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Prevalence of serrated polyps and their association with synchronous colorectal advanced adenomas

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HIGLIGHTS

- This study revealed a similar prevalence of clinically significant serrated polyps and advanced adenomas among patients who underwent colonoscopy.
- Multivariate analysis demonstrated an association between clinically significant serrated polyps and synchronous advanced adenomas, though the strength of this association was stronger for proximal advanced adenomas.
- Large serrated polyps and sessile serrated adenomas were associated with proximal advanced adenomas.

ABSTRACT – Background – Serrated lesions are the precursors of up to one-third of colorectal cancer (CRC) cases and share molecular and epidemiological features with interval CRC. Previous studies have reported wide variation in serrated polyp prevalence and diverse magnitude of its relationship with synchronous advanced adenomas. **Objective –** Describe the prevalence of serrated polyps and evaluate their association with synchronous advanced adenomas. **Methods –** The study is a retrospective analysis of 1208 colonoscopies performed in patients aged 45 to 75, predominantly for CRC screening. Data on the prevalence of serrated polyps subsets and advanced adenomas were collected, and multivariate analysis were performed to identify the association between serrated polyps and synchronous advanced adenomas. **Results –** The prevalence of clinically significant serrated polyps (CSSP), large serrated polyps (LSP), and sessile serrated adenomas (SSA) were 11.3%, 6%, and 3.7%. CSSP were associated with synchronous advanced adenomas (OR 2.121, 95%CI 1.321–3.406), regardless of proximal (OR 2.966, 95%CI 1.701–5.170) or distal (OR 1.945, 95%CI 1.081–3.499) location, while LSP (OR 2.872, 95%CI 1.425–5.787) and SSA (OR 5.032, 95%CI 2.395–10.576) were associated with proximal advanced adenomas. **Conclusion –** The prevalence of CSSP and advanced adenomas were alike. CSSP is a risk factor for advanced adenomas, and the strength of this association is stronger for proximal advanced adenomas. LSP and SSA are associated with proximal advanced adenomas.

Keywords – Cancer screening; colonic polyps/classification; colonic polyps/epidemiology; colonoscopy; colorectal cancer.

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INTRODUCTION

Colorectal cancer (CRC) is the third most common cause of cancer worldwide, and adenomatous polyps are the most common premalignant lesions for this neoplasia[1]. However, there is now unequivocal evidence that the serrated pathway may account for up to 30% of all cases, which leads the serrated polyps to be an important focus of CRC screening[2].

Serrated polyps are classified as hyperplastic polyp (HP), sessile serrated adenoma (SSA), and traditional serrated adenoma (TSA), according to World Health Organization criteria[3]. Different subtypes of serrated polyps have different molecular profiles and variable potential to develop into malignant disease[4], and individuals with large serrated polyps (LSP) have an increased risk of CRC, comparable with individuals with advanced adenomas[5]. Moreover, subsets of serrated polyps share molecular and epidemiological features with interval CRC[6,7], and this finding could be explained by their typical presentation, often quite subtle (flat lesions with indistinct borders), leading to significant variation in detection rates among endoscopists and to incompleteness of resection[8,9].

It is critical to determine the prevalence and clinical significance of serrated polyps in different continents with diverse CRC incidence and mortality rates to support appropriate screening and surveillance strategies. There is limited published data about the prevalence of serrated polyps in Brazil. To the best of our knowledge, no previous study has reported the association between serrated polyps and advanced adenomas in Latin America. The present study aimed to evaluate the prevalence of serrated polyps and their association with synchronous advanced adenomas in Southern Brazil.

METHODS

Patients

This study is a retrospective analysis of all routine colonoscopies performed by a single experienced gastroenterologist between 1 January 2014 and 31 December 2018.

We included all patients from 45 to 75 years of age regardless of the indication for colonoscopy. Exclusion criteria were patients with a personal history of CRC, history of colorectal resection for indications other than CRC, acute gastrointestinal bleeding, and high risk for CRC due to inflammatory bowel disease and familial adenomatous polyposis syndrome. This study was approved by the local Ethics Committee.

Colonoscopy

Conventional white light colonoscopes or high-definition colonoscopes with air insufflation were used. Standardized preparation included two bisacodyl tablets the day before colonoscopy and 500 mL of 20% mannitol diluted in 500 mL of juice 6 hours preceding colonoscopy. Colonoscopy reports were standardized for quality control, including photographic documentation of the appendiceal orifice, quality of bowel preparation, mean withdrawal time and detailed description of all detected lesions. The Paris classification was used for the morphological description of the polyps. Colonic mucosal surface evaluation and polyp removal were performed during colonoscope withdrawal.

