

Colorectal Cancer Screening and Surveillance in the Elderly: Updates and Controversies

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Colorectal cancer is common worldwide, and the elderly are disproportionately affected. Increasing age is a risk factor for the development of precancerous adenomas and colorectal cancer, thus raising the issue of screening and surveillance in older patients. Elderly patients are a diverse and heterogeneous group, and special considerations such as comorbid medical conditions, functional status and cognitive ability play a role in deciding on the utility of screening and surveillance. Colorectal cancer screening can be beneficial to patients, but at certain ages and under some circumstances the harm of screening outweighs the benefits. Increasing adverse events, poorer bowel preparation and more incomplete examinations are observed in older patients undergoing colonoscopy for diagnostic, screening and surveillance purposes. Decisions regarding screening, surveillance and treatment for colorectal cancer require a multidisciplinary approach that accounts not only for the patient's age but also for their overall health, preferences and functional status. This review provides an update and examines the challenges surrounding colorectal cancer diagnosis, screening, and treatment in the elderly. (*Gut Liver*, 2015;9:143-151)

Key Words: Colorectal neoplasms; Colonoscopy; Screening; Surveillance; Elderly

INTRODUCTION

Colorectal cancer is the second leading cause of cancer-related mortality worldwide and the fourth most commonly diagnosed malignant disease.¹ In 2012 there were nearly 1.4 million new cases of colorectal cancer diagnosed in the world with over 2.4 million new cases of colorectal cancer expected to be diagnosed worldwide by 2035. Age is an important risk factor

for developing colorectal cancer² and the elderly are disproportionately affected by this disease, thereby necessitating the need for screening and surveillance in this group. Yet, screening and surveillance decisions in the elderly can be quite challenging. For example, the definition of elderly, based on age alone may not properly capture the appropriateness of screening in an individual person. The World Health Organization defines elderly as persons over the age of 65, yet it is well known that persons over 65 are a heterogeneous group ranging from incredibly healthy with a long life expectancy to those with multiple comorbid medical conditions, declining cognitive function and impaired functional status.

The following review will address a number of the challenges and controversies surrounding colorectal cancer and the elderly. First, we will review the epidemiology and clinical presentation of colorectal cancer in the elderly. Second, we will review the efficacy of screening modalities and examine the data regarding when not to screen a patient based on age. Moreover, we will discuss one of the most common colorectal cancer screening modalities, colonoscopy, and how various aspects of this procedure are impacted by age. Finally, we will discuss colorectal cancer treatment and how age influences the efficacy, safety and decision to treat elderly patients with colorectal cancer.

EPIDEMIOLOGY

Colorectal cancer is common in the elderly. Approximately 90% of new colorectal cancers are diagnosed in patients over 50 years³ with the median age of diagnosis being 69 years. Furthermore, the incidence of colorectal cancer dramatically rises as one ages, regardless of sex and racial background (Fig. 1)³ and nearly doubles between the ages of 40 and 80 years.²

Colonic polyps are precursors to the development of colorec-

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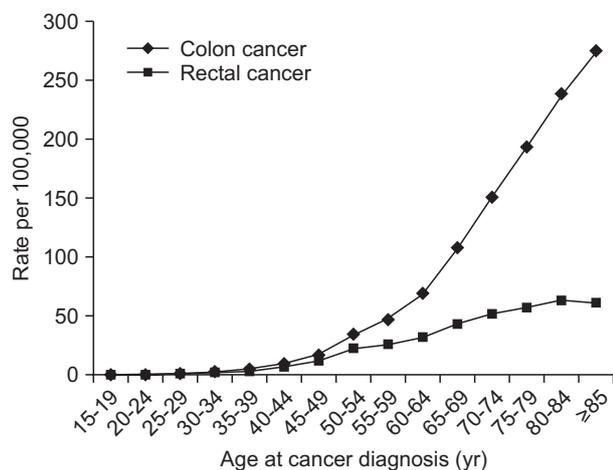


Fig. 1. Incidence rates for colon and rectal cancer for all races and both sexes from 2006 to 2010 in the U.S. population.

tal cancer.⁴ Among precancerous polyps, both adenomatous and advanced adenomatous polyps (defined as polyp size >10 mm, villous/tubulovillous histological features, or having high grade dysplasia) have an increased prevalence and incidence in the elderly.⁵⁻⁷ In fact, adenoma and advanced adenoma prevalence in persons 70 to 75 years of age is more than double that of persons 40 to 49 years.^{5,8,9} In contrast, the prevalence of serrated lesions only slightly increases with age.¹⁰⁻¹⁴ Moreover, age plays a role with respect to a number of other factors related to colonic polyps. Elderly patients are observed to have larger sized and more proximally located adenomatous polyps which may lead to higher rates of colorectal cancer in this population.¹⁵

