

Clinical characteristics of symptomatic young patients with colonic adenomas

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Abstract

Background The incidence of colonic adenomas and colorectal cancer has been on the rise among young patients. In this study, we aimed to describe the characteristics of young patients (<50 years) with adenomatous polyps and to characterize those polyps. We also aimed to determine appropriate surveillance intervals for young patients.

Methods We performed a retrospective chart review of patients <50 years of age who had polypectomy of 1 or more adenomatous polyps on colonoscopy between 2008 and 2021. Patient demographics, colonoscopy indication and polyp characteristics were obtained from the chart. Timing and findings on surveillance colonoscopies were recorded.

Results A total of 610 patients were included: mean age 42.9±5.9 years, 61% males, body mass index 27.5±4.7 kg/m², and over 50% smokers. The most common indications were abdominal pain (23.3%), rectal bleeding (22.3%), and change in bowel habits (17.6%). Almost half of the patients who had adenomas (299) were younger than 45 years. Tubular adenoma was the most frequently encountered type of polyp (571; 93.6%). Mean polyp size was 1.1±0.9 cm. The most common location of adenomas was the sigmoid colon (41%). Of patients with adenomas, 156 (26%) had surveillance colonoscopy within 2.9±2.3 years; 74 patients (47.4%) were found to have new adenomas.

Conclusions Patients aged <50 years with colonic adenomas were mostly males, overweight, and smokers. Further adenomas were found in 47% of surveillance colonoscopies, and most were encountered within 5 years. High rates of recurrent adenomas in people <50 years of age may warrant frequent surveillance.

Keywords Colon adenoma, young patients, tubular adenoma

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Introduction

Colorectal cancer (CRC) is the third most common cancer [1], and the second most common cause of cancer deaths in the US. Over the last 3 decades, the incidence of CRC has been rising among young adults [2], and both the US Preventive Task Force and the American College of Gastroenterology now recommend initiation of colon cancer screening at the age of 45 years in average risk individuals [3,4]. Bailey *et al* predicted that by 2030 the prevalence of colon and rectal cancers will increase by 90% and 124%, respectively, in individuals aged 20-34 years, and by 28% and 46% for individuals aged 35-49 years [5].

CRC usually arises from adenomatous polyps through the adenoma-carcinoma sequence [6]. In Korea, the prevalence of colorectal adenomas was reportedly 3.2% in individuals aged 19-29 years, 13.8% in those 30-39 years, and 21.1% in those aged 40-49 years [7]. Risk factors for the development of colorectal neoplasia in individuals younger than 50 years included being male, being older than 45 years, and having a change in bowel habits [7].

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Studies addressing the clinical characteristics of young patients with colonic adenomas, as well as the type, size and location of those adenomas, are lacking. Very few studies have investigated the appropriate follow-up surveillance colonoscopy intervals for young individuals who have colonic adenomas. One study evaluating endoscopic surveillance practices in young patients with sporadic colorectal adenomas found that, for patients with no high-risk neoplastic findings on colonoscopy (high risk being ≥ 1 advanced neoplasm or ≥ 3 non-advanced neoplasms), 28% of endoscopists recommended repeat colonoscopy in ≤ 3 years, and 99% within 5 years [8]. In view of the increasing incidence of adenomatous polyps in young individuals and the lack of proper management directives, this study aimed to address an area of unmet need.

The aims of our study were to determine the demographic and clinical characteristics of young patients (<50 years) found to have adenomatous polyps on colonoscopy, and to determine the characteristics of those polyps. In addition, we sought to identify appropriate colonoscopy surveillance intervals for the younger patient population.

Patients and methods

Study population

This was a retrospective study of all patients less than 50 years of age who had a colonoscopy and findings of at least 1 adenomatous polyp at our tertiary care referral center between January 2008 and December 2021. Patients were excluded if they were younger than 18 years, had a diagnosis of inflammatory bowel disease (IBD), or if they had a personal or family history of CRC in a first-degree relative. The study was approved by the Institutional Review Board of our institution (Protocol Number: BIO-2021-0057).

Outcomes

Primary outcomes were the clinical and demographic characteristics of young patients with colorectal polyps, including age, sex, body mass index (BMI), vitamin D level, past medical history, past surgical history, family history and medication intake. Colonoscopy reports were reviewed, including all follow-up colonoscopies. Secondary outcomes were to describe the different indications for each colonoscopy, as well as the characteristics of the polyps, including the number of polyps removed, their size, histology, and location.

