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Clinically significant serrated polyp detection rates and risk for postcolonoscopy colorectal cancer: data from the New Hampshire Colonoscopy Registry

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Abstract

Background and Aims: Higher adenoma detection rates reduce the risk of postcolonoscopy colorectal cancer (PCCRC). Clinically significant serrated polyps (CSSPs; defined as any sessile serrated polyp, traditional serrated adenoma, large [≥ 1 cm] or proximal hyperplastic polyp >5 mm) also lead to PCCRC, but there are no data on associated CSSP detection rates (CSSDRs). We used data from the New Hampshire Colonoscopy Registry (NHCR) to investigate the association between PCCRC risk and endoscopist CSSDR.

Methods: We included NHCR patients with 1 or more follow-up events: either a colonoscopy or a colorectal cancer (CRC) diagnosis identified through linkage with the New Hampshire State Cancer Registry. We defined our outcome, PCCRC, in 3 time periods: CRC diagnosed 6 to 36 months, 6 to 60 months, or all examinations (6 months or longer) after an index examination. We excluded patients with CRC diagnosed at or within 6 months of the index examination, with incomplete examinations, or with inflammatory bowel disease. The exposure variable was endoscopist CSSDR at the index colonoscopy. Cox regression was used to model the hazard of PCCRC on CSSDR controlling for age, sex, index findings, year of examination, personal history of colorectal neoplasia, and having more than 1 surveillance examination.

Results: One hundred twenty-eight patients with CRC diagnosed at least 6 months after their index examination were included. Our cohort included 142 endoscopists (92 gastroenterologists). We observed that the risk for PCCRC 6 months or longer after the index examination was significantly lower for examinations performed by endoscopists with CSSDRs of 3% to <9% (hazard ratio [HR], .57; 95% confidence interval [CI], .39–.83) or 9% or higher (HR, .39; 95% CI, .20–.78) relative to those with CSSDRs under 3%.

Conclusions: Our study is the first to demonstrate a lower PCCRC risk after examinations performed by endoscopists with higher CSSDRs. Both CSSDRs of 9% and 3% to <9% had statistically lower risk of PCCRC than CSSDRs of <3%. These data validate CSSDR as a clinically relevant quality measure for endoscopists.

Optimal colorectal cancer (CRC) prevention through colonoscopy depends on complete detection and resection of important polyp precursors. The adenoma detection rate (ADR), which is an endoscopist-specific quality measure, has been shown to be inversely proportional to the risk of postcolonoscopy CRC (PCCRC), which is CRC diagnosed at least 6 months after an index colonoscopy at which no CRC was found.^{1–3} The ADR is calculated as the number of an endoscopist's screening colonoscopies where at least 1 adenoma is detected and resected divided by the total number of that endoscopist's screening colonoscopies.^{4,5} A higher ADR has been shown to be protective from PCCRC.^{1,2} To guide appropriate polyp detection, the current benchmark recommendation is that an endoscopist achieve an ADR of 25% or higher.

In addition to the conventional adenoma pathway, CRC can develop through the serrated pathway, which may account for a large proportion of CRC.^{6–8} The precursors in this pathway are serrated polyps, which include hyperplastic polyps (HPs), sessile serrated polyps (SSPs), and traditional serrated adenomas (TSAs).⁹ As with adenoma detection, it is logical to hypothesize that optimal detection and resection of serrated polyps will enhance CRC prevention.

Attention to endoscopist detection rates improves CRC prevention and may be particularly important for serrated polyps. A unique challenge for endoscopists is that serrated polyps exhibit characteristics that can make them more difficult to detect than conventional adenomas. Thus, it is not surprising that several studies have demonstrated a wide variation in serrated polyp detection rates.^{10–14} In addition, an analysis of data from the New Hampshire Colonoscopy Registry (NHCR) has demonstrated that some endoscopists with varying levels of ADRs may not achieve adequate serrated polyp detection rates.¹⁵ Specifically, 25% of all endoscopists who had an ADR of 25% did not meet the suggested clinically significant serrated polyp detection rate (CSSDR) of 7%. As stated by the American Gastroenterological Association, these results support the need for a benchmark for endoscopist detection of serrated polyps.¹⁶

