

## Retrospective Cohort Study

## Interendoscopist variability in proximal colon polyp detection is twice higher for serrated polyps than adenomas

Jean-François Bretagne, Stéphanie Hamonic, Christine Piette, Jean-François Viel, Guillaume Bouguen

Jean-François Bretagne, Guillaume Bouguen, Service des maladies de l'appareil digestif, hôpital Pontchaillou, Centre hospitalo-universitaire de Rennes, 35033 Rennes, France

Stéphanie Hamonic, Jean-François Viel, Service d'épidémiologie et de santé publique, Centre hospitalo-universitaire de Rennes, 35033 Rennes, France

Christine Piette, Association pour le dépistage des cancers en Ille et Vilaine, 35033 Rennes, France

**Author contributions:** Bretagne JF designed the study and wrote the paper; Hamonic S and Viel JF performed the statistical analyses; Piette C collected the database information; Bouguen G contributed to the writing and the data interpretation; all of the authors contributed to the data analysis and approved the final submitted draft.

**Institutional review board statement:** The study was reviewed and approved for publication by our Institutional Reviewer.

**Informed consent statement:** Participants to the screening program were informed that personal data and colonoscopy findings could be used anonymously for scientific studies.

**Conflict-of-interest statement:** The authors have no potential conflict of interest.

**Data sharing statement:** The original anonymous dataset is available on request from the corresponding author at [jean-francois.bretagne@chu-rennes.fr](mailto:jean-francois.bretagne@chu-rennes.fr).

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Manuscript source:** Invited manuscript

**Correspondence to:** Dr. Jean-François Bretagne, Professor of Medicine, Service des maladies de l'appareil digestif, hôpital Pontchaillou, Centre hospitalo-universitaire de Rennes, 35033 Rennes, France. [jean-francois.bretagne@chu-rennes.fr](mailto:jean-francois.bretagne@chu-rennes.fr)  
Telephone: +33-299-284347  
Fax: +33-299-284189

Received: June 30, 2016

Peer-review started: June 30, 2016

First decision: July 29, 2016

Revised: August 19, 2016

Accepted: September 12, 2016

Article in press: September 12, 2016

Published online: October 14, 2016

### Abstract

#### AIM

To assess the interendoscopist variability in the detection of colorectal polyps according to their location and histological type.

#### METHODS

This study was a retrospective analysis of prospectively collected data from a regional colorectal cancer (CRC) screening program; 2979 complete colonoscopies from 18 endoscopists were included. Variability in performance between endoscopists for detection of at least one adenoma (A), one proximal adenoma (PA), one distal adenoma (DA), and one proximal serrated polyp (PSP) was assessed by using multilevel logistic regression models.

#### RESULTS

The observed detection rates among the 18 endoscopists ranged from 24.6% to 47.6% (mean = 35.7%) for A, from 19.1% to 39.0% (mean = 29.4%) for DA, from 6.0% to 22.9% (mean = 12.4%) for PA, and from 1.3% to 19.3% (mean = 6.9%) for PSP.

After adjusting for patient-level variables (sex, age), the interendoscopist detection rates variability achieved a significant level for A, PA, and PSP but not for DA ( $P = 0.03$ ,  $P = 0.02$ ,  $P = 0.02$  and  $P = 0.08$ , respectively). This heterogeneity, as measured by the variance partition coefficient, was approximately threefold higher for PA (6.6%) compared with A (2.1%), and twofold higher for PSP (12.3%) compared with PA.

### CONCLUSION

These results demonstrate significant interendoscopist variability for proximal polyp particularly for serrated polyps, but not for distal adenoma detection. These findings contribute to explain the decreased effectiveness of complete colonoscopies at preventing proximal CRCs and the need to carefully assess the proximal colon during scope procedure.

**Key words:** Colonoscopy; Colorectal cancer; Adenoma; Serrated polyp; Proximal polyp; Detection rate; Quality performance

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** The present study demonstrates high interendoscopist variability in adenoma, proximal adenoma, and proximal serrated polyp detection rates but not in distal adenoma detection rates. The magnitude of interendoscopist variation was wider for proximal serrated polyps as compared to proximal adenoma detection. Altogether, these findings might explain why complete colonoscopies are less effective at preventing proximal than distal colorectal cancers.

Bretagne JF, Hamonic S, Piette C, Viel JF, Bouguen G. Interendoscopist variability in proximal colon polyp detection is twice higher for serrated polyps than adenomas. *World J Gastroenterol* 2016; 22(38): 8549-8557 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v22/i38/8549.htm> DOI: <http://dx.doi.org/10.3748/wjg.v22.i38.8549>

### INTRODUCTION

Adenoma detection and removal is the basis for the reduction in colorectal cancer (CRC) incidence and mortality achieved by colonoscopy<sup>[1-3]</sup>. However, recent studies raised concerns that screening colonoscopies may not decrease CRC incidence and mortality in the proximal colon to the same extent as in the distal colon<sup>[4-8]</sup>. Although there are multiple plausible explanations for the decreased effectiveness in the proximal colon, the quality of the colonoscopy is a critical issue. Recent studies demonstrated that surrogate indicators for colonoscopy quality performance, such as adenoma detection rates and cecal intubation rates, were predictors of interval CRCs that occur after screening colonoscopies<sup>[9-11]</sup>. A higher

miss rate of proximal adenomas compared to distal adenomas could explain the decreased protective effect of colonoscopy for proximal colon cancer. However, no data are available on the interendoscopist variability of adenoma detection according to the polyp location in the colon, particularly in population-based studies.