On the other hand, the recurrence of adenomas, advanced adenomas, and serrated lesions is less impacted by age. Age does not appear to influence the recurrence of adenomas after diagnosis from an index colonoscopy.¹⁶⁻¹⁸ Other factors such as index polyp size,¹⁷ number of polyps at index colonoscopy,¹⁹ and initial incomplete polyp resection²⁰ are more associated with recurrence. Similar predictors of recurrence are present for advanced adenomas, but age may play a slightly greater role.^{21,22} In addition to polyp characteristics insufficient bowel preparation and incomplete examination have been additional factors noted to predict the recurrence of advanced adenomas detected on surveillance colonoscopies.¹⁹ Limited studies suggest that age does not impact recurrence of serrated polyps²³ and consensus guidelines on surveillance intervals for serrated lesions focus more on the size, number and location of the index serrated lesion(s).²⁴ While colorectal cancer incidence increases with age, the recurrence of it is not. Rather family history, findings on index colonoscopy^{25,26} and presenting symptoms,²⁷ have a much stronger association (Table 1).

Given that age does not strongly influence the recurrence of either colonic polyps or colorectal cancer, surveillance guidelines have not been tailored by age.

Table 1. Factors that Increase the Recurrence Risk of Adenomas, Advanced Adenomas, and Colorectal Cancer

Adenomas
Index polyp size (polyp >1 cm)
Number of index polyps
Incomplete polypectomy
Advanced adenomas
Number of index adenomas
Index polyp size (polyp >1 cm)
Villous histology on pathology
Insufficient bowel preparation
Incomplete examination (unable to reach farther than the distal colon)
Colorectal cancer
Family history of colorectal cancer
Presence of extracolonic malignancy
Detection of synchronous lesions
Coexisting adenomas
Perforation at time of diagnosis
Symptoms

PRESENTATION

Colorectal cancer presentation is similar in younger and older patients although more proximal cancer is detected in older patients.⁷ Likewise older patients may be less likely to present asymptotically.^{28,29} Elderly patients with colorectal cancer may have a range of symptoms that include occult blood loss, rectal bleeding, change in stool caliber, unintentional weight loss or have signs of bowel obstruction or perforation. While no one presenting symptom predominates in elderly patients, it should be recognized that elderly patients may have a more subtle presentation of colorectal cancer such as vague abdominal pain or a new microcytic anemia. Such symptoms cannot be attributed to other etiologies and deserve a thorough cancer evaluation.

SCREENING MODALITIES FOR COLORECTAL CANCER

Colorectal cancer screening, which detects both precancerous polyps and colorectal cancer, can reduce both colorectal cancer incidence and mortality.³⁰⁻⁴⁰ Through screening the incidence of colorectal cancer can be reduced by 17% to 33% with a mortality reduction of 11% to 53% depending on the modality employed.^{30-34,36,37} While no one screening method is advocated a number of consensus documents offer several screening recommendations including those from the U.S. Preventative Services Task Force,⁴¹ American Cancer Society, U.S. Multi-Society Taskforce with the American College of Radiology,⁴² American College of Gastroenterology,⁴³ and the National Comprehensive Cancer Network.⁴⁴ Screening tests available and recommended include examining stool for occult blood or newer tests examin-

ing DNA mutations/alterations,⁴⁵ radiologic or endoscopic methods (Table 2). To date, no one screening test has proven superior for colorectal cancer screening in the elderly.

1. Colonoscopy in elderly patients

Lower endoscopy, specifically colonoscopy, has been shown to significantly reduce both distal and proximal colorectal cancer in older individuals.⁴⁶ As more elderly patients undergo colorectal cancer screening using colonoscopy one has to consider how specific factors, such as age, related to this procedure may interact with one another.

Several reviews⁴⁷⁻⁵⁰ have addressed a number of issues related to the elderly and endoscopy. Few changes are recommended for elderly patients with respect to the preprocedure process and sedation, but some differences have been clarified. During the preprocedure assessment it is recommended that providers assess for elderly patient's cognitive ability and capacity to understand the procedure and that functional status and depression screening be documented in an elderly patient's medical record when they are undergoing endoscopy.^{50,51} Second, providers should use fewer sedative medications, at lower doses and be infused at slower rates when an elderly patient is being sedated.⁵⁰ Furthermore, early recognition by the endoscopist of multiple factors such as an elderly patient's comorbid medical conditions, cognitive function, mobility and polypharmacy need to occur prior to performing endoscopy.

