

New considerations for colorectal cancer screening based on the demographic profile of colorectal cancer in a Greek population

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Abstract. Colorectal cancer screening has long been recommended for middle age and older individuals. Recent evidence indicates increasing incidence and mortality among young adults. Therefore, the present study re-examined the current recommendations using an asymptomatic average-risk population screened by colonoscopy. A total of 716 participants of a wide age range were prospectively enrolled in an open-access endoscopic screening program based on self-referral. Comparisons between different age, gender and location groups, and receiver operating characteristic curves (ROC) curves for best age selection for detection of lesions were employed. Increased incidence of advanced lesions was observed in adults <50 years old. Although the polyp size was <1 cm in 85% of the cohort, a significant number of participants harbored advanced lesions. A disturbing incidence of lesions in women 30-49 years was located mainly in the left colon. One-third of the important pathology resides exclusively in the right colon. ROC curves demonstrated that with the current starting age of screening at 50 years, 92% of polyps and 95% of adenomas could be detected by colonoscopy, but a number of potential precancerous lesions will appear at an earlier age and therefore will be missed. The present study supported the notion that it is critical to reduce screening initiation below the currently accepted age of 50 years. Colonoscopy is a suitable method for addressing the increased prevalence of proximal lesions and the meticulous resection of smaller polyps.

Introduction

It is generally accepted that the management of colorectal cancer (CRC) has been successfully improved. This is indicated by the confirmation of declining incidence and mortality since 1975 and documented in successive annual reports on CRC, spanning over the last decade in the western world. This success has been mainly attributed to identifying modifiable lifestyle risk factors and the wider application of screening and subsequently endoscopic polypectomy (1-3).

Unfortunately, recent evidence tarnished the current euphoria. Increasing incidence and mortality in young adults <50 years old have been reported (3,4). An inconspicuous increase in CRC incidence in younger individuals appeared in the early 1990s (4,5), but it was more widely recognized during the last decade (5,6). This recognition identified CRC as the second most common cancer after the age of 30 years (7) and as the fourth leading cause of mortality in adolescents and young adults (3).

Women seem to be more susceptible to an increased CRC annual percent change (APC) in younger cohorts (30-49 years old), which is higher compared with men and consistent across continents of the western culture (USA, Australia, Europe) (6,8,9). Furthermore, an inverse correlation exists in women where the overall decreasing incidence of CRC is faster in men while the decreasing overall mortality is slower in women (3).

High rates of proximal colon cancers have been estimated to be between 30-42% of the total prevalence, being more common in men compared with women (10,11). Increasing incidences of proximal cancers in young adults 20-49 years old have also been reported, especially after 2010 (5,12).

The vast majority (80%) of polyps found during average-risk screening colonoscopy are subcentimetric polyps (<10 mm) (13,14). At the same time, they constitute a potential cause of pitfalls for the endoscopist since they may harbor significant lesions, such as advanced adenomas ($\leq 12.8\%$) (15), while the methods for their resection are imperfect (16,17).

Screening has been considered to contribute to the decline in CRC incidence and mortality. By contrast, the lack of adequate screening may have threatening repercussions in younger individuals regarding the CRC risk (4,18). To achieve

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this goal, worldwide guidelines recommend the initiation of screening at 50 years old since two-thirds of CRC cases are detected in individuals ≥ 60 years old and 90% in those >50 years old (8,19). Recent recommendations suggest that screening should start earlier at 45 years old (18).

The present study therefore aimed to address the issues aforementioned by analyzing epidemiological data from an average risk asymptomatic screening cohort of a wide age range that was submitted to colonoscopy in an open-access manner in the endoscopy unit of a tertiary hospital. Since there is no national organized screening program in Greece, the current study will provide the opportunity to collect and interpret real-life data from a population sample in a densely populated urban area of westernized lifestyle to demonstrate actual needs for health policymaking.