Serrated polyps might be another significant contributor to the decreased protective effect of colonoscopies for proximal colon cancer. Serrated lesions can be challenging to visualize because of their morphologic characteristics and could be more likely overlooked as compared to conventional adenomas. Cohort studies demonstrated a wide variation rate among endoscopists of the proximal serrated polyps detection rates<sup>[12-14]</sup>, but no study aimed to compare adenomas detection and serrated polyps detection variability amongst endoscopists, especially for proximal colon location.

This population-based study aimed to test the hypothesis that the variations in adenoma detection rates between colonoscopists are wider for the proximal colon compared with the distal colon, and to compare interendoscopist variability in polyp detection rates in the proximal colon between serrated polyps and adenomas.

### MATERIALS AND METHODS

#### Study population

The study was conducted in "Ille et Vilaine", which has a population of approximately one million and was one of the first French districts to implement a national screening program at the end of 2002. The mass screening is based on biennial guaiac fecal occult blood tests. The target population for the screening includes asymptomatic men and women between 50 and 74 years of age with no other CRC risk factors. Individuals with a family history of CRC or a personal history of CRC or adenomas, those with inflammatory bowel disease, and those who had undergone a total colonoscopy in the previous five years were excluded from the screening program.

There were 96054 (51.8%) and 89309 (46.7%) participants in the first and second rounds, respectively. The proportion of positive tests amongst the participants was 2.58% and 2.26%, respectively. Positive testing was followed by a colonoscopy in 92.6% and 91.4% of the subjects, respectively. Finally, 2295 and 1848 colonoscopies were performed from 2003 to 2007 in the first and second rounds, respectively.

The 18 endoscopists who had performed at least 30 colonoscopies following a positive test in each of the first two rounds of the screening program were included. Fourteen of the 18 endoscopists were in private practice, and 4 worked in public hospitals. Overall, the 18 endoscopists performed 3487 (84.2%) of the 4143 white-light colonoscopies of the 2

screening rounds. Although high cecal intubation rates were recorded for rounds 1 and 2 (96.3% and 95.9%, respectively), we included only complete examinations of the colon in this study. The data from both rounds were pooled because no difference in the colonoscopy findings was noted between the two rounds. We previously reported that individual endoscopists who had participated in the CRC screening program as a factor was not a significant predictor of CRC detection but was a significant predictor of adenoma detection<sup>[15]</sup>. In the present study, a secondary analysis of the colonoscopy data was done to explore variations in the detection rate of at least one adenoma according to its location in the colon and to compare interendoscopist variability in polyp detection rates in the proximal colon according to histological subtype (serrated polyps and adenomas). The CRC screening program was declared and approved by the CNIL "Commission Nationale de l'Informatique et des Libertés" on August 30<sup>th</sup> 2002 (n° 812571). Research was approved by the CCTIRS "Comité Consultatif pour le Traitement de l'Information en matière de Recherche dans le domaine de la santé".

### Study design and outcomes

This was a cross-sectional study that used data retrieved from a prospectively collected database. Three adenoma detection rates, which were expressed as the proportion of complete colonoscopies with at least one adenoma, were calculated for each endoscopist as follows: The distal adenoma detection rate (DA.DR) for at least one adenoma detected in the distal colon (*i.e.*, below the splenic flexure including the flexure), the proximal adenoma detection rate (PA.DR) for at least one adenoma in the proximal colon (*i.e.*, proximal to the splenic flexure) and the A.DR for at least one colorectal adenoma regardless of its location in the colon. Colonoscopies with CRC, including those with malignant polyps harboring intramucosal carcinoma, were not included in the analysis because additional polyps in these patients were not recorded in the database. The individual detection rates for serrated polyps in the proximal colon (PSP.DR) were also calculated for each endoscopist. Serrated polyps were defined as an entire group of polyps that included traditional hyperplastic polyps, sessile serrated adenomas/polyps and traditional serrated adenomas.

The observed and adjusted (*i.e.*, according to patient age and gender) adenoma detection rates were calculated for each endoscopist and each site. Similarly, the observed and adjusted (*i.e.*, according to patient age and gender) proximal serrated polyp detection rates were calculated for each endoscopist. The variability between endoscopists in the probability to detect one adenoma/one adenoma in the distal colon/one adenoma in the proximal colon/one serrated polyp in the proximal colon was assessed by multilevel logistic regression models.

Additional analyses were performed after defining a proximal polyp as proximal to the hepatic flexure instead of proximal to the splenic flexure. Furthermore, we assessed the interendoscopist variability for polyps of size  $\geq 10$  mm.

### Statistical analysis

Continuous variables were expressed as the mean, standard error, median and interquartile range, and extremes values; categorical variables were expressed as numbers and percentages. The observed detection rates were compared between males and females and then between age classes using the Wilcoxon test; the use of the Cochran-Mantel Haenszel test permitted endoscopists to be adjustment variables. The patient age- and gender-adjusted adenoma detection rates for each endoscopist (and the corresponding 95%CI) were defined as the observed proportion of colonoscopies with at least one adenoma detected amongst all subjects multiplied by the ratio of the observed to the predicted number of detected adenomas for one endoscopist. The predicted number of detected adenomas for each endoscopist was assessed using logistic regression. Multilevel logistic regression models were used given the hierarchical structure of the sample (*i.e.*, patients are aggregated at the endoscopist level) and binary outcomes (*i.e.*, at least one adenoma/at least one distal adenoma/at least one proximal adenoma/at least one proximal serrated polyp). Each model was a two-level model in which age and gender were included as fixed effects (first or patient level) and in which the endoscopist was introduced as a random effect (second or endoscopist level). The fixed effect results are presented as odds ratios with 95%CI. To determine the proportion of total variance of the outcome that is explained at the endoscopist level, the variance partition coefficient was calculated using the Snijders and Bosker approximation<sup>[16,17]</sup>.

$$VPC = \sigma^2_{u0} / (\sigma^2_{u0} + \pi^2/3)$$

where  $\sigma^2_{u0}$  is the variance of the endoscopist-level random effect representing the between-endoscopist variability in terms of the outcome. The correlations between adjusted values of polyp detection rates were tested using the Spearman rank test. For all tests, the significance threshold was  $\alpha = 5\%$ . The analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC, United States).