However, there is no clear consensus regarding which serrated polyps should be included in a detection rate. Distinguishing HPs from SSPs may be challenging, and studies have shown low rates of agreement among pathologists in diagnosing serrated polyps as HPs or SSPs.^{17,18} As a result, we and other authors have suggested that those serrated polyps that pose the greatest risk for cancer should be classified as clinically significant serrated polyps

(CSSPs).^{15,19} These include SSPs, which have dysplastic potential; TSAs, which exhibit dysplasia; and large HPs or proximal 5- to 9-mm HPs, which may have a similar risk for future large serrated polyps as SSPs.^{17,20}

Currently, no data have examined the risk for PCCRC based on an endoscopist serrated detection rate. We used data from the NHCR to examine the association between CSSDRs and risk of PCCRC.

METHODS

Population

Our analysis examined NHCR data, including patient demographics and examination characteristics from index and follow-up colonoscopies. Individuals undergoing colonoscopy in New Hampshire complete an NHCR patient questionnaire before colonoscopy, which includes detailed demographics, health behavior, and personal and family history data. Endoscopists and/or endoscopy nurses complete the NHCR colonoscopy procedure form during or immediately after colonoscopy, recording detailed examination indications, completion status, withdrawal time, bowel preparation quality, recommended follow-up, and the location, size, and treatment method for all findings.

Endoscopists are asked to score the bowel preparation based on the worst prepped segment after cleaning all colon segments. Furthermore, the specific ratings (excellent, good, fair, or poor) are based on specific descriptive instructions, thus ensuring uniformity in the colon preparation data collected. The following detailed descriptions of each preparation-quality option are noted on every colonoscopy procedure form: excellent, defined as only scattered, tiny particles and/or clear liquid, with 100% visualization possible throughout the colon; good, defined as easily removable small amounts of particles and/or liquid, which is very unlikely to impair visualization throughout the colon; fair, described as residual feces and/or nontransparent fluid, possibly impairing visualization; and poor, defined as feces and/or nontransparent fluid, definitely impairing visualization.

Pathology reports are obtained directly from the pathology labs for each New Hampshire endoscopy site, preventing any need for endoscopy personnel to collect and send the reports. Trained NHCR abstractors match polyp-level pathology results with the corresponding polyp information from the colonoscopy procedure form.²¹ All data collection and study procedures were approved by the Committee for the Protection of Human Subjects at Dartmouth College (CPHS no. 00015834).

Analyzed sample

Our analysis included all patients with an index colonoscopy in the NHCR and at least 1 follow-up colonoscopy performed 6 months or more after the index examination or a diagnosis of CRC as recorded in the New Hampshire State Cancer Registry. Thus, we defined follow-up time as months to first post-index colonoscopy or CRC diagnosis. We excluded patients with poor bowel preparation, inflammatory bowel disease, CRC diagnosed at index or within 6 months of the index examination, and incomplete examinations.

Outcomes

Our main outcome was PCCRC, which was defined as any CRC diagnosed 6 months or longer after the index examination recorded either in the NHCR on subsequent colonoscopy or in the New Hampshire State Cancer Registry. As done in previous studies,²² we examined PCCRC diagnosed during 3 time periods as defined from the date of index colonoscopy: 6 to 36 months after the index colonoscopy, 6 to 60 months after the index colonoscopy, or all examinations occurring 6 months or longer after the index colonoscopy. In addition, to account for patients with multiple follow-up surveillance examinations, we performed a sensitivity analysis where we restricted outcomes to those found on the first follow-up event, whether a first follow-up colonoscopy in the NHCR or a diagnosis of CRC through the New Hampshire State Cancer Registry.

Exposure variable

Our exposure of interest was endoscopist-level CSSDR. This was calculated by dividing the number of complete screening examinations with adequate preparation with at least 1 CSSP (all TSAs or SSPs, all HPs \leq 1 cm, and all proximal HPs $>$ 5 mm) by the total number of complete screening examinations with adequate preparation. Our calculations for detection rates included only screening colonoscopy examinations and excluded any diagnostic or follow-up examinations such as those for fecal immunochemical test–positive indications.

Covariates

Covariates were patient age and sex, index colonoscopy findings (large serrated polyps or conventional advanced adenomas), index examination indication, family history of CRC, and whether the patient had 2 or more surveillance or follow-up examinations.

