

Benedito Rodrigues da Silva Neto
(Organizador)

MEDICINA:



A ciência e a tecnologia em busca da cura

4


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Editora
Ano 2021

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APRESENTAÇÃO

Ciência é uma palavra que vem do latim, “*scientia*”, que significa conhecimento. Basicamente, definimos ciência como todo conhecimento que é sistemático, que se baseia em um método organizado, que pode ser conquistado por meio de pesquisas. Já a tecnologia vem do grego, numa junção de “*tecno*” (técnica, ofício, arte) e “*logia*” (estudo). Deste modo, enquanto a ciência se refere ao conhecimento, a tecnologia se refere às habilidades, técnicas e processos usados para produzir resultados.

A produção científica baseada no esforço comum de docentes e pesquisadores da área da saúde tem sido capaz de abrir novas fronteiras do conhecimento, gerando valor e também qualidade de vida. A ciência nos permite analisar o mundo ao redor e ver além, um indivíduo nascido hoje num país desenvolvido tem perspectiva de vida de mais de 80 anos e, mesmo nos países mais menos desenvolvidos, a expectativa de vida, atualmente, é de mais de 50 anos. Portanto, a ciência e a tecnologia são os fatores chave para explicar a redução da mortalidade por várias doenças, como as infecciosas, o avanço nos processos de diagnóstico, testes rápidos e mais específicos como os moleculares baseados em DNA, possibilidades de tratamentos específicos com medicamentos mais eficazes, desenvolvimento de vacinas e o consequente aumento da longevidade dos seres humanos.

Ciência e tecnologia são dois fatores que, inegavelmente, estão presentes nas nossas rotinas e associados nos direcionam principalmente para a resolução de problemas relacionados à saúde da população. Com a pandemia do Coronavírus, os novos métodos e as possibilidades que até então ainda estavam armazenadas em laboratórios chegaram ao conhecimento da sociedade evidenciando a importância de investimentos na área e consequentemente as pessoas viram na prática a importância da ciência e da tecnologia para o bem estar da comunidade.

Partindo deste princípio, essa nova proposta literária construída inicialmente de quatro volumes, propõe oferecer ao leitor material de qualidade fundamentado na premissa que compõe o título da obra, isto é, a busca de mecanismos científicos e tecnológicos que conduzam o reestabelecimento da saúde nos indivíduos.

Finalmente destacamos que a disponibilização destes dados através de uma literatura, rigorosamente avaliada, fundamenta a importância de uma comunicação sólida e relevante na área da saúde, assim a obra “Medicina: A ciência e a tecnologia em busca da cura - volume 4” proporcionará ao leitor dados e conceitos fundamentados e desenvolvidos em diversas partes do território nacional de maneira concisa e didática.

Desejo uma ótima leitura a todos!


Benedito Rodrigues da Silva Neto

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EVALUATION OF THE SERRATED LESIONS DETECTION RATE AND ITS ROLE AS A COLONOSCOPY QUALITY CRITERIA

Data de aceite: 01/12/2021

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ABSTRACT: Objectives To evaluate the serrated lesion detection rate in colonoscopy at a specialized clinic and its role as quality criteria for endoscopic examination. Methods This is an observational cross-sectional study with all patients that underwent colonoscopy between October 2018 and May 2019, performed by an experienced physician. A questionnaire was answered before the examination by the patient, and another questionnaire after the colonoscopy was answered by the medical team. All polyps identified were removed and sent to the same pathologist for analysis. Results A total of 1,000 colonoscopies were evaluated. The average age of the patients was 58.9 years old, and most of them were female (60.6%). In 62.5% of the procedures, polyps were removed, obtaining a total of 1,730 polyps, of which 529 were serrated lesions, being 272 sessile serrated lesions (SSL). This data resulted in a serrated lesion detection rate (SDR) of 29.2%, and of

14% when considering only the SSL detection rate (SSDR). The right colon had higher rates, with 22.3% SDR and 15.3% SSDR. Screening colonoscopies also presented a higher serrated detection rate, of 20%, followed by diagnostics and follow-up exams. Smoking was the only risk factor associated with higher serrated detection rate. Conclusions The serrated lesion detection rate is higher than the ones already previously suggested and the higher rates were established in the right colon and on screening exams.

KEYWORDS: Colonoscopy, colorectal cancer, polyps.

