Publication status: Not informed by the submitting author

ARE SUPERFICIAL SERRATED LESIONS IN EARLY STAGES HYPERPLASTIC OR SESSILE SERRATED LESIONS?

Matheus Degiovani , Osvaldo Malafaia, Artur Adolfo Parada , Fernando Issamu Tabushi , Marcos Fabiano Sigwalt , Paulo Afonso Nunes Nassif , Luiz Martins Collaço, Cláudio Luciano Franck

https://doi.org/10.1590/SciELOPreprints.8352

Submitted on: 2024-03-28
Posted on: 2024-03-28 (version 1)
(YYYY-MM-DD)

Original Article

ARE SUPERFICIAL SERRATED LESIONS IN EARLY STAGES HYPERPLASTIC OR SESSILE SERRATED LESIONS?

LESÕES SERRILHADAS SUPERFICIAIS NAS FASES INICIAIS SÃO HIPERPLÁSICAS OU LESÕES SÉSSEIS SERRILHADAS?

Matheus Degiovani[1,2], Osvaldo Malafaia[1], Artur Adolfo Parada[2], Fernando Issamu Tabushi[1], Marcos Fabiano Sigwalt[1], Paulo Afonso Nunes Nassif[1], Luiz Martins Collaço[1], Cláudio Luciano Franck[1]

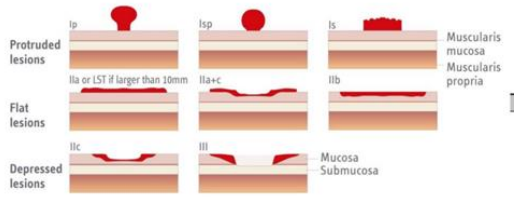
Author´s affiliation: [1]Faculdade Evangélica Mackenzie do Paraná, Curitiba, PR, Brasil; [2]Center for Endoscopic Diagnosis and Therapeutics of São Paulo, 9 de Julho Hospital, São Paulo, SP, Brasil.

ORCID
Matheus Degiovani - https://orcid.org/0000-0002-8242-5314
Osvaldo Malafaia - https://orcid.org/0000-0002-1829-7071
Artur Adolfo Parada - https://orcid.org/0000-0002-3563-7998
Fernando Issamu Tabushi - https://orcid.org/0000-0002-3150-2164
Marcos Fabiano Sigwalt - https://orcid.org/0000-0002-9899-5493
Paulo Afonso Nunes Nassif - https://orcid.org/0000-0002-1752-5837
Luiz Martins Collaço - https://orcid.org/0000-0002-3215-1650
Cláudio Luciano Franck - https://orcid.org/0000-0002-4326-8109

Corresponding Author:
Matheus Degiovani
Email: degiovani.endoscopia@gmail.com

Conflict of interest: The authors declare that there are no conflicts of interest.
Financial Source: Partly by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brazil (CAPES) – Financial code 001

Image



Paris classification of the superficial lesions of the colon

Central Message

Currently, it is supposed that at least 20% of colorectal adenocarcinomas arise from serrated lesions. The diagnosis and study of these lesions during the early stages are important in colorectal cancer prevention. Thus, it is important to know how to analyze and compare the endoscopic and histopathological elements of the serrated lesions resected by colonoscopies. This study aims to offer their classification to improve the prognosis predictions and the risk of malignant transformations.

Perspective

For many years, all lesions identified during colonoscopies have been completely resected. Despite the lack of long follow-up of these lesions, there are no ways to ensure the percentage of them that develop into carcinomas. It is recommended that the advanced lesion´s nature is pointed out and the need to continue the short-term endoscopic follow-up to verify if the lesion has been completely resected. Remember, lesions larger than 7mm that present structural changes must be resected completely, ideally, through mucosectomy or endoscopic submucosal resection.

Author´s contribution

Conceptualization: Matheus Degiovani
Methods: Artur Adolfo Parada
Project administration: Matheus Degiovani
Essay (original sketch): All authors
Essay (review and edition): All authors

ABSTRACT - BACKGROUND: At least 20% of colorectal adenocarcinomas arise through serrated lesions and studying them in early stages is important in prevention. **AIM**: To analyze and compare the endoscopic and histopathological characteristics of superficial serrated lesions in early stages, greater than 5 mm in length, completely resected during colonoscopies, and classified. **METHOD**: Retrospective and observational study evaluating 12,653 colonoscopy exams where 217 cases were selected that underwent endoscopic resections of superficial serrated lesions measuring more than 5 mm in diameter, addressed in terms of anatomical location, endoscopic findings, the average size of the lesions, average age, gender, and anatomopathological result. **RESULTS**: There were 2 groups G1 and G2. G1 had 126 hyperplastic lesions (HL) and G2 had 91 sessile serrated lesions. The anatomical location was 57.9% proximal and 42.1% distal in G1 and 94.5% and 5.5% respectively in G2. In G1, type 0-IIa was found in 26.2% and lateral spreading in 73.8%; in G2, 15.4% and 84.6%, respectively. The average size of the lesions in G1 was 15.4 mm and in G2, 16.7 mm. The average age G1 was 62.6 and G2, 63.5. Women were predominant in the total number of patients. No invasive adenocarcinomas were observed in the 2 groups. **CONCLUSIONS**: Superficially elevated serrated lesions, measuring more than 5 mm and resected by colonoscopies, were hyperplastic (58%). HL was observed throughout the colon and rectum and SSL was predominantly in the proximal colon. HL did not present dysplasia and SSL did. No invasive adenocarcinomas were observed in the submucosa.
KEYWORDS: Colorectal neoplasms. Adenocarcinoma. Colon. Rectum.