Data collection

Patients were identified through reviewing pathology reports from the Pathology Department. All patients younger than 50 years who had a pathology reading for a colorectal polyp between 2008 and 2021 were identified. Data were collected from each patient's medical chart for demographic

characteristics. Colonoscopy reports were reviewed, including all follow-up colonoscopies. The indication for each colonoscopy was recorded, as well as the number of polyps seen and removed, and the polyp characteristics.

All endoscopists involved in this study are either American or European board-certified, see a high volume of patients, perform a large number of colonoscopies, and have a high level of expertise performing polypectomies. For the past 5 years, the average adenoma detection rate (ADR) of these endoscopists was above the benchmark rate approved by professional societies.

All excised polypectomy tissues were histopathologically evaluated in the Pathology Department. Adenomatous polyps included tubular, tubulovillous, villous, or sessile serrated adenomas.

Statistical analysis

Variables of interest were described as mean \pm standard deviation for continuous variables and n, frequency, for categorical variables. For the analysis, our study sample consisted of patients <50 years of age harboring adenomatous polyps. A descriptive analysis of baseline demographics, medical characteristics, indications for colonoscopy, location of polyps, polyp size, and colonoscopy follow-up periods was carried out for our study sample. Patient and polyp characteristics were divided into 2 subgroups: 1) patients with high-risk adenomas, defined as those with 3 or more adenomas on colonoscopy or an advanced adenoma; and 2) patients younger than 45 years of age with adenomatous polyps. Comparisons between the study sample and specific subgroups (e.g., patients <50 years of age with colorectal adenomas vs. patients <50 years of age with high-risk adenomas) were performed using the independent-samples *t*-test for continuous variables and the chi-squared test for categorical variables. A *P* value <0.05 was considered statistically significant. All analyses were performed using SPSS Statistics version 28.0 for Windows.

Results

A total of 1007 patients aged <50 years had colorectal polyps on colonoscopy. Patients with the following characteristics were excluded: age <18 years (*n*=3), patients with IBD (*n*=36), or a personal or family history of CRC in a first-degree relative (*n*=91). Of the remaining 877 patients, 267 (30.5%) had only hyperplastic polyps and were excluded. The rest of the patients (*n*=610) had adenomatous polyps and were included in this study (Fig. 1).

Patients <50 years of age with colorectal adenomatous polyps

Baseline clinical characteristics

At least 1 adenomatous polyp was found in each of 610 young patients. Baseline clinical characteristics are summarized in Table 1.

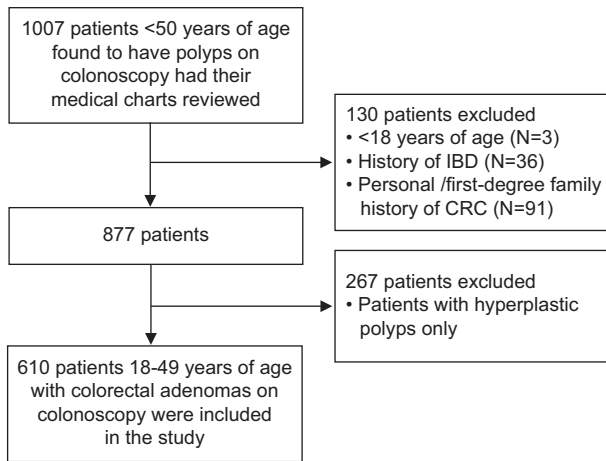


Figure 1 Flow chart representing patients' inclusion and exclusion criteria CRC, colorectal cancer; IBD, inflammatory bowel disease

Table 1 Baseline clinical characteristics of 610 young patients with adenomatous polyps

Variable	(% or SD)
Mean age (years)	42.95 (5.97)
Sex	
Male	371 (60.8%)
Female	239 (39.2%)
BMI*	27.51 (4.71)
Smoking history*	279 (50.8%)
Aspirin intake (Y/N)*	41 (7.4%)
Vitamin D use (Y/N)*	101 (18.1%)
Mean vitamin D Level (ng/mL)*	22.14 (10.29)
Colon cancer family history (second-degree)*†	9 (1.5%)

*This variable was not documented on all medical charts

†Family history was defined as having second-degree relatives with CRC. Patients with a family history of CRC in first-degree relatives were excluded SD, standard deviation; BMI, body mass index; CRC, colorectal cancer

