Original Article

Detection Rate, Distribution, Clinical and Pathological Features of Colorectal Serrated Polyps

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Abstract

Background: Colorectal serrated polyp is considered as histologically heterogeneous lesions with malignant potential in western countries. However, few Asian studies have investigated the comprehensive clinical features of serrated polyps in symptomatic populations. The aim of the study was to evaluate the features of colorectal serrated polyps in a Chinese symptomatic population.
Methods: Data from all consecutive symptomatic patients were documented from a large colonoscopy database and were analyzed. Chi-square test or Fisher's exact test and logistic regression analysis were used for the data processing.
Results: A total of 9191 (31.7%) patients were detected with at least one colorectal polyp. The prevalence of serrated polyps was 0.53% (153/28,981). The proportions of hyperplastic polyp (HP), sessile serrated adenoma/polyp (SSA/P), and traditional serrated adenoma (TSA) of all serrated polyps were 41.2%, 7.2%, and 51.6%, respectively, which showed a lower proportion of HP and SSA/P and a higher proportion of TSA. Serrated polyps appeared more in males and elder patients while there was no significant difference in the subtype distribution in gender and age. The proportions of large and proximal serrated polyps were 13.7% (21/153) and 46.4% (71/153), respectively. In total, 98.9% (89/90) serrated adenomas were found with dysplasia. Moreover, 14 patients with serrated polyps were found with synchronous advanced colorectal neoplasia, and large serrated polyps (LSPs) (odds ratio: 3.446, 95% confidence interval: 1.010–11.750, $P < 0.05$), especially large HPs, might have an association with synchronous advanced neoplasia (AN).
Conclusions: The overall detection rate of colorectal serrated polyps in Chinese symptomatic patient population was low, and distribution pattern of three subtypes is different from previous reports. Moreover, LSPs, especially large HPs, might be associated with an increased risk of synchronous AN.

Key words: Colorectal Cancer; Colorectal Serrated Polyps; Hyperplastic Polyp; Traditional Serrated Adenoma; Sessile Serrated Adenoma/Polyp

Introduction

Colorectal cancer (CRC) is the third most frequent cancer worldwide and the fourth most common cause of cancer deaths.[1] Growing evidence supports that 15%–20% of CRC arise through the serrated pathway, which is characterized by widespread gene inactivation via hypermethylation of promoter regions (the CpG island methylator phenotype), *BRAF* mutations, and frequent microsatellite instability.[2,3] Colorectal serrated polyps are histologically typical for a serrated or "sawtooth-like" appearance of the crypt epithelium[4] and have been recognized as precursor lesions for CRC in western countries over the last decade, especially for interval or missed CRC.[5,6] Currently, serrated polyps are classified by the World Health Organization (WHO) into three distinct subtypes: Hyperplastic polyp (HP), sessile serrated adenoma/polyp (SSA/P) with or without cytological dysplasia, and traditional serrated adenoma (TSA), and each has specific features.[4] Autopsy studies demonstrated

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the variable prevalence of serrated lesions but collectively indicate that 25%–50% of Caucasians have one or more serrated lesions.[7-9] Colonoscopic studies also showed similarly variable but lower prevalence rates.[4] Recent studies in western countries reporting on the prevalence of colorectal serrated polyps in patients with average risk of CRC showed that HP might account for 70%–95% of all serrated polyps, SSA/P for 5%–25%, and TSA for <2%.[10-16]

The overall prevalence of serrated polyps increases only slightly with age during adulthood,[17] and these lesions are most common in the sigmoid colon and rectum, but the distribution varies by histological subtype. HP, typically ≤5 mm in size,[4] appears more in the distal colon and rectum,[18] as well as TSA.[19] As the second frequent subset in serrated polyps, SSA/P occurs predominantly in the proximal colon and in older women.[20] As HP and SSA/P have the similarity in color and vessel distribution,[20] some important features can help identify SSA/P including flat morphology, red-colored surface, mucus cap, lateral growth of crypts at the base, dilation in the lower third of crypts, and hyperserration of the crypt bases, sometimes with branching.[18,21] TSA is a relatively rare lesion and the only member of the serrated class that is uniformly dysplastic.[18] In addition, studies also suggested that large serrated lesions, proximal serrated polyps,[5] or proximal hyperplasic polyps[22] were associated with synchronous advanced neoplasia (AN).