## RESULTS

### Distribution of the adenomas and serrated polyps within the population

After excluding incomplete examinations ( $n = 210$ ) and colonoscopies harboring CRC ( $n = 298$ ), 2979 colonoscopies were included for the analysis. Of these, 1531 (51.4%) were performed in males and

**Table 1** Observed polyp detection rates amongst the 18 colonoscopists

Endoscopist (No.)	Colonoscopies ( <i>n</i> )	A.DR	DA.DR	PA.DR	PSP.DR
A	273	33.33%	29.67%	7.33%	4.40%
B	272	24.63%	19.49%	6.25%	5.51%
C	213	46.48%	38.97%	17.84%	19.25%
D	210	47.62%	38.10%	18.57%	6.19%
E	207	28.99%	25.12%	7.25%	5.31%
F	185	30.81%	27.57%	5.95%	2.70%
G	172	32.56%	29.07%	9.88%	7.56%
H	164	31.71%	28.05%	8.54%	8.54%
I	160	35.63%	30.00%	11.25%	3.13%
J	157	47.13%	35.67%	22.93%	15.92%
K	148	33.11%	29.05%	11.49%	2.03%
L	148	36.49%	31.76%	11.49%	10.14%
M	135	37.04%	25.19%	17.78%	4.44%
N	135	40.74%	31.11%	14.07%	5.93%
O	132	34.85%	33.33%	6.82%	2.27%
P	105	30.48%	19.05%	21.90%	15.24%
Q	85	38.82%	31.76%	12.94%	4.71%
R	78	32.05%	25.64%	11.54%	1.28%
N	18	18	18	18	18
mean	165.50	35.69%	29.37%	12.43%	6.92%
SD	54.65	6.41%	5.41%	5.36%	5.14%
Median	158.50	34.09%	29.37%	11.49%	5.41%
Q1-Q3	135-207	31.71%-38.82%	25.64%-31.76%	7.33%-17.78%	3.13%-8.54%
Min-Max	78-273	24.63%-47.62%	19.05%-38.97%	5.95%-22.93%	1.28%-19.25%

A.DR: Adenoma detection rate; DA.DR: Distal adenoma detection rate; PA.DR: Proximal adenoma detection rate; PSP.DR: Proximal serrated polyp detection rate.

1448 (48.6%) in females. The overall mean age of the patients was  $61.7 \pm 7.2$  years. The number of colonoscopies performed by each of the 18 endoscopists ranged from 78 to 273 (mean =  $165.5 \pm 54.7$ ). At least one adenoma was detected in 1057 subjects as follows: 707 (66.9%) in men and 350 (33.1%) in women. Amongst the patients with at least one adenoma, 703 (66.5%) had only distal adenomas, 180 (17.0%) had only proximal adenomas, and 174 (16.5%) had at least one adenoma in both regions. At least one proximal serrated polyp was detected in 210 subjects as follows: 130 (61.9%) in men and 80 (38.1%) in women. The number of colonoscopies harboring both types of proximal polyps, *i.e.*, at least one adenoma and at least one serrated polyp, was 59 (2.0%).

#### Individual endoscopists' neoplasia detection rates

Table 1 shows the observed detection rates per endoscopist for each of the following four indicators: Adenoma detection rate (A.DR), DA.DR, PA.DR, and proximal serrated polyp detection rate (PSP.DR). The mean detection rates were 35.7%, 29.4%, 12.4% and 6.9%, respectively.

The mean and median values of these four indicators according to gender and age are provided in Tables 2 and 3. For each of the measures related to adenoma detection, the median values were significantly higher in males compared with females, and the values increased with increasing age. The median PSP.DR values did not differ significantly according to age group, but there was a trend for a

higher detection rate in males compared with females (7.0% vs 4.3%, respectively,  $P = 0.06$ ).

#### Factors associated to the adenoma and serrated polyp detection rates from multilevel logistic regression

The results of the multilevel logistic regressions are presented in Table 4. Age and gender were significant factors for polyp detection regardless of the indicator used. After adjusting for patient-level variables, the interendoscopist variability achieved a significant level for A.DR, PA.DR, and PSP.DR but not for DA.DR ( $P = 0.03$ ,  $P = 0.02$ ,  $P = 0.02$  and  $P = 0.08$ , respectively). The corresponding variance partition coefficients were as follows: 2.1%, 6.6%, 12.3%, and 1.3%. The heterogeneity between endoscopists was approximately threefold higher for PA.DR compared with A.DR, and twofold higher for PSP.DR compared with PA.DR.

#### Complementary analyses

The abovementioned results were not affected when the proximal colon was defined as proximal to the hepatic flexure (data not presented).

Amongst the 18 colonoscopists, the median gender- and age-adjusted values for the detection of polyps  $\geq 10$  mm were 17.5%, 16.2%, 2.6% and 0.6% for A.DR, DA.DR, PA.DR and PSP.DR, respectively, without significant statistical interendoscopist variability.

