The relationship between proximal and distal colonic adenomas: is screening sigmoidoscopy enough in the presence of a changing epidemiology?

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Background and study aims **Because the relationship between distal and proximal colonic findings remains uncertain, controversy exists over whether proctosigmoidoscopy or colonoscopy is more suitable for colorectal cancer (CRC) screening. We aim to describe the distribution and characteristics of polyps removed in colonoscopy screening.**

Patients and methods **A prospective registry of a colonoscopy-based CRC screening program was developed on asymptomatic individuals over 50 years. All polyps were removed and characterized. Polyp size and histology were noted. Adenomas were considered advanced if they measured greater than 10 mm or were tubulovillous, villous, or malignant. The prevalence of advanced proximal polyps was determined and patients were categorized according to their family history of CRC.**

Results **A total of 696 individuals (418 women), aged 57.7±10.3 years, were examined; 45.8% presented a colonic lesion, being adenomatous polyps in 32.7% individuals. Among these, 24.7% were advanced adenomas. Three patients (0.6%) presented invasive CRC. There were no significant differences with respect to sex and family history of CRC between patients with or without adenomas. Adenomas were more prevalent in individuals aged at least 65, irrespective of location ($P<0.001$). In 65.1% of individuals with adenomatous polyps in the right colon, there were no synchronous adenomas in the left colon ($P<0.001$). More adenomas were also present in the right colon of patients with no family history of CRC ($P<0.001$).**

Conclusion **Most patients with adenomatous polyps in the right colon showed no synchronic adenomas on the left side. Lesions on the right side would have gone undetected if the individuals undergoing CRC screening had been explored with proctosigmoidoscopy. *Eur J Gastroenterol Hepatol* 00:000–000 © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Introduction

Colorectal cancer (CRC) represents the second leading cause of cancer-related death in Europe [1]. The majority of CRCs grow from adenomatous polyps that progress from a small size to a larger one, later developing into dysplasia and cancer over a period of 5–10 years. Colonoscopic removal of adenomatous polyps has been proven to prevent ~80% of CRCs [2,3], as well as to reduce the overall death rate from the disease [4]. In this context, several studies have shown that CRC screening is both clinically useful [5,6] and cost-effective [7] in the average-risk population, leading to a significant reduction in mortality [8]. CRC is thus considered a preventable disease and an optimal candidate for national screening programs [9–12]. However, several European countries, including Spain, have yet to implement a nation-wide CRC screening program [13], although some regions and scientific societies are now beginning to set up preliminary programs [12,14].

Although it is well established that any strategy is better than not screening for CRC, no consensus has been reached with respect to the optimal screening method. Over the past few years, we have moved from screening with digital rectal examinations, guaiac-based fecal occult blood tests (FOBTs), and rigid sigmoidoscopy to more sophisticated fecal immunochemical testing (FIT) for human hemoglobin [15], colonoscopies, CT colonography [16], and even analysis of stool for mutated DNA [17]. Stool tests for occult blood are predominantly used in Europe [18] and Australia, whereas colonoscopy is the predominant screening method in the USA. Both FIT and colonoscopy have shown similar efficacy in the detection of CRC, but more adenomas are identified in patients screened with the latter method [12].

Endoscopic procedures, including colonoscopy and flexible proctosigmoidoscopy (PS), have the advantage of

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detecting both adenomas and carcinomas, and also of allowing endoscopic polypectomy and removal of in-situ cancers during a single examination. However, they are invasive procedures that are not always accepted by asymptomatic patients referred for screening purposes. Moreover, even though they have been shown to be highly cost-effective, they are still more expensive than FIT.

Despite a lack of definitive studies comparing different screening tools in terms of cost-effectiveness, colonoscopy is considered the most accurate method for early detection and prevention of CRC and premalignant precursor lesions. Although it is the most expensive method, patients who undergo colonoscopic screening and present no colonic lesions can delay repeating this screening test for at least 10 years [19,20]. In contrast, the advantages of PS over colonoscopy include the fact that it requires less bowel preparation and can be performed without sedation by paramedical personnel. This results in a less expensive, less invasive procedure with very little associated morbidity [21]. Recently published results from large, average-risk population trials of 'once-only' PS screening showed a significantly reduced CRC incidence and mortality [22,23]. This has led to renewed interest in implementing this methodology, as it now seems that only patients at high risk for cancer or with advanced adenomas or adenomas found in PS should undergo a complete colonoscopy.

