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Comparative analysis of endoscopic and histopathological features of superficial elevated lesions resected by endoscopic mucosal resection in the distal and proximal colon

Análise comparativa dos aspectos endoscópicos e histopatológicos das lesões superficialmente elevadas ressecadas por mucosectomias no cólon distal e proximal

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ABSTRACT

Objective: to compare endoscopic and histopathologic features of superficial, elevated lesions with one or more centimeters in diameter, diagnosed by videocolonoscopy on the distal and proximal colon, and subjected to mucosal resection. **Methods:** we conducted a retrospective, cross-sectional, observational study involving 8,075 videocolonoscopies. From this total, we evaluated 166 mucosectomies in 145 patients with superficial, elevated lesions with a diameter equal to or greater than 1cm. **Results**: the lesion prevalence was lower in G1 than in G2 (34.9% vs. 65%). The mean age, gender distribution and size (1.9cm in G1 versus 2.0cm in G2, p=0.921) were similar. There was no difference of mucosal surfaces in relation to the location (p=0.575). Considering Intraepithelial neoplasias, both the low grade, high grade (including carcinomas) and hyperplasic ones showedd no difference (p=0.527), nor did the neoplastic lesions when divided into serrated and non-serrated (p=0.124). Excluding 13 hyperplastic lesions and two carcinomas, 124 (82.1%) were non-serrated and 27 (17.9%), serrated. **Conclusion**: were found no significant differences between endoscopic and histopathological aspects of superficial, elevated lesions of 1cm or more in diameter in distal colon compared with the proximal, when resected by mucosectomy. Although not significant, there was a tendency of association between the location of the lesion and the presence of serrated features.

Keywords: Colorectal Neoplasms. Endoscopy. Mucous Membrane. Colon. Colonoscopy.

INTRODUCTION

Colorectal cancer is one of the major medical problems throughout the world[1-3]. The proportion of proximal carcinomas has increased relative to the distal ones[4] and the protection afforded by colonoscopy in the proximal colon is lower than in the distal[5]. Many studies suggest that the interval carcinomas, which are diagnosed few years after colonoscopy, are more proximal, and whose diagnosis was missed, among various factors, due to the development from superficial lesions[5,6]. At the same time, endoscopists started to increasingly diagnose non-polypoid or superficial lesions, and Laterally Spreading Tumor (LST) lesions[7].

In recent years the serrated lesions, which are often superficially elevated lesions, have been subject of much discussion, but there are still some disagreements and difficulties in their diagnosis and characterization by endoscopists and pathologists. Even so, they are now considered important, representing 7.5% to 30% of all colorectal carcinomas according to several authors[8].

This work, emphasizing the histogenesis of colorectal cancer, aimed to study mucosectomy specimens of superficially elevated lesions of 1 cm or more in diameter, comparing their endoscopic and pathologic features in the distal and proximal colon.

METHODS

The study was retrospective, cross-sectional, observational, in which we evaluated the specimens from patients undergoing colonoscopies with endoscopic mucosectomies of superficially elevated lesions with

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more than 1 cm in diameter, in the period from 2011 to 2014 at the Hospital Nove de Julho, São Paulo, SP, Brazil. The examinations were performed with sedation controlled by an anesthesiologist and the lesions were resected by the mucosectomy technique. We considered both the 0-LST and 0-IIa lesions (classification of Paris) as superficially elevated lesions. We classified their surfaces as granular, nodular and smooth after chromoendoscopy with indigo carmine 0.4%. Lesions 2-2.5 cm in diameter were resected en bloc and with more than 2.5-3 cm by fragment (piecemeal) mucosectomy.

We stretched the specimens in cardboard with needles and fixed them in 10% formalin. Subsequently, we cut every 2mm, and microscopically examined them with hematoxylin and eosin. We divided the invasion of the submucosa into three levels: sm1, sm2 and sm3. We histologically classified lesions by the Vienna classification. Lesions with cellular atypia and cytoarchitecture were subdivided in serrated and not serrated, keeping hyperplastic polyps as a separate group.

