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Retrospective Cohort Study

Adenoma and advanced neoplasia detection rates increase from 45 years of age

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statement: This retrospective study does not require approval from an ethics committee, in accordance with French ethics law. However, this study was undertaken as a retrospective audit of patient care as part of service evaluation under the authorization of our local audit and governance guidelines.

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Abstract

BACKGROUND

Colonoscopy is considered a valid primary screening tool for colorectal cancer (CRC). The decreasing risk of CRC observed in patients undergoing colonoscopy is correlated with the adenoma detection rate (ADR). Due to the fact that screening programs usually start from the age of 50, very few data are available on the risk of adenoma between 40 and 49 years. However, the incidence of CRC is increasing in young populations and it is not uncommon in routine practice to detect adenomas or even advanced neoplasia during colonoscopy in patients under 50 years.

AIM

To compare the ADR and advanced neoplasia detection rate (ANDR) according to age in a large series of patients during routine colonoscopy.

METHODS

All consecutive patients who were scheduled for colonoscopy were included. Exclusion criteria were as follows: patients scheduled for partial colonoscopy or interventional colonoscopy (for stent insertion or stenosis dilation). Colonoscopies were performed in our unit by a team of 30 gastroenterologists in 2016. We determined the ADR and ANDR in each age group in the whole population and in the population with an average risk of CRC (excluding patients with personal or family history of advanced adenoma or cancer).

RESULTS

6027 colonoscopies were performed in patients with a median age of 57 years (range, 15-96). The ADR and ANDR were 28.6% and 9.7%, respectively, in the whole population. When comparing patients aged 40-44 ($n = 382$) and 45-49 years

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($n = 515$), a strong increase in all parameters from 45 years was observed, with the ADR rising from 9.7% in patients aged 40-44 to 21.2% between 45 and 49 ($P < 0.001$) and the ANDR increasing from 3.1% in patients aged 40-44 to 6.4% in those aged 45-49 years ($P < 0.03$). With regard to patients aged 50-54 ($n = 849$), a statistically significant increase in the ADR and ANDR was not observed between patients aged 45-49 and those aged 50-54 years. In the population with an average risk of CRC, the ADR and ANDR were still significantly higher in patients aged 45-49 compared with those aged 40-44 years.

CONCLUSION

This study shows a significant two-fold increase in the ADR and ANDR in patients aged 45 years and over.

Key words: Colorectal cancer; Screening; Adenoma detection rate; Colonoscopy; Cohort study

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Core tip: Despite the fact that the incidence of colorectal cancer (CRC) in individuals less than 50 years seems to have increased in the last decade, there are very few data on adenoma and advanced neoplasia in this age group. This is the first large study to evaluate the adenoma detection rate (ADR) and advanced neoplasia detection rate (ANDR) in patients under 50 years during routine colonoscopy in average-risk and high-risk CRC patients. This study showed a significant two-fold increase in the ADR and ANDR in patients aged 45 years and older, irrespective of a personal or family history of polyps or cancer. Such high rates in those aged 45 years and over should be taken into account in CRC screening campaigns.

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INTRODUCTION

Colorectal cancer (CRC) is one of the most frequent cancers worldwide, and the second most common cause of cancer-related deaths^[1,2]. It is now well established that screening programs can reduce CRC mortality through the detection of both precancerous lesions and early-stage cancer^[3-8]. Different screening modalities are available, ranging from stool-based tests (guaiac test, immunochemical test or DNA assays) to endoscopy with varying sensitivity and specificity^[9,10]. The choice of screening method usually depends on the national screening program policy. Irrespective of the method used, most scientific organizations recommend beginning screening at 50 years of age in average-risk populations^[11]. Colonoscopy is considered a valid primary screening tool for CRC when performed every 10 years, usually from the age of 50 years^[11,12]. Optimizing the quality of screening colonoscopy is necessary to improve CRC prevention^[13]. One of the best indicators of the quality of colonoscopy is the adenoma detection rate (ADR) which is correlated with the polyp detection rate and the mean number of adenomas per colonoscopy^[14-16].