RESUMO - RACIONAL: Pelo menos 20% dos adenocarcinomas colorretais surgem através de lesões serrilhadas e estudá-los em estágios iniciais é importante na prevenção. **OBJETIVO**: Analisar e comparar as características endoscópicas e histopatológicas de lesões superficiais serrilhadas em estágios iniciais, maiores que 5 mm de comprimento, completamente ressecadas durante colonoscopias e classificadas. **MÉTODO**: Estudo retrospectivo e observacional avaliando 12.653 exames de colonoscopia, onde foram selecionados 217 casos submetidos às ressecções endoscópicas de lesões superficiais serrilhadas medindo mais de 5 mm de diâmetro, abordados quanto à localização anatômica, achados endoscópicos, tamanho médio das lesões, idade média, sexo e resultado anatomopatológico. **RESULTADOS**: Houve 2 grupos, G1 e G2. O G1 apresentou 126 lesões hiperplásicas (HL) e o G2 91 lesões serrilhadas sésseis. A localização anatômica foi 57,9% proximal e 42,1% distal no G1 e 94,5% e 5,5% respectivamente no G2. No G1, o tipo 0-IIa foi encontrado em 26,2% e o espalhamento lateral em 73,8%; no G2, 15,4% e 84,6%, respectivamente. O tamanho médio das lesões G1 foi de 15,4 mm e G2 de 16,7

mm. A média de idade do G1 foi de 62,6 anos e do G2, 63,5 anos. As mulheres predominaram no total de pacientes. Não foram observados adenocarcinomas invasivos nos 2 grupos. **CONCLUSÕES**: Lesões serrilhadas superficialmente elevadas, medindo mais de 5 mm e ressecadas por colonoscopia, eram hiperplásicas (58%). O HL foi observado em todo o cólon e reto e o SSL foi predominantemente no cólon proximal. HL não apresentou displasia e SSL sim. Não foram observados adenocarcinomas invasivos na submucosa.
DESCRITORES: Neoplasias colorretais. Adenocarcinoma. Cólon. Reto.

INTRODUCTION

Colonoscopy is the main exam made to detect and eventually resect premalignant colorectal lesions, considered by diverse colorectal cancer (CRC) screening guidelines[22]. Although the regular adenoma has been, for a long time, recognized as the forerunner and the main driver of post-polypectomy surveillance guidelines, during the last decades it was identified and distinguished other forerunner lesions. Currently, it is known that at least 20% of the CRCs arise from serrated lesions and not from regular adenomas. [24,27] There is diversity in these lesions' morphology, which varies from polyps with only superficial serrations to excessive serrations and discernible dysplasia. They are also molecularly different and can develop divergent clinical outcomes carcinomas.

There are many high-risk reports on developing CRC through sessile serrated adenomas – now referred to as sessile serrated lesions (SSL) – mostly on patients with serrated polyposis syndrome[10] and in the elderly when these lesions are larger and with associated sessile components.

With the knowledge evolution, technological improvements, and the refinement of endoscopists´ skills, currently it is possible to diagnose these lesions in their early stage, which means, in its superficial form, that usually presents as the Paris Classification as slightly elevated (type 0-IIa), flat (type 0-IIb) or laterally spreading tumors (LST).

Therefore, these lesions' detection and study during their early stages would be of great value to CRC prevention. When diagnosed and resected prematurely, most of the lesions are histologically defined as hyperplastic lesions (HL) or sessile serrated lesions (SSL), and, if they are completely resected, it may interrupt the serrated neoplastic pathway, probably related to arise CRC.

This study aims to analyze and compare endoscopic and histopathological elements of the superficial serrated lesions in the early stage, larger than 5 mm in extension, completely resected during colonoscopies and defined as hyperplastic lesions or sessile serrated lesions, to focus on identifying predictive and evolutionary specifications of these lesions in the development of CRC.

METHODS

The study project was approved by the Evangélica Mackenzie University of Paraná, Curitiba, PR, Brazil, Ethics Committee on Human Research, under number CAAE 53377816.0.0000.0103, with the patient's previous authorization through informed consent. Subsequently, the project was formalized on the Brazil Platform.

This is a retrospective cross-sectional and horizontal study conducted on a private gastrointestinal endoscopy service in the city of São Paulo, SP, Brazil, between January 2012 and January 2021, involving consecutive patients who underwent colonoscopy. It used anatomical nomenclature based on the International Anatomical Terminology, published by the Brazilian Society of Anatomy, affiliated with The Federative Committee on the Anatomical Terminology (Brazilian Society of Anatomy, 2001).

Sample

The study evaluated 12.653 colonoscopies. A total of 217 patients who underwent endoscopic resection of superficially elevated lesions, larger than 5 mm of extension, and with a histological diagnosis of serrated lesions were selected. Thereupon, the patients were distributed in pre-selected groups, as follows: G1= 126 hyperplastic lesions (HL); and G2 = 91 sessile serrated lesions (SSL), with 88 SSL low-grade dysplasia (SSL-BG) and with 3 SSL high-grade dysplasia (SSL-AG).

The lesions, up to 3 cm in diameter, were removed through endoscopic mucosal en-block resection or submucosal endoscopic dissection, starting from this size. Both procedures were performed using their specific materials. The cases that were removed with the use of biopsy forceps were excluded.

All cases were stratified by gender, age, lesion location, size, and macroscopic type according to the Paris Classification.

Colonoscopy

The examinations were performed with endoscopes from Olympus, Pentax, or Fujinon, after the patients' usual preparations for examining the colon, which includes a liquid diet and the use of laxatives a day before, combined with a 10% mannitol (1.000ml) solution on the examination day. It used chromoscopy with 0,4% indigo carmine, and 4% acetic acid, and digital chromoscopy, with or without image magnification, to better evaluate the lesions. Intravenous sedation, to perform the procedure, was administered at the discretion of the anesthesiologist.

According to the endoscopic aspect of the lesions, they were classified according to the Paris Classification, modified by the Japanese concerning laterally spreading lesions (LSL, Figure 1).[14,26,32]

Therefore, there were included superficial lesions with the following characteristics: types 0-IIa and 0-IIb (slightly elevated and superficially flat, respectively) and LST-G (larger than 1 cm in diameter, superficially elevated and with a slightly granulating surface). Any other lesions, even if histopathologically diagnosed as serrated lesions, were excluded.