RESUMO: Objetivos Avaliar a taxa de detecção de lesões serrilhadas na colonoscopia em clínica especializada e seu papel como critério de qualidade para o exame endoscópico. Métodos Trata-se de um estudo transversal observacional com todos os pacientes submetidos à colonoscopia entre outubro de 2018 e maio de 2019, realizada por médico experiente. Um questionário foi respondido antes do exame pelo paciente, e outro questionário após a colonoscopia foi respondido pela equipe médica. Todos os pólipos identificados foram removidos e enviados ao mesmo patologista para análise. Resultados Um total de 1.000 colonoscopias foram avaliadas. A idade média dos pacientes era de 58,9 anos, sendo a maioria do sexo feminino (60,6%). Em 62,5% dos procedimentos, os pólipos foram removidos, obtendo-se um total de 1.730 pólipos, dos quais 529 eram lesões serrilhadas, sendo 272 lesões serrilhadas sesséis (SSL). Esses dados resultaram em uma taxa de

detecção de lesão serrilhada (SDR) de 29,2%, e de 14% quando considerada apenas a taxa de detecção SSL (SSLDR). O cólon direito apresentou taxas mais elevadas, com 22,3% de SDR e 15,3% de SSLDR. As colonoscopias de triagem também apresentaram maior taxa de detecção serrilhada, de 20%, seguida de diagnósticos e exames de acompanhamento. O tabagismo foi o único fator de risco associado a uma maior taxa de detecção serrilhada. Conclusões A taxa de detecção da lesão serrilhada é maior que as já sugeridas anteriormente e as maiores taxas foram estabelecidas no cólon direito e nos exames de rastreamento.

KEYWORDS: Colonoscopia, câncer colorretal, pólipos.

INTRODUCTION

Colorectal cancer (CRC) is the third most common cause of cancer, when excluding skin cancer, and the fourth most common cause of death by cancer worldwide. There were ~1.8 million new cases in 2018, and > 800,000 deaths in the same year, corresponding to 10.2% of all cancers diagnosed.¹ From a morphologic point of view, CRC develops following two main pathways: adenomatous and serrated. The first one is well known and studied by the medical community; it arises through an adenoma-carcinoma sequence and is responsible for 60% of sporadic cancers.²

The second one, the serrated pathway, is gaining notoriety recently and is considered responsible for between 20 and 30% of sporadic CRCs. It has, in the epigenetic instability, also known as CpG Island Methylator phenotype, its main mechanism.^{3,4} Serrated lesions (SL) are the precursors of this pathway and are classified as: hyperplastic polyps (HP), which usually are < 5mm, flat, and have a star-shaped crypt when identified with chromoendoscopy; sessile serrated lesions (SSL) with or without dysplasia, which are also flat, covered with a mucus cap, may present depressed areas, have an open shaped crypt, cloud shape surfaces, and irregular boundaries. Traditional serrated adenoma (TSA) and unclassified serrated adenoma are usually pedunculated and similar to conventional adenoma lesions.^{5,6}

Colonoscopy has high sensibility and specificity and is considered the gold standard test for CRC screening in the United States. Patients that underwent at least one colonoscopy in the past 10 years have a much lower risk of having CRC.⁷

Besides the progress achieved with colonoscopy in preventing CRC, between 5 and 9% of the patients with this malignant neoplasm have had a colonoscopy considered as normal performed in the past 3 years that preceded their diagnosis. Therefore, they were labeled as carriers of interval cancer.⁸

Interval cancer is strongly related to SL, since the serrated pathway leads to CRC in a shorter period and these types of lesions are usually flat, depressed, and covered with mucus cap, which makes them harder to be identified and removed.⁹ The location in the proximal colon and the presence of epigenetic instability are also factors that reassure the association between SL and this type of cancer.¹⁰

The literature shows that the detection of SL varies significantly and is endoscopist-related.¹¹ It has been noticed that the prevalence of these lesions, especially of SSLs, which have a higher malignant potential, presents an important variation among medical centers and endoscopists, so the numbers presented in the literature seem to be lower than those observed on a daily practical basis.¹²

It is also known that the risk of advanced adenomas is lower in patients who have undergone a previous colonoscopy, although this same effect is not seen in patients with SL; therefore, colonoscopy shows to be more effective in the prevention of cancers arising from the adenomatous pathway than from the serrated pathway.¹³

