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ORIGINAL ARTICLE

Detection of Colorectal Neoplasia by Colonoscopy in Average-Risk Patients Age 40–49 Versus 50–59 Years

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Abstract

Background The USPSTF recommends beginning colorectal cancer screening at age 50. A recent study showed prevalence of colorectal adenomas among individuals aged 40–49 was similar to that among those aged 50–59.

Aim To assess the prevalence of colorectal neoplasia, detected during colonoscopy, by age among average-risk patients.

Methods Nine-hundred and ninety-four colonoscopies were analyzed (247 ages 40–49, 747 ages 50–59). We included consecutive patients of ages 40–59 undergoing their first colonoscopy. Colonoscopies that did not reach the cecum and patients at increased risk of colorectal cancer were excluded. The primary endpoint was the prevalence of colorectal neoplasia by age. Secondary endpoints included the prevalence of colorectal neoplasia by gender, ethnicity, and BMI.

Results The prevalence of colorectal neoplasia was 12.1% in patients aged 40–49 and 22.6% in those aged 50–59. Compared with individuals aged 40–49 there was a significantly greater prevalence of adenomas (chi-squared = 12.72, $P = 0.0004$) and of advanced adenomas or cancer (chi-squared = 5.73, $P = 0.01$) in individuals aged 50–59. After adjusting for gender, race, and BMI the effect of age remained significant (OR 0.5, 95% CI 0.33–0.76). Higher BMI was associated with increased risk of colorectal neoplasia (OR 1.03, 95% CI 1.00–1.06). The number that had to be screened to detect one advanced lesion in the 40–49 age group was 49 compared with 20 in those aged 50–59.

Conclusion Individuals aged 40–49 have a lower but measurable risk of colorectal neoplasia compared with those aged 50–59. Although there may be population subgroups for which screening below the age of 50 may be indicated, our results do not support lowering the age threshold for colonoscopy in the general population.

Keywords Colorectal cancer · Colonoscopy · Adenoma · Screening

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Introduction

The burden of colorectal cancer in the United States remains significant despite recent literature that suggests a decline in the annual incidence [1, 2]. As the third most common cause of cancer and second leading cause of cancer death colorectal cancer may be prevented, significantly reduced, or diagnosed at an earlier stage by effective screening methods [3]. There are multiple screening modalities including stool testing, flexible sigmoidoscopy, and CT colonography, but colonoscopy is required for follow-up of a positive screening test. Thus colonoscopy has become the preferred screening method recommended by multiple medical societies for detection and prevention of colorectal cancer in average-risk patients [4, 5]. In fact, reduction in the incidence of colorectal cancer (CRC) and a shift toward earlier stage diagnosis of CRC in those with cancer at the time of initial screening has coincided with the advent of screening colonoscopy [6–10].

Current guidelines proposed by the US Preventive Services Task Force and the United States Multi-Society Task Force on Colorectal Cancer (ACS-MSTF) for the prevention of colorectal cancer are to begin screening at the age of 50 years for average-risk patients [3, 11]. These guidelines are based on cancer statistics indicative of a low incidence of colorectal cancer before age 50 with a progressive increase thereafter [12, 13]. A recent study of screening colonoscopy in average-risk individuals showed similar prevalence in colorectal adenomas among individuals aged 40–49 compared with those aged 50–59 [14] which was in contrast with previous literature [15]. These data suggest that earlier screening colonoscopy could facilitate the detection and removal of colorectal neoplasia thus further reducing the incidence of advanced lesions and colorectal cancer. The objective of this study was to assess the prevalence of colorectal neoplasia, detected during colonoscopy, by age, among average-risk patients aged 40–59.

Methods

Patients

As a referral center for a large metropolitan area, screening colonoscopy is often performed on average-risk patients beginning at age 40 in conjunction with executive health programs. In this retrospective review the results of 994 colonoscopies performed in a single endoscopy unit at a community academic institution in Florida were analyzed. This analysis included a total of 247 colonoscopies for patients aged 40–49 and 747 colonoscopies for patients aged 50–59. Consecutive patients undergoing their first colonoscopy from June 2004 to July 2008 ages 40–59 were included. Patients that underwent colonoscopy for screening, altered bowel habits, and abdominal pain were included in the analysis. We excluded colonoscopies that did not reach the cecum and any patients that were at increased risk of colorectal cancer including those with a personal or family history of colorectal neoplasia, inflammatory bowel disease, weight loss, anemia, or bleeding. The study was approved by the Institutional Review Board at Cleveland Clinic Florida.

Endoscopy Equipment

The procedures were performed with either an EPK-1000 processor (Pentax) with EC-3430LK, EC-3830LK, EC-3470LK, and EC-3870LK model colonoscopes (Pentax) or an EPX-4400 digital processor (Fujinon) and EC-450HL5 and EC-450LS5 model colonoscopes (Fujinon). All colonoscopes used had 140° field of view. Previously published data from our institution revealed there was no difference between polyp detection by use of the Pentax and Fujinon systems.