Materials and methods

The present study prospectively included 716 individuals submitted to screening colonoscopy during a period of 2 years (2017-2018). They have been classified as average risk since those with a personal or family history of polyps and colorectal cancer and those with prior positive fecal hemoglobin tests, blood per rectum or inflammatory bowel disease and anemia were excluded. They were all asymptomatic except for the occasional sporadic abdominal discomfort, which was considered non-significant. Their examination was performed on an open-access endoscopy screening program after self-referral and personal informed consent. The procedure was completed under conscious sedation after bowel cleansing using a polyethylene glycol preparation. The bowel cleansing was graded on a three-class scale (good, adequate, poor) similar to the Boston Preparation Scale. In case polyps were discovered during colonoscopy, they were excised by cold biopsy forceps or by cold or hot snaring at the endoscopist's discretion. The size of the polyps was estimated compared with open biopsy forceps with an opening diameter of 7 mm. The extend of the right colon was considered up to the splenic flexure and that of the left colon from the splenic flexure and peripherally up to the anal verge. Information was collected from the endoscopic and pathologic reports. During endoscopic sessions, both consultants and trainees were involved. Per patient analysis was performed according to the maximum polyp size when more than one polyp of different sizes was found. Advanced adenomas (AA) were defined as polyps with size ≥ 10 mm or with high-grade dysplasia (hgd). Since there was a substantial inter-observer variation for recognizing a villous component, this parameter was not included in the definition of AA (20). The protocol of the present study was accepted by the Sismanogleio-Amalia Fleming Hospital's scientific review committee (approval number 399/18-4-2019) and conformed to the amendments of the Helsinki Declaration.

Statistical analysis. Continuous variables were compared between groups using the t-test and for more than two levels of explanatory variables using one-way ANOVA. Ordinal data were compared using the χ^2 and post hoc comparisons were performed by the Bonferroni method. Receiver operating characteristic curves (ROC) were produced to define the appropriate age providing optimum sensitivity for adenoma

detection. The number needed to screen (NNS) to detect one adenoma was estimated across different age and gender groups. The α -level was defined as significant at 0.05. All P-values were 2-sided. The statistical package used for analytical statistics was the SPSS 27 (IBM Corp.).

Results

General overview. There were 716 participants with a median age of 63 years (range 30-87 years), and 51.3% were males. The cecum was reached in 95.7% of the cases. The preparation was considered as good or adequate in 92% of the endoscopies. A consultant performed the colonoscopy in 69% of the sessions and the rest by a trainee under supervision with an overall adenoma detection rate of 28.4%. The prevalence of lesions including polyps, adenomas, advanced adenomas, high-grade dysplasia, and cancer are shown in Table I. Polyps were found in 52.4% ($n=375$) of the entire cohort. The median number of polyps/person was 2. Marked proportions of the lesions above were found in this average risk screening cohort. This has important implications concerning the epidemiologic burden and the risk of future cancer development in the population.

Associations of polyp size and location with important lesions. Most subjects with polyps (58.1%) had a maximum polyp size of 6-9 mm. Only 14.7% of them had polyps ≥ 10 mm. There is a linear association between increasing polyp size and age as well as the prevalence of adenomas, hgd, cancer, serrated pathology, and the location at the right colon. Nonetheless, a significant proportion of the diminutive and small polyps harbor important lesions (48% adenomas, 5.6% hgd, 12.9% serrated, and 0.9% coexist with cancer lesions) while 15% of the screened participants present with isolated right colon lesions of this size (Table II).

AA appeared in 9.6% of the attendees, mostly in men (67% of AA), in the intermediate age group (50-69 years old; 56.2% of AA), with a significant proportion of them located at the right colon (39%) and 25% of those were found in 6-9 mm polyps. The mean size of AA was 15 mm, and the median number per patient was 1. In Table III, the distribution of characteristics between the isolated right and left colon lesions was shown. Isolated right colon lesions were found in older individuals with increasing frequency, with no significant gender difference but with a male predominance, harboring important pathology (~one-third of serious lesions reside in that part of the bowel). As maximum polyp size increases >9 mm, almost half (43.3%) of the participants accommodate lesions in the right colon.

The epidemiologic profile according to different age groups. A comparison between age groups is presented in Table IV. It seems that between the early (30-49 years old) and intermediate (50-69 years old) age groups, there is no quantitative or qualitative difference in important pathologies (mean number and size of lesions, proportion of AA, hgd, cancer and isolated right colon lesions). Apart from the prevalence of polyps and adenomas that follow a linear association with increasing age and the disparities in the presence of SSP/A (sessile serrated polyp/adenoma) that in any case represent an alternative cancer pathway, it seems that younger individuals (30-49 years old)

Table I. Characteristics of participants.