The interendoscopist variability amongst the 18 colonoscopists remains significant for the detection rate of proximal polyps of any histological subtype (*i.e.*, proximal serrated polyp and/or proximal

**Table 2** Comparison of polyp detection rates (%) between males and females amongst the 18 colonoscopists using the Wilcoxon test

		Males	Females	Total	P value
A.DR	<i>n</i>	18	18	18	< 0.0001
	mean	46.3	24.5	35.7	
	Median	44.9	23.7	34.1	
	Q1-Q3	40.7-50.0	20.0-27.7	31.7-38.8	
	Min-Max	35.8-67.3	12.5-39.3	24.6-47.6	
DA.DR	<i>n</i>	18	18	18	< 0.0001
	mean	38.2	20	29.4	
	Median	37.7	20.6	29.4	
	Q1-Q3	32.4-40.0	17.9-22.7	25.6-31.8	
	Min-Max	27.9-54.8	11.0-29.2	19.0-39.0	
PA.DR	<i>n</i>	18	18	18	< 0.0001
	mean	17.8	7.1	12.4	
	Median	15.3	6.6	11.5	
	Q1-Q3	11.0-22.4	3.6-10.8	7.3-17.8	
	Min-Max	8.6-40.0	1.3-18.0	5.9-22.9	
PSP.DR	<i>n</i>	18	18	18	0.06
	mean	8.3	5.3	6.9	
	Median	7.0	4.3	5.4	
	Q1-Q3	4.5-10.8	1.5-6.6	3.1-8.5	
	Min-Max	2.2-25.6	0.0-16.9	1.3-19.2	

A.DR: Adenoma detection rate; DA.DR: Distal adenoma detection rate; PA.DR: Proximal adenoma detection rate; PSP.DR: Proximal serrated polyp detection rate.

**Table 3** Comparison of polyp detection rates (%) according to age groups amongst the 18 colonoscopists using the Wilcoxon test

		< 55	55-59	60-64	65-69	≥ 70	Total	P value
A.DR	<i>n</i>	18	18	18	18	18	18	< 0.0001
	mean	29.5	28.6	36.7	42.3	42.2	35.7	
	Median	28.5	29.6	38.8	43.5	43.0	34.1	
	Q1-Q3	24.4-34.8	21.4-33.3	29.4-41.4	28.6-50.0	37.5-45.5	31.7-38.8	
	Min-Max	16.7-42.9	12.5-42.6	18.4-52.9	21.7-73.0	29.0-53.8	24.6-47.6	
DA.DR	<i>n</i>	18	18	18	18	18	18	0.0003
	mean	23.9	23.6	31.9	35.3	33.4	29.4	
	Median	22.7	23.8	33.0	39.0	33.3	29.4	
	Q1-Q3	17.6-31.8	18.5-27.8	29.4-37.5	22.7-44.4	26.5-37.5	25.6-31.8	
	Min-Max	11.1-35.3	12.5-36.8	14.3-42.9	13.6-54.1	23.1-51.6	19.0-39.0	
PA.DR	<i>n</i>	18	18	18	18	18	18	0.0006
	mean	9.1	8.8	11.7	15.9	17.4	12.4	
	Median	8.3	9.5	9.1	17.5	15.9	11.5	
	Q1-Q3	5.9-9.3	4.3-11.8	5.0-18.2	11.9-20.0	12.5-20.6	7.3-17.8	
	Min-Max	0-25.0	0-17.9	0-31.0	2.5-32.4	0-46.2	5.9-22.9	
PSP.DR	<i>n</i>	18	18	18	18	18	18	0.37
	mean	6.1	6.5	6.2	8.1	8.6	6.9	
	Median	5.0	4.7	1.8	5.8	8.0	5.4	
	Q1-Q3	0.0-7.4	3.2-10.0	0.0-10.0	2.5-10.2	3.2-12.9	3.1-8.5	
	Min-Max	0.0-20.9	0.0-21.4	0.0-23.1	0.0-26.5	0.0-20.6	1.3-19.2	

A.DR: Adenoma detection rate; DA.DR: Distal adenoma detection rate; PA.DR: Proximal adenoma detection rate; PSP.DR: Proximal serrated polyp detection rate.

adenoma) (data not presented). The corresponding variance partition coefficient was 9.6%, which was an intermediary value between the PSP.DR and PA.DR values.

#### Correlation studies between adjusted values of polyp detection rates

PSP.DR values were not correlated with A.DR values ( $\rho = 0.19$ ,  $P = 0.45$ ), but were significantly correlated with PA.DR values ( $\rho = 0.55$ ,  $P < 0.002$ ). PA.DR values were highly significantly correlated with A.DR values ( $\rho$

$= 0.83$ ,  $P < 0.0001$ ).

## DISCUSSION

Colonoscopies are known to display great variability in A.DRs between endoscopists in various settings, including in academic<sup>[18]</sup>, mixed community-academic<sup>[19]</sup>, community practices<sup>[20,21]</sup> and population-based studies<sup>[15,22]</sup>. However, no study focused on the variability in A.DRs according to the proximal or distal location of the adenomas in the colon. Although

**Table 4 Results of multilevel logistic regression analysis for assessing the interendoscopist variability**

			Coefficient (standard error)	P value	OR	95%CI
Adenoma detection rate	Patient level	Constant	-2.37 (0.356)	< 0.0001		
		Age	0.036 (0.006)	< 0.0001	1.037	1.025-1.048
		Gender (ref = male)	-1.019 (0.082)	< 0.0001	0.361	0.308-0.424
	Endoscopist level	$\sigma^2 u^0$	0.070 (0.032)	0.03		
Distal adenoma detection rate	Patient level	Constant	-2.498 (0.369)	< 0.0001		
		Age	0.033 (0.006)	< 0.0001	1.033	1.022-1.045
		Gender (ref = male)	-0.932 (0.085)	< 0.0001	0.394	0.333-0.466
	Endoscopist level	$\sigma^2 u^0$	0.044 (0.025)	0.08		
Proximal adenoma detection rate	Patient level	Constant	-4.169 (0.538)	< 0.0001		
		Age	0.041 (0.008)	< 0.0001	1.042	1.025-1.059
		Gender (ref = male)	-1.065 (0.127)	< 0.0001	0.345	0.269-0.442
	Endoscopist level	$\sigma^2 u^0$	0.234 (0.101)	0.02		
Proximal serrated polyp detection rate	Patient level	Constant	-4.049 (0.677)			
		Age	0.025 (0.010)	0.02	1.025	1.004-1.046
		Gender (ref = male)	-0.498 (0.150)	< 0.001	0.608	0.453-0.816
	Endoscopist level	$\sigma^2 u^0$	0.460 (0.199)	0.02		