Endoscopic Procedures

The colonoscopies were performed by twelve physicians including eight gastroenterologists and four colorectal surgeons. Each physician had performed a minimum of 1,000 colonoscopies and all of the endoscopists were fellowship-trained and board-certified in their respective field. Each endoscopist performed a similar percentage of procedures among the two age groups. The procedures were performed under nurse-administered standard sedation with meperidine and midazolam or anesthesiologist-administered propofol. The endoscopy reports were generated by the physician using EndoPro management system v6.2.5 licensed by Pentax and EndoProse v12.18.9 licensed by Summit Imaging. Depth of insertion and cecal intubation were required fields for report completion. Cecal intubation was documented by the endoscopist using landmark descriptions including “ileocecal valve” and “appendiceal orifice” with an associated photograph. Bowel-preparation agents used were predominantly sodium phosphate and poly(ethylene glycol)-based. Bowel preparation quality was determined by the physician, who used the descriptors excellent, good, adequate, fair, sub-optimal, and poor. Documentation of preparation quality was required by the reporting software for completion of the report. Those labeled “sub-optimal” and “poor” were included in the analysis as poor preparation. Only procedures with adequate preparation were included in the final analysis for those patients that underwent repeat procedures because of poor preparation. No patient was included in the analysis more than once.

Data Collection

Patient information including demographics, procedure results, and pathology reports were accessed for this study after review of the electronic medical record. The primary endpoint was the prevalence of colorectal neoplasia by age. Secondary endpoints included the prevalence of colorectal neoplasia by gender, ethnicity, and BMI. We also included data on the number of adenomas per patient and the size and location of all lesions detected. Advanced adenomas were defined as those polyps with villous features, high grade dysplasia, or $\geq$1 cm.

Statistical Analysis

The chi-squared test was used to test whether there was association between age groups and having adenomatous polyps. For some subtypes of adenomatous polyps, if the assumption of the chi-squared test was not satisfied, the continuity-adjusted chi-squared test was used rather than Fisher's exact test, because of the limitation of heavy computation. In order to control other covariates for example gender, race, and BMI, the binary logistic regression model was also applied. All analyses were performed with SAS (Cary, NC, USA; version 9.2).

Results

The baseline characteristics of the 994 patients included in the study are reviewed in Table 1. The mean age of those in the 40–49 age group was 45.2 (SD 2.9) years and that of those in the 50–59 age group was 53 (SD 3.0) years. There was a significant difference in BMI between the two groups with those aged 50–59 having a mean BMI of 28.64 compared with a mean BMI of 27.61 in those aged 40–49 ($P = 0.01$). No significant difference was noted in preparation quality between the two cohorts and poor preparation was reported in only 5% of each group. There were more females in the 40–49 age group but no difference was noted in race/ethnicity. Withdrawal time was not recorded for many of these procedures so this variable could not be included in the final analysis.

Primary Endpoint

The total number of adenomatous polyps detected and the percentages of patients with adenomas are listed in Table 2. Among patients aged 40–49 the prevalence of colorectal neoplasia was 12.1% (95% CI 8.6–16.9) with a total of 30 patients having adenomas; five of the latter had advanced polyps but no overt malignancies were detected (0/247, 95% CI 0–1.89). For patients aged 50–59 the prevalence of colorectal neoplasia was 22.6% (95% CI 19.8–25.8) with 169 patients having adenomas, including 37 individuals with advanced adenomas and three with cancer. All three adenocarcinomas found arose from the left colon in white patients (2 male, 1 female). The female patient underwent the procedure for screening, however she was noted to have a BMI of 53.7 kg/m^2 with the lesion occurring in the descending colon. Both male patients were overweight (BMI 25.0–29.9 kg/m^2) one undergoing colonoscopy for altered bowel patterns and the other for abdominal pain, with cancers identified in the sigmoid colon and splenic flexure, respectively. Chi-squared analysis showed that compared with individuals aged 40–49 there was a significantly higher prevalence of colorectal neoplasia in individuals aged 50–59 (chi-squared 12.72, $P = 0.0004$). The number that had to be screened to detect one additional adenomatous lesion or cancer was four among those aged 50–59 compared with eight for those aged 40–49. After adjusting for gender, race, and BMI by logistic regression the effect of age remained statistically significant (OR 0.5, 95% CI 0.33–0.76). The prevalence of advanced adenomas was also higher in the 50–59 age group at 4.95% (95% CI 3.40–6.51) compared with 2.02% (95% CI 0.30–3.78) of those aged 40–49 ($P = 0.03$). The number that had to be screened to detect one advanced polyp in the 40–49 age group was 49 compared with 20 for those aged 50–59. The number of adenomas per patient among those with adenomas is listed in Table 3. Of patients with adenomas, those aged 50–59 were more likely to have three or more adenomas ($P = 0.004$).