It is worth discussing the age at which screening is initiated. It is not uncommon in routine practice to detect adenomas or advanced neoplasia during colonoscopy in patients aged less than 50 years. Moreover, the incidence of CRC is increasing in young populations (particularly in the United States)^[17], and non-negligible rates of colonic adenomas and advanced neoplasia (13.3% and 3.4%, respectively) have already been reported in patients aged 40 to 49 with a family history of cancer^[18]. However, due to the fact that screening programs frequently start from the age of 50, few recent data on the risk of adenoma in patients aged 40-44 and 45-49 years are available. The only way to estimate the incidence of adenomas is to determine the risk in a population referred for colonoscopy for indications other than screening. The aim of the current study was to determine, in routine practice, the adenoma detection rate

(ADR) and advanced neoplasia detection rate (ANDR) according to age in a large population of consecutive patients admitted to our digestive endoscopy unit for colonoscopy over a period of one year.

MATERIALS AND METHODS

This observational monocentric study was conducted in our unit from January 1, 2016 to December 31, 2016, by a team of 30 gastroenterologists. All patients were informed in writing of the use of their endoscopic procedure data for clinical research purposes and none expressed opposition. The data were retrospectively collected by extraction from our medical patient management software. Therefore, in accordance with French ethics law, this retrospective study did not require approval from an ethics committee. All authors declare that they have access to the study data and have reviewed and approved the final manuscript.

Patients

All consecutive patients who were scheduled for colonoscopy were included. Exclusion criteria were as follows: patients scheduled for partial colonoscopy or interventional colonoscopy (for stent insertion, stenosis dilation or hemostasis).

Data collection

The following data were collected using dedicated software: Age, gender, indication for colonoscopy, preparation procedure and quality of preparation [assessed by the Boston Bowel Preparation Scale (BBPS)]^[19,20], cecal intubation, withdrawal time, number and size of polyps (< 1 cm or ≥ 1 cm) and polyp histopathology. Personal history of adenoma/cancer was defined as: a patient in whom a previous colonoscopy had found at least one adenoma or who was previously diagnosed with CRC. Family history of adenoma or cancer was defined as: a patient with at least one first-degree relative diagnosed with CRC, a patient with at least two second-degree relatives diagnosed with CRC or a patient with at least one first-degree relative with adenoma irrespective of the age of the relative. Patients with personal or family history of adenoma or cancer were considered high-risk patients for CRC while patients with other indications were considered average-risk patients for CRC. We determined the ADR (percentage of colonoscopies with at least one adenoma) and the ANDR (percentage of colonoscopies with at least one advanced neoplastic lesion as defined below).

Colonoscopy considerations

The videocolonoscopes used were EVIS EXERA III CF-H190 (Olympus Co.) and more rarely EC-690 WM, and EC-600WM (Fujifilm Co.). Good preparation was defined as a BBPS score ≥ 6 with no sub-score < 2^[14]. Withdrawal time was determined from the cecum to the anal verge, expressed in seconds and calculated on colonoscopies with no polyps.

Histopathological considerations

An adenoma was defined as a tubular or tubulo-villous adenoma. Serrated polyps (SP) were defined as hyperplastic polyps, sessile serrated adenomas/polyps and traditional serrated adenomas. Hyperplastic polyps of the rectum and sigmoid colon were excluded, as they are not considered a risk for CRC^[21]. Advanced neoplasia were defined as grade 4 or grade 5 of the Vienna classification (grade 4 corresponding to a non-invasive high-grade neoplasia, *i.e.*, high-grade adenoma/dysplasia, non-invasive carcinoma and suspicion of invasive carcinoma; grade 5 corresponding to an invasive neoplasia, *i.e.*, intramucosal carcinoma, submucosal carcinoma or beyond) or a polyp 1 cm or greater^[22].