2. Adverse events

The occurrence of adverse events during colonoscopy and how age may modify this risk are important considerations for the elderly patient. Age does not play a role in minor adverse events such as abdominal pain.⁵² Yet, major adverse events such as perforation, bleeding and cardiopulmonary complications are all affected by age, though the individual risk varies and can be influenced by additional factors. Of all adverse events associated with colonoscopy, the greatest risk associated with age is perforation.

For example, elderly patients have a 30% higher risk of experiencing a perforation than younger patients undergoing colonoscopy and a 14-fold higher risk of having a perforation than patients of the same age who do not undergo the procedure.⁵³ Lastly, older patients with more comorbid medical conditions have a greater risk of experiencing an adverse event if the colonoscopy is performed under general anesthesia.⁵⁴

3. Bowel preparation

Bowel preparation is a significant issue to consider in patients undergoing colonoscopy. Two agents are available (polyethylene glycol electrolyte lavage solution [PEG] and oral sodium phosphate [OSP]). A number of adverse events are observed in elderly patients taking PEG and OSPs (Table 3). PEG has a much better safety profile compared to OSPs with a major concern that elderly patients taking OSPs are at greater risk of having electrolyte disturbances^{55,56} and experiencing acute kidney injury.^{15,57} It is for this reason that OSPs are no longer recommended in the elderly and that PEG is the preferred bowel preparation

Table 3. Adverse Events Associated with Bowel Preparation in Elderly Patients

PEG (%)	
Dizziness	(48)
Fecal incontinence	(27-39)
Abdominal pain	(7-23)
Nausea	(2-17.5)
Insomnia	(13)
Fatigue	(12.7)
Headache	(7.9)
Hypokalemia	(2.9-20.5)
Dysnatremia (hyponatremia/hypernatremia)	(4.1)
Emesis	(3.2)
Aspiration pneumonia	(<1)
Pancreatitis	(<1)
Ischemic colitis	(<1)
OSP (%)	
Hyperphosphatemia	(58.1-100)
Fecal incontinence	(23-55)
Elevated creatinine/renal injury	(55.2)
Hypocalcemia	(5.1-58)
Hypokalemia	(5.4-56)
Abdominal pain	(11-32)
Nausea	(9-36)
Insomnia	(15)
Dizziness	(3-55)
Emesis	(4-7)
Hypotension	(4)

PEG, polyethylene glycol; OSP, oral sodium phosphate.

Table 2. Colorectal Cancer Screening Tests

Occult blood	
High sensitivity guaiac-based fecal occult blood test (gFOBT)	
Fecal immunochemical test (FIT)	
Multitarget stool DNA test*	
Endoscopy	
Colonoscopy	
Flexible sigmoidoscopy	
Radiology	
Double contrast barium enema	
Computerized tomography colonography	

*Quantitative molecular assays for KRAS mutations, aberrant NDRG4 and BMP3 methylation and β -actin, in addition to a hemoglobin assay performed on stool samples.

agent for this patient population.

However, there are concerns with PEG in regards to tolerability and compliance in the elderly with noncompliance rates of 3% to 32%.⁵⁸ Also concerns do remain with the elderly being able to tolerate such a large volume of fluid required with PEG. While split PEG dosing regimens have been shown to be more effective⁵⁹ versus standard one time dosing, this approach has not been well studied in the elderly. Finally, of critical importance is that elderly patients remain adequately hydrated when taking PEG.⁶⁰

Poor bowel preparations in the elderly undergoing colonoscopy range from 4% to 57%^{29,61-69} with bowel preparation being more difficult to achieve in very elderly patients (e.g., patients >80 years).^{63,67} Poorer bowel preparations observed in the elderly can occur for a variety of reasons including altered gastrointestinal motility, increased rates of medication-related constipation, previous surgeries, decreased understanding of bowel preparation instructions, greater burden of comorbid medical conditions, and/or functional limitations.