Finally, evaluations of serrated lesions were reconsidered in accordance with the guidance of the World Health Organization (WHO), including hyperplastic polyps with 1cm or more in diameter as serrated lesions[8-10]. These, when with atypia (sessile serrated adenomas/polyps – SSA/Ps) were considered low-grade or high-grade intraepithelial neoplasias, serrated type (IN-LG-S or IN-HG-S). The adenomatous lesions were considered as low-grade or high-grade intraepithelial neoplasias, or as non-serrated low-grade or high-grade intraepithelial neoplasia.

The splenic flexure is considered proximal by some authors[11] and distal by others[12]. In this work, we considered the splenic flexure, descending and sigmoid colon as distal (G1), and the cecum, ascending and transverse colon as proximal (G2).

We described the results of the variables evaluated in the study as frequencies and percentages (qualitative variables). For the age of the patients, we present the mean values and standard deviation. For the comparison of lesions' locations (distal and proximal) with the qualitative variables, we used the Fisher exact test or chi-square test. W considered p values < 0.05 as statistically significant. Data were analyzed with the software IBM SPSS Statistics v.20.

RESULTS

We carried out 166 mucosectomies (2% of total colonoscopies) in 145 patients. Of these, 52 (35.9%) had 58 lesions in G1. The mean age was 64.2 years (+/- 12.3 years, 33-89); 25 (48.1%) were men and 27 (51.9%), women. In G2, 100 individuals (69%) had 108 lesions, with a mean age of 65.4 years (+/- 10.2 years, 38-89); 45 (45%) were men and 55 (55%), women.

Table 1 shows the frequencies and percentage of lesions according to ranges in size at each location.

When comparing the size of lesions in the distal colon with the proximal one, there was no significant difference (p=0.921). We also show the frequencies and percentage of lesions according to the surface's characteristics at each location. There was no significant difference between the locations of the injury and the surface's characteristics (p=0.575).

For the statistical test, we considered low grade, high-grade and hyperplastic intraepithelial neoplasia. The two cases of carcinoma were grouped with the high-grade intraepithelial neoplasias (Table 2).

When comparing G1 with G2 lesions, there was no significant difference (p=0.527). Table 3 shows the comparison between non-serrated intraepithelial neoplasias and serrated ones, excluding the hyperplastic polyps (n=13) and carcinomas (n=2).

In Table 3 we divided these 151 lesions in two groups, considering them as serrated and non-serrated and showed the results restricted to lesions with low-grade and high-grade intraepithelial neoplasia. In all analyzes, there were no significant differences between the types of lesions and their locations between G1 or G2.

Tables 4 and 5 present the frequencies and percentages according to the surface and size, with the histopathology, at each location.

When considering the 13 hyperplastic lesions and serrated lesions (would be sessile serrated adenomas without dysplasia), the serrated lesions would total 41 (Table 6).

The statistical analysis, although without significance, indicated a trend of association between the location and the presence of serrated lesions.

Table 1. *Frequencies and percentages of lesions according to ranges of sizes, surfaces, and histopathology in the distal and proximal colon.*

Size (cm)	Distal	Proximal	Total
1	13 (22.4%)	28 (25.9%)	41 (24.7%)
1.1 a 2	27 (46.6%)	45 (41.7%)	72 (43.4%)
2.1 a 3	12 (20.7%)	22 (20.4%)	34 (20.5%)
> 3	6 (10.3%)	13 (12%)	19 (11.4%)
Total	58	108	166
Surface	Distal	Proximal	Total
Granular-G	45 (77.6%)	88 (81.5%)	133 (80.1%)
Nodular-N	10 (17.2%)	19 (17.6%)	29 (17.5%)
Smooth-S	3 (5.2%)	1 (0.9%)	4 (2.4%)
Total	58	108	166
Histopathology	Distal colon	Proximal colon	Total
Hyperplasic	3 (5.1%)	10 (9.2%)	13 (7.8%)
Low-grade IN	38 (65.5%)	56 (51.8%)	94 (56.6%)
Low grade-serrated IN	6 (10.3%)	18 (16.6%)	24 (14.5%)
High degree IN	10 (17.2%)	20 (18.5%)	30 (18.1%)
High degree-serrated IN	0 (0%)	3 (2.8%)	3 (1.8%)
sm1 Carcinoma	1 (1.7%)	1 (0.9%)	2 (1.2%)
TOTAL	58 (100%)	108 (100%)	166