Statistical analysis

The ADR and ANDR were analyzed in each age group in the whole population and in the population with an average risk of CRC (excluding patients with personal or family history of advanced adenoma or cancer). The NCSS v 10.0 was used to perform the statistical analysis. Quantitative variables were expressed as mean (SD) or as median and interquartile range (IQR). Qualitative variables were expressed as numbers and percentages. Continuous variables were compared using a Student's *t* test or Wilcoxon-Mann-Whitney *U* test, as required. Categorical variables were compared using the chi-squared test or Fisher's exact test, as required. Logistic regression analysis used a forward hierarchical stepwise method with switching to select independent variables related to the ADR. All significant variables in the univariate analysis were included in the model and were retained at each step if *P* >

0.05. Odds ratios (OR) and 95% confidence intervals (CI) are also provided.

RESULTS

During the study period, 6335 colonoscopy procedures were performed. We excluded 278 sigmoidoscopies and 30 interventional procedures (Figure 1), leaving 6027 colonoscopies in 3308 women (54.9%) and 2719 men (45.1%) with a median age of 57 years (range, 15-96; IQR 18). The indication for colonoscopy was a personal history of adenoma or cancer in 1512 patients, family history of adenoma or advanced adenoma or cancer in 2534, a positive fecal immunochemical test in 391, digestive symptoms or hematochezia in 2306, screening colonoscopy in 320 and other causes in 476 (mainly inflammatory bowel disease in remission follow-up, suspected colonic lesions after computed tomography scan and post-diverticulitis colonoscopy). Sub-optimal preparation was noted in 6.2% of the patients. Cecal intubation was obtained in 99%. Median withdrawal time was 470 seconds (range 55-3840; IQR 240).

Results in the whole population

Of the 6027 colonoscopies, 2054 detected 3914 lesions or polyps with adenomas in 2914 (74.5%), SP in 788 (20.1%) and other polyps in 212 (5.4%). The ADR was 28.6% in this series. We found 690 advanced neoplasia in 584 patients leading to an ANDR of 9.7%. The serrated lesion detection rate (SDR) was 9.2%. In the multivariate analysis (Table 1), the variables associated with a higher ADR were: a personal history of polyps or cancer (OR 1.5), a positive fecal immunochemical test (OR 2.7), male gender (OR 1.7) and the age of the patient (≥ 45 years: OR 1.3). Colonoscopy for symptoms was associated with a lower risk of adenoma (OR 0.7).

Results according to age intervals

We examined the ADR and ANDR according to age using age intervals of 5 years. The results are presented in Figure 2. The ADR and ANDR markedly increased from 9.7% and 3.1% to 21.2% ($P < 0.001$) and 6.4% ($P < 0.03$), respectively, in patients aged 40-44 and in those aged 45-49 years (Figure 2). The SDR also increased from 6% to 11.7% ($P < 0.005$) between patients aged 40-44 and those aged 45-49 years. When considering only asymptomatic patients ($n = 3267$), the ADR and ANDR also increased between patients aged 40-44 and those aged 45-49 years from 7.5% to 25.4% ($P < 0.001$) and 3.4% to 6% ($P = 0.3$), respectively.

A comparison of colonoscopy data and detection rates between patients aged 45-49 and those over 50 years is provided in Table 2. With regard to patients' characteristics, the two groups were comparable, except for personal or family history of CRC or polyps and a higher proportion of patients over 50 years having no symptoms. Considering all patients over 50 years ($n = 4436$), the ADR and ANDR were significantly higher than those in the 45-49 years of age group with 34.6% *vs* 21.2% ($P < 0.001$) and 11.8% *vs* 6.4% ($P < 0.001$), respectively. In contrast, the SDR was not significantly different in those aged over 50 than in those aged 45-49 years, with 10.1% *vs* 11.7% ($P = 0.32$), respectively.

