

# Colorectal Cancer Screening in the Elderly: Does Increased Prevalence Necessitate Tighter Surveillance

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**ABSTRACT** **Background:** With age, colorectal cancer (CRC) prevalence rises. The elderly (> 75 years), and the very elderly (> 85 years) are especially vulnerable. The advantages of screening must be assessed in the context of diminished life span and co-morbidities.

**Objective:** To compare CRC findings in colonoscopies that were performed following a positive fecal occult blood test/fecal immunochemical test (FOBT/FIT) in both elderly and very elderly age groups with those of younger patients.

**Methods:** We identified colonoscopies conducted between 1998 and 2019 following a positive stool test for occult blood in asymptomatic individuals. A finding of malignancy was compared between the two patient age groups. Furthermore, a sub-analysis was performed for positive malignancy findings in FOBT/FIT among patients > 85 years compared to younger than < 75 years.

**Results:** We compared the colonoscopy findings in 10,472 patients: 40–75 years old (n=10,146) vs. 76–110 years old (n=326). There was no significant difference in prevalence of CRC detection rate between the groups following positive FOBT/FIT (2.1% vs. 2.7%,  $P = 0.47$ ). Similar results for non-significant differences were obtained in the sub-analysis compared to malignancy detection rates in the very elderly 0% (n=0) vs. 2.1% for < 75 years old (n=18),  $P = 0.59$ .

**Conclusions:** Although the prevalence of CRC increases with age, no significant increase in the detection rate of CRC by FOBT was found in either the elderly or very elderly age groups. Screening colonoscopies in elderly patients should be performed only after careful consideration of potential benefits, risks, and patient preferences.

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**KEY WORDS:** colorectal cancer (CRC), fecal occult blood test (FOBT), fecal immunochemical test (FIT), screening colonoscopy, very elderly

Colorectal cancer (CRC) is a major cause of death among the elderly (age > 75 years). This group of patients represents a growing cohort presenting for colonoscopy [1]. Moreover, they often have a higher risk burden for CRC than their younger counterparts, suggesting that they benefit more from CRC screening. Despite this finding, there is reluctance in referring the elderly for screening for CRC due to high complication rates. Several issues have contributed to this, including reservations regarding their procedural risk-to-benefit ratio due to a shorter life expectancy and the presence of co-morbidities. However, advances in sedation and endoscopic techniques, as well as wider cancer therapy options, have led to better outcomes and lower risk of complications. The existing body of evidence now indicates that the very elderly actually derive more relative benefit from screening colonoscopy than the younger population [2].

The U.S. Preventive Services Task Force (USPSTF) recommends screening for men and women ages 50–75 with a life expectancy of 5 years or more, like other age groups. The USPSTF also recommends selective screening for those aged 76–85 years, a recommendation that is supported by a weaker level of evidence [3]. According to their recommendations, screening would be most appropriate for adults who are either healthy enough to undergo treatment if CRC is detected or who do not have co-morbid conditions that would significantly limit their life expectancy.

Methods that are considered acceptable tests for screening for CRC include: high-sensitivity fecal occult blood tests (FOBT), stool DNA test (FIT-DNA), sigmoidoscopy, standard colonoscopy, and virtual colonoscopy [4]. Screening with a guaiac-based fecal occult blood test has been shown to reduce CRC deaths [5]. The fecal immunochemical test (FIT), which identifies intact human hemoglobin in stool, has improved sensitivity compared to FOBT for detecting CRC [6].

We compared the rate of CRC findings in colonoscopy between two age groups: older than 75 year and younger than 75 years, with positive FOBT/FIT tests performed as part of screening for CRC. We then evaluated the specificity of the screening tool in the two age groups. Our null hypothesis was that CRC screening with FOBT/FIT has a better yield when performed in the very elderly.

## PATIENTS AND METHODS

Our study included colonoscopies performed between 1998 and 2019 at department of gastroenterology in Hillel Yaffe Medical Center, a major hospital on the western edge of Hadera, Israel, serving a population of about 450,000 residents. Indicated for the tests were asymptomatic ambulatory patients with positive FOBT/FIT (PF), as well as others with an indication of family history of CRC (FH) or primary screening colonoscopy (PS). Data were obtained based on registration data for age, sex, examination findings, preparation quality, and examination completeness.

Age was restricted to between 40 and 110 ( $n=66,255$ ) years and divided into two groups: 40–75 years old defined as the control group (younger) and older than 75 years of age were the study group (older). Data on preparation quality and completion of examination were com-

pared between the two groups. A scale of preparation performed according to the average of all colon parts given by Boston Bowel Preparation Scale (0= inadequate, 1=poor, 2=good, and 3=excellent) [7]. Scores of 0 or 1 were considered as poor preparation.