However, several recent retrospective studies have noted a shift in the epidemiology of CRC, with an increased frequency of tumors in proximal colonic segments [24]. It is clear today that right-sided neoplasia may occur in the absence of a distal lesion, as 37–60% of advanced proximal neoplasias were found not to be associated with distal ones [25,26]. Increased age, smoking, and a family history of CRC have been proposed as predictors of isolated proximal adenomas [27], which have a worse overall prognosis [28]. This is important because the premalignant precursors of these tumors may remain undetected by PS if no lesions are present in the distal colon.

The aim of our study is to analyze the results of a prospective 5-year CRC colonoscopy-based pilot screening program that was conducted on outpatients with and without a family history of CRC to assess the prevalence, location, and histology of all the colonic polyps detected among them and to define the reliability of partial examinations in detecting neoplastic changes.

Patients and methods

Study setting

The recruitment area of the Tomelloso General Hospital is a predominantly rural area located in the center of Spain in the autonomous region of Castilla-La Mancha. The hospital offers universal coverage for specialist services, including endoscopy units and trained gastrointestinal endoscopists, for a reference population of roughly 67 360 inhabitants (on the basis of data from the year 2009).

As no specific screening program for CRC has been implemented by the public health authorities of the region, our hospital developed a CRC screening program among patients referred to the gastroenterology department between June 2007 and August 2012. The study was approved by our hospital Research Committee.

Patients

All consecutive adult patients referred to the gastroenterology clinic of our hospital who fulfilled the study criteria were recruited for the program. The inclusion criteria were as follows: aged at least 50 years, being naive for CRC screening with any method, signing the informed consent form after receiving the pertinent medical information, and agreeing to undergo an exploration of the entire colon (including cecal intubation) in a subsequent exam. The exclusion criteria were as follows: a personal history of CRC, adenoma, or inflammatory bowel disease; family history suspicious for hereditary nonpolyposis colon cancer syndrome or familial polyposis, a severe coexisting illness contraindicating a colonoscopy exam; insufficient bowel cleaning (defined as a score <7 in the Boston bowel preparation scale [29]) or not achieving cecal intubation; a previous colectomy or the presence of symptoms indicating the possibility of colorectal disease (rectal bleeding, changes in bowel habits, lower abdominal pain requiring medical evaluation); and patients who had previously undergone any type of CRC screening.

Colonoscopy procedure

Exams were carried out by licensed gastroenterologists from our department, all of whom generally perform more than 250 colonoscopies per year. A low-fiber diet (mainly avoidance of fruits and vegetables) for 2 days before the colonoscopy was recommended to all individuals. An adequate colonic cleansing was achieved with 4 l of polyethylene glycol oral solution administered the day before (Solucion Evacuante Bohm; Bohm Laboratories, Fuenlabrada, Spain). Having completed bowel preparation, the patients were allowed to drink only clear fluids up to 2 h before the colonoscopic procedure. All procedures were performed using a white light colonoscope Pentax EC-3870 LZK (Pentax of America Inc, Montvale, New Jersey, USA) equipped with magnification imaging. Cecal intubation was defined as identification of the appendix hole. Colonoscopic exams were carried out in accordance with the current national guidelines to ensure quality in explorations [30], especially in terms of bowel preparation (good or optimal colonic cleanliness) and scope removal time (>6 min). Conscious sedation was provided in all the colonoscopies, either by endoscopists or by anesthesiologists, depending

on the American Society of Anesthetics class, in compliance with regional legislation.

All polyps identified during the colonoscopy were endoscopically removed and submitted separately to the pathology department in formalin 4% containers. For each polyp, the morphology (sessile, semipedunculated, pedunculated), location [ascending colon (which included the right angle), transverse colon, descending colon (which included the left angle), sigmoid, and rectum], and size (estimated using an 8-mm diameter open-biopsy forceps) were documented.

For analysis, for each colonic segment, patients were classified on the basis of their most advanced lesion (e.g. a patient with a villous adenoma and a tubular adenoma within a same segment was classified as having a villous adenoma). To compare the results, 'right colon' included those segments proximal to the left angle, with the remaining segments considered to be 'left colon'.