4. Completion of colonoscopy

Key to a high quality colonoscopy is the successful completion of it (e.g., intubation of the cecum). Endoscopists subjectively judge a colonoscopy to be more difficult in an elderly patient,⁷⁰ but completion rates vary from 78% to 86% in the elderly and 52% to 95%^{61,62,71} in the very elderly.^{29,63-65,67-69} Age may be an independent risk factor for lower completions rates, but it is apparent that other factors such as poor bowel preparation and a patient's underlying disease process play a stronger role.^{61,72}

DECISIONS REGARDING NOT TO SCREEN FOR COLORECTAL CANCER IN THE ELDERLY

1. Comorbid medical conditions in the elderly and screening

Elderly patients have a greater number and severity of comorbid medical conditions with over one-quarter of patients >65 years of age having more than five comorbid medical conditions.⁷³ This increase in comorbid medical conditions can impact not only the development of colorectal cancer, but can also reduce the benefit from screening and treatment in older patients. It is evident that the benefit of screening is reduced with increasing disease burden. For example, the greatest number needed to screen to prevent a colorectal cancer death is in older, more ill patients. Compounding this issue further is that screening related adverse events are greater than the benefit in this same group of patients.^{74,75} Furthermore, patients with greater comorbid medical conditions have lower survival rates after an initial diagnosis of colorectal cancer,⁷⁶⁻⁷⁸ poorer survival after chemotherapy^{78,79} and prolonged hospitalizations as a consequence of their colorectal cancer.⁸⁰

2. Debate on when to discontinue colorectal cancer screening in the elderly

Detecting colorectal cancer earlier is clearly beneficial but several controversial questions remain.

One important question is: Does screening extend life in older patients who may have a shorter life expectancy? On this topic a number of modeling studies have examined the impact of various colorectal screening methods on life expectancy at different age groups.⁸¹⁻⁸³ Younger patients have a greater decrease in life expectancy than do elderly patients after a diagnosis of colorectal cancer. At the same time, there is a 75% reduction in the benefit of screening for elderly patients when compared with younger patients regardless of which screening modality is used. Identical results have been noted in clinical studies addressing this same question. These studies have illustrated that the benefit of screening, after an initial negative screening test, is reduced in elderly patients as this group has a greater chance of passing away from other illnesses besides colorectal cancer.⁷⁶ As a further example, in a recent study of elderly patients who had a positive fecal occult blood test, nearly half of the patients who did not undergo colonoscopy died from other causes. Of those who underwent colonoscopy 10% experienced an adverse event and the overwhelming majority of patients with a worse life expectancy obtained little benefit from screening.⁸⁴

A second question that arises is: At what point does colorectal cancer screening cease to provide an important extension in life expectancy and therefore not be offered? Multiple studies have tackled this question and examined various ages at which colorectal cancer screening should be discontinued. A number of ages at which to stop screening have been proposed. Some have demonstrated that decreasing the screening age from 85 to 75 years yields small reductions in life years gained as well as utilizes fewer resources, and have concluded that stopping screening at 75 provides almost the same benefit as stopping at 85 years.⁸⁵ Others have demonstrated diminishing returns for days of life lost after the age of 70 for any form of screening⁸⁶ and that after the age of 60 the percentage of life years saved declines precipitously after a single colonoscopy.⁸² While this debate continues at lower ages, there does appear to be clear evidence and consensus on an age in which some patients achieve no benefit from screening. Men >85 years and women >90 years do not achieve any benefit from colorectal cancer screening regardless of modality,⁷⁴ and patients over 80 years have a shortened life expectancy (median survival of <5 years) after a diagnosis of colorectal cancer regardless of comorbid medical conditions or functional status.⁷⁶ Unfortunately, there is very little guidance on when to stop screening from national medical societies (Table 4).

In summary, health, life expectancy and functional status as well as age should all play a role when considering the option to discontinue colorectal cancer screening. However, this

Table 4. Colorectal Cancer Screening Guidelines and the Elderly

Society	Recommendation
U.S. Multi-Society Task Force and the American Cancer Society (USMSTF/ACS)	In those with a prior polyp: discontinuation of surveillance colonoscopy should be considered in persons with serious comorbidities and with less than 10 years of life expectancy.
American Gastroenterological Association (AGA)	No comment on when to stop screening. Comment on need for shared decision making and individualized approach.
American Geriatrics Society (AGS)	Not recommended in those unlikely to live more than 5 years or who have significant comorbidity that would preclude treatment.
British Society of Gastroenterology	Fecal occult blood test every 2 years offered to all persons 50–69 years of age (depending on location) with current plans to extend to age 75 in most areas.
Kaiser Permanent Care Management Institute (KPCMI)	Discontinuation of screening is generally recommended at age 75, provided that there is a history of routine screening. Discontinuation is recommended at age 80 for those with no history of routine screening. The decision to discontinue screening should be based on physician judgment, patient preference, the increased risk of complications in older adults, and existing comorbidities.

practice is quite variable. Some providers take an individualized approach with their elderly patients and colorectal cancer screening with more physicians choosing to engage healthier elderly patients.⁸⁷ Whereas, a larger body of evidence suggests that others perform inappropriate colorectal cancer screening in patients with severe comorbid medical conditions and low life expectancies.^{88,89} Such disparities in practice highlight the need for greater education among providers on colorectal cancer screening in the elderly.