<sup>1</sup>Variance of the endoscopist-level random effect representing the heterogeneity between endoscopists in terms of the outcome.

the present study confirms significant variability for adenoma detection amongst colonoscopists, these data indicate that interendoscopist variability achieves a significant level for proximal adenomas but not distal adenomas detection. Serrated polyps were included to demonstrate that interendoscopist variability was also significant for proximal serrated polyp detection, even higher. These findings which resulted from in-depth statistical analyses using multilevel logistic regressions, demonstrate a higher heterogeneity for proximal serrated polyp than proximal adenoma detection amongst endoscopists. Detection rates for distal serrated polyps were not assessed because we hypothesised that variability between colonoscopists could be related to other factors than the quality of performance by colonoscopists. Some endoscopists might intentionally avoid performing a biopsy or discard small rectal polyps that have the appearance of hyperplastic polyps in the rectosigmoid.

All of these findings contribute to underline that the proximal colon is a difficult issue for colonoscopists. Otherwise, the performances of colonoscopists are more variable for proximal adenomas compared with distal adenomas and within the proximal colon for serrated polyps compared with adenomas. A correlation between adenomas and serrated polyps detection rates is debatable in the literature. No significant correlation between both rates was found similarly to some studies<sup>[23,24]</sup>. On the opposite, other studies reported a significant correlation between adenoma detection rate and detection rate of polyps with other histological type (sessile serrated polyps, serrated polyps and proximal serrated polyps)<sup>[12,14,25-29]</sup>, but all underlined the poor correlation between A.DR and PSP.DR. Moreover, the significant correlation we found between both proximal polyps detection rates is in accordance with results from one large cohort study<sup>[23]</sup>.

The mean detection rate for proximal adenomas

(12.4%) was significantly lower than the 38% rate reported by Kahi *et al.*<sup>[30]</sup> in a recent series of 6681 screening colonoscopies. The anatomical distribution of adenomas in the large bowel is debatable. A right-sided dominance of adenomas has been reported in some studies for both sexes<sup>[12]</sup>, or for women only<sup>[31]</sup>. Of note, we did not observe such distribution for adenomas. But, our findings are in line with data of colonoscopies following a positive FOBT in France<sup>[32]</sup>. Interestingly, data of 2821392 nationwide screening colonoscopies in Germany indicated that only 28.7% of adenomas detected were proximal to the sigmoid colon<sup>[33]</sup>.

The ranges of proximal serrated polyp detection rates amongst endoscopists were 1.3%-19.3% in the present study. Two other studies by Kahi *et al.*<sup>[13]</sup> (1%-18%) and Ijspeert *et al.*<sup>[29]</sup> (2.9%-18.6%) reported similar rates but one study of 7215 screening colonoscopies including 32 endoscopy centers observed lower detection rate of proximal serrated polyps (mean 2.8%, range 0-9.8%)<sup>[14]</sup>. This discrepancy may be secondary to the selected population, bowel preparation quality, endoscopists' technique or skill. While the rate of clinically relevant serrated polyps was recently reported to be similar in FOBT-based screening cohorts and in primary colonoscopy screening cohorts<sup>[14]</sup>, the strengths of the current cohort remains its homogeneity due to the population selection by a single indication. With regard to the population, our study underlines the fact that the prevalence of proximal serrated polyps does not differ according to age and gender<sup>[13,14,24]</sup>. The trend for a higher detection rate in males compared with females that we found in the present study is in accordance with recent findings from post-FOBT colonoscopies<sup>[34]</sup>.

These results point out the substantial numbers of undetected lesions in the proximal colon in clinical practice. The wider variability observed for serrated polyps compared to adenomas amongst endosco-

pists support a more subtle appearance of serrated polyps<sup>[35,36]</sup>, particularly of small and diminutive polyps because we did not find any significant variation in the detection rates for proximal polyps of a size greater than 10 mm for either adenomas or serrated polyps. We speculate that education and training are important not solely for adequate mucosal exposure, but also for identification of subtle lesions such as serrated polyps.

Individual endoscopists' adenoma detection rates have been demonstrated to be associated with interval cancer risk<sup>[9,11]</sup>. The hypothesis that the proximal serrated polyp detection rate or a composite measure for proximal polyp (*i.e.*, adenoma and/or serrated polyp) detection could predict interval CRCs even more accurately than the adenoma detection rate remains to be established.

The present study has several limitations. The preparation quality was not considered in our study. In a recent prospective study, sessile serrated polyps were detected in a significantly smaller proportion of patients with intermediate-quality preparation than high-quality preparation for the whole colon and the right colon<sup>[37]</sup>. However, it seems unlikely that it could explain the wider magnitude of variation for proximal serrated polyp detection compared with proximal adenoma detection. The withdrawal time was not considered in our study. It has been recently reported that it could affect serrated polyp detection<sup>[23,24,38]</sup>. Thus, we cannot exclude that a given withdrawal time could affect differently serrated polyp and adenoma detection. Furthermore, patient-related factors known to modify adenoma prevalence, such as smoking, obesity, or aspirin use, were not considered. By contrast, one strength of our study was the exclusion of subjects with a family history of CRC because of their particular distribution of adenomas in the colon<sup>[39]</sup>. Overall, it seems unlikely that patient-related factors could have explained the magnitude of the variability observed in our study. Nevertheless, as suggested by the variance partition coefficient values found in the current study, other factors than endoscopists could explain interendoscopist variability. Another limitation might be related to the absence of distinction of subtypes of serrated polyps. However, pooling the different histopathological types of serrated polyps is justified when considering the considerable interobserver variation in the differentiation of serrated polyps<sup>[12,40,41]</sup> and the significant correlation between both detection rates of proximal serrated polyps and clinically relevant serrated polyps<sup>[29]</sup>. Lastly, we have no information regarding the endoscopes used by the endoscopists during the study period. We hypothesize that all colonoscopies were performed with standard definition endoscopes. Thus, it remains to demonstrate that high definition endoscopes could reduce the variability for serrated polyp detection amongst endoscopists and the gap between proximal serrated polyp and proximal adenoma detection amongst endoscopists.