Histopathological features

Pathology specimens were evaluated by local board-certified pathologists who classified the polyps according to the criteria established by the WHO in 1982 [31]. As indicated above, all removed specimens were categorized as either hyperplasic or adenomatous polyps. The latter included tubular adenomas, tubulovillous adenomas, and villous adenomas, depending on their architecture. For adenomatous polyps, the grade of dysplasia (low/medium/high) was also assessed. As in previous research, advanced adenomas were defined as adenomatous polyps with high-grade dysplasia/in-situ carcinoma and/or with (tubulo)-villous characteristics (> 25%), and/or adenomas measuring at least 1 cm in diameter [25,32]. Invasive carcinomas were also examined.

Statistical analysis

Results were expressed as mean and SD (continuous variables) or as percentages (categorical data). The differences in clinical characteristics depending on colonic segment were explored using the χ^2-test (categorical variables) and an analysis of variance (quantitative variables). When appropriate, nonparametric tests were used, namely, Fisher's exact test and the Mann–Whitney test. Analyses were carried out using PASW v18.0 software (SPSS Inc., Chicago, Illinois, USA). Values of P less than 0.05 were considered to be statistically significant.

Results

Characteristics of the study population

During the study period, 696 outpatients (418 women and 278 men) underwent complete colonoscopy for CRC screening purposes. No differences were found between sexes for age and family history of CRC. The mean age of the individuals was 57.7 years (SD 10.3; rank 50–89 years). Four hundred and sixty-three individuals (66.5%) were selected solely because they were older than 50 years of age, whereas 233 patients (33.5%) also had a family history of CRC. Among the 215 cases for whom the degree of kinship was recorded, most (191, 88.9%) had a first-degree relative affected by CRC whereas 24 (11.1%) had a second-degree relative and 39 (18.7%) reported having more than one affected relative. The median age of the youngest relative affected by CRC was 64 years (rank 23–91 years). Table 1 summarizes these results.

Table 1 Characteristics of participants included in our colonoscopy-based colorectal cancer screening registry

Number of patients	N=696 [N (%)]
Age (mean±SD) (years)	57.7±10.3
Age strata (years)	
50–59	406 (58.3)
60–69	210 (30.2)
70–79	73 (10.5)
80–90	7 (1.0)
Sex	
Female	418 (60.1)
Male	278 (39.9)
Family history of CRC	
No	458 (68.1)
First degree	191 (28.4)
Second degree	34 (3.6)
Unknown	23
Total patients with neoplasia	
Yes	227 (32.6)
No	469 (67.4)

The term neoplasia includes adenomatous polyps, advanced adenomas, and colorectal cancer (CRC).

Identifying and removing polyps

Of the 696 colonoscopies performed, 319 (45.8%) presented some type of polyp. A total of 664 identified polyps (an average of 0.97 polyps per explored patient, with a range of 0–18 polyps) were removed. Over half of the positive cases had lesions in only one colonic segment (208; 65.2%); the remainder had lesions in two or more colonic locations (111; 34.8%) (Table 2).

All removed polyps were analyzed with respect to morphology, histology, and degree of dysplasia (Table 3). The majority of polyps detected (87.1%) presented a sessile morphology. The most prevalent histology was that of adenomatous polyps, with 59.5% being tubular adenomas, 4% tubulovillous adenomas, and 0.6% being villous adenomas. Three of the removed lesions (0.45%) showed in-situ carcinoma and three patients (0.43%) were diagnosed with invasive carcinoma. A mild-grade dysplasia was described in 12 polyps, whereas nine lesions presented with severe dysplasia (high-grade dysplasia also included invasive carcinoma).

The median age of the patients presenting invasive carcinoma was 59 years (range 50–70 years); one patient had a positive family history.

Table 2 Distribution, location, and size of polyps endoscopically removed from 696 consecutive patients included in our colorectal cancer screening program

Colonic segment location	Positive patients [*N* (%)]	Polyps removed (*N*) [median (rank)]	Polyp size (mm) [median (rank)][a]	Polyp size ≥ 10 mm [*N* (%)][a]
Ascending colon[b]	119 (17.1)	168 [1 (1–12)]	3 (1–40)	20 (16.8)
Transverse colon	81 (11.7)	119 [1 (1–5)]	3 (1–20)	9 (11.1)
Descending colon[c]	77 (11.3)	93 [1 (1–4)]	4 (1–30)	9 (11.78)
Sigmoid colon	123 (17.7)	168 [1 (1–10)]	3.5 (1–20)	18 (14.8)
Rectum	82 (12.7)	116 [1 (1–6)]	3 (1–15)	3 (3.7)

[a]For each patient, the maximum polyp size was recorded.
[b]Ascending colon included the right angle of the colon.
[c]Descending colon included the left angle of the colon.