However, few Asian studies have investigated the comprehensive clinical features of colorectal serrated polyps. To address this issue and also provide more evidence for the management of colorectal serrated polyps in clinical practice, we evaluated the detection rate and the features of serrated polyps in a Chinese symptomatic patient population.

Methods

Patients

All consecutive symptomatic patients who underwent routine colonoscopy at the Digestive Endoscopy Center of Tianjin Medical University General Hospital, between January 2010 and December 2014, were investigated. The indications for colonoscopy were due to various symptoms, such as abdominal pain, diarrhea, and change of bowel habits. Other kinds of endoscopies such as emergent and therapeutic colonoscopy were not included. The pathological sections of suspected colorectal serrated polyps were reevaluated and reclassified by one experienced pathologist (Wen-Jing Song) using the WHO criteria.[23] The demographic and clinicopathological data of all colorectal serrated polyps with a final diagnosis and classification were further collected, including patient age and gender, lesion size, polyp number, and location.

The size of colorectal serrated polyps was determined on the basis of endoscopic descriptions, and large serrated polyps (LSPs) were defined as a diameter ≥10 mm. The proximal polyps refer to the polyps which locate in the cecum, ascending colon, and transverse colon including the splenic flexure, and distal polyps define as polyps in the descending colon, sigmoid colon, and rectum. The AN included adenocarcinomas, adenomas with high-grade dysplasia (HGD), adenomas with any villous histology, or adenomas ≥10 mm.

Exclusion criteria were as follows: (1) <20 years old, (2) patients with any kinds of polyposis syndromes, (3) patients with a history of CRC or inflammatory bowel disease, (4) patients with a history of colonic resection or polypectomy, (5) patients with any emergent and therapeutic colonoscopy, and (6) patients with inadequate bowel preparation and had incomplete colonoscopy.

Informed consents for colonoscopy were granted from all the patients before the procedure, and ethical approval was obtained from the Ethics Committee of Tianjin Medical University General Hospital.

Endoscopic procedure and pathological evaluation

Colonoscopy (Olympus CF-Q260, Olympus Optical Co., Tokyo, Japan) was used for all procedures by the experienced endoscopists. Patients were prescribed polyethylene glycol lavage (PO) for bowel preparation. Patients were orally lavaged, and watery diarrhea excretion before the procedure indicated adequate intestinal preparation. All collected specimens were fixed in 10% formalin and then fixed for a minimum of 4 h. Hematoxylin and eosin staining was used for histopathological evaluation and classification. All the serrated lesions were divided into three subtypes: HP, SSA/P with or without dysplasia, and TSA. The histopathological criteria used for diagnosis were those described by Rex *et al*.[4] and East *et al*.[21] The defining histologic feature of HP is a sawtooth pattern of epithelial infolding in the upper half of the crypt with a lack of cytologic dysplasia.[6] The typical SSA/P has the "boot", "L", or "anchor"-shaped crypts above the muscularis mucosae, serration in the lower third of the crypts with and without branching of the crypts, inverted crypts below the muscularis mucosae, and columnar dilation in the lower third.[21] These crypts may appear dilated and/or branched, particularly in the horizontal plane. Distinguishing the TSA from the other polyps is the unique characteristics described as a serrated architecture and at least a focal area with tall columnar cells having elongated nuclei and an abundant eosinophilic cytoplasm. The budding of proliferative crypts situated perpendicular to the long axis of filiform or villous structures (ectopic crypt formation) also helps identify TSA.[24,25]

Statistical analysis

All statistical analyses were performed using SPSS 19.0 (SPSS Inc, Chicago, IL, USA) for Windows. Risks of colorectal serrated polyps were compared by Chi-square test or Fisher's exact test. Means and standard deviation were calculated for continuous variables. Logistic regression analysis was used to evaluate the odds ratio (*OR*) and 95% confidence interval (*CI*) for colorectal synchronous AN (sAN). Age, gender, size, location, and dysplasia were selected as possible confounding factors. The level of statistically significance was set at two-tailed $P < 0.05$.

