 colonoscopies in one 2010 review and when only colonoscopy-specific mortality studies were examined it was reported at 0.007%. (55, 70, 72-80)

Enhanced Optics/Ancillary Equipment

It has become widely accepted that the ADR is the main target of effective CRC screening and that colonoscopy is the most effective screening test to accomplish that goal. What has yet to be decided is what endoscopic techniques, assist-devices, and image-enhancing options will allow us to more effectively perform these screening and surveillance procedures. What has also yet to be determined is whether the ADR is the best quality indicator for colonoscopy or is the absolute number of adenomas per patient a better marker of effective CRC screening. These various new techniques, devices, and scope optics are all designed to allow us a more careful and complete mucosal inspection of the colon with the goal of improving our ADR. Though it is unlikely that CRC can be completely eliminated, hopefully these areas of research will help optimize colonoscopic screening.

Device manufacturers have developed a number of advanced imaging systems (narrow-band imaging, FICE, iscan, etc.) designed to enhance the identification of colonic lesions. Unfortunately, studies to date have not shown any of these technologies to be superior to standard definition white light endoscopy (SD-WLE). This area of colonoscopy is rapidly evolving, and will be discussed in a separate publication in this issue.

Though originally studied in the hopes of decreasing discomfort during colonoscopy, and potentially reducing or eliminating the need for sedation, water immersion/water exchange colonoscopy has shown promise in increasing ADR as well. This technique involves the use of water instead of air for colonic distention during scope insertion. Though not the primary endpoint for the original trials, the authors showed an overall ADR of 26.8% vs. 34.9% for adenomas >9 mm using the air and water technique, respectively. (81) A larger study in 2011 confirmed these findings.(82) ADR with water immersion was 57.1 vs. 46.1% with standard technique. After controlling for various factors like age, BMI, and bowel prep, they showed an 81% higher chance of finding an adenoma with the water immersion technique. Importantly, they showed a benefit in the right colon specifically, with a right colonic ADR of 45.8% vs. 34.6%. Though these findings need to be confirmed in additional studies, this represents an area of promising research.

Given the recent trials showing a diminished benefit of colonoscopy in the prevention of right sided cancers, investigators have been interested in enhancing visualization of the posterior aspect of the colonics folds, where, based on CT colonography data, many of the missed polyps reside. Retroflexing the colonoscope in the proximal colon is one methods of achieving this end. Hewett *et al.* examined the safety and yield of retroflexion in the right colon after a standard forward-viewing examination. They showed a high technical success rate of 94.4% and with an enhancement in proximal colonic ADR to studies with tandem examinations. (83) The per-protocol adenoma miss rate was 9.8% and the intention-to-treat miss rate was 4.4%. This study was completed in high-volume academic centers with experienced endoscopists and has yet to be reproduced so whether their results are transferable to the general population is still a matter of debate.

Retroscope

The Third Eye© retroscope (TER) is a device specifically designed to evaluate the proximal side of folds, especially in the right colon. The TER is a disposable device which is inserted via the working channel of the colonoscope and which is designed to automatically retroflex once a certain distance beyond the scope tip. Three studies involving over 900 patients examined the TER in regard to both polyp and adenoma detection rates. (84-86)(See table 2.) All of the studies showed an increase in the PDR and ADR and the results were similar among the three groups with respect to the right colon. An interesting and unexpected finding was that a high number of additional polyps and adenomas detected on the left side with the third eye retroscope. The withdrawal times were not statistically different from the quality standard of ≥ 6 minutes and did improve with operator experience in one of the studies. (85) It remains to

be seen if these results are replicable in a community setting. Given the additional costs of the equipment, studies demonstrating an additional benefit in either detection or safety over simple retroflexion in the right colon are needed. The one study looking at retroflexion in the right colon mentioned earlier had an adenoma detection rate for missed lesions in the right colon of 9.8% which is similar to that in these studies.

Table 2. Increase in polyp and adenoma detection when using the Third Eye™ retroscope.