Table 3 Classification of all colonic polyps removed according to localization, morphology, and histology

	Ascending colon	Transverse colon	Descending colon	Sigmoid	Rectum	Total
Polyp morphology [*N* (%)]						
Pedunculated	6 (5.2)	3 (3.8)	12 (16.0)	17 (14.0)	4 (4.9)	42 (8.9)
Semipedunculated	4 (3.4)	1 (1.3)	3 (4.0)	7 (5.8)	4 (4.9)	19 (4.0)
Sessile	107 (91.4)	75 (94.9)	60 (80.0)	97 (80.2)	73 (90.1)	412 (87.1)
Histopathology [*N* (%)]						
Hyperplasic	23 (19.5)	15 (18.5)	12 (16.2)	44 (36.1)	53 (64.6)	147 (30.8)
Tubular adenoma	79 (66.9)	60 (74.1)	57 (77.0)	67 (54.9)	21 (25.6)	284 (59.5)
Tubulovillous adenoma	3 (2.5)	2 (2.5)	4 (5.4)	5 (4.1)	5 (6.1)	19 (4.0)
Villous adenoma	1 (0.8)	–	–	1 (0.8)	1 (1.2)	3 (0.6)
Invasive carcinoma	–	1 (1.2)	–	2 (1.6)	–	3 (0.6)
Other	12 (10.2)	3 (3.7)	1 (1.4)	3 (2.5)	2 (2.4)	21 (4.4)
Dysplasia [*N* (%)]						
Low grade	69 (95.8)	43 (86.0)	43 (91.5)	75 (93.8)	59 (96.7)	289 (93.2)
Mild grade	2 (2.8)	5 (10.0)	2 (4.3)	2 (2.5)	1 (1.6)	12 (3.9)
High grade[a]	1 (1.4)	2 (4.0)	2 (4.3)	3 (3.8)	1 (1.6)	9 (2.9)

[a]Including advanced adenomas and invasive carcinomas.

Table 4 Distribution of all adenomas and advanced adenomas endoscopically removed from asymptomatic patients undergoing colorectal cancer screening

		Patients with advanced adenomas [*N* (%)]	
Location	Patients with adenomatous polyps *N* (prevalence) [*N* (%)]	*N* (prevalence)	% adenomas
Ascending colon	82 (11.8)	17 (2.4)	17/82 (20.7)
Transverse colon	62 (8.9)	7 (1.0)	7/62 (11.3)
Overall in right colon	126 (18.1)	21 (3.0)	21/126 (16.7)
Descending colon	63 (9.1)	13 (1.9)	13/63 (18.5)
Sigmoid colon	76 (10.9)	20 (2.9)	20/76 (26.3)
Rectum	27 (3.9)	8 (1.2)	8/27 (29.6)
Overall in left colon	145 (20.8)	38 (5.5)	38/145 (26.2)
Any location	227 (32.7)	56 (8.1)	56/227 (24.7)

The number of adenomas in each colonic location was not taken into account.
Adenomatous polyps included tubular, tubulovillous, and villous adenomas.
Advanced adenomas were defined as an adenoma measuring ≥ 10 mm in diameter, and/or with villous architecture (>25%), and/or high-grade dysplasia or in-situ carcinoma.
Prevalence: proportion of lesions in the overall number of patients; % adenomas: proportion of advanced adenomas in the overall number of adenomatous polyps.

Prevalence and topographical distribution of colorectal polyps, adenomas, and cancer

Among the 696 asymptomatic individuals, potentially premalignant adenomatous polyps were found in 227 (32.7%) individuals. In this group, advanced adenomas were found in 56 individuals (8.1%), representing 24.7% of the total number of adenomatous polyps detected. No differences in age, family history of CRC, or sex were observed between patients with or without polyps.

The topographical distribution of adenomas and advanced adenomas detected in recruited patients is summarized in Tables 4 and 5. Overall, adenomas were not more frequent in left (20.8%) than in right (18.1%) colon segments ($P = 0.18$). Of the 227 patients from whom adenomatous polyps were removed, 126 patients (55.5%) had them in the right colon whereas in 145 patients (63.9%), they were located in the left colon. In only 19.4% of cases (44/227) were there synchronous adenomatous polyps in both locations. This means that 65.1% of all patients with adenomatous polyps located in the upper colon (82/126) had no synchronous adenomatous polyps in the distal colon, which means that the upper colon polyps would have been missed by PS screening.