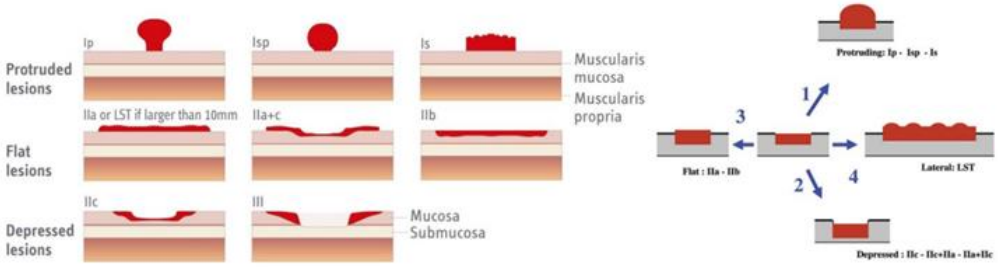


FIGURE 1 – Paris classification for colon superficial lesions and their subtypes

For the anatomic-endoscopic location of the lesions, all segments of the colon and rectum were included, with the cecum, ascending and transverse colon as long as the proximal location; splenic flexure, descending and sigmoid colon and rectum, and distal location.[2,34]

Inclusion and exclusion criteria

Inclusion criteria were superficially elevated lesions (0-IIa and 0-IIb) and LST-G, all measuring 5mm or more in diameter and with a previous histological diagnosis of serrated lesion. Resections would be performed completely on lesions with good clinical conditions and with the ideal preparation of the colon, which allows the procedure from a technical point of view.

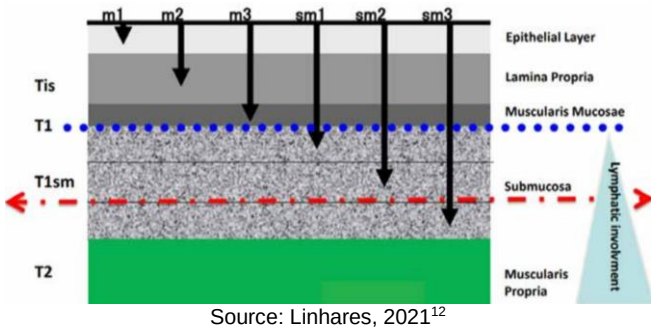
Exclusion criteria were intestinal polyposis, inflammatory bowel diseases, fragmentation or non-retrieval of the specimen after the procedure, lesions that did not elevate after submucosal injections, the very extensive ones, and those located in difficult places to access through the endoscope.

Histopathologic study

After resection, the specimens were stretched with needles on Styrofoam, cark, or cardboard, fixated in 10% formalin, and subsequently sent to histological analysis, where they were cut every 2 mm and microscopically examined with H&E, evaluating the histological lesions type and their lateral and vertical margins.

Histopathologic diagnoses were conducted by pathologists specialized in the gastrointestinal area. The lesions were separated initially based on architectural changes and secondly on cytological features.

The submucosal invasion was subdivided into three different levels (Figure 2): sm1, sm2, and sm3.[11,13] The measurement limit, which considered patients to be practically cured with minimal lymph node metastasis risk, was 1000 µM (sm1).[14]



Source: Linhares, 2021[12]

FIGURE 2 – Submucosal invasion

For histological evaluation, the Vienna Classification was used, which defines the categories from 1 to 5. Category 1 is negative for neoplasia/dysplasia (including reacting lesions); 2 is indefinite for dysplasia/neoplasia; 3 is noninvasive low-grade intraepithelial or mucosal neoplasia (LGIN, equivalent to low-grade dysplasia and corresponding to mild and moderate dysplasia on the 3 grades system, low-grade adenoma/dysplasia); 4 is noninvasive high grade intraepithelial or mucosal dysplasia (HIGN, equivalent to high-grade dysplasia, adenoma with high-grade dysplasia or intense dysplasia on the 3 grades system, noninvasive carcinoma *in situ* and carcinoma in the mucosa that invades the lamina propria); and 5 is invasive neoplasia or carcinoma, that invades into the submucosa or deeper.[6,30]

For serrated lesions, the World Health Organization classification was used: hyperplastic polyp; serrated sessile lesion; traditional serrated adenoma; and unclassified serrated adenomas.[23]

Superficially elevated lesions were considered as SSL, when they presented one or more crypts with distorted growth, with dilatation of their basal portion, with the shape of a boot, capital letter L, or anchor, near the base. Regarding the pattern and/or architectural changes, with or without mild dysplasia, there were considered serrated low-grade intraepithelial neoplasia (SSL-BG). The ones with severe dysplasias were considered serrated high-grade intraepithelial neoplasia (SSL-AG). Carcinomas were considered only in cases where the submucosa was invaded (Figure 2).

Statistical analysis

To assess the association between two categorical variables, the Fisher's exact test or the chi-square test was used. The value of $p<0.05$ indicated statistical significance. Data were analyzed using the computer program IBM SPSS Statistics version 20.0 (IBM Corp, Armonk, NY, USA) and GraphPad Prism 8.0.

RESULTS

Considering the pre-established groups (G1, n=126 HL; G2, n=91 SSL with SSL-BG= 88 and SSL-AG=3), the data was established based on the studied items.

Lesion´s anatomic and colonoscopic location

G1= 73 (57,9%) proximal (cecum, ascending and transverse colon) and 53 (42,1%) distal (descending, sigmoid colon, and rectum); G2= 86 proximal (94,5%) and 5 distal (5,5%, Table 1A Figures 3A and 3B)

Endoscopic aspects: colorectal lesions morphology

On G1, LH presented macroscopically based and according to Paris Classification as type 0-IIa (26,2%); and LST type (73,8%). In the G2 (SSL): type 0-IIa (15,4%); and LST type (84,6%). There was no statistically significant difference (p=0,067) between the endoscopic findings in the two groups (Table 1b and Figure 3C). In the SSL-BG and SSL-AG groups, the endoscopic findings were: SSL-BG type 0-IIa (15,9%) and LST (84,1%); SSL-AG: LST (100%). There was no statistical difference between these groups (p=0,067, Table 1B and Figures 3C and 3G).