Total no.	716
Age, median, (range)	63 (30-87)
Sex, n (%)	
Male	367 (51.3)
Female	349 (48.7)
Prevalence of lesions, n (%)	
Any polyp	375 (52.4)
Adenoma	205 (28.6)
Advanced Adenoma	69 (9.6)
High grade dysplasia	31 (4.3)
Cancer	10 (1.4)
SSP/A	54 (7.5)
Location	
Right colon lesions, n (%)	156 (21.7)
No polyps/pt, median	2
No adenoma/pt, median	1

Any polyp: all screens with polyp of any type. SSP/A, sessile serrated polyp/adenoma.

have acquired a risk profile that needs to be taken into account by future screening policy recommendations.

Gender influences across different age groups. In Table V, the findings showed that women 30-49 years old have a higher prevalence of polyps of larger size and cancer cases compared with men, although this was not statistically significant. There was no significant difference in frequency characteristics between women of 30-49 years old and women of 50-69 years old (data not shown) except for the prevalence of SSP/A. Females of a younger age had their polyps, AA and hgd located in the left colon (absence of isolated right colon lesions). By contrast, men show a marked increase in the prevalence and size of polyps and prevalence of adenomas and AA at the next age group of 50-69 years old, with frequencies higher compared with the respective age group of females. Men 30-49 years old show polyps distributed throughout the left and right colon and important lesions, such as AA and hgd in the right colon (absence of isolated left colon lesions). There was a linear association for right colon lesions with increasing age in women. Nonetheless, males maintain the majority of proximal lesions in all age groups. These findings indicate a trend towards an additional disease burden in young women, which is located in the easily accessible left colon.

Implications based on ROC curves analysis. ROC curves (Table VI) were generated to predict the detection of adenomas at each age group by colonoscopic screening. In every screening program, one of the most important determinants is the sensitivity of the detection method. The area under the curve predicted that at 50 years old, a colonoscopy will detect 92% of the polyps (Fig. 1), 95% of the adenomas (Fig. 2), and 93% of the AA (Fig. 3) and proximal lesions (Fig. 4). When ROC curves were applied for males and females separately

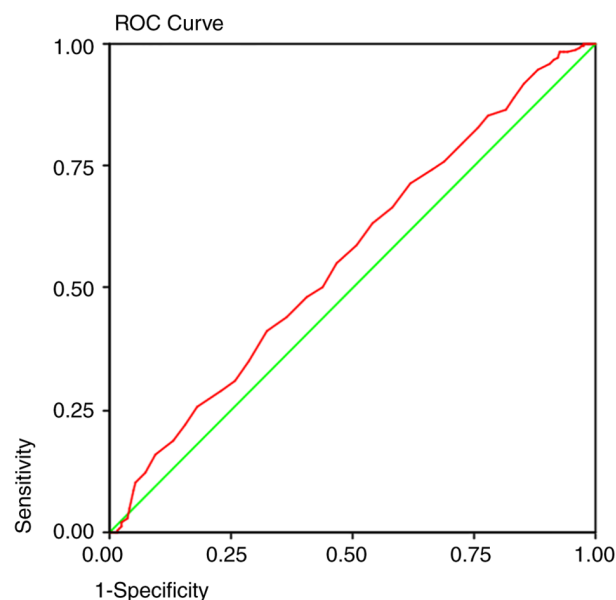


Figure 1. ROC curve for polyp detection. ROC, receiver operating characteristic.