The primary outcome was the comparison of positive results of colonoscopies for CRC screening in those 40–75 years old and > 75 years old. Both groups had been referred to our department after a positive FOBT/FIT test. A further sub-analysis was performed, in which the ages were split into three groups: < 76 years, 76–85 years, and > 85 years. Both analyses included comparisons of sex, completeness of exam, and preparation.

The study was approved by Helsinki Committee, the local medical ethics board (HYMC-0102-19).

## STATISTICAL ANALYSIS

Descriptive statistics in terms of mean  $\pm$  SD and percentiles were performed for all parameters of the study. Differences between the two groups (age 40–75 vs. age >75) were assessed by *t*-test and Fisher's exact tests. Differences between the three groups (age 40–75, age 76–85, and age > 85) were tested by ANOVA with multiple comparisons and Pearson chi-square. Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 25 (SPSS, IBM Corp, Armonk, NY, USA).  $P < 0.05$  was considered as significant.

## RESULTS

Of a total of 10,472 patients, 38.8% had PF ( $n=4064$ ), 39.8% had a FH ( $n=4166$ ), and 21.4% underwent colonoscopy as PS ( $n=2242$ ). Table 1 shows the characteristics of the study population. The mean age of the control group was  $58.1 \pm 8.2$  ( $n=10,146$ ) versus  $79.0 \pm 3.9$  in the study group ( $n=326$ ). Female patients were 48.0% and 45.7% of the total, respectively. PF was 37.9% in the younger group vs. 68.4% in the older group, indicating a significant difference the two age ( $P < 0.001$ ). The greater incidence for malignancy was 0.9% in the younger group vs. 1.8% in the older group ( $P = 0.07$ ) suggesting the difference was non-significant. No statistically significant difference between the two groups was noted for both achieving a complete exam (87.4% in the younger group vs. 84.0% in the older group,  $P = 0.072$ ), and poor preparation 24.2% vs. 28.5%, respectively).

Table 2 shows the ratio of malignancy findings by indication for each study group. Younger patients with PF had 2.1% ( $n=80$ ) malignancy findings, compared to 2.7%

**Table 1.** General characteristics

	Control group (n=10,146)	Study group (n=326)	P-value
Age, in years			
Range	40–75	> 75	
Mean ± SD	58.1 ± 8.2	79.0 ± 3.9	
Sex			
Female	4875 (48.0%)	149 (45.7%)	0.43
Male	5271 (52.0%)	177 (54.3%)	
Indication			
PF	3841 (37.9%)	223 (68.4%)	< 0.001
PS	2194 (21.6%)	48 (14.7%)	0.004
FH	4111 (40.5%)	55 (16.9%)	< 0.001
Malignancy	87 (0.9%)	6 (1.8%)	0.07
Full exam	8872 (87.4%)	274 (84.0%)	0.072
Poor preparation	2455 (24.2%)	93 (28.5%)	0.075

FH = family history of colorectal cancer, PF = fecal occult blood test / fecal immunochemical test, PS = primary screening colonoscopy, SD = standard deviation

**Table 2.** Diagnosis of malignancy by indication and age group

Age in years	Fecal occult blood test/fecal immunochemical test			Primary screening colonoscopy			Family history of colorectal cancer		
	40–75 (n=3841)	> 75 (n=223)	P-value	40–75 (n=2194)	> 75 (n=48)	P-value	40–75 (n=4111)	> 75 (n=55)	P-value
Malignancy	80 (2.1%)	6 (2.7%)	0.47	2 (0.1%)	0	1.00	5 (0.1%)	0	1.00

(n=6) in the older group. This difference was not significant,  $P = 0.47$ . No significant difference was noted in the diagnosis of malignancy for the other indications as well (screening and family history of CRC).

When focusing on patients with PF only [Table 3], no difference between the control group (40–75 years old) and the study group (> 75 years old) was observed in sex ( $P = 0.63$ ), exam completeness ( $P = 0.49$ ), preparation quality ( $P = 0.36$ ), and the rate of malignancy detection (2.1% vs. 2.7% respectively,  $P = 0.47$ ).