Statistical analysis

Means and standard deviations were calculated for continuous variables, whereas numbers and percents were derived for proportions. We used the χ^2 test for trend and the Fisher exact test to evaluate categorical variables. Wilcoxon rank sum and Mann-Whitney tests were used for nonparametric continuous variables. Cox regression was used to model the hazard of PCCRC on detection rates controlling for age, sex, findings at the index examination, having $>$ 1 surveillance examination, and family history of CRC. For each patient, we calculated follow-up time from the time of index examination until the time (months) of first surveillance colonoscopy or CRC diagnosis either on any colonoscopy in the NHCR or as reported in the State Cancer Registry. All statistics were analyzed with SPSS, version 26 (IBM, Armonk, NY, USA).

RESULTS

Our analyzed sample included 19,532 patients with a follow-up event 6 months or longer after the index colonoscopy. Of 128 CRCs diagnosed at least 6 months after an index examination, 40 were diagnosed 6 to 36 months, 36 diagnosed 36 to 60 months, and 52 diagnosed 60 months or longer after the index examination. One hundred forty-two endoscopists (92 gastroenterologists) performed colonoscopies for our cohort. The 50 nongastroenterologist endoscopists comprised general and colorectal surgeons and family

practitioners. We categorized CSSDR into approximate terciles, using the cutoffs of 3% and 9%. CSSDR intervals were <3%, 3% to <9%, and 9% or higher. When stratified into the CSSDR categories, gastroenterologists were more likely to be in higher CSSDR categories than nongastroenterologist endoscopists (gastroenterologists vs nongastroenterologist for <3%, 3% to <9%, and 9+%: 15.2% [n = 14] vs 46.0% [n = 23], 50.0% [n = 46] vs 44.0% [n = 22], and 34.8% [n = 32] vs 10.0% [n = 5], respectively; $P = .00005$).

As compared with patients with no diagnosed PCCRC, those with PCCRC were more likely to be older, have a shorter interval between the index and follow-up event, and have had their index examination from an endoscopist with a lower CSSDR. These data are shown in Table 1.

We examined the absolute risk for PCCRC across separate time intervals (6 to <36 months, 36 to <60 months, and 6+ months or total sample). Across all time periods, the absolute risk for PCCRC was lower with higher CSSDRs; patients whose index examinations were performed by endoscopists with CSSDRs of 3% to <9% or >9% were at lower risk for PCCRC than patients whose examinations were performed by endoscopists with CSSDRs <3% (Table 2). After adjusting for covariates, Cox regression analyses demonstrated that higher CSSDR categories had lower hazard ratios (HR) for PCCRC across all time periods (Table 3).

Because some patients had more than 1 surveillance colonoscopy, we conducted a subanalysis in which we excluded all patients with more than 1 surveillance or follow-up colonoscopy, restricting the analysis to those with only a follow-up event. The results were largely unchanged (Table 4). To compare the results with ADR, we examined the risk for PCCRC in examinations performed by endoscopists with an ADR $\geq 25\%$. The HRs for an ADR $\geq 25\%$ were .43 (95% CI, .22–.82) for the 6- to 36-month period, .61 (95% CI, .38–.97) for the 6- to 60-month period, and .70 (95% CI, .49–1.00) for the entire period after 6 months. When we examined risk of CRC as stratified by location, we observed that higher CSSDRs were associated with lower risk for right-sided and left-sided CRCs (Table 5). When stratified by ADRs of $\geq 25\%$, higher CSSDR categories were associated with lower risks for PCCRC for examinations performed by endoscopists with ADRs $\geq 25\%$ and those with ADRs <25% (Table 6).

We performed a cluster analysis with Cox regression to examine the potential impact of endoscopists on the outcome for all examinations (6+ months). We observed the following HRs for CSSDRs of 3% to <9%: for the 6- to 36-month group, .45 (95% CI, .23–.86); for the 6- to 60-month group, .48 (95% CI, .24–.98); and for the entire sample, .57 (95% CI, .32–1.00). In addition, we observed the following HRs for CSSDRs of 9% or higher: for the 6- to 36-month group, .16 (95% CI, .06–.49); for the 6- to 60-month group, .33 (95% CI, .13–.77), and for the entire sample, .39 (95% CI, .15–1.00) (data not shown). Furthermore, we examined only those patients whose endoscopists had at least 100 colonoscopies and observed that the HRs were similar for the 3% to <9% group (HR, .56; 95% CI, .38–.83) and the 9% or higher group (HR, .40; 95% CI, .20–.79) (data not shown).