Outcome variables

Data were collected on age, sex, indication for colonoscopy, and the location, size, and histology of all resected lesions. According to location, the lesions were classified as proximal colon (proximal to the splenic flexure) or distal colon (from the splenic flexure to the rectum). Regarding the size, they were classified as diminutive (≤5 mm), small (6–9 mm), or large (≥10 mm). Polyp detection rate (PDR) was defined as the proportion of colonoscopies with at least one polyp detected. Adenoma detection rate (ADR) was the proportion of colonoscopies with at least one adenoma detected. Advanced adenoma (AA) was defined as an adenoma ≥10 mm, with villous architecture (>25%) or high-grade dysplasia. Advanced adenoma detection rate (AADR) was the proportion of colonoscopies with at least one advanced adenoma detected. Serrated polyp detection rate (SPDR) was the proportion of colonoscopies with at least one serrated polyp detected. Clinically significant serrated polyps (CSSP) were SSA, TSA, HP ≥10 mm anywhere in the colon, or HP >5 mm proximal to the sigmoid. Clinically significant serrated polyp detection rate (CSSPDR) was the proportion of colonoscopies with at least

one CSSP detected. Large serrated polyp detection rate (LSPDR) was the proportion of colonoscopies with at least one serrated polyp ≥10 mm detected. Sessile serrated adenoma detection rate (SSADR) was the proportion of colonoscopies with at least one sessile serrated adenoma detected.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software, version 16 (Statistical Package for the Sciences – SPSS Inc., Chicago, IL, USA). Categorical variables were presented as numbers and percentages and compared using the chi-square test. Continuous variables were presented as means with standard deviations and analyzed by using *t* test. The prevalence rate was defined as the proportion of individuals with at least one determined lesion detected. Association between serrated polyps and advanced adenomas was evaluated by multivariate analyses, adjusted by age and sex, and presented using odds ratio (OR) and 95% confidence interval (CI). A *P* value <0.05 was considered to be statistically significant.

RESULTS

The study analyzed 1208 colonoscopies. The average patient age was 58.7 years (±7.7 years), and 74.3% of the patients were female (TABLE 1). The indications for colonoscopy were screening (64%), surveillance (18.4%), and diagnostic (17.6%). The PDR, ADR, AADR, and SPDR were 67.6%, 42.9%, 10.9%, and 33.6%, respectively, with significant differences between male and female patients (TABLE 2). Colorectal cancer was detected in 1.2% of the patients.

Once one adenoma was identified, the mean number of adenomas per positive patient was 2.4 among men and 1.9 among women. Furthermore, since one serrated polyp was detected, male and female individuals presented a mean number of serrated polyps per positive patient of 1.7 and 1.6, respectively.

A multivariate analysis, including age (≥60 years old), gender (male), and indication for colonoscopy (not screening), showed that only age was associated with the presence of serrated polyps (OR 1.562; 95%CI, 1.029–2.371).

TABLE 1. Characteristics of patients included in the study.

	Total	Male	Female
Number of colonoscopies, n (%)	1208 (100%)	310 (25.7%)	898 (74.3%)
Age, mean (s.d.)	58.7 (7.7)	59.1(7.6)	58.5(7.7)
Age range, n (%)			
45–49 yr	131 (10.8%)	27(8.7%)	104 (11.6%)
50–59 yr	556 (46.0%)	133 (42.9%)	423 (47.1%)
60–69 yr	390 (32.3%)	117 (37.7%)	273 (30.4%)
70–75 yr	131 (10.8%)	33 (10.6%)	98 (10.9%)

TABLE 2. Prevalence of lesions detected by colonoscopy.

	Total	Male	Female	OR (95%CI)	*P*
PDR	816 (67.6%)	233 (75.2%)	583 (64.9%)	1.635 (1.221–2.189)	0.001
ADR	518 (42.9%)	165 (53.2%)	353 (39.3%)	1.757 (1.354–2.279)	0.000
AADR	132 (10.9%)	49 (15.8%)	83 (9.2%)	1.843 (1.261–2.695)	0.002
SPDR	406 (33.6%)	114 (36.8%)	292 (32.5%)	1.373 (1.041–1.812)	0.024
CSSPDR	137(11.3%)	38 (12.3%)	99 (11.0%)	1.128 (0.757–1.680)	0.555
LSPDR	73 (6%)	18 (5.8%)	55 (6.1%)	0.945 (0.546–1.635)	0.839
SSADR	45 (3.7%)	12 (3.9%)	33 (3.7%)	1.056 (0.538–2.070)	0.875

PDR: polyp detection rate; ADR: adenoma detection rate; AADR: advanced adenoma detection rate; SPDR: serrated polyp detection rate; CSSPDR: clinically significant serrated polyp detection rate; LSPDR: large serrated polyp detection rate; SSADR: sessile serrated adenoma detection rate.