From the 584 patients diagnosed with advanced adenoma during the study period, 71 underwent complementary treatment such as surgery, chemotherapy, radiotherapy or a combination of these treatments. The results showed that endoscopic resection was curative in 513 (88%) patients. When considering only patients aged under 50 years, 10 of 61 with advanced adenoma received additional treatment, resulting in a curative endoscopic resection rate of 51/61 (84%) ($P = 0.7$ compared with the whole population).

Results in patients with an average risk for CRC

To rule out the possibility that our results were driven by patients at high risk for CRC, we excluded patients with personal or family history of polyps or cancer. In this average-risk population, we also observed a significant increase in both the ADR and ANDR in patients aged 40-44 and in those aged 45-49 years, from 11% to 19% ($P < 0.01$) and 2.7% to 6.4% ($P < 0.05$), respectively. The extent of this increase was therefore similar to that observed in the whole population (Figure 3).

DISCUSSION

This study demonstrated that adenoma and advanced neoplasia (*i.e.*, a polyp greater than 1 cm in size or an adenoma with at least high-grade dysplasia) detection rates start to increase from 45 years of age, with a two-fold increase compared to those aged

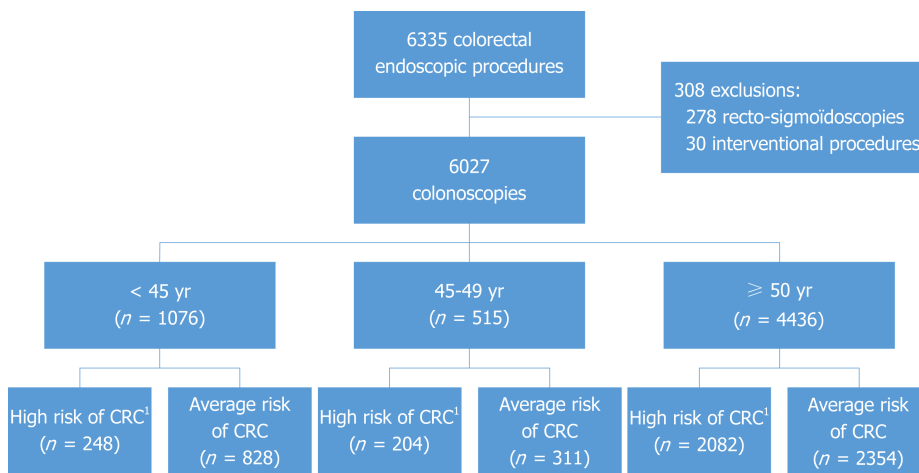


Figure 1 Register flow chart. Patients admitted, exclusions and breakdown of patients with high risk and average risk of colorectal cancer. ¹Personal or family history of colonic polyps or colorectal cancer.

40-44 years. These data were confirmed whether or not there was a personal or family history of polyps or cancer. Moreover, we did not observe any significant difference in the ADR and ANDR between patients aged 45-49 and those aged 50-54 years in the whole population. Of note, the increase in these detection rates from age 45 years also concerned SP.

This is one of the first large studies to evaluate adenoma and ANDR in patients under 50 years old during routine colonoscopy in average-risk and high-risk CRC patients. To our knowledge, the study by Regula *et al*^[18] is the only published report to evaluate CRC screening in a young population aged 40 to 66 years. This very large Polish colonoscopy-based screening program on more than 50000 participants included patients aged 40 to 49 years, but only in cases with a family history of cancer of any type. These young patients constituted only 14.2% of the participants (*vs* 26.4% in our study). In the Polish study, the ANDR and ADR were 3.4% and 8.5%, respectively. The ANDR and ADR in our patients aged 45 to 49 were much higher at 9.7% and 21.2%, respectively. This discrepancy could be explained by the sharp rise in the ADR between 40-44 and 45-49 years and to a lesser degree by the high rate of completed colonoscopy (1% in our series *vs* 9% in the Polish study). However, the same difference was observed in those aged over 50 years, with an ADR of 13.1% in the Regula study *vs* 34.6% in our patients, the latter being much closer to other published data^[14].