Table 1 Patient characteristics

Characteristic	Age 40–49 ($n = 247$)	Age 50–59 ($n = 747$)	*P* value
Mean age, years	45.2	53	N/A
Indication (*n*)			
Screening	64	679	<0.001
Diagnostic	183	68	
BMI (mean)	27.6	28.6	0.01
Gender (%)			0.003
Men	107 (43)	406 (54)	
Women	140 (57)	341 (46)	
Race (%)			0.53
White	119 (48)	396 (53)	
Black	35 (14)	97 (13)	
Hispanic	59 (24)	151 (20)	
Other	34 (14)	103 (14)	
Prep Quality (%)			0.62
Acceptable	236 (95)	706 (95)	
Poor	11 (5)	41 (5)	

Table 2 Detection of colorectal neoplasia

Finding	Age 40–49 ($n = 247$)	Age 50–59 ($n = 747$)	*P* value
Total polyps detected	40	284	0.0001
Adenomas	34	230	0.0001
Advanced adenomas	6	51	0.01
Cancer	0	3	0.34
AA[a] or cancer	6	54	0.005
Patients with neoplasia (%)			
Adenomas	25 (10)	129 (17)	0.003
Advanced adenomas	5 (2)	37 (5)	0.027
Cancer	0 (0)	3 (0.4)	0.288
AA[a] or cancer	5 (2)	40 (6)	0.016
Any neoplasia	30 (12)	169 (23)	0.0004

[a] Advanced adenoma defined as any polyp >1 cm in diameter or that contained villous features or high-grade dysplasia

Table 3 Distribution of adenomas

Patients with adenomas	Age 40–49 ($n = 247$)	Age 50–59 ($n = 747$)	P value
One adenoma (%)	21 (8.5)	111 (14.9)	0.009
Two adenomas (%)	8 (3.2)	30 (4)	0.85
Three or more adenomas (%)	1 (0.4)	28 (3.7)	0.004

Secondary Endpoints

Higher BMI was associated with an increased risk of colorectal neoplasia in both age groups (OR 1.03, 95% CI 1.00–1.06). After logistic regression the effect of BMI remained significant with the odds of having an adenoma increasing by 3.3% for every 1 unit increase in BMI. There was no difference in adenoma size or location between the two age groups. The odds of having an adenomatous polyp was 45% higher in males than in females (OR 1.47, 95% CI 1.06–2.02). No difference was noted in adenoma rate by ethnicity but there was a trend toward non-African–American patients having fewer adenomas (OR 0.62, 95% CI 0.36–1.07).

Discussion

The recently reported reduction in the incidence of colorectal cancer correlates with the advent and increased use of screening [1, 2]. Guidelines for initiation of colorectal cancer screening are based on cancer statistics that show a dramatic rise in the occurrence of colorectal cancer after the age of 60 [12, 13]. This fact, in combination with the recognized model of colorectal cancer in which the sequence of adenoma to cancer takes at least 10 years, has led to the recommendation to begin screening of average-risk patients at age 50 [16]. The guidelines for adenoma detection and quality indicators in colonoscopy are based on published literature that demonstrates adenoma detection of 25% among individuals age 50, increasing to 50% by age 70 [17, 18]. Only two studies have addressed the occurrence of adenomas detected during colonoscopy in average-risk patients aged 40–49 years. The first study published in 2002 by Imperiale involved 906 asymptomatic average-risk patients aged 40–49 and found 11% overall adenoma prevalence with a 3.5% prevalence of advanced neoplasia and no cancers detected [15]. This study did not compare overall adenoma prevalence in those aged 40–49 with older age groups although they did find a statistically significant trend for advanced neoplasia with advancing age after they stratified their screening colonoscopy patients according to the age groups 40–49, 50–59, 60–69, and 70 or older. It was concluded that screening colonoscopy was a low-yield procedure in the 40–49 age group. More recently, Rundle et al. analyzed results of screening colonoscopies in average-risk patients ages 40–49 versus those aged 50–59 and found a similar prevalence of colon adenomas: 14% versus 16%, respectively. However, this study reported a higher prevalence of advanced neoplasia in those aged 50–59 although this difference was not statistically significant, probably because of insufficient patient numbers. Interestingly, the prevalence of adenomas and advanced neoplasia in Rundle's 40–49-year-old cohort was similar to that reported by Imperiale [14]. These results are reviewed in Table 4.