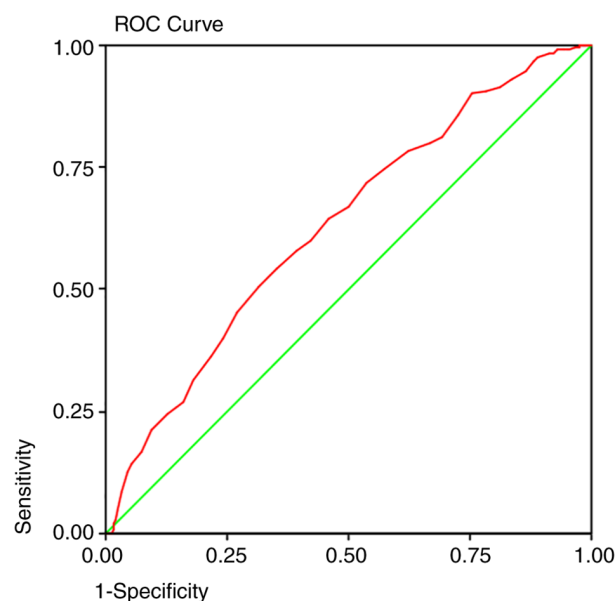


Figure 2. ROC curve for adenoma detection. ROC, receiver operating characteristic.

(Figs. 5 and 6 respectively), the area under the curve for the detection of adenomas demonstrated 95 and 93% sensitivity, respectively, at the same age limit (50 years old).

Discussion

Since 2003, when the European Council recommended implementing CRC screening, a number of European countries have initiated screening programs starting at the age of 50 years (21). In Greece, although there has been an attempt for an organized screening program according to the National Oncological Plan during 2008-2012, until now, screening has been applied only in certain hospitals on an individual basis (22). The present

Table II. Frequency of lesions by patient according to maximum polyp size.

Characteristics					P-value
Maximum polyp size, mm	≤5	6-9	10-20	21-40	
Patients, n	101	218	46	10	
Age, mean	61	64	65.3	71	0.001
Male (n)	59.4% (60)	58.7% (128)	63% (29)	90% (9)	0.25
Lesions (n)					
Adenomas	25.7% (26)	58.3% (127)	91.3% (42)	100% (10)	0.0001
HGD	0%	8.3% (18)	19.6% (9)	40% (4)	0.0001
Cancer	1% (1)	0.9% (2)	4.3% (2)	10% (1)	0.049
SSP/A	7.9% (8)	15% (33)	28.3% (13)	0%	0.009
Isolated Rcolon (n)	12.5% (11)	23.6% (37)	39.3% (11)	50% (2)	0.007
No polyps, mean	1.9	2.5	3.2	3.2	0.003
No adenomas, mean	1.4	1.7	1.8	2.6	0.02

HGD, high grade dysplasia; SSP/A, sessile serrated polyp/adenoma; Isolated Rcolon, (right colon); No polyps, No adenomas, mean number of polyps, adenomas.

Table III. Distribution of characteristics in isolated left and right colon lesions.

Characteristics	Right colon	Left colon	P-value
Participants, n	61	217	
Age, years, mean	65.3	62.7	0.05
Age category %			0.35
30-49	16.7	83.3	
50-69	20	80	
70-87	27.5	72.5	
Sex %			0.08
Male	25.8	74.2	
Female	16.5	83.5	
Lesions %			
Adenomas	29.9	70.1	0.002
AA	39	61	0.007
HGD	27.8	72.2	0.55
SSP/A	34.4	65.6	0.1
No polyp, mean	1.8	1.9	0.9
AA size, mm, mean	14.2	15.3	0.6
Max polyp size %			0.009
1-9 mm	19.5	80.5	
10-40 mm	43.3	56.7	

AA, advanced adenoma; HGD, high grade dysplasia; SSP/A, sessile serrated polyp/adenoma.

study revealed an overall prevalence of adenomas, AA, and cancer of 28.6, 9.6 and 1.4%, respectively, among asymptomatic average risk first-time participants presented by self-reference in an open access colonoscopy screening program. Similar studies of asymptomatic average-risk screening programs

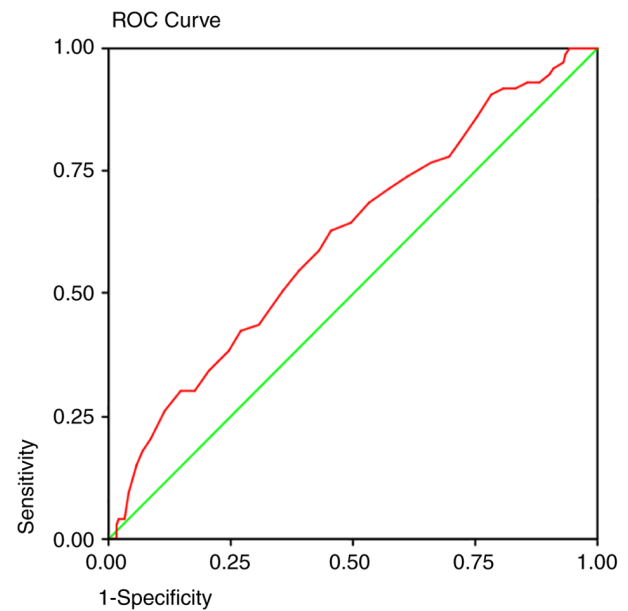


Figure 3. ROC curve for advanced adenoma detection. ROC, receiver operating characteristic.