Table 5 Relationship between age and the prevalence of adenomas in patients

		Adenomas [*N* (%)]			Advanced adenomas [*N* (%)]		
Age (years)	Patients	Any location	Right colon	Left colon	Any location	Right colon	Left colon
<65	522	155 (29.7)	83 (15.9)	97 (18.6)	33 (6.3)	10 (1.9)	24 (4.6)
≥ 65	174	72 (41.4)	43 (24.7)	48 (27.6)	23 (13.2)	11 (6.3)	14 (80)
P value		0.004	0.009	0.011	0.004	0.003	0.08

The number of adenomas in each colonic location was not taken into account.
Adenomatous polyps included tubular, tubulovillous, and villous adenomas.
Advanced adenomas were defined as an adenoma measuring ≥ 10 mm in diameter, and/or with villous architecture (>25%), and/or high-grade dysplasia or in-situ carcinoma.

Considering age as a risk factor, adenomas were more prevalent at each location analyzed in individuals 65 years of age and older ($P < 0.05$). With respect to overall advanced adenomas, these were also more prevalent in patients older than 65 years of age ($P = 0.004$), especially those located in the right colon ($P = 0.003$) (Table 5).

No significant statistical differences in colonic localization were observed with respect to size, average number, morphology, histological type, presence of dysplasia in the polyps, or a positive family history of CRC. Overall, 70 patients with no polyps in the left colon presented adenomatous polyps in more proximal segments, with 14 patients presenting advanced adenomas. Finally, 18 hyperplasic polyps were also detected, but were not considered a risk factor for proximal neoplasia [33].

Family background and risk of polyps/colorectal cancer

Patients with a family history of CRC (including first-degree and second-degree relatives) showed no significant differences in terms of the number of polyps identified and removed in comparison with patients with no family background of CRC. However, considering the number of adenomatous polyps removed, more polyps tended to be present in the distal colon of patients with a family history of CRC, especially if a first-degree relative was affected, but this did not reach statistical significance (37.7 vs. 31.9%; $P = 0.08$). The number of relatives with CRC was not related to the presence of polyps in the right ($P = 0.76$) or the left ($P = 0.77$) colon.

Discussion

This research confirms that asymptomatic individuals frequently show a high proportion of premalignant adenomas when explored with a complete colonoscopy for CRC screening purposes. More importantly, our results clearly show that nearly three of four colonic polyps in general, and adenomatous polyps in particular, appearing in the right colon are not accompanied by synchronous lesions on the left-hand side. These right-sided lesions would have thus remained undetected if the individuals undergoing CRC screening had been explored with PS. In this respect, the entire colon should be considered as a potential target for neoplastic changes.

Colonoscopy is widely recommended as a screening procedure with high diagnostic and therapeutic yield; however, its use has become a subject of debate in recent years [20]. Even though it has been shown that colonoscopic removal of adenomatous polyps prevents death from CRC [4], a limited number of studies have sought to measure the 'real' efficacy of screening colonoscopies in the prevention of CRC, considered in terms of overall reduction in mortality [20]. Thus, compared with FOBT alone, trials using FOBT followed by colonoscopy in the case of a positive result have been shown to reduce CRC mortality [34–36].

Currently, the presence of sentinel polyps in the rectum and sigmoid is considered as a warning sign of the risk of finding proximal lesions, making PS a valid alternative for CRC population screening. This technique, which has advantages both in economic terms and in acceptance when provided without sedation, has recently been shown to be useful in reducing CRC-related mortality. However, as this is true of all screening techniques, economic concerns have given rise to various studies seeking to optimize the differential use of colonoscopy and PS for distinct patient patterns. Unfortunately, the size of distal adenomas as a predictor of proximal advanced adenomas produced contrasting results in research carried out at the end of the 20th century. Although some authors reported that patients with a single tubular adenoma measuring 5 mm or less had a low prevalence of advanced proximal polyps [37], other researchers, after observing that distal adenoma size was not a significant predictor in any of the analyses carried out, called for age-based screening with PS in patients aged 50–55 years and older, and with colonoscopy in patients older than 65 years of age [38].

