

C. S. Pitchumoni, M.D., T. S. Dharmarajan, M.D., Series Editors

Colorectal Cancer (CRC) Screening in the Geriatric Population: Factors in Risk Assessment and Outcome Benefits

by C. S. Pitchumoni, Shivani Sharma

INTRODUCTION

In our previous articles in this series we have emphasized the growing number of elderly in the USA, bringing to light the importance of identifying measures to keep the older adults healthy, vigorous and disability free (1). Indeed the older adults today are living longer, and healthier because of the many successful measures taken in the past three decades. One of the very successful measures that have been acclaimed is colorectal cancer (CRC) screening (2,3). Lifetime risk of developing CRC in the USA is one in 17, the risk alike in men and women, with 90% of the cases occurring beyond age 50 years. Overall five-year survival rates have improved during the past two decades; from 50% to 60% (4). Implementing CRC screening in eligible individuals has excellent effectiveness clinically and economically. CRC screening is the search for polyps and cancer in individuals who have not been previously diagnosed with colonic neoplasms, and surveillance implies follow-up of patients who have had the diagnosis of colonic neoplasms. Diagnostic examinations are different from screening and surveillance and are per-

formed to evaluate a patient with symptoms indicative of colonic neoplasms.

Many randomized controlled studies have clearly shown that screening colonoscopy for colorectal cancer reduces mortality by recognition of polyps and cancer in earlier stages (by Duke's classification) (2,5–9). However, these observations are not specific to the older adults, since most studies group all individuals over 65 years of age in one group, with no subgroups.

In this review we have briefly addressed the current status of CRC screening followed by our analysis on the recent controversies in discontinuing screening colonoscopy after a certain age. Obviously, discontinuing arbitrarily a well accepted procedure such as screening colonoscopy based solely on the chronological age can neither be too early—which will limit the value of a proven technique in reducing CRC related deaths—nor too late in advanced age (with a lower life expectancy) when the risks of colonoscopy begin to out-weigh the benefits. Many debates on screening colonoscopy in older adults are also prompted by a desire to free up endoscopic resources to screen younger individuals with a longer life expectancy. The demand for screening colonoscopy continues to strain the USA health care system despite overall low participation rates (10).

Epidemiology of CRC in different population groups is presented here to provide another facet in the controversy in order to understand the relative importance of the incidence of the disease. The aim certainly is not to exclude any ethnic or racial group from screen-

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ing, but the need to intensify screening in certain groups such as African Americans and solely to provide an idea about the relative risks in different ethnic groups. For example, a 75-years-old Asian Indian who has recently migrated to the USA certainly has a lower risk for colon cancer as compared to an African American or a Caucasian of the same age in the USA. Important differences in the data on screening colonoscopies in different ethnic groups may help us to justify customization of the screening recommendations based on race and ethnicity (11). And this appears to be a need in view of the current limited capacity that constrains our ability to meaningfully improve CRC screening rates (10).

EPIDEMIOLOGY OF COLORECTAL CANCER IN RELATION TO AGE/RACE/ETHNICITY

An understanding of the incidence of CRC risk based on race, gender, and age may help us to assess risk and justify customizations of screening recommendations. In the USA, where there is a “melting pot” or “salad bowl” of different ethnic groups, CRC screening recommendations are already complex. Many may object to adding another layer of complexity based on race or ethnicity or any one of the other factors to the general recommendations which might add a new barrier, perhaps even reducing the overall efficiency of screening programs (12). National guidelines of CRC screening are the same for all ethnic groups in the USA and at this time certainly do not exclude Asians, Indians, or others based on a lower incidence of CRC (6,13).

Epidemiology of CRC in the USA

CRC continues to be the number one cause of GI related mortality and is the second leading cause of cancer-related deaths in the USA (14). While SEER (Surveillance, Epidemiology, and End Results Program) (<http://seer.cancer.gov>) data demonstrates modest decreases in both the incidence and mortality rates, CRC dwarfs all the other GI malignancies both in incidence and in mortality in the USA (15).

Approximately 148,610 new cases of CRC are diagnosed each year, of which 106,680 are colon and the remainder rectal cancers. In 2006, more than 55,000 Americans were expected to die of CRC, accounting for approximately 10% of all cancer deaths (16).

Effect of Age

CRC is a rare diagnosis before the age of 40, the incidence begins to increase significantly between the ages of 40 and 50, and age-specific incidence rates increase progressively thereafter to 3.7/1000 per year by age 80 (15). The incidence of CRC approximately doubles during each successive decade from age 40–80 years (17) This is well illustrated in Figure 1.

A progressive increase in the frequency of advanced CRC occurs with age. The risk of having advanced colonic lesions increases by 1.05-fold for every single-year increase in age. A 4-fold increase in prevalence of advanced colonic neoplasm is seen in patients more than 70 years old compared with those less than 50 years of age (18). Hence, the older the patient the greater the likelihood of a benefit from CRC screening procedures, not considering other conflicting factors discussed.

Prevalence of CRC in Different Groups

The USA is a country of immigrants and the prevalence of CRC in immigrants from different parts of the world is useful information for practitioners of medicine in major metropolitan areas. The following is an analysis of epidemiologic observations on the differences in the incidence of CRC based on data from different coun-

(continued on page 21)

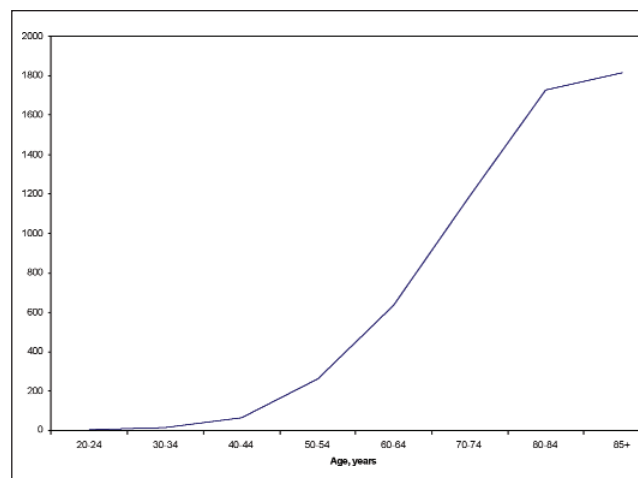


Figure 1. Age-Specific (Crude) SEER incidence rates in the general population for both Sexes and all races based on SEER 13 Registries for 1994-2003. Data from SEER program, 1994-2003. (www.seer.cancer.gov) accessed on Feb 5, 2007