have shown rates of adenomas, AA and cancer of 12.3-29, 2.5-7.1 and 0.7%, respectively (13,23,24). The results of the present study indicated an increased prevalence rate, although the higher mean age of the participants compared with the other studies may account for the difference.

The present study demonstrated a substantial rate of adenomas in the 30-49 year old group (10.4%) and also a high prevalence of AA (4.5%) and cancer (1.5%). Previous publications from the USA, the Middle, and the Far East, including asymptomatic average risk cohorts spanning from 1994-2014, have demonstrated a similar prevalence of adenomas (8.3-17.3%) but lower AA (1-2.5%) and cancer (0.2%) at 40-49 years old (25-29). Consequently, it has been

Table IV. Frequency of lesions by patient-Comparison between early-intermediate-late age groups.

Age (mean)	n (%)	Sex, male	Any polyp	Adenoma	AA	HGD	Cancer	SSP/A	Rcolon	No polyp mean	No adenoma mean	HGD size, mm	AA size, mm	1-10 mm
30-49 (43)	67 (9.4)	41.8%	34.3%	10.4%	4.5%	4.5%	1.5%	0	16.7%	2	1	10	9.5	91.3%
50-69 (60.4)	463 (64.7)	48.8%	52.7%	26.3%	8.2%	4.1%	0.4%	10.2%	20%	2.5	1.8	11.4	15.3	89.6%
70-87 (74)	186 (26)	60.8%	58.1%	40.9%	15.1%	4.8%	3.8%	3.8%	27.5%	2.4	1.7	15.3	15.4	79.6%
P-value		0.006	0.004	0.0001	0.012	0.84	0.004	0.001	0.36	0.57	0.17	0.5	0.4	0.16

AA, advanced adenoma; HGD, high grade dysplasia; SSP/A, sessile serrated polyp/adenoma; Rcolon, isolated right colon lesions; 1-10 mm, patients with 1-10 mm maximum polyp size.

Table V. Gender differences in different age groups.

Age category Participants, n	30-49 (birth cohort 1980s)			50-69 (birth cohort 1960s)			70-87 (birth cohort 1940s)		
	67			463			186		
	Male	Female	P-value	Male	Female	P-value	Male	Female	P-value
M/F % (n)	41.8 (28)	58.2 (39)		48.8 (226)	51.2 (237)		60.8 (113)	39.2 (73)	
Any polyp %	28.6	38.5	0.44	64.6	41.4	0.0001	63.7	49.3	0.06
No polyps, mean	2	2.13	0.8	2.7	2.3	0.2	2.6	2	0.07
Polyp location			0.04			0.07			0.2
L %	57.1	100		74.2	83.5		66.7	82.8	
R %	42.9	0		25.8	16.5		33.3	17.2	
Adenoma %	14.3	7.7	0.44	33.2	19.8	0.001	44.2	35.6	0.28
No adenoma, mean	1	1	NS	1.8	1.6	0.3	1.8	1.5	0.3
HGD %	7.1	2.6	0.56	5.3	3	0.24	3.5	6.8	0.3
HGD size, mm, mean	9	12	NS	9.8	13.8	0.16	25.7	8.8	0.2
HGD location			NS			0.6			NS
L %		100		50	62.5		66.7	60	
R %	100			50	37.5		33.3	40	
AA %	7.1	2.6	NS	10.6	5.9	0.08	17.7	11	0.3
AA size, mm, mean	9	10	NS	15	16	0.6	16.3	13.2	0.45
AA location			0.33			0.09			0.2
L %		100		48.1	78.6		42.1	75	
R %	100			51.9	21.4		57.9	25	
Cancer %	0	2.6	NS	0	0.8	0.49	4.4	2.7	0.7
Serrated polyp/adenoma %	0	0		11.5	8.9	0.36	5.3	1.4	0.25
Maximum polyp size, mm			0.27			0.5			0.14
≤5	62.5%	26.7%		28.1%	31.6%		19.4%	16.7%	
6-10	37.5%	60%		58.9%	55.1%		54.2%	75%	
11-20	0	13.3%		11%	13.3%		18.1%	5.6%	
21-40	0	0		2.1%	0		8.3%	2.8%	
NNS-adenoma	18	22		6	10		4	7	