TREATMENT

Treatment for colorectal cancer (both surgical and medical) in the elderly differs in comparison with younger patients. First, age plays a role in outcomes and the type of colorectal cancer surgery selected. Laparoscopic colorectal cancer surgery in the elderly appears to be a more effective procedure compared with an open approach with equal cure rates between the two procedures, but less adverse events,⁹⁰ less blood loss⁹⁰⁻⁹² and shorter postoperative hospitalizations⁹⁰⁻⁹² noted with laparoscopic colectomy performed in elderly patients with colorectal cancer. Also, older patients are observed to have higher mortality rates after colorectal cancer surgery.⁹³ Second, age impacts medical treatment for colorectal cancer, but to a lesser degree. Many oncologists reduce the dose of chemotherapy for perceived risks of impaired liver or renal function in older patients.⁹⁴ However, most chemotherapeutic agents are safe in the elderly and can achieve the same therapeutic benefits of reduced recurrence and mortality as observed in younger patients, especially in the adjuvant setting.⁹⁵⁻⁹⁷ Given this data most advocate that age alone not factor into one's decision to treat colorectal cancer.^{95,98,99} One limitation of the current literature on chemotherapy data for colorectal cancer and the elderly is that advanced age is an exclusion factor in many clinical trials.^{98,100-102} In fact, comor-

bid medical conditions play a much larger role in the decision to proceed with chemotherapy as this has a more pronounced impact on life expectancy after colorectal cancer diagnosis and treatment.⁷⁸

Likewise, age appears to factor into colorectal cancer treatment on a number of other fronts. Elderly patients with colorectal cancer are less frequently discussed at multidisciplinary cancer team meetings,^{103,104} undergo less surgery,^{103,104} have less adjuvant chemotherapy prescribed,^{103,105,106} and undergo less palliative therapy.¹⁰⁵ Furthermore, colorectal cancer is more complicated in older patients at diagnosis¹⁰⁵ with more emergency surgery performed in the elderly.¹⁰⁴ Also, while elderly patients represent half of metastatic colorectal cancer diagnoses, their survival is significantly less compared to younger patients with metastatic colorectal cancer.¹⁰⁷ These data do not suggest these differences are appropriate or inappropriate, but rather that age impacts colorectal cancer treatment.

As a final point, with respect to colorectal cancer treatments in the elderly, oncologists do advocate the use of a variety of tools and approaches to help guide treatment decisions. The Comprehensive Geriatric Assessment was developed to evaluate elderly patients being considered for colorectal cancer treatment and its use has proven effective in reducing adverse outcomes among the elderly.^{108,109} Also, oncologists promote a multidisciplinary approach in treating elderly patients with colorectal cancer. A patient's functional status, comorbid medical conditions, and preferences as well as cancer stage all have to be factored into the decision of determining what regimen (if any) to use when treating the elderly patient with colorectal cancer.^{98,100}

SUMMARY

Overall, a disproportionate number of colorectal cancer diagnoses and deaths occur in elderly patients. Advancing age is an

independent risk factor associated with both colorectal cancer and adenomas whereas the detection of recurrent colorectal cancer and adenomas after a screening colonoscopy is not affected by age. A number of colorectal cancer screening modalities are available for elderly patients, but it is important to remember that at specific ages the risks and increased resources may outweigh the benefit of screening in some elderly patients. Controversy exists over when to discontinue colorectal cancer screening and surveillance in the elderly. Yet, most agree that the decision to proceed with screening and surveillance requires an individualized assessment of the elderly patient that takes into account the risks and benefits and balances this with the patients' health, functional status, and preferences. Some aspects of screening, such as with colonoscopy, need to be factored into this decision making process. Older patients have a higher risk of adverse events during a colonoscopy, poorer bowel preparations and possibly lower successful completion rates. Finally, a variety of colorectal cancer treatments are available for elderly patients and, just as with decisions about when to discontinue screening, a patient's functional status, comorbid medical conditions, and preferences have to be factored into the decision making process when determining which treatment regimen to offer.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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