The establishment of an endoscopic quality criteria that quantifies the adenoma detection rate (ADR) turned up to be really effective in obtaining good results regarding the prevention of CRC emerging from the adenomatous pathway.^{7,8}

However, for the SL, a detection rate to be achieved has not been defined yet. In this scenario, some studies indicate that more than half of the SLs in the right colon are not identified by most endoscopists, and that, in average, 25% of the lesions are not detected.¹⁴

This important gap between data from different medical centers and specialists shows the need to bring awareness to the importance of proper diagnosing and removal of SLs. The establishment of a minimum rate to be reached could encourage doctors and help to improve these data.¹⁵

In the present research, we aimed to evaluate the serrated lesions detection rate (SDR) in colonoscopies performed in a specialized center and its role as a quality criterion in endoscopic exams.

METHODS

A cross-sectional observational study was performed with patients that underwent colonoscopy in a specialized center in Campinas, state of São Paulo, Brazil, between October 2018 and May 2019, by one experimented endoscopist.

The present study was approved by the ethical committee of research in human beings from PUC-CAMPINAS, under the file number 2.908.718, and all patients were asked to sign a Free and Informed Consent Term.

The exams were executed following the American Society for Gastrointestinal Endoscopy (ASGE)¹⁶ quality criteria and had imaging enhanced technology used or second forward view examination performed, when necessary.

Data was compiled with help from two questionnaires, one answered by the patients, informing about symptoms, alcohol intake, previous colonoscopies, family history of CRC, obesity, smoking habits, diabetes, physical activity, and other variables.

A second questionnaire was answered by the medical team at the end of the exams, providing information about the lesions removed, the Boston Bowel Preparation Scale, the

duration of the procedure, the withdraw time, among other variables.

All lesions identified were sent to be analyzed by a single gastrointestinal expert pathologist, except from the non-removable ones, for which biopsies were performed. They were classified by proximal or distal location to the splenic flexure. Hyperplastic areas on the sigmoid and rectum, defined as areas with multiple diminutive polyps with hyperplastic aspect shown by enhanced imaging techniques, were not removed or biopsied, following the ASGE recommendations.¹⁷

Patients < 18 years old, those who did not accept to be a part of the research, who did not sign the consent term, who did not answer the questionnaire or did so in an incomplete way were excluded from the research. Colonoscopies with a score < 6 in the Boston Scale, incomplete, not reaching the cecum, and with < 6 minutes of withdraw time were also removed from data.

For all the statistics analysis, the significance level was defined as 5%. The Student *t*-test was used to compare averages; the chi-squared test and the Poisson regression were used for univariate data analysis. IBM SPSS Statistics for Windows (IBM Corp., Armonk, NY, USA), R software (R Foundation, Vienna, Austria), and Microsoft Excel (Microsoft Corp., Redmond, WA, USA) were chosen to assist on the analysis.

RESULTS

During the predetermined period, 1,000 colonoscopies fulfilled the inclusion criteria for the research.

The mean age of the patients was 58.9 years old, with a standard deviation (SD) of 13.2 years; 60.6% of the patients were female.

Polypectomies were performed in 62.5% of the patients, providing a total of 1,730 polyps. Adenomatous polyps (AP)

		Gender		
Detection Rate	Combined	Female	Male	p-value
ADR	51.7%	48.5%	56.5%	0.961
SDR	29.2%	28.8%	30.4%	
SSLDR	14.0%	15.6%	11.4%	

Abbreviations: ADR, adenoma detection rate; SDR, serrated lesion detection rate; SSLDR, sessile serrated lesion detection rate.

Table 1 Polyps detection rate by histological type and patient gender

represented 69.5% of all polyps. A total of 529 lesions were SLs, including HPs and SSLs, which corresponded to 30.5% of the polyps. No TSA was diagnosed. Sessile serrated lesions had a prevalence of 15.7%. Adenocarcinoma was found in 0.9% of the patients.

The combined ADR was of 51.7%, being 56.5% among males and 48.5% among females.

At least 1 SL was identified in 292 patients, providing an SDR of 29.2%, as shown in ► Table 1. Considering only SSLs, the combined detection rate was of 14.0%, with 15.6% in females and 11.4% in males; however, there was no statistical significance that related gender and a higher SSLDR ($p = 0.961$).