HGD, high grade dysplasia; AA, advanced adenoma; No polyps, No adenomas, mean number of polyps or adenoma per patient; L, left; R, right.

proposed that this age group with risk factors such as obesity should start screening at 45 years old (25).

Subcentimetric polyps constituted 85% of the cohort, which is consistent with other studies previously mentioned (13,14).

Table VI. Area Under The Curve and Cut-off points of screening colonoscopy for identifying disease positive patients.

	Area	Asymptomatic significance	95% CI	Cut-off value	Sensitivity	Specificity
Polyps	0.564	0.003	0.522-0.606	50 years	0.92	0.85
Adenomas	0.631	0.000	0.586-0.675	50 years	0.95	0.86
AA	0.613	0.002	0.545-0.682	50 years	0.93	0.88
Proximal lesions	0.573	0.005	0.523-0.622	50 years	0.93	0.87
Adenomas-male	0.607	0.001	0.548-0.666	50 years	0.95	0.87
Adenomas-female	0.641	0.036	0.569-0.712	50 years	0.93	0.85
Adenomas				48 years	0.98	0.90
Adenomas-male				48 years	0.98	0.92
Adenomas-female				46 years	0.98	0.91

CI, confidence interval.

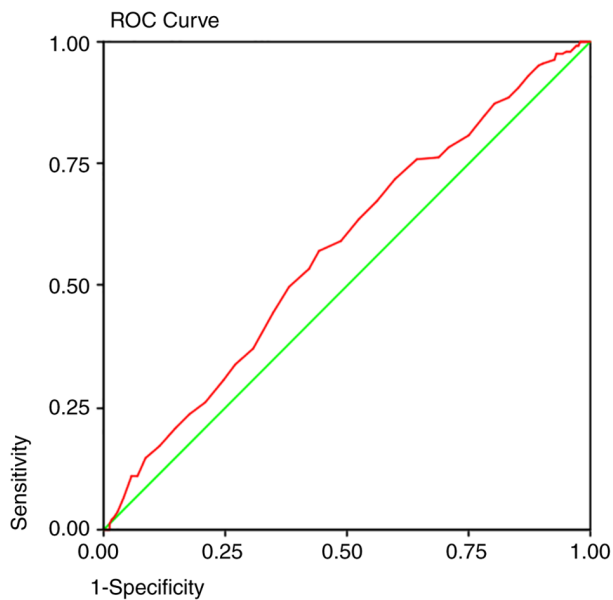


Figure 4. ROC curve for proximal lesions detection. ROC, receiver operating characteristic.

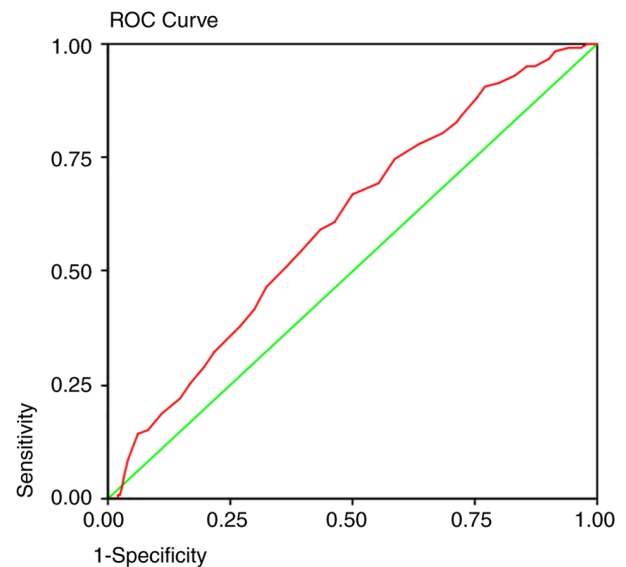


Figure 5. ROC curve for adenoma detection in males. ROC, receiver operating characteristic.