		Polyps			Adenomas		
		Entire Colon	Right Colon	Left Colon	Entire Colon	Right Colon	Left Colon
Author	**Standard Colo**						
Waye et al		257	133	124	136	87	49
DeMarco et al		182	80	102	100	58	42
Leufkens et al		160			107		
	TER						
Waye et al		34	22	12	15	13	2
DeMarco et al		27	12	15	16	7	9
Leufkens et al		34			15		
	%additional yield with TER						
Waye et al		**13.2**	16.5	9.7	**11.0**	14.9	4.1
DeMarco et al		**14.8**	15.0	14.7	**16.0**	12.1	21.4
Leufkens et al		**19.8**			**14.3**	13.0	32.7

Cap-assisted Colonoscopy

Finally, cap-assisted colonoscopy (CAC) is another technique which has been examined as an adjunct to improve ADR. For CAC, a clear transparent cap in inserted over the tip on the colonoscope which helps displace the colonic folds and thus, theoretically, may improve visualization and ADR. Initial studies were done to look at other quality indicators like cecal intubation rates and the proposed surrogate of ADR, polyp detection rates. In all, three studies looked at either adenoma detection or miss rates. The first, by Hewett *et al.* in 2010, showed a lower adenoma miss rate for cap-assisted colonoscopy of 21% versus 33% for conventional colonoscopy (CC). (87) The next two studies involving over 1700 patients showed mixed results with the larger of the two studies showing no difference in ADR overall, in advanced/flat/depressed morphology, or in proximal versus distal. The second study showed a significant difference of 13% higher number of patients with at least one adenomas, though the only difference was for polyps <5 mm. (88-89) These studies differed significantly in their patient demographics with one groups subjects consisting of >90% white males versus 50:50 male:female in the other study. The only significant statistical significant finding in both studies was a longer cecal intubation time of around 1 minute with questionable clinical impact. A recent meta-analysis of 16 randomized controlled trials including nearly 9,000 subjects found only a marginal benefit of CAC for polyp detection (RR 1.08) and cecal intubation time (-0.64 minutes) but not on total colonoscopy time.(90)Whether such marginal benefits are of clinical significance remains to be seen.

4. Conclusion

As outlined above, colonoscopy is a powerful, but imperfect, test for detecting and preventing, colorectal cancer. In 2012, colonoscopy remains the dominant CRC screening method in the United States. The data clearly support the conclusion that colonoscopy significantly reduces left-sided CRC incidence and mortality. The limited benefit for right sided CRC is of great interest to researchers and clinicians alike and is likely multifactorial. Given several studies which show that the type of endoscopists performing the examination has a significant effect on right-sided benefit, further efforts are needed to standardize training for all colonoscopists and to identify and institute adequate quality assurance measures which are not specialty specific. Whether the specialties can agree on certain minimum training standards which include competency (versus number) based assessments remains to be seen. One thing is certain -- colonoscopy performance must improve if we are to realize the full benefits of CRC screening, particularly in the right colon.

From a societal standpoint, redoubled efforts to

educate the public about the importance of colorectal screening are needed. Moreover, clinicians and public health personnel must work together to remove barriers to CRC screening. These efforts should be based on the specific culture and needs of the population in question. There is no "one size fits all solution."

To date, many modifications have been made to the basic colonoscope with the hopes of improving performance for CRC. These have, thus far, proven to be of marginal benefit. With the exception of the TER, ancillary devices have fared no better. Despite it's proven improvement in adenoma yield, the TER remains untested in a non-academic setting and the cost/benefit ratio of using this device for all who undergo colonoscopic CRC screening is yet unknown. For now, colonoscopists are better served by honing their technique than by investing in new equipment.

The future of colorectal screening in the United States will ultimately depend on numerous factors. These include cost, efficacy, acceptability, and insurance coverage of the various options. It may well be that some combination of tests, such as colonoscopy with interval fecal DNA testing, will provide the optimal risk/benefit ratio, provided that costs can be lowered in to an acceptable range. Whatever the future holds, colonoscopy will be the linchpin of CRC screening in the near term. High quality colonoscopy, with tracking of recognized performance improvement measures is paramount to maximizing its effectiveness.

Disclaimer

The views expressed in this manuscript are those of the authors and do not reflect the official policy of the Department of the Army, the Department of Defense.

Competing Interests

The authors have declared that no competing interest exists.

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