Colonoscopy indications and findings

The 2 most common colonoscopy indications for young patients found to harbor adenomatous polyps were abdominal pain (23.3%) and rectal bleeding (22.3%). Other common indications were change in bowel habits (17.6%) and anemia/occult bleeding (11.1%). The rest of the patients had indications of abnormal lab results, such as increased inflammatory markers, or abnormal non-specific imaging results, such as colon thickening on computed tomography scan. Among the 610 patients with adenomas, 275 (45.3%) had 1 polyp, 132 (21.7%) had 2 polyps, 82 (13.5%) had 3 polyps, and 118 (19.4%) had more than 3 polyps. Three patients had missing colonoscopy reports, hence were lacking documentation for the number of polyps. Note that the total number of polyps may include hyperplastic polyps. In fact, 104/610 patients (17%) also had hyperplastic polyps, while 41/610 patients (6.7%) had pedunculated polyps. Diminutive

polyps were present in 163/610 patients (27.9%), small polyps were present in 385/610 patients (65.9%), and large polyps in 78/610 (13.3%). As for the location of polyps, patients with adenomas had their polyps most commonly located in the sigmoid colon (41.3%), followed by the ascending colon (33.6%), transverse colon (26.6%), descending colon (24.4%), rectum (12.5%), and cecum (12.1%). Splenic and hepatic flexures contained 3.3% of adenomatous polyps.

Follow-up colonoscopies

Of the 610 patients harboring adenomatous polyps, 156 (25.6%) had at least 1 documented follow-up colonoscopy performed at our institution within the 14 years of follow up (2008-2021). This first follow-up colonoscopy was performed after a mean of 2.9 ± 2.3 years. Follow-up timing ranged from a few months (typically 6 months) to 9 years. A minority of patients had their first follow up after a few months, and those were to follow-up on piecemeal resections of large polyps (≥ 2 cm) as recommended by guidelines. The most common indication for those subsequent colonoscopies was surveillance of colonic polyps (74.4%). Other indications included change in bowel habits (7.7%), abdominal pain (7.1%), rectal bleeding (3.8%), and anemia/positive fecal occult blood test (FOBT) (3.2%). The remaining follow-up colonoscopies were for abnormal lab results or abnormal non-specific abdominal imaging. Forty-seven percent of patients who underwent a follow-up colonoscopy had new adenomatous polyps.

In patients with adenomatous polyps on baseline colonoscopy, tubular adenoma was the most frequently encountered type (93.2%), followed by tubulovillous (4.7%), sessile serrated (19; 3.1%), and villous adenomas (0.2%). The detailed pathology findings seen at first and second follow up are presented in Table 2.

Patients who only had tubular adenomas (not tubulovillous, villous or sessile serrated pathology) had a follow-up rate of 22.7% and their follow up was performed after a mean of 3.2 ± 2.3 years. Tubular adenomas were found on surveillance colonoscopy in 45.5% of patients, 2 patients (1.5%) had sessile serrated adenomas, while none had tubulovillous or villous adenomas at first follow-up surveillance colonoscopy. Of those who had at least 1 tubulovillous adenoma at initial colonoscopy ($n=29$), 55.2% had a documented surveillance colonoscopy and had their follow up after a mean of 0.8 ± 1.1 years. Those 16 follow ups revealed the following: 10/16 patients (62.5%) were found to have tubular adenomas and 1 patient (6.2%) was found to have a villous adenoma. Regarding villous pathology, only 1 patient had this on their index colonoscopy and this patient was lost to follow up. Patients who had sessile serrated adenomas on index colonoscopy had a follow-up rate of 42.1% after a mean time of 2.0 ± 0.9 years and had no polyps on their follow ups. Thirty-eight patients (24.3%) had a second follow up after a mean of 2.1 ± 1.6 years after the first follow up. Of these, 15 (39.5%) were found to have adenomas, 13 (86.7%) tubular adenomas. One patient had a tubulovillous adenoma at second follow-up colonoscopy and this patient had previously had 1 tubulovillous adenoma at index colonoscopy and 1

Table 2 Polyp histopathology in patients with colorectal adenomatous polyps at baseline colonoscopy, first and second follow up