The diagnosis investigation was the indication for colonoscopy in 48% of the patients, surveillance was responsible for 40% of the exams, and CRC screening for only 12% of the exams. According to ► Table 2, the SSLDR is highest on screening exams (20,0%) ($p = 0.015$).

Regarding the location on the colon, APs were found in the proximal colon in 69.1% of the cases. In the SL group, 55.1% were in the proximal colon, and when only SSLs were considered, 84,9% were in the proximal colon. As demonstrated, there was a higher possibility of identifying an SSL in the proximal colon, as seen on ► Fig. 1 ($p < 0.001$).

The detection rates calculated are shown in ► Table 3. We can observe that, when calculated for SLs, the SDR was of 22.3% and the SSLDR was of 15.3% on the proximal colon, emphasizing that location in the proximal colon is related to a higher SSLDR ($p < 0.001$).

Patients with multiple diminutive polyps in the rectum that appeared to be hyperplastic, as in ► Fig. 2, did not have biopsies performed; therefore, they were not considered as having SLs. This scenario was found in 10% of the patients.

Through a univariate analysis of risk factors linked with SLs, only smoking was associated with a higher risk of developing SLs (PR: 1.18; 95% confidence interval [CI]: 1.00–1.40). Skin color, obesity, alcohol intake, physical activity, diabetes, and use of anti-inflammatories did not present statistical significance.

DISCUSSION

Serrated lesions were seen as benign until a few years ago. They represent a challenge for the endoscopists nowadays, corresponding to up to 30% of sporadic CRCs.⁷ The flatter shape, the fact that they are more often located in the proximal colon, and the presence of a mucus cap covering these lesions make their identification during colonoscopy quite difficult.¹⁸

With a well-defined role on the prevention of CRC, colonoscopy stills needs improvement so that we can identify even more lesions and downsize the impact of interval cancer.

The SDR, besides being as important as the ADR in the prevention of CRC, still does not have a value to be reached defined by specialists, and the attempts of suggesting values varies from 1.5 to 10% in the literature.^{19,20} According to the data obtained in our study,

we can imply that performing colonoscopy following quality criteria, with high-definition colonoscopes, and by an experimented endoscopist, the lesion detection rate will be much higher than expected.

In our data, the ADR was of 51.7%, 2 times higher than the minimum established by the ASGE.¹⁶ When evaluating SLs, the SDR was of 29.2%, and in 140 patients, at least 1 SSL, which has a higher malignifying potential, was detected, establishing an SSLDR of 14.0%.

According to previous studies, the prevalence of SLs varies considerably.^{12,21,22} In a review from researches performed between 2003 and 2014, the prevalence varied from 0.6 to 5.3%.²³ In a systematic review, the average prevalence was of 4% and it varied from 0 to 20%.²⁴

There were some attempts to develop an SDR, as it was done for the adenomas. A multicenter study suggested a 5% SDR, considering only proximal colon lesions; the endoscopists with best results had an SDR of up to 20%,²⁰ while in our study we had a 22.3% SDR considering the same findings. In contrast, Vleugels et al. came up with a 10% value of SDR to be pursued;²⁵ however, considering lesions from the whole colon, our results demonstrated a 29.2% SDR in this scenario.

	Indication						<i>p-value</i>
	Screening		Surveillance		Diagnosis		
Detection Rate	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
ADR	77	64.16%	261	65.25%	199	41.45%	0.818
SDR	43	35.83%	139	34.75%	111	23.12%	0.621
SSLDR	24	20.0%	60	15.0%	55	11.45%	0.015

Abbreviations: ADR, adenoma detection rate; SDR, serrated lesion detection rate; SSLDR, sessile serrated lesion detection rate.