(continued from page 18)

Table 1.
CRC Epidemiology: African Americans vs. Whites (21)

<i>Data</i>	<i>African Americans</i>	<i>Whites</i>	<i>Difference</i>
Age adjusted incidence	63/100,000	53.3/100,000	19% Higher
Age adjusted mortality	28.3	20.3	39% Higher
Five year survival	51%	59%	
Mortality >75 years	219	176	24% difference
Incidence >75 years	403	385	5% difference
Benefit derived from CRC screening measures			
Decrease in incidence	0.4%	0.8%	
Decrease in mortality	0.7%	1.9%	

tries and ethnic groups. Globally, the incidence of CRC varies 10-fold, with the highest incidence rates in North America, Australia, and northern and western Europe; developing countries have lower rates, particularly Africa and Asia. These geographic differences appear to be attributable to differences in dietary and environmental exposures that are imposed upon a background of genetically determined susceptibility (19). We recognize that in many ethnic groups (as in the Japanese) that migrated to the USA decades ago, the incidence of CRC has increased and matches the USA population figures. Similarly, a rapid change in CRC epidemiology is noted in some Asian countries making the data subject to careful and constant scrutiny.

CRC in Caucasians and African Americans

The United States has one of the lowest mortality rates from CRC, despite having a higher incidence than most countries. Data collected by the SEER suggest that 61% of all patients treated for colorectal cancer (all stages and sites combined) survive five years (20). In contrast, the lowest five-year survival rates have been reported by China and Eastern Europe (32% and 30%, respectively) (19).

Based on the most recent data from 1997 to 2001, the age-adjusted incidence of CRC (more likely to be diagnosed with CRC) per 100,000 individuals was 63 for African Americans versus 53.3 for whites, representing a 19% higher incidence rate. The age-adjusted mortality rate (more likely to die from CRC) over the same period

was 28.3 for African Americans versus 20.3 for whites representing a 39% higher mortality rate. Translating these rates into 5-year survival numbers reveals that African-American men with CRC have a 5-year survival of 51% compared with 59% for white men. A similar trend is seen for women (21).

In addition to presenting at more advanced stages of disease, African Americans also present at a slightly younger age with CRC. Among the over three million cases of CRC in the National Cancer Database between 1985 and 1993, African Americans presented at an average age of 66.4 versus 69.7 for whites. Table 1 shows the incidence and mortality rates by age and race based on SEER data from 1997 to 2001. Both incidence and mortality increase with age. The disparity between African Americans and whites also exists among all the age cohorts studied; however, it seems most pronounced for the youngest cohorts. A younger age at onset with greater differences in mortality rates among the younger cohorts raises the question of the role of genetic and lifestyle factors in contributing to the differences (21). An unexplored field is the need to intensify screening of the healthy older African American in the USA.

CRC in Asians

The incidence of CRC in Asians in their home countries may be lower than in western countries (22). Although it is generally believed that CRC is more prevalent in Western countries, there has been a rapid rise over the past few decades in CRC incidences in a few countries

in Asia (23). A comparison of the CRC incidence rates in Japan and the United States has shown a dramatic rise in Japanese rates (22–25). According to the South Korea National Statistical Office, there was a 35% increase in CRC mortality in Korea over the past two decades. In China the data also suggest that the CRC incidence is rising in some urban areas, e.g., Shanghai. The incidence of CRC in Chinese men in Hong Kong has increased from 30 per 100,000 in 1984 to 55 per 100,000 in 2002. The age-standardized incidence rates of CRC in some Asian countries are now comparable with that of Western figures (18,26–28).

CRC ranks number three among the incidence of cancers and one of the three most rapidly increasing cancers in China (28). For reasons unclear the Chinese seem to have a higher risk for developing CRC compared to Malaysians and Indians (29). Further, Chinese patients tend to have the majority of their (65%–71%) cancers in the distal colon (30,31). This increases the yield for screening sigmoidoscopy. There is less advantage of colonoscopy over sigmoidoscopy as a screening tool for CRC in the Chinese compared to American (32). Certainly the alarming increase in the incidence of CRC in China cautions us not to ignore the Chinese population from CRC screening.

The crude prevalence of all colonic neoplasms was highest among Japanese (42.3%) and lowest among Indian patients (8.5%) (18). CRC in Indians appears to be relatively low compared to Westerners and Chinese and Japanese. Large scale migration to the USA from India occurred only in the last three decades. No study has been conducted on the incidence of CRC in Indian immigrants in the USA. It is not known whether the low incidence in India continues to be a feature in Indians in the USA after decades of immigration and in Asian Indians born in the USA. Excluding any ethnic group residing long term in the USA from CRC screening based on epidemiologic data may not be a good practice of medicine in the USA, in a society that is highly litigious, and considering the long term influence of environmental factors or life style changes in the USA.

CURRENT RECOMMENDATIONS FOR CRC SCREENING

The following is a summary of currently accepted guidelines in CRC screening. Current recommenda-

tions for screening for CRC are based on the U.S. Preventive Services Task Force (5) and the American Gastroenterological Association consortium panel updated review (13), both of which have been reviewed and endorsed by the American Cancer Society.

The original guidelines put forth in 1997 were reviewed and updated subsequently taking into account a substantial body of published evidence. The new guidelines were published in 2006 with useful information on surveillance colonoscopy after polyp removal in the initial screening colonoscopy. The widely published guidelines are briefly summarized below.