Results

Detected rate of colorectal serrated polyps

A total of 28,981 symptomatic patients undergoing colonoscopy from 2010 to 2014 were collected in this study. The mean age was 53.2 ± 15.0 years, and 14,332 of the patients (49.5%) were males. The main indications for colonoscopy were abdominal discomfort in 47.2% patients, abdominal pain in 15.9% patients, the change of bowel habits in 10.3% patients, and diarrhea in 9.3% patients. A total of 9191 individuals (31.7%) were found with at least one colorectal polyp and 149 individuals had at least one serrated polyp. Among the 149 patients, a total of 153 serrated polyps were detected. The overall prevalence of colorectal serrated polyps in the current study was about 0.53% (153/28,981). Among the 153 serrated polyps, HP, SSA/P, and TSA accounted for 41.2% (63/153), 7.2% (11/153), and 51.6% (79/153), respectively.

Clinical features of colorectal serrated polyps in symptomatic patients

The demographic characteristics of the patients with colorectal serrated polyps are listed in Table 1. Colorectal serrated polyps appeared more in males ($\chi^2 = 4.785$, $P < 0.05$) and in patients ≥50 years old ($\chi^2 = 5.593$, $P < 0.05$). The mean age of the patients with serrated polyps was 57.4 ± 13.6 years, and HP, SSA/P, and TSA were 56.2 ± 13.0 years, 60.3 ± 9.4 years, and 58.0 ± 14.4 years, respectively. However, there was no significant difference in the subtype's distribution in gender and age [Table 2]. As shown in Figure 1, the detection rates of serrated adenomas (including SSA/P and TSA) in different age decades showed a steadily increased trend with age while HPs showed a light peak in 60–69 years old.

The serrated polyps in the present study tended to have a small diameter (<10 mm). Furthermore, LSPs (diameter ≥10 mm) have a pooled prevalence of 0.2% (21/9191) of all polyps, and the proportion of LSPs in all serrated polyps was 13.7% (21/153). Serrated polyps (53.6% in the distal colon), HPs (60.3% in distal colon), SSA/Ps (54.5% in proximal colon), and TSAs (50.6% in proximal colon) showed no significant difference in anatomic location which was different from previous studies. In total, 98.9% (89/90) serrated adenomas were found with dysplasia, and the low-grade dysplasia was more commonly found. Only one TSA with HGD was found in the present study.

Association of colorectal serrated polyps and synchronous advanced neoplasia

A total of 14 colorectal serrated polyps were found associated with sAN which included adenomas with a size larger than 10 mm, villous component, and HGD and CRC [Table 1]. These included 5 serrated polyps coexisted with invasive adenocarcinoma, 1 with HGD, 1 with villous or tubulovillous adenoma, and 7 with adenoma ≥10 mm in size. Logistic regression analysis indicated that LSPs (*OR*: 3.446, 95% *CI*: 1.010–11.750, $P < 0.05$) had a significant association with sAN [Table 3]. Remarkably, large HPs (*OR*: 11.417, 95% *CI*: 1.474–88.405, $P < 0.05$) showed a strong association with sAN [Table 4].

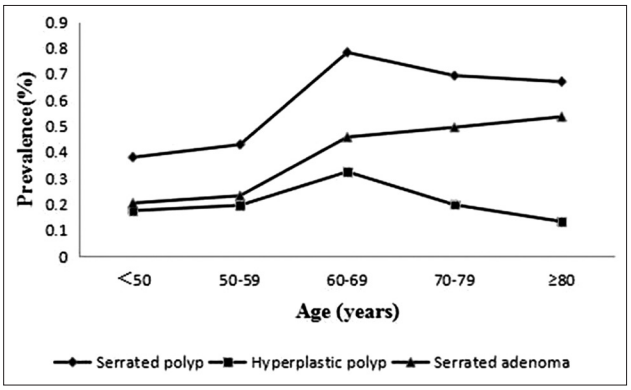

Figure 1: The detection rate of colorectal serrated polyps in different age decades.

Table 1: The characteristics of three subtypes of colorectal serrated polyps in a symptomatic patient population

Characteristics	CSP (*n* = 153)	HP (*n* = 63)	SSA/P (*n* = 11)	TSA (*n* = 79)
Male/female, *n*	93/60	40/23	7/4	46/33
Age (years), mean ± SD	57.4 ± 13.6	56.2 ± 13.0	60.3 ± 9.4	58.0 ± 14.4
Size, *n* (%)				
≥10 mm	21 (13.7)	4 (6.4)	1 (9.1)	16 (20.3)
<10 mm	132 (86.3)	59 (93.6)	10 (90.9)	63 (79.8)
Location, *n* (%)				
Distal	82 (53.6)	38 (60.3)	5 (45.5)	39 (49.4)
Proximal	71 (46.4)	25 (39.7)	6 (54.5)	40 (50.6)
Dysplasia, *n* (%)				
No	64 (41.8)	63 (100)	1 (9.1)	0 (0)
Yes	89 (58.2)	0 (0)	10 (90.9)	79 (100)
With sAN, *n*	14	4	2	8
Adenoma with larger than 10 mm, *n*	7	1	0	6
Adenoma with villous component, *n*	1	1	0	0
Adenoma with high grade dysplasia, *n*	1	1	0	0
Colorectal cancer, *n*	5	1	2	2