In conclusion, our findings demonstrate significant

variability in the detection of proximal polyps, which included both adenomas and serrated polyps, amongst endoscopists. The heterogeneity was approximately twofold higher for proximal serrated polyps than for proximal adenomas detection. These findings might explain why complete colonoscopies are less effective at preventing proximal CRCs than distal ones. Furthermore, our results question the potential of using a proximal serrated polyp detection rate as a surrogate indicator for interval CRC risk.

## ACKNOWLEDGMENTS

The authors would like to thank all of the gastroenterologists and general practitioners who participated in the CRC screening in Ille-et-Vilaine, France.

## COMMENTS

### Background

The variability of detection rate for proximal serrated polyps amongst endoscopists has been reported in the literature. However, no study aimed to compare adenomas and serrated polyps detection variability amongst endoscopists, especially for proximal colon location.

### Research frontiers

The authors indicate that interendoscopist variability achieves a significant level for proximal adenomas but not for distal adenomas detection. Moreover, the heterogeneity was approximately twofold higher for proximal serrated polyps than for proximal adenomas detection.

### Innovations and breakthroughs

The interendoscopist variability in detection of proximal polyps (serrated polyps and adenomas) had never been compared in previous studies.

### Applications

The authors findings might explain why complete colonoscopies are less effective at preventing proximal colorectal cancer (CRCs) than distal ones. Furthermore, our results question the potential of using a proximal serrated polyp detection rate as a surrogate indicator for interval CRC risk.

### Terminology

Proximal polyps are defined as polyps located above the splenic flexure. Serrated polyps were defined as an entire group of polyps that included traditional hyperplastic polyps, sessile serrated adenomas/polyps and traditional serrated adenomas.

### Peer-review

The study was appropriately designed and analysed. Its result has thoroughly strong impact on routine practice, especially on screening colonoscopy program. The manuscript is clearly constructed and written in appropriate English. There is no major issues to be revised in their paper.

## REFERENCES

- 1 **Zauber AG**, Winawer SJ, O'Brien MJ, Lansdorp-Vogelaar I, van Ballegooijen M, Hankey BF, Shi W, Bond JH, Schapiro M, Panish JF, Stewart ET, Wayne JD. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. *N Engl J Med* 2012; **366**: 687-696 [PMID: 22356322 DOI: 10.1056/NEJMoa1100370]
- 2 **Citarda F**, Tomaselli G, Capocaccia R, Barcherini S, Crespi M. Efficacy in standard clinical practice of colonoscopic polypectomy in reducing colorectal cancer incidence. *Gut* 2001; **48**: 812-815