**Table 3.** Patients with PF general characteristics (n=4064)

	Control group (n=3841)	Study group (n=223)	P-value
<b>Age in years</b>			
Range	40–75	> 75	
Mean ± SD	61.3 ± 7.4	79.5 ± 4.4	
<b>Sex</b>			
Female	1847 (48.1%)	103 (46.2%)	0.63
Male	1994 (51.9%)	120 (53.8%)	
Malignancy	80 (2.1%)	6 (2.7%)	0.47
Full exam	3271 (85.2%)	186 (83.4%)	0.49
Poor preparation	1064 (27.7%)	68 (30.51%)	0.36

SD = standard deviation

**Table 4.** Sub-analysis positive fecal occult blood test for age group > 86 years (n=4064)

	Age groups			P-value
Age in years				
Range	40–75 (n=3841)	76–85 (n=205)	> 86 (n=18)	
Mean ± SD	61.3 ± 7.4	78.55 ± 2.5	90.6 ± 6.4	
Sex				
Female	1,847 (48.1%)	90 (43.9%)	13 (72.2%)	0.06
Male	1,994 (51.9%)	115 (56.1%)	5 (27.8%)	
Malignancy	80 (2.1%)	6 (2.9%)	0	0.59
Complete exam	3,271 (85.2%)	170 (82.9%)	16 (88.9%)	0.62
Poor preparation	1,064 (27.7%)	61 (29.8%)	7 (38.9%)	0.47

SD = standard deviation

When looking into the sub-analysis by the three age groups, 40–75, 76–85, and > 86 year olds, still no significant difference in parameters was observed: 0% (n=0) vs. 2.1% (n=80) for malignancy with  $P = 0.59$ , 88.9% (n=16) vs. 85.2% (3271) for achieving a complete exam with  $P = 0.62$ , and 38.9% (n=7) vs. 27.7% (1064) had poor preparation,  $P = 0.47$  [Table 4].

## DISCUSSION

While CRC incidence increases with age [1], we expected an extra benefit from screening older patients using FOBT or FIT for detecting CRC in the general population. However, the results of our study demonstrated no additional benefit for those older than 75 or 85 years of age, compared with the younger group of younger than 76 years of age. We did not find evidence to support the null hypothesis suggesting increased yield from screening, independent of other factors, including complications and patient preferences.

Several studies provided clues regarding lack of evidence for an additional benefit in screening the very elderly compared to younger patients.

In a large population-based, prospective, observational study that included patients aged 70–79 years at average risk for CRC, it was demonstrated that the benefit of screening colonoscopy decreased with age [15]. For patients aged 70–74 years, the 8-year risk of CRC was 2.19% in those who were screened, compared with 2.62% in those who were not, with an absolute difference of only 0.43% [8]. These results are in concordance with ours. The authors stated that no increased cost benefit is to be found in screening the very elderly for CRC.

Further, Pisal and Wallace [9] reviewed the evidence of when to stop CRC screening in older adults, stating that life expectancy and co-morbidities should guide decisions more than age cutoffs.

The potential for increased risk of complications is one of the major concerns with performing a colonoscopy on elderly patients. A systematic review and meta-analysis showed that very elderly patients had a significantly higher rate of overall adverse events, including gastrointestinal bleeding and perforation [10,11]. Nevertheless,

our data showed no difference in exam completion rates or preparation quality when comparing those over 75 and 85 to younger counterparts [12]. This finding contrasts with studies reporting lower completion and poorer preparation in those over 80 vs. younger patients [13].

Updated USPSTF guidelines in 2021 emphasize individualized screening decisions based on life expectancy and co-morbidities rather than blanket age cutoffs for stopping screening [14]. Our study is limited by its retrospective nature and lack of co-morbidity data. However, completely excluding elderly patients over 75 or 85 years of age from CRC screening based on age alone can bias study results. While CRC incidence increases with age, our findings suggested that screening colonoscopy in the elderly solely with a positive FOBT may not substantially improve CRC detection compared to younger individuals. Decisions should weigh the more limited benefits against the risks and patient preferences.

## CONCLUSIONS

While CRC incidence is high in the elderly, screening this age group with PF does not necessarily lead to higher detection rates of CRC. Surprisingly, the rate of completion of the exam and quality of preparation did not differ from the younger group. These findings suggest that the decision on screening colonoscopy should be made only after careful consideration of potential benefits, risks, and patient preferences.

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## Capsule

### Induction of adaptive immune responses

Adaptive immunity evolved in ectothermic jawed vertebrates, yet how and where these immune responses are mounted in the apparent absence of germinal centers is not clear. To determine whether teleost fish have organized lymphoid structures, Shibasaki and colleagues searched the spleens of parasite-infected trout for proliferating lymphocytes. They identified regions of B and T cell proliferation close to melanomacrophage centers (MMCs), which they termed MMC-associated lymphoid aggregates (M-LAs). M-LAs

contained immunoglobulin M+ antigen-specific B cells, which expressed aicda and had undergone somatic hypermutation. M-LA B cells were polyclonal, and a significant portion were apoptotic, indicative of clonal expansion. These findings demonstrate that induction of adaptive immune responses in teleost fish occurs in organized secondary lymphoid structures that are functionally analogous to germinal centers.

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