Table 2 Polyp detection rate by polyp histological type and exam indication

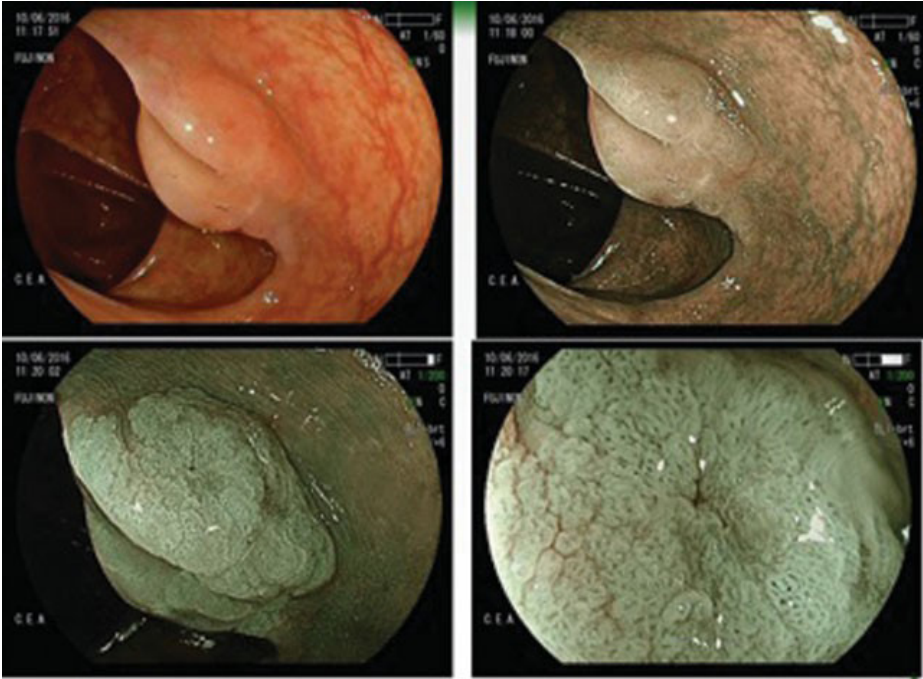


Fig. 1 Sessile serrated lesion identified on the proximal colon; colonoscopy performed with assistance of Blue Light Imaging technology.

	Location		<i>p</i> -value
	Proximal colon	Distal colon	
Detection Rate	%	%	< 0.001
ADR	42.3%	24.8%	
SDR	22.3%	10.8%	
SSLDR	15.3%	2.5%	

Abbreviations: ADR, adenoma detection rate; SDR, serrated lesion detection rate; SSLDR, sessile serrated lesion detection rate.

Table 3 Polyp detection rate by the location in the colon

Another research suggested an 11% SDR and a 7% SSLDR, and concluded that using the SDR with all the SLs was easier to adjust to a daily basis, without damaging the results, given that both rates are directly related.¹⁹ Besides suggesting values much lower than those we have identified, this conclusion does not transfer to our reality, considering that we had a very important difference between a 29.2% SDR and a 14% SSLDR, even though they are correlated ($p < 0.001$). Using only the SDR to evaluate the endoscopist's performance, considering all SLs, could generate a false sense of prevention, since these lesions have different malignant potential, and a high SDR could be secondary to a high prevalence of HPs that are not the main focus on preventing CRC arising from the serrated pathway.

Analyzing several studies available, it is clear that, before setting an SDR, it is

mandatory to define which sample of lesions and patients will be considered. The different methodologies used, considering different types of SLs and the

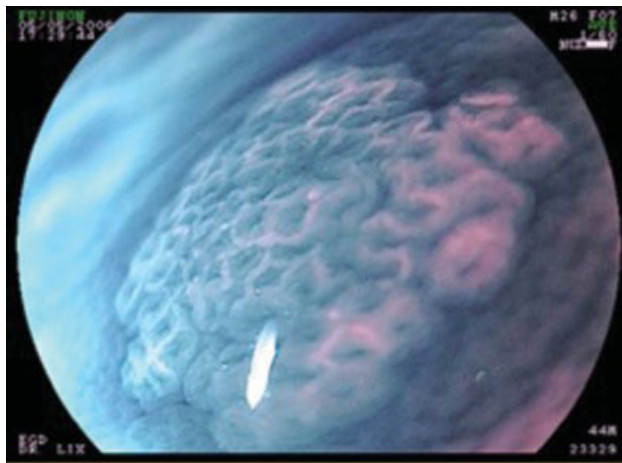


Fig. 2 Hyperplastic polyp diagnosed with chromoendoscopy and enhanced imaging technique.

location on proximal or on the whole colon, all these points makes the comparisons between data hard to be unbiased. Another point that needs to be highlighted is that the population studied to define ADR consisted of screening patients; in other words, asymptomatic patients, aged > 50 years old, and who were undergoing their first colonoscopy.