A reduction in the ADR and ANDR may have been expected by excluding patients with a personal or family history of polyps or CRC as previously described^[2,18], but this was not the case. As familial syndromes account for no more than 20% of young-onset CRC^[23], the high rates of detection in our series could have minimized the difference between high-risk and average-risk patients. This study raises questions regarding screening in patients less than 50 years. Most scientific organizations such as the French Society of Digestive Endoscopy or the American College of Gastroenterology agree that colonoscopy or other methods of CRC screening for average-risk patients must enroll patients aged 50 to 75 years^[3,5,15], but little is known about the ADR and ANDR outwith this range. The incidence of CRC in individuals less than 50 years seems to have increased in the last decade^[2,17,23]. In two recent studies involving approximately 600 patients in each study, young patients were diagnosed with significantly more advanced CRC in comparison to older patients^[24,25]. Therefore, earlier screening may improve disease stage on presentation and the prognosis of CRC. Indeed, the United States multi-society task force on CRC recently recommended providing screening to African Americans as early as 45 years of age^[26], thus confirming the validity of rethinking the "50-year-old barrier".

If adenomas are detected as early as 45 years of age, they could be resected at 50 years of age. While this assertion may be acceptable for small and low-grade dysplastic adenomas, it is highly questionable for advanced adenomas. However, the medical benefit of performing colonoscopy as early as 45 years has to be balanced by the medico-economic feasibility of such a screening policy. Nevertheless, whatever the screening method, the high ANDR observed in our young patients has to be taken into account in order to improve the prevention of CRC and disease stage on presentation and prognosis.

Our study had some limitations. First, while this study has the advantage of

Table 1 Multivariate analysis of the adenoma detection rate in the whole population (*n* = 6027)

Variable	Univariate analysis		Multivariate analysis		
	Odds ratio	P	Odds ratio	95%CI	P value
Male gender	1.8	10 ⁻⁵	1.7	1.5-1.9	10 ⁻⁵
Age > 45 yr	1.5	10 ⁻⁵	1.3	1.1-1.6	0.0005
Good prep	1.3	0.02			
Screening	REF		REF		
Family history	0.60	0.0006	0.65	0.5-0.0	0.004
Personal history	1.5	0.001	1.53	1.2-2.0	0.002
FIT +	2.7	10 ⁻⁵	2.7	1.9-3.6	10 ⁻⁵
Digestive symptoms	0.6	0.0005	0.7	0.5-0.9	0.02
Other indications	0.36	10 ⁻⁵	0.4	0.3-0.5	10 ⁻⁵

FIT: Fecal immunochemical test.

describing “real-life” conditions, socio-economic level and environmental exposure as well as the way-of-life of a population of a major European capital could represent some biases compared to national screening campaigns which are more representative of the population of the entire country. Moreover, as 38% of our patients underwent colonoscopy due to symptoms, our population cannot be considered a screening population. However, such symptoms are not known to increase the risk of polyps and were not correlated with a high ADR in the multivariate analysis in our series (OR 0.7). A personal or family history of polyps or CRC (defined as high-risk patients) may also bias the results. For this reason, we have detailed the results obtained for high-risk and average-risk patients. However, the ADR and ANDR significantly increased in both populations (Figure 3). The number of patients in our study who underwent colonoscopy for screening was only 320 (approximately 5% of our population). Most of these patients were older than 50, as colonoscopy screening is not recommended for younger patients in France. The size of the screening population was too small to perform a reliable analysis. The conclusions of our study, as obtained on routinely explored patients, should therefore be transposed to screening with caution. In addition, it is well known that age is not the only risk factor for the development of adenomas. Therefore, it could be speculated that other confounding factors may be associated with our ADR and ANDR. We acknowledge that we did not consider ethnicity (which is not allowed in France), smoking or obesity, which are other known risk factors for CRC^[27-30]. Nevertheless, we showed that age was an independent factor associated with a high ADR in the multivariate analysis (OR 1.3). Lastly, the colonoscopy quality criteria obtained in a single team such as ours with a long-standing awareness policy (sub-optimal preparation in only 6.2%, median withdrawal time of 490 s, cecal intubation rate of 99%) undoubtedly had a positive impact on detection rates and may thus moderate the reproducibility of these results.