The prevalence of CSSP, LSP and SSA were 11.3%, 6% and 3.7%, with similar results among subjects of both genders (TABLE 2). Among 137 patients with at least one CSSP, 73 (53,3%) presented large serrated polyps, and among 45 patients with at least one SSA, 13 (28.9%) presented large SSA.

In the studied population, three patients (0.3%) presented five or more serrated polyps, all being at least 5 mm in size, two of these polyps ≥10 mm, reaching the criteria for serrated polyposis syndrome[10].

Predictors of advanced adenoma in patients with serrated polyps

The multivariate analysis demonstrated that CSSP and SSA were significantly associated with synchronous advanced adenomas. Since clinical and biological differences exist between colorectal neoplasia in the proximal and distal colon[11,12], we analyzed the association between serrated polyps and synchronous advanced adenomas at these segments. Clinically significant serrated polyps were associated with synchronous advanced adenomas at both sites (proximal colon: OR 2.966, 95%CI 1.701–5.170; distal colon: OR 1.945, 95%CI 1.081–3.499). Large serrated polyps and SSA were associated with proximal advanced adenomas, with an approximately threefold and fivefold increased risk, respectively (TABLE 3).

DISCUSSION

Serrated lesions are the precursors of up to one-third of CRCs and account for a disproportionate fraction of cancer identified after colonoscopy. An expert panel suggests that all serrated lesions proximal to the sigmoid colon and all serrated lesions in the rectosigmoid larger than 5 mm in size should be completely removed. However, closer surveillance intervals are recommended only for clinically significant serrated polyps[2].

Although previous studies have observed variation in serrated polyp detection rates[13,14] and a CSSPDR benchmark has not yet been recommended, a systematic review of 74 colonoscopy studies demonstrated a mean CSSP prevalence of 12.3% (9.3–15.4%)[15]. A recent large retrospective observational study at five institutions in the United States concluded that among endoscopists with adequate ADR (median 43%), the median CSSPDR was 8.4% (7.3–11.4%), and the median AADR was 9.3% (6.4–12.6%)[16]. Moreover, according to Anderson JC et al.[17], CSSPDR varied from 1.3% for endoscopists with ADR <15% to 10% for endoscopists with ADR ≥35%. All these findings corroborate the results of the present study, which describes ADR of 42.9% and CSSPDR of 11.3%.

The SSADR was 3.7%, and 28.9% of the SSA were classified as large size, analogous to the results of Meester RGS et al.[15], that described a pooled SSA prevalence of 4.6% (2.6–10.5%), and 19.3% of the SSA presented with a diameter of 10 mm or more.

The studied population presented a serrated polyposis syndrome (SPS) prevalence of 0.3%. In European screening populations, the prevalence of SPS varies from 0% to 0.7%[18], and the Netherlands primary colonoscopy cohort described a 0.4% overall rate[19].

TABLE 3. Serrated polyps as predictive factors for advanced adenomas (multivariate analysis).

	AA OR (95%CI) †	AAp OR (95%CI) †	AAd OR (95%CI) †
Any serrated polyp			
No	1	1	1
Yes	1.395 (0.960–2.028)	1.287 (0.792–2.091)	1.618 (1.018–2.573)*
CSSP			
No	1	1	1
Yes	2.121 (1.321–3.406)**	2.966 (1.701–5.170)***	1.945 (1.081–3.499)*
LSP			
No	1	1	1
Yes	1.780 (0.941–3.367)	2.872 (1.425–5.787)**	1.754 (0.803–3.830)
SSA			
No	1	1	1
Yes	2.209 (1.053–4.634)*	5.032 (2.395–10.576)***	1.632 (0.616–4.324)

AA: advanced adenoma; AAp: proximal advanced adenoma; AAd: distal advanced adenoma; CSSP: clinically significant serrated polyp; LSP: large serrated polyp; SSA: sessile serrated adenoma. †Odds ratio adjusted by age and gender. *P<0.05; **P<0.01; ***P<0.001.

Thereafter, the prevalence of CSSP, LSP, SSA, and SPS in Southern Brazil is similar to those of developed countries.