CSP: Colorectal serrated polyps; HP: Hyperplastic polyp; SSA/P: Sessile serrated adenoma/polyp; TSA: Traditional serrated adenoma; sAN: Synchronous advanced neoplasia; SD: Standard deviation.

Table 2: Distribution of colorectal serrated polyps according to gender and age

Items	CSP, *n*	HP, *n* (%)	SSA/P, *n* (%)	TSA, *n* (%)	χ^2	*P*
Gender						
Male	93	40 (43.0)	7 (7.5)	46 (49.5)	0.473	0.842
Female	60	23 (38.3)	4 (6.7)	33 (55.0)		
Age (years)						
<50	39	18 (46.2)	1 (2.6)	20 (51.3)	1.639	0.439
≥50	114	45 (39.5)	10 (8.8)	59 (51.7)		
Total	153	63 (41.2)	11 (7.2)	79 (51.6)		

CSP: Colorectal serrated polyp; HP: Hyperplastic polyp; SSA/P: Sessile serrated adenoma/polyp; TSA: Traditional serrated adenoma.

Table 3: Characteristics of colorectal serrated polyps associated with synchronous advanced neoplasia

Characteristics	*n*	CSP without sAN (*n* = 139)	CSP with sAN (*n* = 14)	Univariate analysis		Multivariate analysis	
				OR (95% *CI*)	*P*	*OR* (95% *CI*)	*P*
Gender, *n*							
Male	93	85	8	0.847 (0.279–2.576)	0.77		
Female	60	54	6				
Age (years), mean ± SD		56.6 ± 13.4	64.8 ± 12.3	1.056 (1.004–1.111)	0.036	1.052 (0.996–1.112)	0.067
Size, *n*							
<10 mm	132	122	9	4.271 (1.272–14.336)	0.019	3.446 (1.010–11.750)	0.048
≥10 mm	21	17	5				
Location, *n*							
Distal	82	76	6	1.608 (0.530–4.880)	0.401		
Proximal	71	63	8				
Dysplasia, *n*							
Yes	89	79	10	1.899 (0.568–6.349)	0.298		
No	64	60	4				
Type, *n*							
HP	63	59	4	1.251 (0.690–2.266)	0.460		
SSA/P	11	9	2				
TSA	79	71	8				

CSP: Colorectal serrated polyps; sAN: Synchronous advanced neoplasia; *OR*: Odd ratio; *CI*: Confidence interval; HP: Hyperplastic polyp; SSA/P: Sessile serrated adenoma/polyp; TSA: Traditional serrated adenoma; SD: Standard deviation.

Discussion

The current study suggested a lower detection rate of colorectal serrated polyps of 0.53% (153/28,981) and a different distribution of subtypes compared with available previous reports.[26-33] These also led to a lower overall detection rate of LSPs; however, the proportion of LSPs among colorectal serrated polyps corresponded with lately reports.[5,34-36] After being fully recognized and classified in 2005,[37] colorectal serrated polyps were always reported to have a flat or sessile appearance and paler than surrounding mucosa under white light colonoscopy. This may contribute to a high missing rate even when the polyp detection rate and withdraw time correspond with standards recommended worldwide. It has been reported that the prevalence of proximal colorectal serrated polyps in western countries ranged from 1% to 18% (average 13%).[10,38,39] The endoscopy detection rates of HP (5.7%–44%)[4,15,26-31] and SSA/P (1%–14%)[14,15,26-28,30,31] also varied significantly among different studies. To the best of our knowledge, the prevalence of colorectal serrated polyps also varied a lot.[40,41] Some studies in Chinese population also suggested the similar low prevalence of SSA/Ps.[42,43] Various factors including the patients' population, colonoscopy quality, pathologic validation, variation between centers, and ethnicity might cause these differences.[10,21] In addition, inadequate communication between pathologists and endoscopists, ignorance of inconspicuous rectal polyps, and lack of validated classification criterion may also contribute to the missing rate in Chinese patients. Furthermore, dietary habit may possibly contribute to this difference. Lately, a body of evidence indicated that the western diet habit (with higher total energy intake and red-meat intake) was a high risk of development of colorectal polyps in both number and size, as well as the left-sided advanced serrated lesions.[44-47] Further investigation is needed to find the exact reason for the lower prevalence of colorectal serrated polyps and different distribution of subtypes.