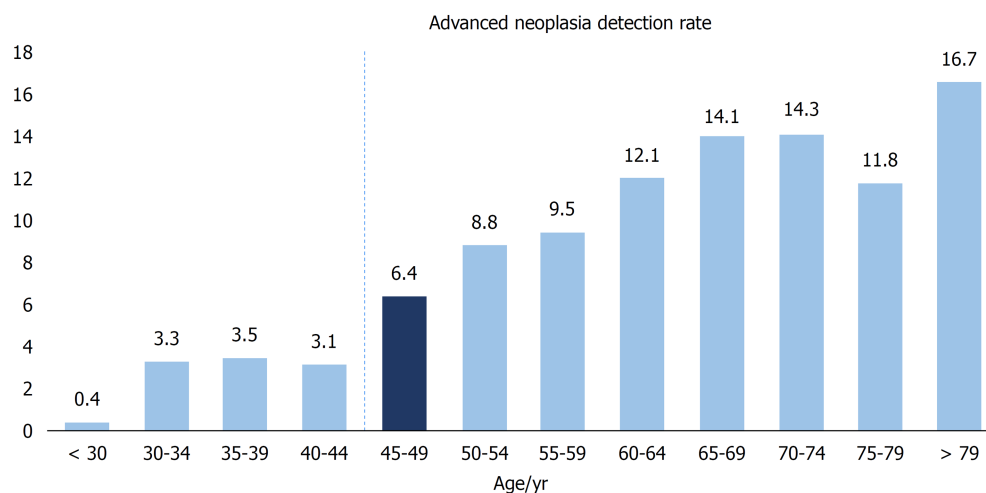
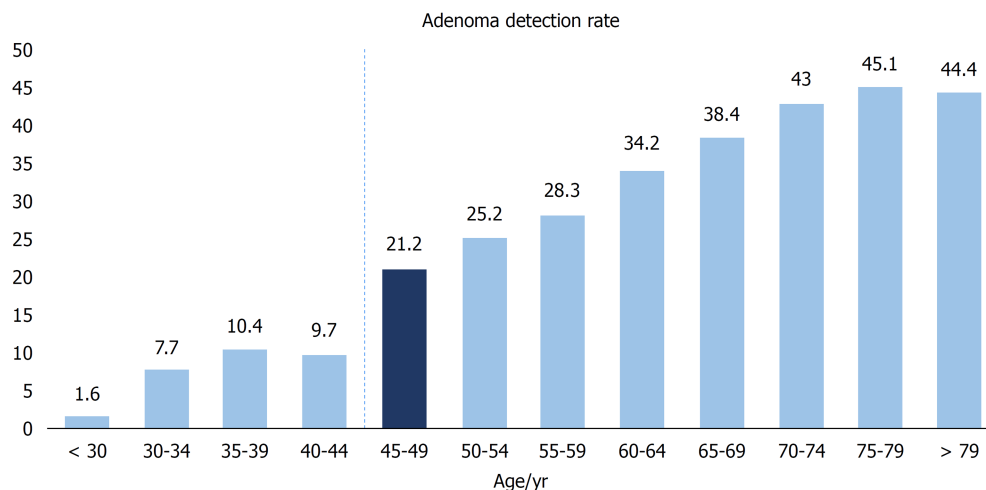
To summarize, in this large monocentric cohort of consecutive colonoscopies, we found a two-fold increase in the ADR and ANDR in patients aged 45 years and over, irrespective of a personal or family history of polyps or CRC.