DISCUSSION

In our study, we observed that the risk (HR) for PCCRC was lower for those patients whose index examination was performed by an endoscopist with a higher CSSDR than those who had an endoscopist with a lower CSSDR. PCCRC is defined as any CRC diagnosed after a colonoscopy in which no cancer was found.^{6,23,24} Previous studies have demonstrated lower rates of PCCRC in patients whose index examinations were performed by endoscopists with a higher ADR. Kaminski et al² found a decreased incidence of PCCRC to be associated with an ADR of 20%, whereas Corley et al¹ showed that a higher ADR of 34% may offer even more protection. Recent data on patients with high-risk index findings suggest that those whose index examinations were performed by an endoscopist with a higher ADR have a lower risk of PCCRC.²⁵

Only 1 study has examined the impact of serrated detection rate on subsequent risk of CRC.³ A modeling study compared the impact of endoscopist proximal serrated detection rates with that of ADR on future risk of CRC in a population screened with the fecal immunochemical testing.³ Although an increase in ADR reduced the CRC risk, an increase in the proximal serrated detection rate did not alter CRC risk. The authors concluded that the lack of positive findings for proximal serrated detection rate could be because of the low sensitivity of the fecal immunochemical test for serrated polyps.²⁶ Thus, patients with serrated polyps are less likely to have a positive fecal immunochemical test and to be sent for colonoscopy as opposed to patients with conventional adenomas, decreasing the impact of high endoscopist proximal serrated detection rates on PCCRC risk in this study of fecal immunochemical test–positive patients.

Our study is the first to examine the association between PCCRC risk and endoscopist serrated detection rates using actual data from patients having colonoscopy as opposed to models. We observed that the mean CSSDR for those examinations with a PCCRC was significantly lower than that for examinations without PCCRC (5.3% vs 6.8%, respectively; $P < .0001$). Because PCCRC is more likely to arise from “missed precursors,” it is logical that the detection rates are lower for endoscopists who performed those index examinations with subsequent PCCRC. To examine the association between CSSDRs and PCCRC in more detail, we stratified the CSSDR into 3 categories, <3%, 3% to <9%, and 9% \geq . In our analyses, we observed that a CSSDR of 9% or higher was associated with the lowest risk for PCCRC as compared with a CSSDR of <3%, although the 2 CIs did overlap. We also examined the impact on PCCRC of an ADR cutoff of 25% and observed that the HR was similar to that for the 3% to <9% CSSDR category, suggesting that a CSSDR of 3% or more may offer similar protection as an ADR of 25%.

It may be reasonable to question whether a separate serrated detection rate is needed in addition to ADR. In our analysis, when we stratified by ADR, even in the higher ADR category (>25%), higher CSSDR categories were associated with lower PCCRC rates. Furthermore, a significant proportion of endoscopists in a prior NHCR analysis had an ADR of 25% but a CSSDR below the median of 7%.¹⁵ These data support our suggestion that endoscopists, even those with an ADR >25%, calculate their serrated detection rate at least once, a recommendation supported by a recent review of the American Gastroenterological

Association.¹⁶ In support of their recommendation, they cite published data documenting variation in serrated detection rates. The American Gastroenterological Association review also notes that our previous study demonstrating a strong association between withdrawal time and serrated polyp detection suggests that serrated detection rates provide a meaningful measure of inspection quality.^{27,28}

Our novel findings have important implications for endoscopists. Detecting serrated polyps is important because the serrated pathway may be responsible for 20% to 30% of all CRCs.²⁹ Of the 3 main subgroups of serrated polyps, HPs, SSPs, and TSAs, many small and distal HPs are believed to have a benign course, whereas TSAs and SSPs have the potential for malignant transformation. In particular, SSPs can be difficult to detect endoscopically because they are often flat with indistinct borders. Significant variation in detection of serrated polyps, especially those that are clinically significant such as SSPs, TSAs, and large or proximal HPs >5 mm, has been documented in numerous studies.^{11, 12, 14, 15, 30-32}