Compared with the prevalence of conventional adenomas which sharply increased with age,[48] the age-specific prevalence of serrated polyps was found to increase steadily with age in the current study which was similar with some recent findings.[15,30,49] We also found the prevalence of HPs

Table 4: Association of colorectal serrated subtypes and synchronous advanced neoplasia

Serrated polyps	*n*	Serrated polyps with sAN, *n*	Univariate analysis		Multivariate analysis	
			OR (95% *CI*)	*P*	*OR* (95% *CI*)	*P*
Proximal HP						
No	128	13	0.810 (0.214–3.073)	0.757		
Yes	25	1				
Proximal SSA/P						
No	147	12	0.000	0.999		
Yes	6	2				
Proximal TSA						
No	113	9	0.780 (0.206–2.956)	0.715		
Yes	40	5				
Large HP (≥10 mm)						
No	149	12	11.417 (1.474–88.405)	0.020	11.417 (1.474–88.405)	0.020
Yes	4	2				
Large SSA (≥10 mm)						
No	152	14				
Yes	1	0				
Large TSA						
No	137	12	2.643 (0.653–10.703)	0.173		
Yes	16	2				

sAN: Synchronous advanced neoplasia; *OR*: Odd ratio; *CI*: Confidence interval; HP: Hyperplastic polyp; SSA/P: Sessile serrated adenoma/polyp; TSA: Traditional serrated adenoma.

in different age decades reached a light peak at 60–69 years old and serrated adenomas steadily increased with age. However, it is still controversial that some studies indicated that increasing age was not materially associated with risk of serrated polyps.[48] Therefore, further study is needed to determine whether aging is significantly associated with the development of colorectal serrated polyps.

To investigate the predictors of sAN in colorectal serrated polyps in Chinese symptomatic patient population, the current study analyzed multiple factors including age, gender, size, location, and dysplasia. By logistic regression analysis, we found that LSPs, especially large HPs, are associated with sAN. Previous studies in asymptomatic screening population reported that large and proximal serrated polyps were the independent predictors of sAN.[10,34,35,40] Multiple SSAs, hyperplastic polyposis, proximal and large HPs, as well as proximal and large SSA/Ps, were further distinguished to be associated with sAN.[10,27,50] However, a large, nationwide, population-based, multicenter, randomized study in average-risk individuals showed that LSPs, but not proximal serrated polyps, were the independent risk factor of sAN.[10] The investigation of genetic or environmental risk factors may be needed to confirm the exact predictors.

Some strengths are included in the present study. First, the study chose a simply and widely used and accepted method (white light colonoscopy), so the results could coincide with the common prevalence standards. Second, we chose a recent period to reduce the influences of inadequate knowledge and less attention of serrated polyps. Third, the relatively large sample size was based on the results of 28,981 colonoscopy of consecutive patients referred to clinic in a comprehensive clinical center. However, some limitations should be mentioned simultaneously. First, the present study was a retrospective study, so the observational design was an important limitation. Second, the current study was conducted in a tertiary endoscopic center, so selection bias might not be ignored. Third, our population was from symptomatic patients undergoing colonoscopy, while previous reports might include average-risk, asymptomatic patients aged ≥50 years who underwent screening colonoscopy, and thus these comparisons among different studies should be made with caution.

In conclusion, our data showed that the detection rate of colorectal serrated polyps in a Chinese symptomatic patient population was low, and distribution pattern of the three subtypes is different from previous reports. The detection rates with age increasing of serrated adenomas showed a steadily increased trend while HPs showed a light peak in 60–69 years old. Moreover, LSPs, especially large HPs, might be associated with an increased risk of sAN. Prospective studies may be necessary to evaluate the accurate prevalence and subtypes distribution of colorectal serrated polyps in Chinese population. This article may provide a reference for the future studies about Chinese colorectal serrated polyps.

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Conflicts of interest

There are no conflicts of interest.

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