IN = intraepithelial neoplasia

DISCUSSION

The sessile serrated adenomas / polyps (SSA/Ps) predominate in the right colon[13]. They tend to be flat in the proximal colon (75%), 64% being bigger than 5mm, and 17% bigger than 10mm. The proximal hyperplastic polyps with more than 5mm could be classified as serrated[8], while most non-serrated or adenomatous lesions would occur in the left colon[14]. Authors state that the proximal hyperplastic polyps, greater than 10mm may be considered sessile serrated adenomas. With these criteria, we would have had 41 serrated lesions, nine (22%) in G1 and 32 (78%) in G2. In G1, they correspond to 15.5% of 58, and in G2, including the sm1 serrated carcinoma, 29.6% of 108. Of the 125 non-serrated lesions, 49 (39.2%) occurred in G1 and 76 (60.8 %), in G2. The statistical test (0.061) was not significant, but showed a tendency to the association between the location and the presence of serrated lesions.

In an American study of 100 serrated lesions, 88 were located in the colon proximal to the splenic flexure. The vast majority were superficially elevated lesions[15]. This paper presents similar data, ie, of the 41 serrated (including hyperplastic polyps), 32 (78%) were located in the G2 and nine (21.9%), in G1.

A Japanese multicenter study analyzed 154 hyperplastic polyps with 1cm or more in diameter. Most sessile serrated adenomas with atypia (SSA/Ps), 90 of 107 (84.1%), and those who were not sessile serrated adenomas (non-SSA/Ps, thus without atypia), 33 of 47 (70.2%) were in the proximal colon[16], as observed in this study, where 77.7% of serrated lesions with atypia (21 of 27 lesions) and 76.9% of serrated lesions without atypia (10 of 13 hyperplastic lesions) were located in the proximal colon (G2).

A very large series of a Korean group of 28,544 colonoscopies diagnosed 143 sessile serrated adenomas / polyps (SSA/Ps) (0.5%). Of these, 123 (86%) were proximal to the splenic flexure and nine (6.3%) had more than 1cm in diameter[17]. In the literature, the average size of sessile serrated adenomas was 8.1mm[16]. We diagnosed 27 sessile serrated adenomas with 1cm or more in diameter, six in G1 (22.2%) and 21 in G2 (77.7%).

In this series, with these criteria, four of 41 serrated lesions (9.7%) and 31 of 125 non-serrated (24.8%) had high-grade IN or sm1carcinomas. In G1, of the 49 non-serrated lesions, 11 had high-grade IN or sm1 carcinomas (22.4%) and

Table 2. *Histopathological aspects of the sample (n = 166).*

Histopathology	Distal	Proximal	Total
Low-grade IN	44 (75.9%)	74 (68.5%)	118 (71.1%)
High-grade IN and carcinoma*	11 (19%)	24 (22.2%)	35 (21.1%)
Hyperplastic polyp	3 (5.2%)	10 (9.3%)	13 (7.8%)
Total	58	108	166

** Two cases of adenocarcinoma (one distal non-serrated on and one proximal, serrated)*

none in the serrated lesions. In G2, 20 of the 76 non-serrated lesions (26.3%) and four serrated (4/32 = 16.7%) were high-grade intraepithelial neoplasia or sm1carcinomas.

In a Brazilian publication, it was shown that lesions larger than 1 cm tend to be pedunculated, with adenomatous component, and patients over 50 years of age are more likely to present sessile polyps in the proximal colon[18]. In an American study with 2400 patients, 10% of diagnosed polyps were serrated. The right colon lesions, when compared by size, were more likely to be dysplastic[19]. In this study we diagnosed 41 serrated lesions in 166 mucosectomies' specimens (24.7%), 55 being lesions with atypia in G1 (94.8%) and 98 in G2 (90.4%), with no statistical difference between the two groups.

In a Korean study of 47 proximal serrated lesions, 43 were slightly elevated lesions, and of these, nine were at high risk, two with dysplasia and seven with diameter greater than 10mm. The average size was 6mm[20]. In this study, 32 were slightly elevated lesions in G2, all with 1 cm or more in diameter, and four were high-grade IN or sm1 carcinomas.