The present study noted that 8.3% of the 6-9 mm polyps could host advanced lesions, such as hgd, or coexist with cancer in 0.9% of the cases. In the literature so far, the pooled rate of AA in small polyps (6-9 mm) is ~4.9% (30) in asymptomatic average-risk groups. Other studies from Europe and America, including asymptomatic but not exclusively average-risk individuals, report the presence of AA in 1.6-12.8% of the small polyps (15,31,32). This is to remind the endoscopists that participate in screening programs not to dismiss subcentimetric polyps easily and to be cautious about the radical excision of such lesions.

These data regarding young adults and small polyps necessitate reconsideration of current recommendations. The natural history of precancerous lesions suggests that 37% of the adenomas and 91% of AA will eventually progress to cancer with an annual rate of 2.5-5.5% for AA, while ~6% of subcentimetric adenomas will become AA in 2-3 years (33-35). This

indicates that advanced lesions at the early age group will become cancer almost by certainty after 20-30 years, meaning in the 6th or 7th decade of life.

There are several but consistent data gathered from different continents (America, Australia and Europe) (6,9,11) noting that although absolute CRC incidence rates are lower in women compared with men (8,11), the annual percentage changes for women 30-49 years old are higher between 1994 and 2016 ranging between APC 4.73-6.8% (6,10) and they appeared to have been tripled (APC: 12) since 2009 (5). In Europe, this percentage change was associated with a cohort effect, with the turning point being in the early 1990s (5,6). Another study, including first-time asymptomatic average-risk individuals, showed that women <50 years old had more advanced neoplasia compared with men (6.2 vs. 0.6% respectively) (23). The present study noted an increase in prevalence rates of polyps and a larger maximum polyp size in women 30-49 years old relative to men. The majority of the serious

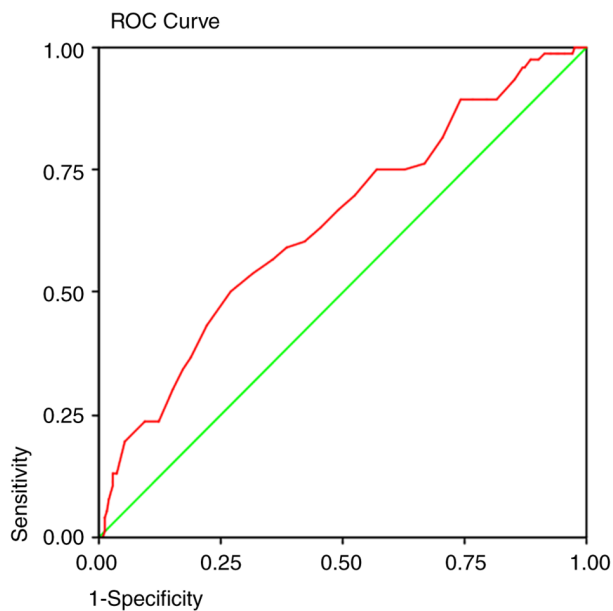


Figure 6. ROC curve for adenoma detection in females. ROC, receiver operating characteristic.

lesions were located in the left colon the opposite to that in men. If this tendency is validated in other studies, it would be reasonable to lower the screening age for younger women <50 years old with a flexible sigmoidoscopy as the initial examination followed by colonoscopy at a later age according to current guidelines.

The above findings differed in older age groups, where men >50 years had statistically more serious lesions compared with women while maintaining an increased prevalence of right colon lesions. These findings were consistent with other studies presenting increased incidence of proximal malignant neoplasia in men 20-39 years old, especially since 2010 (5,12), with higher left-sided lesions in women (10).