Risk Stratification

Clinicians should determine an individual patient's risk status well before initiation of screening. The individual's risk status determines when screening should be initiated and what tests and frequency are appropriate.

Risk stratification is accomplished by asking several questions aimed at uncovering the risk factors for CRC (13):

- Has the patient had CRC or an adenomatous polyp?
- Does the patient have an illness (e.g., inflammatory bowel disease) that predisposes him or her to CRC?
- Has a family member had CRC or an adenomatous polyp? If so, how many, was it in a first degree relative (parent, sibling, or child), and at what age was the cancer or polyp first diagnosed?
- Does the family history suggest one of the genetic syndromes (familial adenomatous polyposis or hereditary non-polyposis colorectal cancer)?

A positive response to any of these questions should prompt further efforts to identify and define the specific condition associated with increased risk.

Recommendations for the Average Risk Population

According to current recommendations average risk individuals should be offered options for screening for CRC at the age of 50 years. These updated 2003 options include FOBT annually without slide rehydra-

(continued on page 25)

(continued from page 22)

tion, flexible sigmoidoscopy every five years, combined FOBT and sigmoidoscopy, colonoscopy every 10 years, or Double Contrast Barium Enema (DCBE) every five years (33). These recommendations differ slightly from organization to organization and are constantly updated. We have compared the relative merits and weaknesses of the options in Table 2.

Recommendations for Men and Women at Increased Risk of CRC

According to the current data, recommendations should be individualized for above-average risk persons. Decision should be tailored to the individual's level of risk based on the personal, family and medical history. A complete visualization of the colon should be advised if the results are abnormal. Colonoscopy is the preferred test for abnormal results but some physicians may recommend flexible sigmoidoscopy with DCBE in case colonoscopy is unavailable. Usually one positive FOBT out of six samples is considered to be positive screening test and should be followed by diagnostic colonoscopy (33).

CURRENT OPTIONS ARE SUMMARIZED BASED ON NEWER DATA

FOBT

In a recent issue of the *American Journal of Gastroenterology* the current status of FOBT in CRC screening was discussed in an editorial as well as in three articles one each from the UK, China and the USA. Although the USA has accepted colonoscopy as the mainstay in screening, the above articles reemphasized the role of FOBT for its simplicity, cost and reliability, although much limited. In many other countries colonoscopy is considered impractical, costly, and perhaps even an unwanted risk (34). Sung, from China, noted a point relevant to this article; he pointed out that FOBT remains the most affordable test, with good evidence for life saving and the most likely accepted method of screening. Further, because of the enormous aging population and minimally subsidized health care system, FOBT is the only viable option for that country for a long time to come (35). FOBT despite its sim-

plicity is noted to reduce CRC mortality by 33% in the USA (36). FOBT which is considered by all the three countries (UK, China, and the USA) a viable screening strategy may surprise many readers in the USA who consider colonoscopy as the only option.

Adequate performance of FOBT requires that the patient avoid red meat and peroxidase-rich foods (broccoli, turnips, cantaloupe, cauliflower, radishes), and certain medications such as vitamin C, aspirin, and NSAIDS for three days prior to and during testing. Slides should be developed within four-to-six days. Hydration of the slide by adding a drop of water increases sensitivity but increases false positivity and may lead to many more avoidable colonoscopic examinations.

It is also of interest to note that FOBT is the only screening option that has been shown in randomized controlled trials to reduce both the mortality and the incidence of CRC. Evidence based CRC screening guidelines in the USA include annual FOBT either alone or in combination with flexible sigmoidoscopy as an acceptable screening option (6,13,37). Even in the USA, an affluent country, neither the resources nor the capacity exists to perform general population based colonoscopy screening (36,38).

Sigmoidoscopy

Selby, et al and Newcomb, et al in two separate studies concluded that there is a definite reduction in the distal CRC mortality with screening sigmoidoscopy (2,39). On the contrary, there are studies which highlight a major limitation of flexible sigmoidoscopy, i.e. the inability to visualize the right side of the colon. A case control study by Rex, et al reported that at least 30% of patients with high grade CRC have disease proximal to the splenic flexure with no signs of disease distal to the splenic flexure and can be expected to have a negative flexible sigmoidoscopy (40). Similar findings were reported by Imperiale, et al and Lieberman, et al in separate case control studies (41,42).

Regardless of the limitations, flexible sigmoidoscopy is used in many centers in conjunction with FOBT as a primary screening measure for CRC. Perhaps something is better than nothing, when it comes to a question of mass screening for CRC. Data indi-

Table 2.
Screening Strategies for CRC

<i>Test</i>	<i>Advantage</i>	<i>Disadvantage</i>
Traditional Options		
FOBT	Inexpensive Good compliance Noted to reduce mortality from CRC Detects lesions in the entire colon	Low sensitivity/ specificity Bleeding from upper GI tract may create a dilemma.
Flexible Sigmoidoscopy	Low cost Shown to reduce disease/ death from left sided cancers Biopsy is feasible	Proximal lesions are missed Not ideal for polypectomy Since no sedation is given, often uncomfortable
Double contrast barium enema	Moderate cost Detects polyps >1 cm Low complications	Low sensitivity Biopsy not feasible Colonoscopy is indicated if a lesion is found No study has shown reduction in mortality
Colonoscopy	Entire colon is visualized Polypectomy/ biopsy is feasible	Expensive Patient compliance may be poor Risks for perforation, bleeding, sedation associated risks
Newer Options		
Virtual Colonoscopy	Good sensitivity for polyps >1 cm Low risk of perforation Can be followed by traditional colonoscopy if positive Detection of extra colonic findings (e.g. aortic aneurysms)	Expensive Poor results for small polyps Requires bowel preparation
PillCam Colonoscopy	Increased patient acceptability Good sensitivity/ specificity in early studies	Requires bowl preparation No therapeutic options

cates that in the older adults the yield of sigmoidoscopy may be less as compared to young individuals. Older age increases the absolute risk of advanced neoplasia in the right half of the colon (5.6% in >65 years versus 0.8% in the group aged 50–54 years) decreasing the sensitivity of sigmoidoscopy which only helps to exclude left sided lesions (43–45).