The significant variation in detection and the importance of the serrated pathway in carcinogenesis support the recommendation that a serrated polyp detection rate benchmark is needed to ensure complete polyp detection by all endoscopists.³³ A challenge in addressing this issue is in determining which serrated polyps should be considered significant and included in serrated detection rates. Although many studies have analyzed proximal serrated polyp detection,^{12,15,30} others have examined detection of only those lesions diagnosed as SSPs.^{30,34} Using SSP detection rates may not be optimal because their diagnosis may depend more on classification by pathologists than on the ability of endoscopists to detect these lesions, as shown in a study.¹⁴

We have proposed the classification of CSSPs,¹⁵ which includes SSPs (with or without dysplasia) of any size, TSAs of any size, any HP \geq 1 cm, and any proximal HP >5 mm. This definition combines important factors associated with long-term CRC risk, such as histology (SSPs and TSAs), size, and proximal location.^{8,35} Because the CSSDR includes lesions with malignant potential as well as larger and proximally located HPs, which may actually represent misdiagnosed SSPs, our results demonstrating a lower risk for PCCRC with increased CSSDRs validates the CSSDR as a quality metric.

Strengths of our analysis include the large number of endoscopists who participated in the NHCR and the longitudinal nature of our database, which can follow individual patients over many years of CRC screening and surveillance examinations. Our database allowed us to examine detection rates that were calculated for screening examinations only, which is the accepted approach for deriving these rates. In addition, the detailed polyp pathology data of the NHCR allowed us to calculate accurate CSSDRs, and standardized collection of key patient and endoscopic variables such as bowel preparation^{36,37} allowed a uniform assessment. We also linked our database with the New Hampshire State Cancer Registry, which allowed us to identify those patients diagnosed with CRC outside of NHCR-captured colonoscopies. Finally, our database captured detailed data on patient risk factors, which are important in examining risk for CRC. For example, based on patient history and examination indication, we were able to exclude all patients with inflammatory bowel disease, which can be a significant risk for PCCRC.³⁸ Thus, our data may be more generalizable to those

patients at risk for sporadic CRC as opposed to those who are at increased risk because of inflammatory bowel disease.

We acknowledge some limitations to our analysis. Similar to other analyses, our study cannot provide information regarding endoscopic techniques such as reexamination of the right-sided colon or cecal retroflexion. Molecular characteristics of the cancers in our study are also not available. For example, information on BRAF versus KRAS was not available. However, prior studies have shown a similar mutational profile in PCCRC and non-PCCRC cancers.³⁹ We also recognize that the possibility of residual confounding cannot be excluded.

In summary, index examinations performed by endoscopists in the 2 higher CSSDR groups (as compared with <3%) were associated with a decreased risk for PCCRC. A CSSDR of 9% or higher was associated with a lower risk of PCCRC than a CSSDR of 3% to <9%, although the 95% CIs overlapped. These results validate CSSDR as an important quality measure for endoscopists, one that broadens our understanding of colonoscopy quality and incorporates the serrated pathway to CRC.

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Abbreviations:

ADR	adenoma detection rate
CRC	colorectal cancer
CSSDR	clinically significant serrated polyp detection rate
CSSP	clinically significant serrated polyp
HP	hyperplastic polyp
HR	hazard ratio
NHCR	New Hampshire Colonoscopy Registry
PCCRC	postcolonoscopy colorectal cancer
SSP	sessile serrated polyp
TSA	traditional serrated adenomas

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TABLE 1. Patient and colonoscopy characteristics stratified by the presence or absence of PCCRC

Characteristic	Follow-up with no PCCRC (n = 19,404)	Patients with PCCRC (n = 128)	P value
Patient data			
Sex, male	48.3 (9365)	45.3 (58)	.52
Mean age, y (SD)	58.4 (9.6)	65.8 (10.4)	.0001
Mean body mass index, kg/m ² (SD)	28.4 (6.0)	28.6 (6.4)	.71
Family history of colorectal cancer	26.5 (5151)	22.7 (29)	.27
Race, white	92.3 (17,906)	93.8 (120)	.54
Index examination characteristics			
Cecal intubation	97.5 (18,926)	97.7 (125)	.16
Mean follow-up time to first examination or diagnosis, mo (SD)	59.4 (30.0)	54.6 (31.8)	.07
Mean clinically significant serrated polyp detection rate (SD)	6.8 (4.0)	5.3 (3.2)	.0001
Mean adenoma detection rate (SD)	27.4 (8.2)	23.9 (8.2)	.001
Performed by gastroenterologists	91.3 (17,719)	76.6 (98)	.001

Values are % (n) unless otherwise defined.