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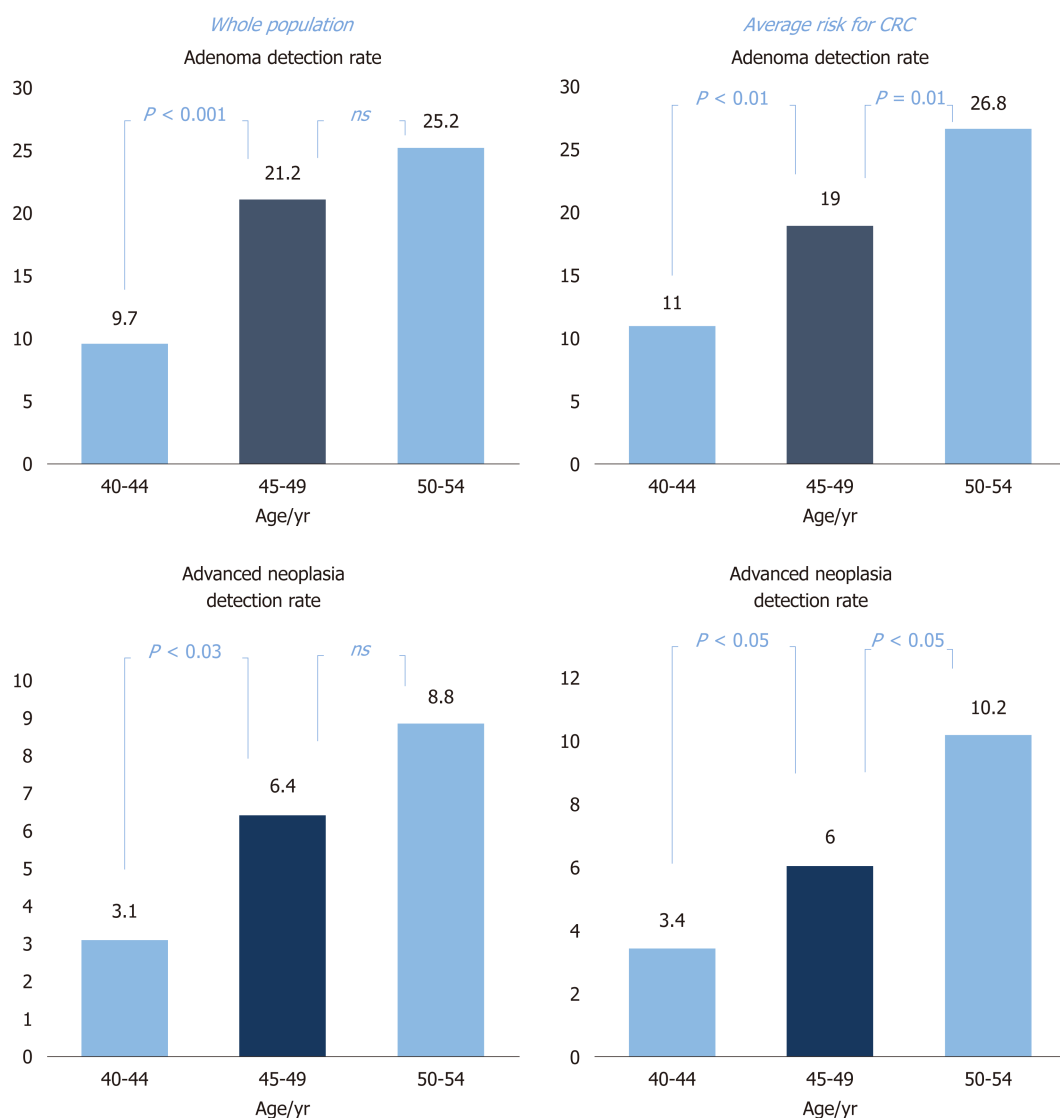
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Table 2 Comparison of patients' characteristics, colonoscopy data and detection rates in patients aged 45-49 years and over 50 years *n* (%)