Colonoscopy

Screening colonoscopy is considered the best option for CRC screening although there are no randomized

controlled studies. Colonoscopy is the only method for total colonic evaluation, detection of early cancers by biopsy, detection and resection of polyps. The questions which are posed on the feasibility of mass screening are based on the cost, risk, compliance, and finally the capacity of the medical system. Certainly most countries other than the USA do recognize the superiority of colonoscopy, but have not followed the recommendations in the USA. Seeff and colleagues rightly pointed out the colonoscopy capacity even in the USA is seriously limited and other screening strategies are needed to reach the estimated 41.8 mil-

lion people above age 50 years, who have not been screened for CRC (46). The risks of colonoscopy, albeit small, and other issues are discussed subsequently in relation to its application in the elderly.

Double Contrast Barium Enema (DCBE)

The national guidelines in CRC screening recommend DCBE once in five years as an acceptable substitute for colonoscopy (47). There are no randomized trials evaluating whether screening with DCBE reduces the incidence or mortality from CRC.

In three separate studies Winawer, et al, Rex, et al, and Rockey, et al reported the sensitivity and specificity of DCBE to be very low as compared to screening colonoscopy (47–49).

THE FUTURE ALTERNATIVES TO TRADITIONAL COLONOSCOPY

It is estimated that currently there are more than 40 million adults over the age of 50 who have never been screened for colon cancer. Newer options to traditional colonoscopy might improve compliance if they are less invasive, less time consuming and less expensive and associated with no complications.

Virtual Colonoscopy (VC)

Virtual colonoscopy (VC) known as CT colonography has shown mixed results. In the Pickhardt trial 50 VC showed excellent results, not demonstrated in two other studies (49,51). The American College of Radiology Imaging Network's (ACRIN) national trial to be published is expected to offer useful data.

VC and Capsule Colonoscopy, if shown to be sensitive enough to detect polyps are likely to be preferred by many as screening procedures. However, most of the patients who have undergone colonoscopy dislike the ritual of colon preparation the day before more than the procedure itself. Most patients requiring VC require the same preparation that traditional colonoscopy demands. The success rates on polyp detection are quite variable (52–54). A significant improvement for VC would be effective polyp detection without bowel preparation (55–57).

Stool DNA Tests for Colon Cancer

Cancers develop as a result of alteration in the genes that regulate growth, survival and other cellular behaviors. Tumor cells and DNA are shed into the lumen of colon. Uniquely mutated genes can be identified in the feces that would indicate the presence of a neoplasm (58). Stool based DNA testing is likely to be much better accepted by the public but the utility is yet to be studied (59).

Wireless Capsule Endoscopy (WCE) (Pillcam Colon): A Promising Tool to Visualize the Colon

WCE to visualize the colon is in its early phase of investigation. It is likely that Pillcam colonoscopy may become an excellent alternative to colonoscopy which needs IV sedation. The elderly may be reluctant to undergo sedation and an invasive test associated with potentially life threatening complications. Initial studies on WCE have shown a good sensitivity to detect polyps. WCE has shown promise as a new technology for visualizing the colon in a serially blinded study; data was presented at the 2006 Annual American College of Gastroenterology meeting. Dr. Lewis reported that WCE might complement traditional colonoscopy in those unwilling to undergo standard colonoscopy. WCE was compared in a serially blinded study of 51 volunteers aged >50 years. WCE was reported to be more sensitive than VC in detecting small polyps (60).

The small chance of perforation and complications including those associated with IV sedation can be avoided with VC or Pillcam Colonoscopy (Pillcam colon). The group supportive of traditional colonoscopy as the sole procedure will argue that the use of the non-invasive studies such as VC or WCE when positive lead to traditional colonoscopy increasing the cost of health care. Certainly many older adults will prefer less invasive procedures and if found negative for polyps/cancer feel relieved that they do not require a tube test. The overall benefit will be that more geriatric patients would undergo CRC screening.

THE CONTROVERSIES ON CRC IN THE ELDERLY

A number of recent studies have raised questions on the value of screening for CRC in particular by

colonoscopy in the growing number of elderly after a certain age. The controversies relate to

1. the availability of resources,
2. the benefit of detecting a polyp or cancer in an advanced age with a limited life expectancy, and
3. the wisdom of subjecting a large number of elderly to a screening procedure that is potentially associated with complications, and many other minor issues (61–63).

Overall the decision to screen or not at any age is based on careful weighing of the benefits and risks of screening procedures, in particular colonoscopy. CRC screening even in the young with poor health and severe comorbidity is questioned (64). Obviously, in the elderly it is a major challenge to weigh the risks and benefits (65,66). Potential benefits of CRC screening decreases with age and multimorbidity as competing risks for mortality become more prominent. In their study Ko and Sonnenberg found that one cancer death would be prevented by screening 42 healthy men aged 70–74 years with colonoscopy, 178 healthy women aged 70–74 years with fecal occult blood tests, 431 women aged 75–79 years in poor health with colonoscopy, or 945 men aged 80–84 years in average health with fecal occult blood tests. The potential for screening-related complications was greater than estimated benefit in some population sub-groups aged 70 years and older. However at all ages, the potential reduction in mortality from screening outweighed the risk of colonoscopy-related death (67). Guidelines currently do not explain a maximum age beyond which screening is not endorsed (13,68).

In the debate on CRC screening in the elderly an issue that is often critically analyzed is the potential capacity that the health care system has in implementing screening to all. If our capacity is limited then there is a need to offer it to the most deserving population group that is expected to have a good life expectancy. In 2002 approximately 14.2 million colonoscopies were performed (46). There are currently 14.8 million people who are unscreened. There is insufficient capacity to serve the entire population with sigmoidoscopy and/or colonoscopy demanding substantial investment in space, equipment or personnel. It is reported that the demand for screening colonoscopy

continues to strain the USA health care system despite the fact that the overall population sites participating in screening are low (10). In this context it is economically a worth while discussion to see whether CRC screening is being offered to population groups such as the very elderly with limited life expectancy.