Recent evidence from PS studies showing a reduction in CRC mortality [22,23] can be extrapolated to colonoscopy as it provides a more complete examination of the colon [19]. However, definitive data on the advantages of colonoscopy over PS have yet to be provided. Several studies developed in the last decade have already shown that the prevalence of right-sided advanced adenomas in patients with no left-sided adenomas was in the 2–5% range [39–42], and that patients with distal tubular adenomas were at a similar risk for advanced proximal neoplasia as those without distal adenomas [25,26,43]. The validity of a strategy that encourages individuals with small tubular adenomas visible on PS to undergo follow-up

colonoscopy (excluding those with nonadenomatous lesions) is thus questionable. Indeed, our results show that 65.1% of patients with right-sided neoplasia presented no synchronous lesions in the left colon, a finding that underscores the advantage of colonoscopy over PS when considering invasive CRC screening techniques. In fact, recent epidemiological observations have described a change in the trends of CRC location toward more proximal sections in high-incidence countries such as the USA, Israel, and parts of Europe [24,44–47]. This differs from the countries in Africa and Turkey, in which there is still a high proportion of distal tumors [48,49]. This epidemiological trend has also been confirmed in two large prospective studies on colonoscopy screening in which about half the patients with advanced proximal neoplasia presented no distal colonic neoplasia [40,41]. This new evidence on the prevalence of advanced right-sided neoplasia occurring in the absence of polyps in the left colon thus seems to favor the use of colonoscopy over PS as the primary CRC screening method [44,50,51], especially considering that 24.7% of the adenomas removed in our study were advanced adenomas and that the prevalence of asymptomatic, invasive CRC was 0.43%. Moreover, and in contrast to previous results [27], the prevalence of adenomas did not correlate with age, sex, colonic location, or a family history of CRC in our study population. Differences in study designs, age of the recruited patients, and geographical or genetic variations may have produced some discrepancies; further studies involving a higher number of patients are required to define the impact of each risk factor on the development of CRC.

Considerable research has been carried out with respect to the possible switch in CRC location toward more proximal colonic segments during the last decades, with several explanations of the differing trends across populations being offered. These include genetic and ethnic differences [52], exposure to various environmental and dietary risk factors [53], and the effect of CRC screening and its associated variations in prevalence and efficacy [54]. Because the population included in our study was naive for any type of CRC screening method, the latter explanation could not have influenced our results. In contrast, increasing evidence shows that proximal and distal CRC differ in clinical, pathological, and molecular features [55], which supports the hypothesis that right-sided and left-sided CRCs are distinct clinicopathological entities [56] with different epidemiologies.

Among the strengths of our study is its prospective design and the consecutive inclusion of all individuals explored with the aid of colonoscopy as the initial screening technique in the same hospital over a 5-year period. The prevalence of adenomatous lesions detected in our study was identical to other recently published results for Spain and Italy, in which 32% of the patients explored also presented premalignant lesions in the colon [12,57]. Our study, however, is based on a prospective register of our clinical practice and shows the effectiveness of CRC screening programs developed in 'closed communities.'

However, our study also has several limitations: our pilot CRC screening program was not developed at the population level, but rather on patients enrolled in our digestive clinics, which excluded the presence of any condition associated with a rectocolonic pathology, with or without a family history of CRC. In the absence of a standard screening program mandated by regional health authorities, the option of screening in 'closed communities' has proven to be a valid and efficient strategy in different parts of Europe, especially as a preliminary to the establishment of a universal coverage program [58,59]. Also, because some studies seem to show that the risk for developing colon neoplasia is principally related to age and family history [60], on the basis of our exclusion criteria, we believe that our results can be extrapolated to a standard population.

Another limit of screening colonoscopy is that it has imperfect sensitivity, depending on the quality of the procedure in terms of the cecal intubation rate, missed lesions, and withdrawal time. Although we attempted to control for these variables, it is also true that previous studies based on colonoscopic screening have had the same limitations. Considerable attention has been paid in recent years to the importance of sessile serrated adenomas, especially in the proximal colon. However, we did not consider this histopathologic description, first introduced in the WHO classification for lower gastrointestinal tract lesions in 2010, as our study consistently used the diagnostic criteria established by the WHO in 1982 [31]. Finally, colonoscopy involves greater cost, risk, and inconvenience to patients than other screening tests. However, not only does it offer the possibility of detecting small lesions as well as those located in the proximal colon but also the time between exams can be longer (compared with FIT) in patients who show no colonic neoplasia. Further studies are required to investigate the specific impact of the detection and removal of proximal colonic lesions in preventing the appearance of CRC and reducing CRC mortality rates.

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Conflicts of interest

There are no conflicts of interest.

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