Pathology (adenoma subtype)	Number of polyps	Patients at baseline colonoscopy (n=610)	Patients at first follow up (n=156)	Patients at second follow up (n=38)
Tubular	1	319 (52.3%)	27 (17.3%)	3 (7.8%)
	2	127 (20.8%)	18 (11.5%)	3 (7.8%)
	3	57 (9.3%)	8 (5.1%)	1 (2.6%)
	More than 3	66 (10.8%)	18 (11.5%)	6 (15.7%)
Tubulovillous	1	28 (4.6%)	0 (0.0%)	1 (2.6%)
	2	1 (0.2%)	0 (0.0%)	0 (0.0%)
Villous	1	1 (0.2%)	1 (0.6%)	1 (2.6%)
Sessile/serrated	1	18 (3.0%)	2 (1.3%)	0 (0.0%)
	2	1 (0.2%)	0 (0.0%)	0 (0.0%)

tubular adenoma at first follow up. Follow-up surveillance colonoscopies for this patient were carried out at intervals of 2 years. Another patient had a villous adenoma on second follow up; this patient was found to have a tubulovillous adenoma on index colonoscopy and a villous adenoma at first follow up. Colonoscopies of this patient were done at intervals of 1.5 years. None of the patients in our study had evidence of carcinoma at first or second follow-up colonoscopies.

Specific subgroups

Patients with high-risk adenomas

As per the United States Multi-Society Task Force (USMSTF), individuals with high-risk adenomas are defined as those who have 3 or more adenomas on colonoscopy or an advanced adenoma (adenoma ≥ 1 cm and/or adenomas with villous histology and/or adenoma with high grade dysplasia). Of our 610 patients, 169 (27.7%) satisfied the above criteria. A similar descriptive analysis to the one carried out earlier was applied to patients with high-risk adenomas. Their average age was 43.1 ± 5.7 years at baseline colonoscopy. The most common indication in this subgroup was rectal bleeding (26%). These patients had on average 3.5 ± 1.7 polyps, with an average polyp size of 1.62 ± 0.98 cm. The average number of polyps was calculated after excluding all patients with "multiple" or "few" polyps on colonoscopy ($n=14$), as these cases had no specific number of polyps to be included in the statistical calculation of the average. Thirty of 169 (17.8%) patients of this subgroup had a villous component on histopathology (tubulovillous or villous). A comparison of the characteristics of patients with high-risk adenomas ($n=169$) vs. standard-risk adenomas ($n=441$) showed no statistically significant difference between the clinical variables of the 2 groups. Hence, baseline clinical characteristics were similar between patients with high-risk adenomas and patients with standard-risk adenomas. Indications for colonoscopy were also compared between the 2 groups, and abdominal pain (14.2% in high-risk adenoma group vs. 27.5% in standard-

risk group) was the only indication that significantly differed, P -value < 0.001 . Follow-up rates were compared: 57/169 (33.7%) patients with high-risk adenomas had at least 1 follow-up colonoscopy, compared to 99/441 (22.4%) patients in the standard-risk group ($P=0.007$), implying that patients with high-risk adenomas had a significantly higher follow-up rate.

Patients <45 years of age with colonic adenomas

Patients with adenomas were further divided into 2 groups, one including patients <45 years of age (18-44), the other including patients 45-49 years of age. Of 610 patients with adenomas, 299 (49%) were 18-44 years old. The mean age in this group was 38.3 ± 4.1 years, 58.6% were males, and mean BMI was 26.8 kg/m^2 . The most common indications in this subgroup were abdominal pain (23.7%), rectal bleeding (22.1%), and change in bowel habits (17.1%). Over half of these patients (51.2%) had only 1 adenoma, 21.4% had 2 polyps, and 10.3% had 3 polyps. The remaining (17.1%) had more than 3 polyps on index colonoscopy. Of the 29 patients found to have tubulovillous adenomas in our study, 15 (51.7%) were <45 years of age. The only patient who had a villous adenoma was also in this subgroup and was 41 years old. As for sessile serrated adenomas, 11/19 (57.8%) of patients were <45 years of age. This subgroup (18-44 years of age) had a follow-up rate of 24.7% (74/299 patients had a follow-up colonoscopy), with 40.5% of those found to have adenomas. Follow up was performed after a mean of 2.8 ± 2.4 years. Twenty of 74 patients (27%) had a second follow-up surveillance colonoscopy after 1.9 ± 1.4 years, and 8 (40%) of them again had adenomas. We compared adenoma recurrence between patients aged 18-44 years and patients aged 45-49 years, but we did not find a statistically significant result at either first or second follow up. We also aimed to look for any differences in the clinical characteristics between the 2 groups. Results are shown in Table 3.