This is a limited population, which makes it harder for the endoscopist to use the same data on their practice.

Anderson et al. compared a group of screening colonoscopies with surveillance ones. While there was an important difference in the detection rate for adenomas, the same difference was not significant when the SDR was evaluated.¹³

Therefore, using an SDR in a common population would be an option.

However, in our study, when the SSLDR was evaluated only on screening patients, a higher value was found (20.0%) ($p \approx 0.015$). In this scenario, using a screening population to define the detection rate would generate a higher rate to be achieved than the one expected to be found in a common population.

When considering results from studies that evaluated the performance of a single experimented endoscopist, in 2 of them the ADRs were of 47.8 and 48%, and the SSLDRs were of 8.1 and 20%.^{23,26} Results from a single doctor experiment, just like the present study, seems to present a higher SSLDR. Gathering information from only one endoscopist provides more control of the variants that could generate bias, such as the colonoscopy techniques applied, the quality of the exam performed, as well as the level of experience of the examiner; as Schramm et al. described, the personal ability of the endoscopist has

an important role in having a high SSLDR.²⁷ The literature shows that endoscopists with higher ADRs tend to have higher SDRs and SLLDRs, which could be one of the reasons for finding higher SDRs and SSLDRs in our data. Considering that the ADR was two times higher than the benchmark, a bigger attention to seek adenomas would also allow to identify more SLs.^{21,28} The use of image-enhancing technologies, when there was a doubt regarding the features of the mucosa, is also a factor that could have increased the detection rates, especially of flat lesions that could have been undetected.⁹

Female patients had a higher SDR than males, 15.6 and 11.4%, respectively, but this difference did not have statistical significance ($p = 0.961$). Prior studies have divergent results regarding a higher prevalence of SLs among males or females.

Tumors with epigenetic instability, a factor highly related to the serrated pathway, are more common in females and in proximal colon lesions.²⁹ Meanwhile, some reports highlight a higher SDR in males,²¹ and in a review with 60,000 colonoscopies, there was no important difference on the prevalence of SLs among men and women.²⁴

The SLs were located proximal to the splenic flexure in 68.2% of the cases; regarding SSLs, the number corresponded to 85.4% of the lesions. The SDR and SSLDR were also higher when calculated considering only proximal lesions (22.3 and 15.3%, respectively) ($p < 0.001$). This finding may also be associated with the nonresection of diminutive hyperplastic polyps on the distal colon, affecting 10% of the patients, which reduces the frequency of lesions being removed on the left side. It is known that SLs are more often found on the proximal colon, and that the SSLDR is higher when only proximal lesions are considered.¹⁸

Among the risk factors associated with SLs, only smoking was linked to a bigger chance of having these lesions (PR: 1.18; 95%CI: 1.00–1.40). As other studies have already reported, smoking is a risk factor for all types of polyps, but specially for SLs, enhancing twofold the risk of developing them. However, in disagreement with other research, obesity, alcohol intake, and skin color were not associated with a higher risk in our results.³⁰

Considering the high detection rates obtained, it is possible to imply that a lot of SLs are being undetected during exams, contributing to the rise in incidence of interval cancer. With a higher SDR and SSLDR, colonoscopy can be as effective in preventing cancer developing from SL on the proximal colon as it already is for AP on the distal colon.¹⁸

The present study has some limitations: the fact that the colonoscopies were performed by a single experienced endoscopist allows for a more standardized protocol for the performance of exams, helping to have data with less biases; however, the analysis of data embracing results from other specialists, in different hospitals, with different levels of expertise, would bring richer information to be analyzed. Besides the several advantages of a prospective study, the endoscopist was aware of the research, which may have impacted, even if involuntarily, the execution of the exams. Having a single expert pathologist analyzing the samples gives a high rate of identified SLs, but at the same time, considering multiples disagreement between pathologists on the diagnosis of these lesions can also be a limiting

factor to our results.

CONCLUSION

With the present study, we can conclude that smoking is a risk factor for developing SLs. The SDR and SSLDR are higher than previously suggested, and are even higher when only proximal colon lesions on patients undergoing screening colonoscopy are analyzed. This reassures the need of well- established benchmarks for SL detection, so the number of undetected lesions on colonoscopy can decrease.

CONFLICT OF INTERESTS

The authors have no conflict of interests to declare.

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


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