In an excellent article Walter, et al have critically evaluated the value of colorectal, breast and cervical cancer in the elderly (61). Walter and Covinsky have developed a four point framework for evaluating screening CRC in an individual elderly patient, which nicely identifies the major issues to be recognized. The points include the following:

1. Estimation of life expectancy
2. the benefit of screening
3. the potential harm of screening
4. the value and preferences of the individual patient

Many of these points and others are discussed in many papers already quoted. We have discussed these and other points of interest in this raging debate (69).

Effect of Aging on the Incidence of CRC

While the incidence of CRC increases with age making screening a necessity, the competing risk of mortality from other causes is to be put into the equation in analyzing the cost-benefit ratio (70). Lin's article carefully analyzed the issue. The prevalence of CRC was found to be 13.9% in patients aged 50–54 years, 26.7% in the age group 70–79 years and 28.2% in those 80 and above. Advanced neoplasia including high-grade neoplasia and cancer was found in 3.2%, 4.7%, and 14% of the cohorts aged 50–54 years, 75–79 years, and 80 years and above respectively. The mathematical modeling predicted that the mean extension of life expectancy was greater for those 50–54 years (0.85 years) than for older age groups (0.17 years and 0.13 years for those 75–79 years and those 80 and above) (71).

Although the incidence of CRC increases with advancing age, the risk of mortality from other causes increases simultaneously. The elderly patients 80 years and above gain only 15% of the expected benefit in life expectancy achieved by those aged 50–54 years. However, there is a persistent benefit among the very

(continued on page 33)

(continued from page 28)

elderly although somewhat less than in the younger age groups (70).

The risk for neoplasia in one study was noted to decrease from 19% at age 65–69 to 14% after 70 years with the suggestion to stop CRC screening after age 70 (72). The latter study based on sigmoidoscopy can be challenged since age advanced right sided cancer is noted to increase.

Individuals who inherit mutations in MSH2 and MLH1 genes responsible for Hereditary Nonpolyposis Colon Cancer Syndrome (HNPCC) also show an age related increase in the risk for cancer. The risk for CRC progressively increases from >25% at the age of 50 years to almost 82% by the age of 70 (73,74). Hence there is no reason to believe that the incidence of CRC decreases after a certain age.

Do Comorbid Conditions Decrease the Life Expectancy Making the Benefit of Colon Cancer Screening Worthless?

As age advances obviously there is an accumulation of comorbid conditions which may shorten the life and may markedly negate any benefit that may result from CRC screening. The presence of multiple diseases in an elderly individual conceptualized recently as multimorbidity represents a paradigm shift from the term comorbidity. Multimorbidity (including cognitive impairment) is an important consideration for patients with CRC; the majority of them are aged 65 or older. A substantial proportion of deaths in older patients with CRC are attributable to CHF, Diabetes Mellitus, COPD, a few of the many multimorbidity conditions (75).

More than 90% of all the deaths in a study in a cohort of patients with stage 1 through stage 3 CRC were attributable to CHF, whereas 5% was attributable to COPD and almost 4% to diabetes. Because multimorbidity is so common, the view that many older persons may die with causes other than that from their cancer is to be reckoned with in prescribing screening colonoscopy (75).

Does Colonoscopy Have More Complications in the Elderly than the Young?

The fear of the potential risks and complications including perforation in approximately 1/1000 proce-

dures, serious bleeding in 3/1000 and cardiopulmonary events from IV sedation in 5/1000 (13) generates a legitimate basis for an intellectual discussion on when to stop screening for colon cancer as age advances (62,70,71,76,77). Other problems relating to screening colonoscopy in the elderly are the inconvenience in pre-colonoscopy cleansing of the colon, dehydration, and the frequent inability to cleanse the colon thoroughly with large volume of Pegylated solutions.

Colonoscopy in the geriatric population is most often successful and effective, even in those 80 years or older (63), based on a large retrospective study. Technical difficulties and prior bowel preparation completion rates were comparable with those in younger patients. Poor colonoscopic preparation as an important impediment to adequate colonoscopy was noted in a prospective study of 250 outpatients that included 150 non-octogenarians, and 100 octogenarians (78), but the overall success rate for complete colonoscopy was only 45%. The authors also advised careful use of sedation and minimizing the use of meperidine, a drug associated with side-effects in the older adults.

There is also the nuisance of polypharmacy in the elderly, often including anticoagulants, antiplatelet medications, antihypertensives, and antidiabetics, necessitating appropriate revisions and even discontinuation prior to the procedure, and careful readministration.

The studies have addressed the safety and efficacy of colonoscopy in the elderly. Emergency surgery is associated with a high mortality in older subjects. The usually quoted rates for complication are 0.2% and mortality of 0.1% in the general population (79,80). Perforation and hemorrhage occur in 0.1% to 0.8% of all colonoscopies (80,81).

What About the Cost of Screening Colonoscopy In a Population with a Shortened Life Expectancy?

Cost saving analysis of endoscopic CRC screening is not easy, and likely to be influenced by many factors in the elderly (82). Endoscopic CRC screening has the potential to be cost saving. Whether or not it continues to be cost saving as age advances needs to be determined. A case control study in which half the total number of patients was >70 years noted that those who died of CRC

were less likely to have had a colonoscopy in the prior ten years (OR = 0.43; 95% CI = 0.30 to 0.63) (7).

Does CRC Respond Poorly to Chemotherapy in the Elderly?

The behavior of CRC in the elderly was addressed by Sargent, et al. A pooled analysis of adjuvant chemotherapy for resected colon cancer in older patients indicated that advancing age does not cause CRC to become more indolent or less responsive to surgery or chemotherapy (83). As in the younger individuals, localized CRC in older individuals responds well to treatment and is associated with less mortality and better survival than advanced disease (84).