	45-49 yr (n = 515)	≥ 50 years (n = 4436)	P value
Gender, male/female, <i>n</i>	236/279	2028/2408	0.98
Indications for colonoscopy			
Patients without symptoms	268 (52)	3,006 (68)	< 0.001
High risk			
Personal or family history of polyps	204 (39.6)	2082 (46.9)	0.002
Average risk	311 (60.4)	2354 (53)	< 0.001
Digestive symptoms	247 (48)	1430 (32.2)	
Other	64 (12.4)	924 (20.8)	
Colonoscopy data			
Sub-optimal preparation	30 (5.8)	275 (6.2)	0.84
Mean number of polyps	0.47	0.78	-
Median withdrawal time, s	452	471	0.49
Histological data			
Polyp detection rate, %	29.1	40	< 0.001
Adenoma detection rate, %	21.2	34.6	< 0.001
Serrated polyp detection rate, %	11.7	10.1	0.32
Advanced neoplasia detection rate, %	6.4	11.8	< 0.001



Age, y (<i>n</i>)	< 30 (252)	30-34 (182)	35-39 (260)	40-44 (382)	45-49 (515)	50-54 (849)	55-59 (856)	60-64 (828)	65-69 (775)	70-74 (537)	75-79 (339)	> 79 (252)
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Figure 2 Adenoma and advanced neoplasia detection rates according to age.**Figure 3** Adenoma and advanced neoplasia detection rates. Adenoma and advanced neoplasia detection rates in the 40-44, 45-49 and 50-54 age groups in the whole population and in the average-risk of colorectal cancer population.

ARTICLE HIGHLIGHTS

Research background

Colonoscopy is considered a valid primary screening tool for colorectal cancer (CRC). The decreasing risk of CRC observed in patients undergoing colonoscopy is correlated with the adenoma detection rate (ADR). Due to the fact that screening programs usually start from the age of 50, very few data are available on the risk of adenoma between 40 and 49 years of age. However, the incidence of CRC is increasing in young populations and it is not uncommon in routine practice to detect adenomas or even advanced neoplasia during colonoscopy in patients under 50 years.

Research motivation

It is well known that early detection of adenomas reduces the incidence of CRC and allows the diagnosis and treatment of cancer at an earlier stage. As CRC is increasing in young populations, it is important to know at which age the increase in incidence of colonic adenomas and advanced colonic adenomas occurs.

Research objectives

The purpose of this study was to compare the ADR and advanced neoplasia detection rate (ANDR) according to age in a large series of patients during routine colonoscopy.

Research methods

All consecutive patients who were scheduled for colonoscopy were included in this observational monocentric study conducted in our unit by a team of 30 gastroenterologists.

Research results

6027 colonoscopies were performed in patients with a median age of 57 years (range, 15-96). The ADR and ANDR were 28.6% and 9.7%, respectively, in the whole population. When comparing patients in the 40-44 ($n = 382$) and 45-49 year old groups ($n = 515$), a strong increase in all parameters from 45 years was observed, with the ADR rising from 9.7% in patients aged 40-44 to 21.2% in those aged 45-49 years ($P < 0.001$), and the ANDR increased from 3.1% in patients aged 40-44 to 6.4% in those aged 45-49 years ($P < 0.03$). In contrast, we did not observe a statistically significant increase in the ADR and ANDR between patients aged 45-49 and 50-54 years. When focusing on the population with an average risk for CRC, the ADR and ANDR were still significantly higher in patients aged 45 to 49 compared to patients aged 40 to 44 years.

Research conclusions

This study showed a significant two-fold increase in the ADR and ANDR from 45 years of age, irrespective of a personal or family history of polyps or CRC.

Research perspectives

This study raises questions regarding screening in patients less than 50 years of age. The medical benefit of performing colonoscopy as early as 45 years needs to be balanced by the medico-economic feasibility of such a screening policy. Nevertheless, whatever the screening method, the high ANDR observed in our young patients has to be taken into account in order to improve the prevention of CRC, disease stage on presentation and prognosis.

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