Table 3 Comparison of demographics and polyp characteristics between patients younger than 45 years of age and patients 45-49 years of age with adenomatous polyps

Variable	Patients 18-44 years old (n=299)	Patients 45-49 years old (n=311)	P-value
Mean age at baseline colonoscopy	38.3	47.4	<0.001
Males	58.6%	63.0%	0.256
BMI	26.77	28.20	0.886
Vitamin D level	20.82	23.28	0.403
Smoking	50.0%	51.6%	0.705
Mean size of polyps	1.21	1.01	<0.001
High-risk patients	24.7%	30.2%	0.130
Follow-up rate	24.7%	26.1%	0.713

BMI, body mass index

Discussion

Our study suggests that young patients <50 years with colorectal adenomas were mostly males, in the overweight to obese range, and were frequently smokers. They also had a relatively low mean vitamin D level. A significant number of patients were under 45 years of age, and a substantial proportion turned out to harbor high-risk adenomas. Young patients with adenomatous polyps underwent colonoscopy mainly for abdominal pain or rectal bleeding, and none of the patients developed interval cancer at surveillance colonoscopies.

It is not uncommon in routine practice to find colorectal adenomas in the young population [10]. Many factors have been found to be associated with adenomatous polyps. Male sex has been reported as a risk factor [11], and this may be attributed to the role of male hormones in adenoma formation [12]. An association between a high BMI and colorectal adenomas was recently reported in a meta-analysis involving 36 independent studies [13]. In another study, smoking was found to be a risk factor for early onset metachronous colorectal adenoma [14]. Male sex, high BMI and smoking history were all common among our study population and hence may be contributors to adenoma formation in young patients, similarly to what is known for patients over 50 years of age. Those of our patients who were younger than 45 years had almost the same clinical characteristics as the older group (45-49 years old). This implies that those baseline characteristics could be risk factors for adenomatous polyps, even in younger-range patients. One meta-analysis combining 15 studies suggested that there is an inverse relationship between circulating vitamin D levels and colorectal adenomas, in both Western and Asian populations [15]. Indeed, patients in our study had a mean vitamin D level that was borderline low.

Our cohort's indications for colonoscopy were also similar to those found in other studies. Allison *et al* found that undergoing a diagnostic colonoscopy (i.e., with a symptomatic

indication) was independently associated with adenoma detection (odds ratio [OR] 1.81, 95% Confidence Interval is [1.44-2.29]). Please complete the missing confidence intervals. In our study, 76.4% of the patients with adenomatous polyps had gastrointestinal symptoms, anemia or positive FOBT before colonoscopy. As regards location, our patients with adenomas had their polyps almost uniformly distributed along different segments of the colon, with no predominance of either side (right colon vs. left colon). This is comparable to another study, where no significant difference was found in the incidence of adenomas between proximal and distal colon in young individuals [16]. A very recent study analyzed patients' outcomes after baseline colonoscopies and found that the presence of 5 or more polyps at index colonoscopy is associated with future development of high-risk colorectal neoplasms (OR 2.57, 95% CI: 1.003 - 6.613) [17]. In our study, 18% of patients had 4 or more polyps. A Brazilian study examined associations between patients age, polyp size and histopathological findings [18]. In patients younger than 49 years who had polyps on colonoscopy, 35% had tubular adenomas, 3% had tubulovillous adenomas, 2% had villous adenomas, and 35% had hyperplastic polyps [18]. Our study numbers were somewhat similar to the Brazilian study for all polyp types except for tubular adenomas; 65% in our study vs. 35% in the Brazilian one.

To our knowledge, only 2 previous studies addressed follow-up colonoscopy findings and appropriate surveillance timings in young individuals. The first suggested that current surveillance guidelines for patients >50 years of age may be appropriately used with younger adults [19]. The second study included 10,013 patients, and extended the post polypectomy surveillance interval up to 5 years in patients aged 30-44 years with advanced adenomas, setting surveillance timings in patients aged 45-49 years to the same as those aged ≥50 years [20]. In our study, half of the patients who had follow up after a mean of 3 years had adenomas, suggesting that more frequent surveillance than was suggested in the 2 previous studies may be needed in the young population.