Gender

Regarding gender, women were prevalent, but not between the groups: on G1, 57,1% were women and 42,9% were men, and on G2, 69,2% and 30,8%, respectively (p=0,088, Table 1C and Figure 3E)

TABLE 1- Endoscopic lesions profile

A) Lesions location			
Group	**Proximal**	**Distal**	**Total**
G1 (HL)	73 (57,9%)	53 (42,1%)	126
G2 (SSL)	86 (94,5%)	5 (5,5%)	91
p<0,001 (Fisher´s exact test, p<0,05)			

B) Endoscopic or morphologic aspects			
Group	**0-IIA**	**LST-G**	**Total**
G1 (HL)	33 (26,2%)	93 (73,8%)	126
G2 SSL	14 (15,4%)	77 (84,6%)	91
SSL-BG	14 (15,9%)	74 (84,1%)	88
SSL-AG	0	3 (100%)	3
p=0,067 (Fisher´s exact test, p<0,05)			

C) Lesion type vs gender			
Group	**Feminine**	**Masculine**	**Total**
G1 (HL)	72 (57,1%)	54 (42,9%)	126 (100%)
G2 (SSL)	63 (69,2%)	28 (30,8%)	91 (100%)
p=0,088 (Fisher´s exact test, p<0,05)			

D) Gender vs. anatomopathological			
Group	**Feminine**	**Masculine**	**Total**
SSL-BG	60 (68,2%)	28 (31,8%)	88 (100%)
SSL-AG	3 (100%)	0 (0%)	3 (100%)
p=0,550 (Fisher´s exact test, p<0,05)			

Colorectal lesion size

The results were as follows: G1= less than 20 mm (92,0%); larger than 21 mm (8,0%). G2 = less than 20 mm (75,9%); larger than 21 mm (24,2%, p<0,05, Table 2A). The mean size of the lesions in mm and the standard deviation in the groups were: G1=15,4±8,8 mm; G2=16,7±10,3 mm.

When the size of the lesions and the anatomopathological findings were correlated, a statistically significant relation was found: 5-10 mm= HL (61,7%) and SSL (38,3%); 11-20 mm= HL (63,1%) and SSL (36,9%); >21 mm= HL (31,3%) and SSL (68,7%, p=0,005, Figure 3D and Table 3).

Age structure

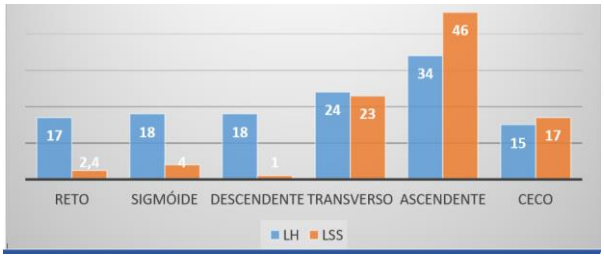
The mean age and the standard deviation of G1 were 62,6±10,1 years old, with a minimum age of 32 and a maximum of 85, and of G2, 63,5±11,2 years old, with a minimum age of 28 and a maximum of 86.

There was no statistically significant difference between the two groups (p=0,861). Below 50 years, 12,7% of HL and 11% of SSL were diagnosed; above 70 years, 20,7% of HL and 25,3% of SSL; above 80 years, 4% of HL and 5,5% of SSL (Table 2B, Figure 3D).

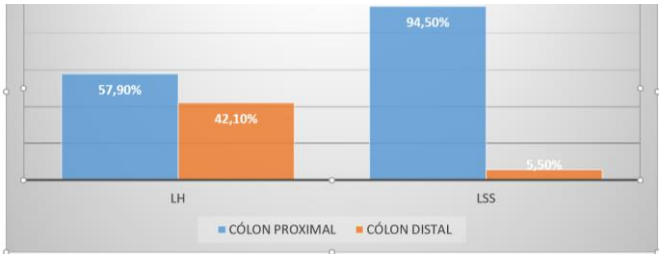
TABLE 2 – Age structure and the size of the lesion

A) Size of the lesion					
Type	**5 to 10**	**11 to 20**	**> 21**	**Average**	**Total**
G1 (HL)	29 (23,1%)	87 (69,0%)	10 (7,9%)	15,4	126
G2 (SSL)	18 (19,8%)	51 (56,0%)	22 (24,2%)	16,7	91
TOTAL	47	138	32		217
p=0,005 (Chi-square test, p<0,05)					

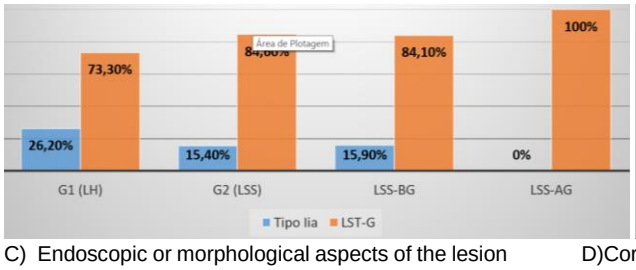
B) Lesion type vs. age structure					
Type	**≤ 50**	**51 to 70**	**71 to 80**	**> 80**	**Total**
G1 (HL)	16 (12,7%)	84 (66,7%)	21 (16,7%)	5 (4,0%)	126
G2 (SSL)	10 (11%)	58 (63,7%)	18 (19,8%)	5 (5,5%)	91
p=0,861 (Chi-square test, p<0,05)					



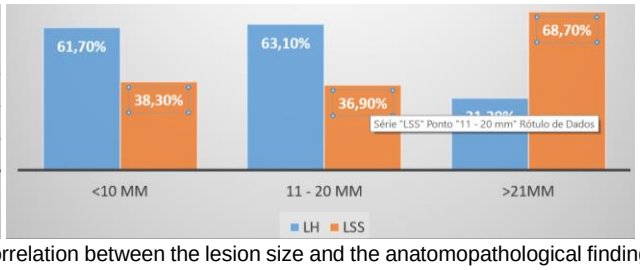
A) Segmental anatomical location of the colorectal lesions



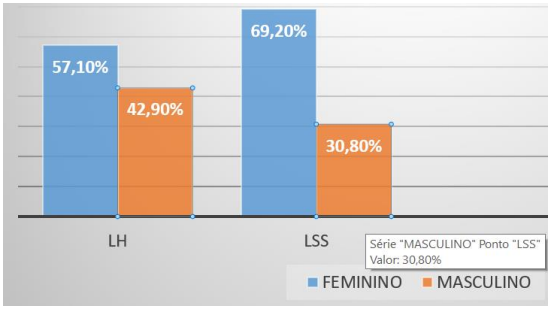
B) Endoscopic colonic location of the lesions