Recent publications of few cases series (n=12)[21] demonstrated that even small serrated lesions may have invasive carcinoma, with sizes between 8.5 and 11.3 mm, suggesting malignant transformations are rare, but fast. This rapid progression aspect was not confirmed in another study, in which the average age of patients with sessile serrated adenomas was 61, of the sessile serrated adenomas with high-grade atypia, 72, and of the cancer related to sessile serrated adenomas, 76[22].

A Japanese research evaluated 141 serrated lesions, 107 being slightly elevated lesions, preferably in the right colon (81.8%), with an average size of 13 mm, with intramucosal carcinoma in 13.6% (3/22 SSA/Ps)[23]. In this study, considering the high degree IN as intramucosal carcinoma, we found three lesions of 27 sessile serrated adenomas (11.1%) and one sm1 carcinoma, which would total four carcinomas in 28 SSA/Ps (14 2%), with an average size of 14 mm, all in G2.

Table 3. *Serrated and non-serrated lesions and intraepithelial neoplasia.*

Serrated	Distal	Proximal	Total	
Low-grade IN. non-serrated	38 (70.4%)	56 (57.7%)	94 (62.3%)	
High-grade IN. non-serrated	10 (18.5%)	20 (20.6%)	30 (19.9%)	
Low-grade IN. serrated	6 (11.1%)	18 (18.6%)	24 (15.9%)	p=0.278
High-grade IN. serrated	0 (0%)	3 (3.1%)	3 (2%)	
Total	54	97	151	
Serrated	Distal	Proximal	Total	
No	48 (88.9%)	76 (78.4%)	124 (82.1%)	
Yes	6 (11.1%)	21 (21.6%)	27 (17.9%)	p=0.124
Total	54	97	151	
Low-grade serrated	Distal	Proximal	Total	
No	38 (86.4%)	56 (75.7%)	94 (79.7%)	
Yes	6 (13.6%)	18 (24.3%)	24 (20.3%)	p=0.237
Total	44	74	118	
High-grade serrated	Distal	Proximal	Total	
No	10 (100%)	20 (87%)	30 (90.9%)	
Yes	0 (0%)	3 (13%)	3 (9.1%)	p=0.536
Total	10	23	33	

IN= intraepithelial neoplasia

Table 4. *Histopathology and surface features of lesions in the distal and proximal colon*

Histopathology	(Distal. n = 58)			Surface (proximal. n = 108)		
	Granular	Nodular	Smooth	Granular	Nodular	Smooth
Hyperplastic polyp	2 (4.4%)	0	1 (33.3%)	9 (10.2%)	1 (5.2%)	0
Low-grade IN	29 (64.4%)	7 (70%)	2 (66.7%)	42 (47.7%)	13(76%)	1 (100%)
Low-grade IN. serrated	6 (13.3%)	0	0	18 (20.5%)	0	0
High degree IN	7 (15.6%)	3 (30%)	0 (0%)	16 (18.2%)	4(23.5%)	0
High-grade IN. serrated	0	0	0	2 (2.3%)	1 (5.2%)	0
Adenocarcinoma	1 (2.2%)	-	-	1 (1.1%)	0	0
Total	45	10	3	88	19	1

IN= intraepithelial neoplasia

The submucosal invasion index for lateral spreading lesions with homogeneous surfaces is very low (< 2%), even in large lesions, while in those with mixed surfaces, with larger nodules, this ratio is higher (up to 7%)[24]. The two cases of carcinoma in this series occurred lesions with granular surface (1.5% of 133), one being serrated with 1 cm in G2, and the other non-serrated, with a 2.5 cm diameter in G1.

Sessile serrated adenomas and traditional sessile adenomas (TSA) have been considered precancerous neoplastic lesions and the hyperplastic polyp, void of malignant potential. However, one author considers the hyperplastic polyp with more than 1 cm also with malignant potential[24]. Sessile serrated adenomas with obvious dysplasia present, according to some authors, with an estimated higher probability to evolve to cancer than conventional adenomas (5.3% versus 2.2%).