The clinical implications of this work are rather notable. Adenomatous colorectal polyps are often seen in individuals <50 years of age, as has been shown by a study that enrolled 4286 young adults aged 20-39 years old. By age group, the prevalence of colorectal adenoma was 5.4% in participants aged 20-29 years and 12.6% in participants aged 30-39 [21]. Therefore, careful inspection for colonic polyps is recommended during diagnostic and screening colonoscopies in the young population, and endoscopists should aim at a high ADR in the young also. Targeting excellent bowel preparation, adopting the standard withdrawal times, washing, and frequently turning patients during the procedure should also be observed for colonoscopy in young individuals. More importantly, a lower colonoscopy threshold should be considered for males, overweight patients, and individuals presenting with abdominal pain, rectal bleeding or change in bowel habits. Given the uniform distribution of the polyp locations we demonstrated in our study, a sigmoidoscopy may not be enough in young patients and colonoscopy needs to be considered. The high rates of metachronous adenomas found

in our study after an average follow-up period of 3 years (a relatively short period) certainly highlights the importance of specifying a short surveillance interval for younger patients, especially those under 45 years of age, as they have comparable pathology results, proportion of high-risk adenomas and rates of metachronous adenomas, when compared to the older group (45-49 years). Our results should trigger more work on this, especially research addressing the adenoma–carcinoma sequence in the young population, as it might have other implications apart from those found in the literature. Follow-up intervals in the young should certainly be based upon the baseline number of polyps, shape, size, location and pathology, and our work implies that a surveillance interval of 3-5 years might be reasonable in young individuals, unless they present with high-risk polyp features (such as tubulovillous or villous pathology, large size, etc.). Our data suggest that young patients with advanced pathology findings would benefit from follow up at shorter intervals (2-3 years).

There are limitations to our study, the most important being the retrospective nature of the work and the small sample size. Additionally, our data were acquired from a single center, limiting the generalizability of our results. A larger, multicenter prospective study is needed to better confirm our results. Our endoscopists consistently record bowel preparation scores for each procedure; however, these were not collected for this study. Based on the Aronchick bowel preparation scale [22], 78% of patients undergoing colonoscopy at our institution exhibit good or excellent bowel preparation, so we infer that our cohort mirrored the general population we typically encounter. Our study lacks performance indicators for our endoscopists, which is another limitation. Moreover, this study did not have a control group, i.e., matched patients without adenomas on colonoscopy. The presence of such a control group could have helped in calculating prevalence as well as thoroughly addressing differences in clinical characteristics between those with polyps and those without. We also had multiple variables with missing data. For instance, a large proportion of individuals did not have their BMI, vitamin D level or other variables documented on the medical chart. Another limitation was reporting the polyp size as large, diminutive, or small in the majority of cases without stating the precise polyp dimensions. Additionally, since our study looked at patients who had procedures between 2008 and 2021, the majority of the pathology specimens were reported prior to the updated 2019 classification for sessile serrated lesions. Finally, attrition bias is also to be considered.

In conclusion, patients younger than 50 years with colorectal adenomatous polyps were mostly male, overweight, smokers, and half of them were 44 years or younger. For young patients with gastrointestinal complaints, a low colonoscopy threshold should be considered in patients with high-risk baseline characteristics and symptoms of abdominal pain, rectal bleeding or change in bowel habits. Almost half of the patients who had a follow up (mean 3 years) had adenomas found on their surveillance colonoscopy. This high rate may warrant consideration of more frequent surveillance in the young population than is specified in regular follow-up

guidelines. Future studies addressing adenomatous polyps and the adenoma–carcinoma sequence in young individuals are warranted, and prospective work will be able to further enlighten the gastrointestinal community about adenoma characteristics and appropriate surveillance in the young individuals.

Summary Box

What is already known:

- The incidence of colorectal adenomatous polyps and colorectal cancer is on the rise among young individuals
- Our understanding of the clinical and polyp characteristics of this population, as well as their optimal surveillance intervals, remains limited

What the new findings are:

- Young patients (<50 years of age) with colorectal adenomas are mostly males, overweight, smokers, and half of them are 44 years old or younger
- Common symptoms include abdominal pain, rectal bleeding and change in bowel habits, and more than half of the adenomas were found in the rectosigmoid region
- Almost half of the young patients with colorectal adenomas were discovered to have recurrent adenomas within the following 5 years, thereby possibly requiring more frequent surveillance than typically believed

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