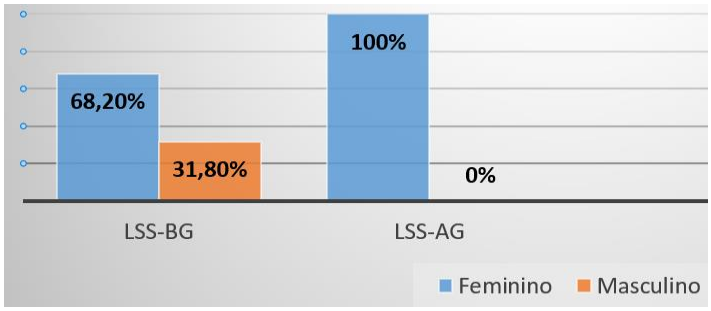
C) Endoscopic or morphological aspects of the lesion



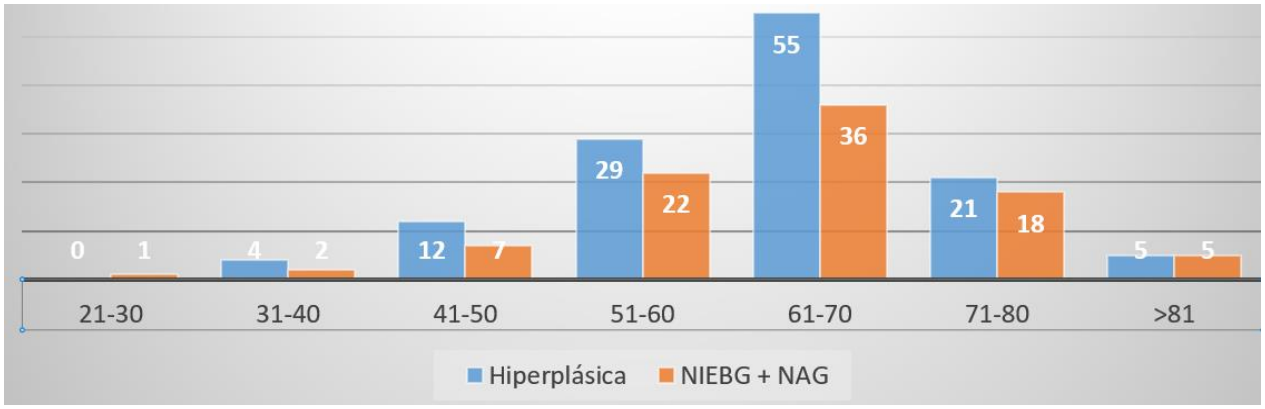
D)Correlation between the lesion size and the anatomopathological findings



E) Type of lesion vs. gender



F) Gender vs. anatomopathological



G) Type of lesion vs. age structure

FIGURE 3 – Epidemiology of the lesions found

When subdivided SSL, with or without low-grade dysplasia (SSL-BG), and SSL with high-grade dysplasia (SSL-AG), women predominated, however, there was no statical difference between the groups (p=0,55, Table 3 and Figure 3F)

TABLE 3 - Correlation between the size of the lesion and anatomopathological

Superficial serrated lesions				
Size	**HL**	**SSL-Bg**	**SSL-Ag**	**Total**
5 to 10 mm	**29 (61,7%)**	18 (39,3%)	0 (0%)	47 (100%)
11 to 20 mm	**87 (63,1%)**	49 (35,5%)	2 (1,5%)	138 (100%)
> 21 mm	10 (31,3%)	**21 (65,6%)**	1 (3,1%)	32 (100%)
Total	126 (100%)	88 (100%)	3 (100%)	217 (100%)

p=0,005 (Chi-square test, p<0,05)

DISCUSSION

Currently, there are many plausible discussions about the CRC (colorectal cancer) oncogenic pathways. The improvement of colonoscopy equipment and the early detection of precursor lesions of carcinoma is a significant challenge for endoscopists.

Despite the diagnostic devices' evolutionary process and other inexplicable causes, there still are a considerable number of small precursor lesions of CRC undiagnosed and, also, patients that present interval carcinomas.

According to several authors, most of the undiagnosed lesions are, probably, superficial, in early stages, originating from the serrated pathway and located in the proximal colon (cecum, ascending and transverse).

Until recently, HL has always considered benign lesions without the potential to evolve into malignancy. However, nowadays there is evidence that these lesions can indeed be precursors of carcinomas (non-adenomatous) and be part of the serrated pathway to cancer. The microvesicular type is the most common, accounting for 66,7% of the hyperplastic lesions and located mostly in the right colon. The globet cells account for 24,4%

and are located mostly in the left colon. Therefore, they gain importance because of their potential to evolve into other types of serrated lesions, mainly to SSL and, consequently, following this carcinogenic pathway, turn into adenocarcinoma.[25,28]

In an interesting study investigating these lesions, it was estimated that HL evolved to SSL in approximately 7,5 years.[35] If this statement is true, in this sample, the HL percentage, larger than 5 mm, that would evolve to SSL, would be very high among superficially elevated lesions, corresponding to 42% of the cases. However, this data indicates that with advancing age the lesion´s size remains practically the same, both for HL and SSL, raising questions about the evolution of HL to SSL.

An important and elucidative fact to this carcinogenic pathway would be the HL growth in the presence of SSL. When comparing the results of this research it was observed that of 47 lesions from 5 mm to 10 mm in diameter, there were 29 HL (61,7%) and 18 SSL (38,3%), which is considered a big amount of HL. This correlation persisted among lesions between 10 and 20 mm diameter (63,1% of HL). From 20 mm diameter onwards this correlation was inverted, that is, out of 32 lesions, 31% were HL and 69% were SSL, with this difference being statistically significant (p=0,005). Therefore, it is suggested and plausible that when these lesions reach a 20 mm size, there may be this progression between HL and SSL.

To elucidate even more this point of view, when the lesions are correlated by their anatomopathological aspect and size, it is evident that 29 (23%) of HL were between 5 and 10 mm in diameter; 87 (69%) between 11 and 20 mm; and 10 (7,9%), larger than 20 mm. In the SSL group, 18 (19,8%) are between 5 and 10 mm; 51 (56,1%) between 11 and 20 mm; and 22 (24,1%) are larger than 20 mm. That means, the larger the size of the superficial elevated lesion, the higher the chance of an SSL diagnosis, mostly when it reaches 20 mm in diameter (p<0,05).