Furthermore, in the present study, proximal lesions were found in a substantial proportion of participants (21.9%) and 39% of AA were located solely in the right colon. Right colon lesions were detected in older age compared with distal lesions with a predilection in men and larger maximum polyp size. This notification is crucial for developing a screening program and the determination of screening methods as sigmoidoscopy and fecal tests are inadequate or less sensitive, respectively, for the detection of proximal lesions (36). The location has significant implications for screening since there is a higher missing rate for proximal lesions (37) and these lesions are out of the reach of sigmoidoscopy. In one meta-analysis, once only sigmoidoscopy at the age of 55 years decreased the incidence and mortality of CRC by 18 and 28%, respectively (38). This could be an option for younger age women in whom the majority of lesions lie in the left colon and since the NNS for the finding of one adenoma is higher compared with men (22 vs. 18), it is difficult to justify a screening colonoscopy at ages <50 years.

The ROC curves revealed that with the current recommendation of screening colonoscopy at 50 years, 5-7% of adenomas will remain undetected either due to the inability of the detection method itself or because of a late referral of individuals. Since the first proposal for initiation of screening

at 45 years for African Americans was suggested in 2005 (39), certain Medical Societies, such as in Saudi Arabia in 2015 (19), the US Multi-society Task Force in 2017 (20) and recently the American Cancer Society (18) have adopted this recommendation for all adult average-risk population. In the present case, we would expect to detect 98% of the overall adenomas in both genders if we decided to lower the screening age at 48 years in men and 46 years in women. This age group is also compatible with epidemiological data showing that CRC is an important health risk, being the fourth most common cancer with 74.3% of its cases clustering in between 40 and 49 years old (40). Cost-effectiveness analysis modeling using estimated adenoma prevalence in different age cohorts similar to the present study has concluded positively for starting screening at 45 years (41). The selection of the acceptable age for initiation of screening is a matter of public health policy and available resources. Since the purpose of screening is to detect precancerous lesions, meaning in practice adenomas, it would be reasonable to detect as many of them as possible and as early in life as possible since the cancers that are diagnosed at the age of 60 years stem from adenomas at the age of 40 years. Following this concept, if it is a public necessity to detect 98% of the adenomas in the screened population, one would need to start screening at the age of 48 years and if one would like to detect the same number in women as in men, then the initiation of screening should be at 46 years for women.

The present study has certain limitations. Some limitations are inherent to the study type and the sample size. Although the participants were prospectively entered into the database, this is an observational cross-sectional study with an adequate overall sample size but with a restricted earlier age cohort and consisted of self-referred individuals since there is no organized national screening program in Greece. This might introduce type II errors and selection bias because the included individuals could be considered more health-oriented with health-seeking behaviors. A future meta-analysis could properly collect and incorporate more data from various studies regarding young adults who unfortunately remain behind screening intentions.

Additionally, in one-third of the procedures, trainees were actively involved, theoretically increasing the risk of missing lesions. The present study was aware that proposals regarding screening procedures at a population level should consider multi-dimensional prerequisites concerning the disease itself, health resources and local cost-effectiveness analysis. This epidemiological analysis aims to provide answers about the active disease profile of the Greek population, which is of fundamental importance in activating the cascade of further endeavor.

In conclusion, this is the largest study of colorectal cancer screening of a Greek average risk population sample so far. It noted emerging trends of increased prevalence in precancerous and malignant colon lesions, especially important for younger adults and, more specifically, women. It also focused on the small polyps that host significant lesions in the screening cohort and also focused on the proximal location of lesions in the right colon as an additional parameter of missing lesions and access strategy. Based on this disturbing data and the corroborative epidemiologic surveillance profile from other countries, it was proposed to lower the initiation age of screening at 48 years for men with colonoscopy and

at 46 years for women with once-only sigmoidoscopy with subsequent surveillance following current guidelines from the age of 50 years by colonoscopy. These proposals are based on a Greek population sample and cannot be extrapolated to other countries.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

VP was responsible for conception and design of the present study. Analysis and interpretation of the data was performed by VP, GF, PK, NV, SV, GL, ID and EK. VP and EK drafted the article and VP, ID and EK critically revised the article for important intellectual content. VP, NV and SV confirm the authenticity of all raw data. All authors reviewed and approved the final manuscript.

Ethics approval and consent to participate

All participants provided written informed consent. The study has been performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. The Institutional Review board of the Sismanogleio General Hospital approved the study protocol (approval number 399/18-4-2019).

Patient consent for publication

Not applicable.

Competing interest

The authors declare that they have no competing interests.

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