Other Issues

Prior to 1998, Medicare did not routinely reimburse for colon cancer screening. The Consolidated Appropriations Act of 2001 extended the screening colonoscopy benefit to all individuals, regardless of risk beginning on July 1st, 2001 making colonoscopy affordable to the elderly (85). Although Medicare reimbursement of colonoscopy to the average risk population was implemented on 1st July, 2001 to reduce the economic access barrier to CRC screening, more than half of the elderly do not utilize the opportunity. It is likely that in certain segments of the society overpopulated by gastroenterologists there is a need to reduce misuse, but the data on a national scale indicates that our efforts should be to strengthen CRC screening and not dilute our efforts. CRC screening in the USA is utilized much less than that for breast or cervical cancers (86).

As Inadomi (70) has concluded commenting on Lin, et al's article (71) that advocating a cut off age of 75 or 80 years may not be appropriate because there might be a persistent benefit derived from CRC screening even in the very old albeit less than the younger patients. Patient's estimated life expectancy, personal preference, and societal resources which determine the analysis of cost-effectiveness, are all crucial factors in determining how far one should go into CRC screening. At this time little consensus has been reached with regards to a specific age beyond which CRC screening should be discontinued (70).

In summary CRC screening is useful in the geriatric population, but the decision to discontinue screening cannot be based on a guideline. CRC screening should be individualized based on quality of life of the patient, comorbid situations, and a rough estimate of the individual's life expectancy. If risks outweigh the benefits, obviously screening for CRC by colonoscopy is not indicated. In the individual evaluation of an older adult for screening colonoscopy it is not enough to find out whether the patient can withstand the procedure, but serious consideration should be given to life expectancy, the effect of multimorbidity on the individual's life and if necessary appropriate risk assessment based on ethnicity (87,88).

There are new technological advances in colonoscopic techniques. Wireless capsule endoscopy is not yet available for colonoscopic examination in the USA, but is likely to be more acceptable than traditional colonoscopy. Virtual colonoscopy is likely to gain popularity. Chromo endoscopy and narrow band imaging (NBI) are not yet recommended for mass screening. Until a new technique excels traditional colonoscopy in detecting polyps, traditional colonoscopy is the choice. ■

References

1. USA Department of Health, Healthy People 2010. 2nd ed. Vol. I-II. 2005, Washington, DC: USA Department of Health and Human Services.
2. Selby V, Friedman GD, Quesenberry CP, et al. A case control study of screening sigmoidoscopy and mortality from colorectal cancer. *NEJM*, 1992;326:653-657.
3. Frazier LA, Colditz GA, Fuchs CS, et al. Cost-effectiveness for the screening for colorectal cancer in the general population. *JAMA*, 2000;284:1954-1961.
4. Greenlee RT, Hill-Harmon MB, Murray T, et al. Cancer Statistics, 2001. *CA Cancer Journal Clin*, 2001;51:15-36.
5. Pignone M, Rich M, Teutsch S, et al. Screening for colorectal cancer in adults at average-risk: a summary of the evidence for the USA Preventive Services Task Force. *Ann Intern Med*, 2002;137:132-141.
6. Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy: the National Polyp Study Workgroup. *NEJM*, 1993;329:1977-1981.
7. Muller AD, Sonnenberg A. Protection by endoscopy against death from colorectal cancer: a case-control study among the veterans. *Arch Intern Med*, 1995; 155:1741-1748.
8. American Cancer Society, Cancer Facts and Figures:2005. <http://www.cancer.org/downloads/STT/CAFF2005f4PWSecured.pdf>. Feb 21, 2005.
9. Ries LAG, Eisner MP, Kosary CL, et al. SEER Cancer Statistics Review, 1975-2001. http://seer.cancer.gov/csr/1975_2001. Dec 1, 2004.
10. Levin TR. Colonoscopy capacity: Can we build it? Will they come? *Gastroenterology*, 2004;127:1841-1849.