There is a lot of discussion involving the size of the lesions, mainly concerning the 10 mm limit, used to define conventional adenomas to advanced ones. Although, it is not clear whether this measure is also applied to SSL.[19] It is also considered that HL, larger than 10 mm, in addition to being associated with dysplasia, would increase the risk of evolving to CRC, since its molecular changes are like those of the corresponding subtypes of this cancer.[1,4,28,33]

There was no evidence of dysplasia in superficially elevated serrated lesions of hyperplastic type. In SSL superficially elevated, with a diameter up to 10 mm, there was also no cytological dysplasia. Among the 77 SSL cases larger than 10 mm, 3 of them presented high-grade dysplasia (3,9%). There was no evidence of carcinomas invading the submucosa, even in lesions larger than 20 mm in diameter. However, as described in the literature, there are carcinomas in smaller lesions that may exhibit quick progression. Therefore, it is recommended to completely resect lesions larger than 7 mm in diameter, mostly when they present endoscopic findings, such as a slight elevation, nodules, reddish lesions, erosions or depressions, or double elevation. In the presence of these findings, dysplasia and carcinomas are predicted and indicate these lesions must be completely removed by endoscopic resections of the mucosa and, preferably, in en-block resection or by endoscopic resection of the submucosa.[21,29]

The cold snare resection has been widely used, but it should be only performed after a thorough analysis of the lesion type, the surface, and the vascularization, even for lesions smaller than 1 cm in diameter.[20]

In a recent publication, clinical and molecular aspects of a large number of SSL with dysplasia or carcinoma were analyzed. It was found that they are mostly small (<10 mm), located in the proximal colon, and affect the elderly (median age of 76,7 years old). The dysplasia cases occurred in patients of similar ages to those with carcinomas, suggesting a quick transformation to malignancy.[3]

In this case series, 126 HL (58% of superficial serrated lesions) and 91 SSL (42%) were diagnosed. Among these 91 SSL, 88 presented architectural typical changes of these lesions, with or without mild cytological dysplasia, considered as SSL-BG (96,7%), and, 3 SSL, intense architectural changes or high-grade dysplasia (3,3%), considered as SSL-AG. These 3 cases were diagnosed in elderly women and located in the ascending colon. No men presented SSL with high-grade dysplasia. These data were similar to those described by some authors, suggesting that elderly and feminine patients present more SSL that evolves into high-grade dysplasia and carcinomas.[15]

Equally important in this carcinogenic pathway context are the interval carcinomas, defined as SSL undiagnosed during the first preventive colonoscopy. Consequently, they will be diagnosed later, 3-5 years after the initial exam, in preventive exams and/or screening exams; however, in this case, with an initial diagnosis of serrated adenocarcinoma, they are responsible for 5% to 7% of the colorectal carcinomas.[22]

Demonstrating this possibility, García-Solano et al.[9] while studying 927 consecutive carcinomas, identified 85 (9,1%) as serrated adenocarcinomas, probably undiagnosed previously, being considered interval carcinomas.

It has been suggested that SSL can evolve quickly to CRC and these CRCs exhibit molecular and genetic characteristics consistent with a big part of these interval carcinomas, presenting high microsatellite instability and CIMP+.[7,25]

Another important fact to be considered in this carcinogenic pathway is the significant variability between the pathologists of the superficial elevated lesions diagnosis, mostly in the differentiation between HL and SSL.[13,25,28]

Associated with the resection pattern of these lesions by the endoscopist, the histopathologic examination should be performed in the completely resected lesion, which is the gold standard for diagnosis. Biopsies isolated are not adequate for their precise diagnosis.

Characteristically serrated lesions can present, in the same lesion, microvesicular hyperplastic histological aspect in one predominant area and SSL in another smaller area, which turns challenging to achieve the final diagnosis. As previously stated, for SSL diagnosis it is recommended, nowadays, to have at least one crypt with a distorted architectural change, dilated or with horizontally branching ramifications, particularly associated with inverted maturation.[16,28]

Elucidating this diagnostic difference between pathologists, a multicenter Japanese study conducted between 2003 and 2010, reviewed 154 lesions considered as hyperplastic, with 1 cm or more in diameter, resected during colonoscopy and described as hyperplastic lesions. After the revisional histopathological analysis, 107 (69,5%) were considered SSL and 47 (30,5%) non-SSL (incomplete SSL and/or hyperplastic polyp). Furthermore, in this study, the majority of the lesions were located in the proximal colon (cecum, ascending, and transverse) when compared to distal (descending and sigmoid)[31], which is consistent with the data of this study.

Therefore, for many years all the identified lesions during colonoscopy have been completely resected. Despite the lack of long-term follow-up of these lesions, there is no way to assure which would be the percentage of these lesions that progressed into carcinomas per se.

To emphasize the importance of the follow-up of these lesions, according to several authors, categorizing serrated lesions with low-grade dysplasia may convey the wrong message to the attending doctors. It is recommended to emphasize the nature of the advanced lesion and the need for short-term endoscopic follow-up to verify if the lesion has been completely resected. Lesions larger than 7 mm, presenting structural changes, as the ones stated previously, must be completely resected, preferably through mucosectomy or endoscopic resection of the submucosa.

Regarding the post-resection follow-up of colorectal lesions, the dysplasia stage, the size of the lesion, and the number of lesions are considered risk factors and, according to different guidelines, change the follow-up proposals, which remains highly controversial. For SSL, with no dysplasia and smaller than 10 mm in diameter, the follow-up is 5 years.[7,8,17] For SSL with more than 10 mm and dysplasia, the follow-up is 3 years. In serrated polyposis, it is recommended annual follow-up[17]. In contrast to the follow-up protocol of the authors in this research, for SSL, no-dysplasia and smaller than 10 mm, the follow-up is 3 years; in SSL with more than 10 mm and with dysplasia and in serrated polyposis the follow-up is annual.