PCCRC, Postcolonoscopy colorectal cancer; SD, standard deviation.

TABLE 2. Absolute risk of postcolonoscopy colorectal cancer by CSSDR category, as stratified by time since index colonoscopy

Time period after index examination	CSSDR <3%	CSSDR 3% to <9%	CSSDR 9% or higher	P value	Total
6 to 36 mo, %	2.6 (n = 15)	1.2 (n = 21)	.3 (n = 4)	<.0001	1.1 (n = 40)
Total = 581					
6 to 60 mo, %	1.8 (n = 29)	.8 (n = 36)	.4 (n = 11)	<.0001	.9 (n = 76)
Total = 1199					
Total = 1592					
6 to 60+ mo, %	1.1 (n = 52)	.6 (n = 64)	.3 (n = 12)	<.0001	.7 (n = 128)
Total = 2758					
Total = 4326					
Total = 10,570					
Total = 4741					
Total = 4221					
Total = 19,532					

CSSDR, Clinically significant serrated polyp detection rate.

TABLE 3.

Hazard ratio of postcolonoscopy colorectal cancer by CSSDR category, as stratified by time since index colonoscopy

Time period after index examination	CSSDR <3%	CSSDR 3% to <9%	CSSDR 9% or higher
6 to 36 mo	1.0	.45 (.23–.90)	.16 (.05–.52)
	Total = 581	Total = 1711	Total = 1199
6 to 60 mo	1.0	.49 (.29–.81)	.33 (.15–.69)
	Total = 1592	Total = 4326	Total = 2758
6+ mo	1.0	.57 (.39–.83)	.39 (.20–.78)
	Total = 4741	Total = 10,570	Total = 4221

Values in parentheses are 95% confidence intervals. Adjusted for age, sex, index findings, year of examination, personal history of colorectal neoplasia, and having more than 1 surveillance examination. CSSDR, Clinically significant serrated polyp detection rate.

Sensitivity analysis showing hazard ratios for postcolonoscopy colorectal cancer in patients with only 1 follow-up colonoscopy or event by CSSDR, as stratified by time since index colonoscopy

TABLE 4.

Time period after index examination	CSSDR <3%	CSSDR 3 to <9%	CSSDR 9% or higher
6–36 mo	1.0	.45 (.20–.99)	.17 (.04–.63)
6–60 mo	1.0	.44 (.24–.79)	.32 (.14–.73)
6+mo	1.0	.56 (.36–.88)	.38 (.17–.82)

Values in parentheses are 95% confidence intervals. Adjusted for age, sex, index findings, year of examination, and personal history of colorectal neoplasia. *CSSDR*, Clinically significant serrated polyp detection rate.

TABLE 5.
Absolute risk of postcolonoscopy CRC by CSSDR as stratified by location of CRC

Location	CSSDR <3%	CSSDR 3% to <9%	CSSDR 9% or higher	P value
Right-sided CRC	.6 (29)	.3 (36)	.2 (7)	<.001
Left-sided CRC	.4 (20)	.2 (20)	.1 (4)	.003
Unknown location	.1 (4)	.1 (8)	.0 (1)	.34

Values are % (n). CRC, Colorectal cancer; CSSDR, clinically significant serrated polyp detection rate.

TABLE 6.

Stratification of postcolonoscopy colorectal cancer by CSSDR and ADR of 25%

ADR	CSSDR < 3%	CSSDR 3% to <9%	CSSDR 9% or higher	P value
<25%	1.1 (51/4686)	.6 (19/3292)	.0 (0/7)	.05
25%	1.8 (1/55)	.6 (45/7278)	.3 (12/4214)	.02

Values are % (n/N).

CSSDR, Clinically significant serrated polyp detection rate; ADR, adenoma detection rate.