The progression of sessile serrated adenoma to cancer would be faster than that of conventional adenomas. Progress to invasive carcinoma has already been shown to take place in eight months. The data suggest that the serrated sessile adenomas may be present for many years with few changes; however, they may rapidly progress to invasive carcinomas, even without dysplasia and with less than 10mm in diameter[25.26].

New technologies can help to better distinguish hyperplastic lesions from the serrated and not serrated lesions and to determine the most adequate procedure to adopt in each case during colonoscopy[27.28].

In recent years, serrated lesions were also included in the colonoscopy follow-up recommendation. Nevertheless, it is not yet clear whether the size of 10mm – used to define conventional adenomas as advanced –

Table 5. *Histopathology and lesion size in the distal and proximal colon.*

Histopathology	Lesion size (cm) (Distal. n = 58)				Lesion size (cm) (Proximal. n = 108)			
	1	1.1 a 2	2.1 a 3	> 3	1	1.1 a 2	2.1 a 3	> 3
Hyperplastic polyp	2 (15.4%)	1 (3.7%)			1 (3.6%)	8 (17.8%)		1 (7.7%)
Low-grade IN	10 (76.9%)	19 (70.4%)	7 (58.3%)	2 (33.3%)	15 (53.6%)	21 (46.7%)	13 (59.1%)	7 (53.8%)
Low-grade IN. serrated	1 (7.7%)	2 (7.4%)	1 (8.3%)	2 (33.3%)	7 (25%)	9 (20%)	1 (4.5%)	1 (7.7%)
High-grade IN		5 (18.5%)	3 (25%)	2 (33.3%)	2 (7.1%)	7 (15.6%)	7 (31.8%)	4 (30.8%)
High-grade IN. serrated					2 (7.1%)		1 (4.5%)	
Adenocarcinoma			1 (8.3%)					
					1 (3.6%)			
Total	13	27	12	6	28	45	22	13

IN= intraepithelial neoplasia

Tabela 6. *Results according to the criteria of the World Health Organization (WHO).*

Serrated	Distal	Proximal	Total
No	49 (84.4%)	76 (70.3%)	125 (75.3%)
Yes	9 (15.5 %)	32 (29.6%)	41 (24.7%)
Total	58	108	166

p=0.061

should also be applied to serrated sessile adenomas[28].

In conclusion, there were no significant differences between the endoscopic and histopathological aspects of superficially elevated lesions with more than 1cm in diameter resected by mucosectomy from the distal colon compared with the proximal one. Although not significant, there is a tendency to the association between the location of the lesion and the presence of serrated features.

R E S U M O

Objetivo: *comparar aspectos endoscópicos e histopatológicos de lesões superficialmente elevadas, com um ou mais centímetros de diâmetro, diagnosticadas por videocolonoscopias e ressecadas por mucosectomias do cólon distal com as do cólon proximal.* **Métodos:** *estudo foi retrospectivo, transversal, observacional, envolvendo 8075 videocolonoscopias. Avaliou-se 166 mucosectomias em 145 pacientes com lesões superficialmente elevadas com diâmetro igual ou maior do que 1cm.* **Resultados:** *a prevalência de lesões foi menor no G1 do que no G2 (34,9% x 65%). A média de idade, a distribuição por sexo e o tamanho (1,9cm no G1 e 2cm no G2, p=0,921) foram semelhantes. Não houve diferenças das superfícies em relação à localização (p=0,575). Considerando neoplasia intraepitelial de baixo grau, neoplasia intraepitelial de alto grau (incluindo carcinomas) e hiperplásicas, não houve diferença (p=0,527), assim como quando foram divididas as lesões neoplásicas em serrilhadas e não serrilhadas (p=0,124). Excluindo-se 13 lesões hiperplásicas e duas com carcinomas, 124 (82,1%) foram não serrilhadas e 27 (17,9%) serrilhadas.* **Conclusão:** *não foram observadas diferenças significativas entre os aspectos endoscópicos e os histopatológicos das lesões superficialmente elevadas, com 1cm ou mais de diâmetro, ressecadas por mucosectomia do cólon distal em relação ao proximal. Embora não significante, há tendência à associação entre a localização da lesão e a presença de características serrilhadas.*

Descritores: *Neoplasias Colorretais. Endoscopia. Membrana Mucosa. Cólon. Colonoscopia.*

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