Age above 60 years was an independent predictor of serrated polyps, and the mean number of serrated polyps per positive patient was 1.6; therefore, since one serrated polyp is identified, further careful inspection frequently results in the detection of other serrated polyps.

This study demonstrated that CSSP are a risk factor for advanced adenomas, and the strength of this association is stronger for proximal advanced adenomas. Additionally, we found that LSP and SSA are associated with proximal advanced adenomas.

The proposed serrated pathway in colorectal carcinogenesis is HP→ SSA→ dysplastic SSA→ cancer[4], and there is evidence of a progressive increase in CIMP-high, MSI-high, and BRAF mutations from the distal to the proximal colon[20]. Interval CRC is 2.4 times more frequent in the proximal colon and shares many of the molecular and biological mechanisms of the serrated pathway[2,5]. Previous studies have demonstrated that a high adenoma detection rate reduces the risk of interval CRC[21,22]; however, removing adenomas without adequate resection of serrated polyps may not sufficiently avoid interval CRC. Thus, quality indicators in colonoscopy should include CSSPDR.

Some limitations in our study should be mentioned. First, it was a retrospective single endoscopist study. Second, the pathologic criteria for the diagnosis of serrated polyps were not reviewed by a single pathologist, and the literature describes only moderate interobserver agreement, even among expert pathologists, in the diagnosis of serrated colonic lesions using expert panel recommendations[23]. Finally, screening was not the only colonoscopy indication; however, Rex DK et al.[24] have pointed out that all indications can be used to derive the serrated polyp detection rate and adenoma detection rate.

In conclusion, this study demonstrated that the prevalence of CSSP, LSP, and SSA in Southern Brazil is near those described in literature from developed countries. These lesions were similarly distributed among men and women, with a higher prevalence of serrated polyps among patients with age ≥60 years. The prevalence of CSSP and advanced adenomas were alike. The identification of at least one CSSP represented a threefold increase in synchronous proximal advanced adenoma detection and a twofold increase in synchronous distal advanced adenoma detection. Furthermore, LSP and SSA were associated with a threefold and fivefold increase in synchronous proximal advanced adenomas, respectively. These results suggest that CSSP should be considered a marker of synchronous advanced adenomas. Future studies are needed to elucidate the impact of CSSPDR on colorectal cancer prevention.

Author's contribution

Meine GC: conceived and designed the analysis; collected the data; performed the analysis; wrote the paper and Sander GB: conceived and designed the analysis; revised the paper critically for important intellectual content.

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Meine GC, Sander GB. Prevalência de pólipos serrilhados e sua associação com adenomas avançados colorretais síncronos. Arq Gastroenterol. 2023;60(2):224-9.

RESUMO – Contexto – Lesões serrilhadas são precursoras de até um terço dos casos de câncer colorretal (CCR) e compartilham características moleculares e epidemiológicas com o CCR de intervalo. Estudos prévios relataram ampla variação na prevalência de pólipos serrilhados e na magnitude da sua relação com adenomas avançados sincrônicos. **Objetivo –** Descrever a prevalência de pólipos serrilhados colorretais e avaliar sua associação com adenomas avançados sincrônicos. **Métodos –** O estudo é uma análise retrospectiva de 1208 colonoscopias realizadas em pacientes com idades entre 45 e 75 anos, predominantemente para rastreamento de CCR. Dados sobre a prevalência de subtipos de pólipos serrilhados e de adenomas avançados foram coletados, e análises multivariadas foram realizadas para identificar a associação entre pólipos serrilhados e adenomas avançados sincrônicos. **Resultados** – A prevalência de pólipos serrilhados clinicamente significativos (PSCS), pólipos serrilhados grandes (PSG) e adenomas sésseis serrilhados (ASS) foi de 11,3%, 6% e 3,7%, respectivamente. PSCS foram associados a adenomas avançados sincrônicos (OR 2,121, IC95% 1,321–3,406), independentemente da localização proximal (OR 2,966, IC95% 1,701–5,170) ou distal (OR 1,945, IC95% 1,081–3,499), enquanto PSG (OR 2,872, IC 95%1,425–5,787) e ASS (OR 5,032, IC95% 2,395–10,576) foram associados a adenomas avançados proximais. **Conclusão —** A prevalência de PSCS e de adenomas avançados foi semelhante. PSCS é um fator de risco para adenomas avançados, e a força dessa associação é maior para adenomas avançados proximais. PSG e ASS estão associados a adenomas avançados proximais.

Palavras-chave – Rastreamento de câncer; pólipos colônicos/classificação; pólipos colônicos/epidemiologia; colonoscopia; câncer colorretal.

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