Despite many controversies and much to be learned about colorectal lesions, thorough colonoscopy examination is essential, preferably using high-definition imaging and all the current technological advancements, while not disregarding contrast chromoscopy which still outperforms digital chromoscopy. It must be emphasized the importance of completely resected lesions of any lesion identified during the examination, always prioritizing the safety and risk-benefit of these resections. For instance, for larger lesions located in the right colon, there are significant concerns regarding their resection as the risk of the procedure itself may outweigh the risk of these lesions progressing to CRC. These procedures should always be performed in specialized gastrointestinal endoscopy centers, preferably hospital-based and by teams with adequate training.[7]

CONCLUSION

The majority of superficially elevated serrated lesions, with more than 5 mm and resected by colonoscopy were hyperplastic (58%). The HL was identified throughout the colon and rectum and the SSL, predominantly, in the proximal colon. There was a predominance of females in both groups but without statistical significance. Lesions measuring up to 2 cm in the largest axis were HL and the ones measuring over 2 cm were SSL. Regarding the median age, there was no statistically significance difference between the two groups. The HL did not present dysplasia, whereas SSL did, with severe dysplasia observed in 3,3% of the cases. No invasive adenocarcinomas were observed in the submucosa.

REFERENCES

1. Anderson JC. Pathogenesis and Management of Serrated Polyps: Current Status and Future Directions. Gut Liver. 2014;8(6). Doi: 10.5009/gnl14248
2. Benedix F, Kube R, Meyer F, Schmidt U, Gastinger I, Lippert H, et al. Comparison of 17,641 Patients With Right- and Left-Sided Colon Cancer: Differences in Epidemiology, Perioperative Course, Histology, and Survival. Dis Colon Rectum. 2010;53(1). Doi: 10.1007/DCR.0b013e3181c703a4
3. Bettington M, Walker N, Rosty C, Brown I, Clouston A, McKeone D, et al. Clinicopathological and molecular features of sessile serrated adenomas with dysplasia or carcinoma. Gut. 2017;66(1). Doi: 10.1136/gutjnl-2015-310456
4. Cho H, Hashimoto T, Yoshida H, Taniguchi H, Ogawa R, Mori T, et al. Reappraisal of the genetic heterogeneity of sessile serrated adenoma/polyp. Histopathology. 2018;73(4). Doi: 10.1111/his.13688
5. Degiovani M, Parada AD, Cuenca RM, Torres OJM, Andreollo NA, Possiedi RD, Tabushi FI. Há diferenças endoscópicas e histopatológicas entre lesões serrilhadas superficiais nas suas fases iniciais? BioSCIENCE 2023; 81(2):101-107. Doi:10.55684/81.2.19
6. Dixon MF. Gastrointestinal epithelial neoplasia: Vienna revisited. Gut. 2002;51(1). Doi: 10.1136/gut.51.1.130
7. East JE, Atkin WS, Bateman AC, Clark SK, Dolwani S, Ket SN, et al. British Society of Gastroenterology position statement on serrated polyps in the colon and rectum. Gut. 2017;66(7). DOI: 10.1136/gutjnl-2017-314005
8. Freeman HJ. Heterogeneity of colorectal adenomas, the serrated adenoma, and implications for screening and surveillance. World J Gastroenterol. 2008;14(22). Doi: 10.3748/wjg.14.3461
9. García-Solano J, Pérez-Guillermo M, Conesa-Zamora P, Acosta-Ortega J, Trujillo-Santos J, Cerezuela-Fuentes P, et al. Clinicopathologic study of 85 colorectal serrated adenocarcinomas: further insights into the full recognition of a new subset of colorectal carcinoma. Hum Pathol. 2010;41(10). Doi: 10.1016/j.humpath.2010.04.002
10. Ijspeert JEG, Bastiaansen BAJ, van Leerdam ME, Meijer GA, van Eeden S, Sanduleanu S,et al. Development and validation of the WASP classification system for optical diagnosis of adenomas, hyperplastic polyps and sessile serrated adenomas/polyps. Gut. 2016;65(6). DOI: 10.1136/gutjnl-2014-308411
11. Kikuchi R, Takano M, Takagi K, Fujimoto N, Nozaki R, Fujiyoshi T, et al. Management of early invasive colorectal cancer. Risk of recurrence and clinical guidelines. Dis Colon Rectum. 1995;38(12). Doi: 10.1007/BF02049154