11. Lieberman D. Screening for colorectal cancer in average-risk populations. *Am J Med*, 2006; 119:728-735.
12. Lieberman D. Race, gender, and colorectal cancer screening. *Am J Gastroenterol*, 2005; 100:2756-2758.
13. Winawer S, Fletcher R, Rex D, et al. Colorectal cancer screening and surveillance: clinical guidelines and rationale: updated based on new evidence. *Gastroenterology*, 2003;124: 544-560.
14. Shaheen NJ, Hansen RA, Morgan DR, et al. The burden of gastrointestinal and liver diseases, 2006. *Am J Gastroenterol*, 2006;101:2128-2138.
15. Eddy DM. Screening for colorectal cancer. *Ann Intern Med*, 1990;113:373-384.
16. Jemal A, Siegel R, Ward E, et al. Cancer statistics 2006. *CA Cancer Journal Clin*, 2006; 56:106-130.
17. Arora A, Singh P. Colonoscopy in patients 80 years of age and older is safe, with success rate and diagnostic yield. *Gastrointest Endosc*, 2004;60:408-413.
18. Leung WK, Ho KY, Kim WH, et al. Colorectal neoplasia in Asia: a multicenter colonoscopy survey in symptomatic patients. *Gastrointestinal Endoscopy*, 2006; 64: 751-759.
19. Parkin DM, Pisani P, Ferlay J, et al. Global Cancer Statistics. *CA Cancer Journal Clin*, 1999; 49:33-64.
20. Ries L, Kosary C, Hankey BF, et al. SEER cancer statistics review 1973-1995. Bethesda National Cancer Institute, 1998.
21. Polite BN, Dignam JJ, Olopade OI. Colorectal cancer and race: Understanding the differences in outcomes between African Americans and Whites. *Med Clin N Am*, 2005; 89:771-793.
22. Yu H, Harris RE, Gao YT, et al. Comparative epidemiology of cancers of the colon, rectum, prostate, and breast in Shanghai, China versus the United States. *Internat J Epidemiol*, 1991; 20:76-81.
23. Sung JJ, Lan JY, Goh KL, et al. Increasing incidence of colorectal cancer in Asia: Implications for screening. *Lancet Oncology*, 2005; 6:871-876.
24. Yiu HY, Whittemore AS, Shibata A. Increasing colorectal cancer incidence rates in Japan. *Internat J Can*, 2004;109:777-781.
25. You WC, Jin F, Devesa S, et al. Rapid increase in colorectal cancer rates in urban Shanghai, 1972-1997, in relation to dietary changes. *J Can Epidemiol Prevent*, 2002; 7: 143-146.
26. Hong Kong cancer registry, Hospital authority of Hong Kong special administrative region. <http://www3.ha.org.hk/cancereg/>. Feb 5, 2005.
27. Jin BT, Devesa SS, Chow WH, et al. Colorectal cancer incidence trends by sub site in urban Shanghai 1972-1994. *Can Epidemiol Biomark Prevent*, 1998;661-666.
28. Yang L, Parkin DM, Li LD, et al. Time trends in cancer mortality in China: 1987-1999. *Internat J Can*, 2003;106:771-783.
29. Lee HP, Lee J. Trends and ethnic variations in incidence and mortality from cancers of the colon and rectum in Singapore 1968-1982. *Ann Acad Med Sing*, 1987. 16: 397-401.
30. Qing SH, Rao KY, Jiang HY, et al. Racial differences in the anatomical distribution of colorectal cancer: A study of differences between American and Chinese patients. *World J Gastroenterol*, 2003; 9:721-725.
31. Theuer CP, Taylor TH, Brewster WR, et al. The topography of colorectal cancer varies by race/ ethnicity and affects the utility of flexible sigmoidoscopy. *American Surgery*, 2001; 67:1157-1161.
32. Soon MS, Kozarek RA, Ayub K, et al. Screening colonoscopy in Chinese and Western patients: a comparative study. *Am J Gastroenterol*, 2005;100:2749-2755.
33. Nease DE, Stoffel E, Turgeon DK, et al. Colorectal cancer screening. *Gastroenterology*, 2004; 6:693-695.
34. Achkar E, Moayyedi P. Colorectal cancer screening with fecal occult blood testing (FOBT): An international perspective. *American Journal of Gastroenterology*, 2006;101: 212.
35. Sung J. Does fecal occult blood test have a place for colorectal cancer screening in China in 2006? *Am J Gastroenterol*, 2006;101:213-215.
36. Bond JH. The place of fecal occult blood testing in colorectal cancer screening in 2006: The USA perspective. *Am J Gastroenterol*, 2006; 101:219-221.
37. Smith RA, von Eschenbach AC, Wender R, et al. American cancer society guidelines for the early detection of cancer: update of early detection guidelines for prostate, colorectal, and endometrial cancers. *CA Cancer Journal Clin*, 2001;51: 38-75.
38. Seeff LC, Manninen DL, Dong FB, et al. Is there endoscopic capacity to provide colorectal cancer screening to the unscreened population in the USA? *Gastroenterology*, 2004; 127:1661-1669.
39. Newcomb PA, Norfleet RG, Storer BE, et al. Screening sigmoidoscopy and colorectal cancer mortality. *J Nat Can Inst*, 1992;84:1572-1575.
40. Rex DK, Chak A, Vasudeva R, et al. Prospective determination of distal colon findings in average-risk patients with proximal colon cancer. *Gastrointest Endosc*, 1999; 49: 727-730.
41. Lieberman DA, Weiss DG, Bond JH, et al. Use of colonoscopy to screen asymptomatic adults for colorectal cancer. *NEJM*, 2000; 343:162-168.
42. Imperiale TF, Wagner DR, Lin CY, et al. Risk of advanced proximal neoplasms in asymptomatic adults according to distal colorectal findings. *NEJM*, 2000;343:169-174.
43. Imperiale TF, Wagner DR, Lin CY, et al. Using risk for advanced colonic neoplasia to tailor endoscopic screening for colorectal cancer. *Ann Intern Med*, 2003;139:959-965.
44. Tomoda H, Taketomi A, Baba H, et al. The clinico-pathological characteristics and outcome of patients with right colon-cancer. *Oncology Rep*, 1998;5:481-483.
45. Troisi RJ, Freedman AN, Devesa SS. Incidence of colorectal carcinoma in the USA: and update of trends by gender, race, age, sub site, and stage, 1975-1994. *Cancer*, 1999;85: 1670-1676.
46. Seeff LC, Richards TB, Shapiro JA, et al. How many endoscopies are performed for colorectal cancer screening? Results from CDC's survey of endoscopic capacity. *Gastroenterology*, 2004; 127:1670-1677.
47. Winawer SJ, Stewart ET, Zauber AG, et al. A comparison of colonoscopy and double contrast barium enema for surveillance after polypectomy. *NEJM*, 2000; 342:1766-1772.
48. Rex DK, Cutler CS, Lemmel GT, et al. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. *Gastroenterology*, 1997;112:24-28.
49. Rockey DC, Paulson E, Niedzwiecki D, et al. Analysis of air-contrast barium enema, computed tomography colonography, and colonoscopy: prospective comparison. *Lancet*, 2005; 365:305-311.
50. Pickhardt PJ, Choi R, Hwang I, et al. Computed tomography virtual colonoscopy to screen colorectal neoplasia in asymptomatic adults. *NEJM*, 2003; 349:2191-2200.
51. Cotton PB, Durlaski VL, Pineau BC, et al. Computed tomography colonography (Virtual colonoscopy): a multicenter comparison with standard colonoscopy for detection of colonic neoplasms. *JAMA*, 2004; 291:1713-1719.
52. Rex DK. Current colorectal cancer screening strategies: Overview and obstacles to implementation. *Reviews in Gastroenterological Disorders*, 2002; 2: S2-S10.
53. Spinzi G, Belloni G, Martegani A, et al. Computed tomography colonography and conventional colonoscopy: a developing technology. *Med J Australia*, 2001;173:472-475.
54. Miao YM, Amin A, Healy J, et al. A prospective single center study comparing computed tomography pneumocolon against colonoscopy in the detection of colorectal neoplasms. *Gut*, 2000; 47: 832-837.
55. Callstrom MR, Johnson CD, Fletcher JG, et al. CT colonography without cathartic preparation: feasibility study. *Radiology*, 2001; 219:693-698.
56. Lauenstein T, Holtmann G, Schoenfelder D, et al. MR colonography without colonic cleansing: a new strategy to improve patient acceptance. *Am J Roentgenol*, 2001;117: 823-827.