The objective of our study was to assess the prevalence of colorectal neoplasia detected during colonoscopy among average-risk patients aged 40–59. Included were patients undergoing colonoscopy for colorectal cancer screening, abdominal pain, or altered bowel habits. Although inclusion of non-screening colonoscopies may increase heterogeneity, previous studies indicate that patients undergoing initial colonoscopy for abdominal pain or alteration in bowel habits are not at increased risk of colorectal cancer and seem to have adenoma prevalence similar to that of the asymptomatic screening population [19]. For this reason subset analysis was performed by comparing screening and non-screening indications for colonoscopy included in this study. Compared with the two previous studies by Imperiale and Rundle that included only average risk screening colonoscopies, we, in fact, found similar prevalence of colorectal neoplasia and advanced lesions among patients aged 40–49 (12 and 2% respectively). In addition, as with these two previous studies no cancers were detected in the 40–49 age group. There were three cancers detected (0.4%)

Table 4 Prevalence of colorectal neoplasia by age

Study author	Adenomas per patient (%)	Advanced adenomas per patient (%)	Colorectal cancer per patient (%)
Thoma et al.	40–49 years: 12.1	40–49 years: 2	40–49 years: 0
	50–59 years: 22.6	50–59 years: 6	50–59 years: 0.4
Rundle et al. [14]	40–49 years: 14	40–49 years: 2	40–49 years: 0
	50–59 years: 16	50–59 years: 4	50–59 years: 0.3
Imperiale et al. [15]	40–49 years: 11	40–49 years: 3.5	40–49 years: 0
	50–59 years: ?	50–59 years: 4.1	50–59 years: 0.5

in the 50–59 age group which was similar to the 0.3% prevalence reported by Rundle et al. despite the small sample size.

Unlike Rundle, we found statistically higher overall adenoma prevalence in patients aged 50–59. Our detection of adenomatous polyps in 23% of the older age group is more consistent with the prevalence reported by other studies. We also found that patients aged 50–59 were more likely to have three or more adenomas ($P = 0.004$) compared with those aged 40–49 whereas Rundle found no difference in the number of patients with three or more adenomas between the age groups. Although both Rundle and Imperiale describe a trend associating increasing age with a higher risk of advanced neoplasia, neither reported a statistically significant difference for advanced neoplasia when comparing the 40–49 and 50–59 age groups. We did find a statistically significant higher prevalence of advanced adenomas in the older cohort. Our prevalence of advanced neoplasia of 6% in the 50–59 age group is very similar to the 5.4% reported by Lieberman using a large database [20]. With our data the number that had to be screened to detect one advanced adenoma or cancer in the 40–49 age group was 49 compared with 20 in the 50–59 age group.

Besides age and family history, additional risk factors for colorectal cancer include obesity and African–American race and these are taken into consideration in our analysis [5]. The increased risk posed by obesity is described in a meta-analysis by Bergstrom et al., with an estimated 3% increase in CRC risk per one unit increase in BMI [21]. Several studies have also shown that obesity is associated with colon adenomas and that obesity may double the relative risk of adenomas [21–24]. BMI was not reported in the Imperiale study and Rundle et al. stratified patients as normal, overweight, or obese but no analysis of the effect of BMI on adenoma prevalence was listed. In our study after adjusting for other potential risk factors including age and race increasing BMI was associated with an higher risk of colorectal neoplasia. For each one unit increase in BMI the probability of colorectal neoplasia increased by approximately 3.3%. It is worthy of note that BMI was statistically higher in the group aged 50–59 (mean 28.6) than in those aged 40–49 (mean 27.6, $P = 0.01$).

We did not detect a significant difference in adenoma detection by race, however there was a trend toward more adenomas in African–Americans. This did not reach statistical significance because of the small sample size of African–Americans in our study. Approximately 50% of our patients were non-white, making our study more ethnically diverse than the two previous studies, because most of the patients in these studies were white males.

The retrospective nature of this study poses some limitations. Although we account for several risk factors for colorectal neoplasia, for example race and family history, data on smoking were felt to be incomplete and were not included in the data collected or the statistical review. In addition, although we detected adenoma prevalence similar to that in published literature for both age groups we did have statistically more females in the 40–49 age group; this difference was, however, adjusted for by use of multivariate analysis. Interestingly all of the advanced adenomas detected in the younger group were in females. We theorize that this variance was because of either sample error related to the small sample size or the possibility that those patients were at an increased risk for colorectal cancer that was not disclosed in the medical record.

This study reveals significantly higher overall adenomatous polyp prevalence and advanced adenomatous polyps in patients 50–59 years old as compared with a 40–49 age group. Our study demonstrates that age is the greatest predictor for colorectal neoplasia and adds to the current literature by showing that increasing BMI remains a significant risk factor after adjusting for age, race, and gender. We conclude that individuals aged 40–49 have a lower but measurable risk of colorectal neoplasia compared with those aged 50–59. Although there may be population subgroups for which screening below the age of 50 may be indicated, our results do not support lowering the age threshold for colonoscopy in the general population.

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