- [PMID: 11358901]
- 3 **Cottet V**, Jooste V, Fournel I, Bouvier AM, Faivre J, Bonithon-Kopp C. Long-term risk of colorectal cancer after adenoma removal: a population-based cohort study. *Gut* 2012; **61**: 1180-1186 [PMID: 22110052 DOI: 10.1136/gutjnl-2011-300295]
  - 4 **Brenner H**, Chang-Claude J, Seiler CM, Rickert A, Hoffmeister M. Protection from colorectal cancer after colonoscopy: a population-based, case-control study. *Ann Intern Med* 2011; **154**: 22-30 [PMID: 21200035 DOI: 10.7326/0003-4819-154-1-201101040-00004]
  - 5 **Lakoff J**, Paszat LF, Saskin R, Rabeneck L. Risk of developing proximal versus distal colorectal cancer after a negative colonoscopy: a population-based study. *Clin Gastroenterol Hepatol* 2008; **6**: 1117-1121; quiz 1064 [PMID: 18691942 DOI: 10.1016/j.cgh.2008.05.016]
  - 6 **Baxter NN**, Goldwasser MA, Paszat LF, Saskin R, Urbach DR, Rabeneck L. Association of colonoscopy and death from colorectal cancer. *Ann Intern Med* 2009; **150**: 1-8 [PMID: 19075198]
  - 7 **Singh H**, Nugent Z, Demers AA, Kliewer EV, Mahmud SM, Bernstein CN. The reduction in colorectal cancer mortality after colonoscopy varies by site of the cancer. *Gastroenterology* 2010; **139**: 1128-1137 [PMID: 20600026 DOI: 10.1053/j.gastro.2010.06.052]
  - 8 **Brenner H**, Hoffmeister M, Arndt V, Stegmaier C, Altenhofen L, Haug U. Protection from right- and left-sided colorectal neoplasms after colonoscopy: population-based study. *J Natl Cancer Inst* 2010; **102**: 89-95 [PMID: 20042716 DOI: 10.1093/jnci/djp436]
  - 9 **Kaminski MF**, Regula J, Kraszewska E, Polkowski M, Wojciechowska U, Didkowska J, Zwierko M, Rupinski M, Nowacki MP, Butruk E. Quality indicators for colonoscopy and the risk of interval cancer. *N Engl J Med* 2010; **362**: 1795-1803 [PMID: 20463339 DOI: 10.1056/NEJMoa0907667]
  - 10 **Baxter NN**, Sutradhar R, Forbes SS, Paszat LF, Saskin R, Rabeneck L. Analysis of administrative data finds endoscopist quality measures associated with postcolonoscopy colorectal cancer. *Gastroenterology* 2011; **140**: 65-72 [PMID: 20854818 DOI: 10.1053/j.gastro.2010.09.006]
  - 11 **Corley DA**, Jensen CD, Marks AR, Zhao WK, Lee JK, Doubeni CA, Zuber AG, de Boer J, Fireman BH, Schottinger JE, Quinn VP, Ghai NR, Levin TR, Quesenberry CP. Adenoma detection rate and risk of colorectal cancer and death. *N Engl J Med* 2014; **370**: 1298-1306 [PMID: 24693890 DOI: 10.1056/NEJMoa1309086]
  - 12 **Hetzel JT**, Huang CS, Coukos JA, Omstead K, Cerda SR, Yang S, O'Brien MJ, Farraye FA. Variation in the detection of serrated polyps in an average risk colorectal cancer screening cohort. *Am J Gastroenterol* 2010; **105**: 2656-2664 [PMID: 20717107 DOI: 10.1038/ajg.2010.315]
  - 13 **Kahi CJ**, Hewett DG, Norton DL, Eckert GJ, Rex DK. Prevalence and variable detection of proximal colon serrated polyps during screening colonoscopy. *Clin Gastroenterol Hepatol* 2011; **9**: 42-46 [PMID: 20888435 DOI: 10.1016/j.cgh.2010.09.013]
  - 14 **Payne SR**, Church TR, Wandell M, Rösch T, Osborn N, Snover D, Day RW, Ransohoff DF, Rex DK. Endoscopic detection of proximal serrated lesions and pathologic identification of sessile serrated adenomas/polyps vary on the basis of center. *Clin Gastroenterol Hepatol* 2014; **12**: 1119-1126 [PMID: 24333512 DOI: 10.1016/j.cgh.2013.11.034]
  - 15 **Bretagne JF**, Hamonic S, Piette C, Manfredi S, Leray E, Durand G, Riou F. Variations between endoscopists in rates of detection of colorectal neoplasia and their impact on a regional screening program based on colonoscopy after fecal occult blood testing. *Gastrointest Endosc* 2010; **71**: 335-341 [PMID: 19922930 DOI: 10.1016/j.gie.2009.08.032]
  - 16 **Goldstein H**, Browne W, Rasbash J. Multilevel modelling of medical data. *Stat Med* 2002; **21**: 3291-3315 [PMID: 12375305]
  - 17 **Snijders T**, Bosker R. Multilevel analysis: an introduction to basic and advanced multilevel modelling. London: Sage, 1999
  - 18 **Chen SC**, Rex DK. Endoscopist can be more powerful than age and male gender in predicting adenoma detection at colonoscopy. *Am J Gastroenterol* 2007; **102**: 856-861 [PMID: 17222317]
  - 19 **Imperiale TF**, Glowinski EA, Juliar BE, Azzouz F, Ransohoff DF. Variation in polyp detection rates at screening colonoscopy. *Gastrointest Endosc* 2009; **69**: 1288-1295 [PMID: 19481649 DOI: 10.1016/j.gie.2007.11.043]
  - 20 **Barclay RL**, Vicari JJ, Doughty AS, Johanson JF, Greenlaw RL. Colonoscopic withdrawal times and adenoma detection during screening colonoscopy. *N Engl J Med* 2006; **355**: 2533-2541 [PMID: 17167136]
  - 21 **Shaukat A**, Oancea C, Bond JH, Church TR, Allen JI. Variation in detection of adenomas and polyps by colonoscopy and change over time with a performance improvement program. *Clin Gastroenterol Hepatol* 2009; **7**: 1335-1340 [PMID: 19665583 DOI: 10.1016/j.cgh.2009.07.027]
  - 22 **Atkin W**, Rogers P, Cardwell C, Cook C, Cuzick J, Wardle J, Edwards R. Wide variation in adenoma detection rates at screening flexible sigmoidoscopy. *Gastroenterology* 2004; **126**: 1247-1256 [PMID: 15131784]
  - 23 **Lee CK**, Kim YW, Shim JJ, Jang JY. Prevalence of proximal serrated polyps and conventional adenomas in an asymptomatic average-risk screening population. *Gut Liver* 2013; **7**: 524-531 [PMID: 24073309 DOI: 10.5009/gnl.2013.7.5.524]
  - 24 **de Wijkerslooth TR**, Stoop EM, Bossuyt PM, Tytgat KM, Dees J, Mathus-Vliegen EM, Kuipers EJ, Fockens P, van Leerdam ME, Dekker E. Differences in proximal serrated polyp detection among endoscopists are associated with variability in withdrawal time. *Gastrointest Endosc* 2013; **77**: 617-623 [PMID: 23321338 DOI: 10.1016/j.gie.2012.10.018]
  - 25 **Zorzi M**, Senore C, Da Re F, Barca A, Bonelli LA, Cannizzaro R, de Pretis G, Di Furia L, Di Giulio E, Mantellini P, Naldoni C, Sassatelli R, Rex DK, Zappa M, Hassan C; Equipe Working Group. Detection rate and predictive factors of sessile serrated polyps in an organised colorectal cancer screening programme with immunochemical faecal occult blood test: the EQuiPE study (Evaluating Quality Indicators of the Performance of Endoscopy). *Gut* 2016; Epub ahead of print [PMID: 26896459 DOI: 10.1136/gutjnl-2015-310587]
  - 26 **Kim HY**, Kim SM, Seo JH, Park EH, Kim N, Lee DH. Age-specific prevalence of serrated lesions and their subtypes by screening colonoscopy: a retrospective study. *BMC Gastroenterol* 2014; **14**: 82 [PMID: 24775268 DOI: 10.1186/1471-230X-14-82]
  - 27 **Sanaka MR**, Gohel T, Podugu A, Kiran RP, Thota PN, Lopez R, Church JM, Burke CA. Adenoma and sessile serrated polyp detection rates: variation by patient sex and colonic segment but not specialty of the endoscopist. *Dis Colon Rectum* 2014; **57**: 1113-1119 [PMID: 25101608 DOI: 10.1097/DCR.000000000000183]
  - 28 **Occhipinti P**, Saettone S, Cristina S, Ridola L, Hassan C. Correlation between adenoma and serrated lesion detection rates in an unselected outpatient population. *Dig Liver Dis* 2015; **47**: 508-511 [PMID: 25659823 DOI: 10.1016/j.dld.2015.01.003]
  - 29 **IJspeert JE**, van Doorn SC, van der Brug YM, Bastiaansen BA, Fockens P, Dekker E. The proximal serrated polyp detection rate is an easy-to-measure proxy for the detection rate of clinically relevant serrated polyps. *Gastrointest Endosc* 2015; **82**: 870-877 [PMID: 25935704 DOI: 10.1016/j.gie.2015.02.044]
  - 30 **Kahi CJ**, Li X, Eckert GJ, Rex DK. High colonoscopic prevalence of proximal colon serrated polyps in average-risk men and women. *Gastrointest Endosc* 2012; **75**: 515-520 [PMID: 22018551 DOI: 10.1016/j.gie.2011.08.021]
  - 31 **Forsberg AM**, Kjellström L, Agréus L, Nixon Andreasson A, Nyhlin H, Talley NJ, Björck E. Prevalence of colonic neoplasia and advanced lesions in the normal population: a prospective population-based colonoscopy study. *Scand J Gastroenterol* 2012; **47**: 184-190 [PMID: 22229966 DOI: 10.3109/00365521.2011.647062]
  - 32 **Denis B**, Sauleau EA, Gendre I, Piette C, Bretagne JF, Perrin P. Measurement of adenoma detection and discrimination during colonoscopy in routine practice: an exploratory study. *Gastrointest Endosc* 2011; **74**: 1325-1336 [PMID: 21958899 DOI: 10.1016/j.gie.2011.07.038]
  - 33 **Pox CP**, Altenhofen L, Brenner H, Theilmeier A, Von Stillfried