12. Kim JH, Kang GH. Evolving pathologic concepts of serrated lesions of the colorectum. Journal of Pathology and Translational Medicine. 2020. Doi: 10.4132/jptm.2020.04.15
13. Kitajima K, Fujimori T, Fujii S, Takeda J, Ohkura Y, Kawamata H, et al. Correlations between lymph node metastasis and depth of submucosal invasion in submucosal invasive colorectal carcinoma: a Japanese collaborative study. J Gastroenterol. 2004;39(6). Doi: 10.1007/s00535-004-1339-4
14. Kudo S, Lambert R, Allen JI, Fujii H, Fujii T, Kashida H, et al. Nonpolypoid neoplastic lesions of the colorectal mucosa. Gastrointestinal Endoscopy. 2008;68(4). Doi: 10.1016/j.gie.2008.07.052
15. Lash RH, Genta RM, Schuler CM. Sessile serrated adenomas: prevalence of dysplasia and carcinoma in 2139 patients. J Clin Pathol. 2010;63(8). Doi: 10.1136/jcp.2010.075507
16. Li SC, Burgart L. Histopathology of Serrated Adenoma, Its Variants, and Differentiation From Conventional Adenomatous and Hyperplastic Polyps. Arch Pathol Lab Med. 2007;131(3). Doi: 10.5858/2007-131-440-HOSAIV
17. Lieberman D, Moravec M, Holub J, Michaels L, Eisen G. Polyp Size and Advanced Histology in Patients Undergoing Colonoscopy Screening: Implications for CT Colonography. Gastroenterology. 2008;135(4). DOI: 10.1053/j.gastro.2008.06.083
18. Linhares M, Pinto JD, Caldeira A, Sousa R, Banhudo A. Cancro colorretal e lesões pré-malignas: a propósito de dois casos clínicos. Revista Portuguesa de Coloproctologia. 2021;18(3):48-55. ISSN 2183-3729
19. Moss A, Bourke MJ, Williams SJ, Hourigan LF, Brown G, Tam W, et al. Endoscopic Mucosal Resection Outcomes and Prediction of Submucosal Cancer From Advanced Colonic Mucosal Neoplasia. Gastroenterology. 2011;140(7). Doi: 10.1053/j.gastro.2011.02.062
20. Muniraj T, Sahakian A, Ciarleglio MM, Deng Y, Aslanian HR. Cold Snare Polypectomy for Large Sessile Colonic Polyps: A Single-Center Experience. Gastroenterol Res Pract. 2015;2015. Doi: 10.1155/2015/175959
21. Murakami T, Sakamoto N, Ritsuno H, Shibuya T, Osada T, Mitomi H, et al. Distinct endoscopic characteristics of sessile serrated adenoma/polyp with and without dysplasia/carcinoma. Gastrointest Endosc. 2017;85(3). Doi: 10.1016/j.gie.2016.09.018
22. Muzny DM, Bainbridge MN, Chang K, Dinh HH, Drummond JA, Fowler G, et al. Comprehensive molecular characterization of human colon and rectal cancer. Nature. 2012;487(7407). Doi: 10.1038/nature11252
23. Nagtegaal ID, Odze RD, Klimstra D, Paradis V, Rugge M, Schirmache P, et al. The 2019 WHO classification of tumours of the digestive system. Histopathology. 2020;76(2). Doi: 10.1111/his.13975
24. Nishizawa T, Yoshida S, Toyoshima A, Yamada Y, Sakaguchi Y, Irako T, et al. Endoscopic diagnosis for colorectal sessile serrated lesions. World Journal of Gastroenterology. 2021;27(13). Doi: 10.3748/wjg.v27.i13.1321
25. Pai RK, Bettington M, Srivastava A, Rosty C. An update on the morphology and molecular pathology of serrated colorectal polyps and associated carcinomas. Modern Pathology. 2019;32(10). Doi: 10.1038/s41379-019-0280-2.
26. Participants in the Paris Workshop. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon. Gastrointestinal Endoscopy. 2003;58(6). Doi: 10.1016/s0016-5107(03)02159-x
27. Phipps AI, Limburg PJ, Baron JA, Burnett-Hartman AN, Weisenberger DJ, Laird PW, et al. Association between molecular subtypes of colorectal cancer and patient survival. Gastroenterology. 2015;148(1). Doi: 10.1053/j.gastro.2014.09.038
28. Rex DK, Ahnen DJ, Baron JA, Batts KP, Burke CA, Burt RW, et al. Serrated Lesions of the Colorectum: Review and Recommendations From an Expert Panel. American Journal of Gastroenterology. 2012;107(9). Doi: 10.1038/ajg.2012.161
29. Sano W, Fujimori T, Ichikawa K, Sunakawa H, Utsumi K, Iwatate M, et al. Clinical and endoscopic evaluations of sessile serrated adenoma/polyps with cytological dysplasia. J Gastroenterol Hepatol. 2018;33(8). Doi: 10.1111/jgh.14099
30. Schlemper RJ, Riddell RH, Kato Y, Borchard F, Cooper HS, Dawsey SM, et al. The Vienna classification of gastrointestinal epithelial neoplasia. Gut. 2000;47(2). Doi: 10.1136/gut.47.2.251
31. Shida Y, Ichikawa K, Fujimori T, Fujimori Y, Tomita S, Fujii T, et al. Differentiation between sessile serrated adenoma/polyp and non-sessile serrated adenom'a/polyp in large hyperplastic polyp: A Japanese collaborative study. Mol Clin Oncol. 2013;1(1). Doi: 10.3892/mco.2012.20
32. Tanaka S, Kashida H, Saito Y, Yahagi N, Yamano H, Saito S, et al. Japan Gastroenterological Endoscopy Society guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. Dig Endosc. 2020;32(2). Doi: 10.1111/den.12456
33. Tate DJ, Jayanna M, Awadie H, Desomer L, Lee R, Heitman SJ, et al. A standardized imaging protocol for the endoscopic prediction of dysplasia within sessile serrated polyps (with video). Gastrointest Endosc. 2018;87(1). Doi: 10.1016/j.gie.2017.06.031
34. Weiss JM, Pfau PR, O'Connor ES, King J, LoConte N, Kennedy G, et al. Mortality by Stage for Right- Versus Left-Sided Colon Cancer: Analysis of Surveillance, Epidemiology, and End Results–Medicare Data. J Clin Oncol. 2011;29(33). Doi: 10.1200/JCO.2011.36.4414
35. Yang S, Farraye FA, Mack C, Posnik O, O'Brien MJ. BRAF and KRAS Mutations in Hyperplastic Polyps and Serrated Adenomas of the Colorectum. Am J Surg Pathol. 2004;28(11). Doi: 10.1097/01.pas.0000141404.56839.6a

This preprint was submitted under the following conditions:

- The authors declare that they are aware that they are solely responsible for the content of the preprint and that the deposit in SciELO Preprints does not mean any commitment on the part of SciELO, except its preservation and dissemination.
- The authors declare that the necessary Terms of Free and Informed Consent of participants or patients in the research were obtained and are described in the manuscript, when applicable.
- The authors declare that the preparation of the manuscript followed the ethical norms of scientific communication.
- The authors declare that the data, applications, and other content underlying the manuscript are referenced.
- The deposited manuscript is in PDF format.
- The authors declare that the research that originated the manuscript followed good ethical practices and that the necessary approvals from research ethics committees, when applicable, are described in the manuscript.
- The authors declare that once a manuscript is posted on the SciELO Preprints server, it can only be taken down on request to the SciELO Preprints server Editorial Secretariat, who will post a retraction notice in its place.
- The authors agree that the approved manuscript will be made available under a Creative Commons CC-BY license.
- The submitting author declares that the contributions of all authors and conflict of interest statement are included explicitly and in specific sections of the manuscript.
- The authors declare that the manuscript was not deposited and/or previously made available on another preprint server or published by a journal.
- If the manuscript is being reviewed or being prepared for publishing but not yet published by a journal, the authors declare that they have received authorization from the journal to make this deposit.
- The submitting author declares that all authors of the manuscript agree with the submission to SciELO Preprints.