57. Zallis ME, Hahn PF. Digital subtraction bowel cleansing in CT colonography. *Am J Roentgenol*, 2001;176:646-648.
58. Boland RC. Molecular basis for stool-based DNA tests for colorectal cancer: A primer for clinicians. *Reviews in Gastroenterological Disorders*, 2002;2:S12-S19.
59. Traverso G, Shuber A, Levin B, et al. Detection of APC mutations in fecal DNA from patients with colorectal tumors. *NEJM*, 2002;346:311-320.
60. Kuznar W. Capsule Endoscopy Promising Tool to Visualize the Colon. *Internal Medicine World Report*, 2006. Nov. issue.
61. Walter LC, Lewis CL, Barton MB. Screening for colorectal, breast and cervical cancer in the elderly: A review of the evidence. *Am J Med*, 2005;118:1078-1086.
62. Stevens T, Burke CA. Colonoscopy screening in the elderly: When to stop? *Am J Gastroenterol*, 2003; 98:1881-1885.
63. Lagares-Garcia JA, Kurek S, Collier B, et al. Colonoscopy in octogenarians and older patients. *Surg Endosc*, 2001;15:262-265.
64. Sultan S, Conway J, Edelman D, et al. Colorectal cancer screening in young with poor health and severe comorbidity. *Arch Int Med*, 2006;166:2209-2214.
65. Welch HG. Right and wrong reasons to be screened. *Ann Int Med*, 2004; 140:754-755.
66. American Geriatrics Society Ethics Committee, Health screening decisions for older adults: AGS position paper. *J Am Geriat Soc*, 2003;51:270-271.
67. Ko CW, Sonnenberg S. Comparing risks and benefits of colorectal cancer screening in elderly patients. *Gastroenterology*, 2005;129:1163-1170.
68. Byers T, Levin B, Rothenberger D, et al. American cancer society guidelines for screening and surveillance for early detection of colorectal polyps and cancer: update 1997. American cancer society detection and treatment advisory group on colorectal cancer. *CA Can J Clin*, 1997;47:154-160.
69. Walter LC, Covinsky KE. Cancer screening in elderly patients: A framework for individualized decision making. *JAMA*, 2001; 285:2750-2756.
70. Inadomi JM. When to stop screening for colorectal cancer. *Gastroenterology*, 2006;131: 1355-1357.
71. Lin OS, Kozarek RA, Schembre DB, et al. Screening colonoscopy in very elderly patients: Prevalence of neoplasia and estimated impact on life expectancy. *JAMA*, 2006; 295:2357-2365.
72. David J, Totta F, Shaukat M, et al. At what age is it appropriate to stop screening flexible sigmoidoscopy? *Am J Gastroenterol*, 2000;95:2531.
73. Lynch HT, Smyrk TC, Watson P, et al. Genetics, natural history, tumor spectrum and pathology of hereditary nonpolyposis colorectal cancer: An updated review. *Gastroenterology*, 1993; 104:1535-1549.
74. Lynch TH, Kaul K. Micro satellite instability, clinical implications, and new methodologies. *J Nation Can Inst*, 2000;92:511-512.
75. Gross CP, Guo Z, McAvay GJ, et al. Multimorbidity and survival in older persons with colorectal cancer. *J Am Ger Soc*, 2006;54:1898-1904.
76. Inadomi JM, Sonnenberg A. The impact of colorectal cancer screening on life expectancy. *Gastrointest Endosc*, 2000;51:517-523.
77. Walter LC, Bertenthal D, Lindquist K, et al. PSA screening among elderly men with limited life expectancies. *JAMA*, 2006;296:2336-2342.
78. Lukens FJ, Loeb DS, Machicao VI, et al. Colonoscopy in octogenarians: A prospective outpatient study. *Am J Gastroenterol*, 2002; 97:1722-1725.
79. Kassa E. Colonoscopy in the investigation of colonic diseases. *E African Med J*, 1996; 73:741-745.
80. Wexner SD, Forde KA, Sellers G, et al. How well can surgeons perform colonoscopy? *Surgical Endoscopy*, 1998;12:1410-1414.
81. Garbay JR, Suc B, Rotman N, et al. Multicenter study of the complications of colonoscopy. *Brit J Surg*, 1996;83:42-44.
82. Loeve F, Brown ML, van Balleqooijen M, et al. Endoscopic colorectal cancer screening: a cost-saving analysis. *J Nat Can Inst*, 2000;92:557-563.
83. Sargent DJ, Goldberg RM, Jacobson SD, et al. A pooled analysis of adjuvant chemotherapy for resected colon cancer in elderly patients. *NEJM*, 2001; 15:1091-1097.
84. Balducci L. Geriatric oncology: Challenges for the new century. *Eur J Can*, 2000; 36: 1741-1754.
85. Federal Registry - Centers for Medicare and Medicaid Services. Medicare program; revisions to payment policies and five-year review of and adjustments to the relative value units under the physician fee schedule for calendar year 2002: final rule with comment period. *Fed Regist*, 2001;66:55246-5503.
86. Shih YC, Zhao L, Elting LS. Does Medicare coverage of colonoscopy reduce racial/ethnic disparities in cancer screening among the elderly? *Health Affairs*, 2006; 25: 1153-1162.
87. Rex DK. Who is the best colonoscopist? *Gastrointestinal Endoscopy*, 2007;65:145-150.
88. Rex DK, Petrini JL, Baron TH, et al. Quality indicators for colonoscopy. *Gastrointestinal Endoscopy*, 2006; 63:S16-S28.

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