- D, Schmiegel W. Efficacy of a nationwide screening colonoscopy program for colorectal cancer. *Gastroenterology* 2012; **142**: 1460-1462 [PMID: 22446606 DOI: 10.1053/j.gastro.2012.03.022]
- 34 **IJspeert JE**, Bevan R, Senore C, Kaminski MF, Kuipers EJ, Mroz A, Bessa X, Cassoni P, Hassan C, Repici A, Balaguer F, Rees CJ, Dekker EI. Detection rate of serrated polyps and serrated polyposis syndrome in colorectal cancer screening cohorts: a European overview. *Gut* 2016; Epub ahead of print [PMID: 26911398 DOI: 10.1136/gutjnl-2015-310784]
- 35 **Huang CS**, Farraye FA, Yang S, O'Brien MJ. The clinical significance of serrated polyps. *Am J Gastroenterol* 2011; **106**: 229-240; quiz 241 [PMID: 21045813 DOI: 10.1038/ajg.2010.429]
- 36 **Rex DK**, Ahnen DJ, Baron JA, Batts KP, Burke CA, Burt RW, Goldblum JR, Guillem JG, Kahi CJ, Kalady MF, O'Brien MJ, Odze RD, Ogino S, Parry S, Snover DC, Torlakovic EE, Wise PE, Young J, Church J. Serrated lesions of the colorectum: review and recommendations from an expert panel. *Am J Gastroenterol* 2012; **107**: 1315-1329; quiz 1314, 1330 [PMID: 22710576 DOI: 10.1038/ajg.2012.161]
- 37 **Clark BT**, Laine L. High-quality Bowel Preparation Is Required for Detection of Sessile Serrated Polyps. *Clin Gastroenterol Hepatol* 2016; **14**: 1155-1162 [PMID: 27060426 DOI: 10.1016/j.cgh.2016.03.044]
- 38 **Butterly L**, Robinson CM, Anderson JC, Weiss JE, Goodrich M, Omega TL, Amos CI, Beach ML. Serrated and adenomatous polyp detection increases with longer withdrawal time: results from the New Hampshire Colonoscopy Registry. *Am J Gastroenterol* 2014; **109**: 417-426 [PMID: 24394752 DOI: 10.1038/ajg.2013.442]
- 39 **Wark PA**, Wu K, van 't Veer P, Fuchs CF, Giovannucci EL. Family history of colorectal cancer: a determinant of advanced adenoma stage or adenoma multiplicity? *Int J Cancer* 2009; **125**: 413-420 [PMID: 19358277 DOI: 10.1002/ijc.24288]
- 40 **Khalid O**, Radaideh S, Cummings OW, O'Brien MJ, Goldblum JR, Rex DK. Reinterpretation of histology of proximal colon polyps called hyperplastic in 2001. *World J Gastroenterol* 2009; **15**: 3767-3770 [PMID: 19673017]
- 41 **Wong NA**, Hunt LP, Novelli MR, Shepherd NA, Warren BF. Observer agreement in the diagnosis of serrated polyps of the large bowel. *Histopathology* 2009; **55**: 63-66 [PMID: 19614768 DOI: 10.1111/j.1365-2559.2009.03329.x]

**P-Reviewer:** Lakatos PL, Mori Y **S-Editor:** Qi Y  
**L-Editor:** A **E-Editor:** Zhang FF





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>



ISSN 1007-9327



9 771007 932045