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Characterization of the mucin phenotype can predict gastric cancer recurrence after endoscopic mucosal resection

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ABSTRACT – Background – Endoscopic mucosal resection is still considered an accepted treatment for early gastric cancer for selected cases. Histopathologic criteria for curative endoscopic resection are intramucosal well-differentiated adenocarcinoma, lateral and deep margins free of tumor, no histological ulceration, and no venous or lymphatic embolism. A 5% local recurrence rate has been described even when all the above-mentioned criteria are met. On the other hand, antigen expression by tumoral cells has been related to the biological behavior of several tumors. **Objective** – To evaluate whether early gastric cancer mucin immunoexpression, p53 and Ki-67, can predict recurrence after endoscopic mucosal resection, even when standard histopathologic criteria for curative measures have been attempted. **Methods** – Twenty-two patients with early gastric cancer were considered to have been completely resected by endoscopic mucosal resection. Local recurrence occurred in 5/22 (22.7%). Immunohistochemical study was possible in 18 (81.8%) resected specimens. Patients were divided in two groups: those with and those without local recurrence. They were compared across demographic, endoscopic, histologic data, and immunohistochemical factors for MUC2, MUC5a, CD10, p53, and Ki-67. **Results** – Mucin immunoexpression allowed a reclassification of gastric adenocarcinoma in intestinal (10), gastric (2), mixed (4), and null phenotypes (2). Mixed phenotype (positive for both MUC2 and MUC5a) was found in 80% of cases in the local recurrence group, while the intestinal type (positive MUC2 and negative MUC5a) was found in 76.9% of cases without local recurrence (P=0.004). Other observed features did not correlate with neoplastic recurrence. **Conclusion** – The mixed phenotype of early gastric adenocarcinoma is associated with a higher probability of local recurrence after endoscopic mucosal resection.

HEADINGS – Stomach neoplasms. Endoscopic mucosal resection. Gastric mucins.

INTRODUCTION

Gastric adenocarcinoma that is limited to the mucosal layer, with no ulcer or scar tissue, does not usually present lymph node involvement[47]. This is the rationale for local resection with endoscopic mucosal resection (EMR), or mucosectomy. The local recurrence rate after EMR for gastric adenocarcinoma ranges from 2% to 35%[11,59]. This is usually minimal for well-differentiated adenocarcinoma: *en bloc* resected, measuring up to 20 mm in size, restricted to the mucosa, and presenting without ulceration.

However, neoplastic cells may express some antigens, which are markers of a tumor's biological behavior. Moreover, well-differentiated gastric carcinoma (Lauren's intestinal carcinoma) may display different phenotypic properties at an early stage, as demonstrated by mucin expression[23].

Mucins are glycoproteins, the main component of the protective mucous layer of the mucosa. Twelve types of mucins have already been identified: Muc1, 2, 3, 4, 5a, 5b, 6, 7, 8, 9, 11, and 12. Muc1, Muc5a, and Muc6 expressions are present in the normal gastric mucosa, whereas Muc2 expression is the typical mucin of intestinal epithelium with goblet cells. Depending on mucin expression, metaplasia is divided into two groups: gastric and intestinal metaplasia. Muc5a, Muc6, and galactose are markers of gastric phenotype, whereas Muc2 and CD-10 are the intestinal subtype[43,65]. Similar to metaplasia, a subclassification of well-differentiated (Lauren's intestinal) cancer in phenotypes was established to better understand the biological x of these lesions[2,7,19,49,57,64,69]. This type is also known as intestinal cancer, presenting with different phenotypes based on mucin expression: gastric, intestinal, mixed, or indeterminate types[10,50]. Gastric and mixed types tend to show greater agressive behavior, with increased potential for invasion and metastasis (even in early phases, similar to undifferentiated gastric carcinoma of the stomach)[5,29,46,50,53].

The aim of this study was to evaluate whether expression of mucins, p53 and Ki-67, could predict risk of local recurrence of well-differentiated gastric adenocarcinoma (completely resected through EMR in patients followed for at least 1 year).

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METHODS

This was mostly a retrospective study in which patients with early gastric cancer who underwent EMR, by a single endoscopist, at Hospital das Clinicas of São Paulo University from June 1994 to December 2005 were included. The histologic evaluation of the specimens including immunohistochemistry studies were performed prospectively. Patients who had a complete resection were followed for one year. Those patients who were not submitted to surgical treatment after endoscopic resection were considered as cured.

Histopathologic complete resection was defined by the criteria below[18]:

1. Intramucosal cancer;
2. Well-differentiated adenocarcinoma;
3. No histological ulcerations;
4. No lymphatic or venous invasion;
5. Lateral margins free of neoplasia.

The endoscopic follow-up consisted of quarterly scar biopsies in the first year, every 6 months in the second year, and annually thereafter. Patients were divided according to local recurrence during endoscopic follow-up. The two patient groups (with and without local recurrence of gastric adenocarcinoma) were compared for demographic, clinical, endoscopic, and histopathological aspects.

Demographic data

Gender (male or female), age (younger than 60 years old, or older than 60 years old), and race (white, black, or Asian origin).

Endoscopic features

Lesion size: lesions were classified according to size, and grouped as 2 cm or larger. To define lesion size, measurements by macroscopic examination of the resected specimen (and defined by the pathologist) were used for cases of *en bloc* resection. In piecemeal resection, measurements taken by the pathologist were also used; however, when lesion reconstruction was not possible, endoscopic measurement was considered.

Lesion location: according to the Japanese Gastric Cancer Association[18], this was classified in terms of upper, middle, and lower third of the stomach; in addition, it was classified by gastric circumference, either having a greater or lesser curvature as seen in the anterior and posterior wall.

Macroscopic type: this was used for Japanese classification, established by the Japanese Research Society for Gastric Cancer[38]. This classification includes lesions that present slight alterations on the mucosal surface, which may be assessed by endoscopic examination.

Techniques applied to endoscopic resection

a) Strip-biopsy or lift-and-cut technique (Figure 1 A-C) were first described by Tada et al.[54].

b) Suck-and-cut or cap technique (Figure 1 D-E) were described by Inoue et al.[16] and later modified by Torii et al.[60].

Number of resected fragments during mucosectomy: lesions were grouped into *en bloc* resection (single fragment) and piecemeal resection (two or more fragments).

Immunohistochemical profile of gastric adenocarcinoma: two pathologists prospectively reviewed all fragments of endoscopic or surgical resection. The resected specimens had a high likelihood of cure, and were submitted for another immunohistochemical profile prospectively. The immunohistochemical panel included the expression of Muc5A, Muc2, CD-10, p53, and Ki-67 markers.

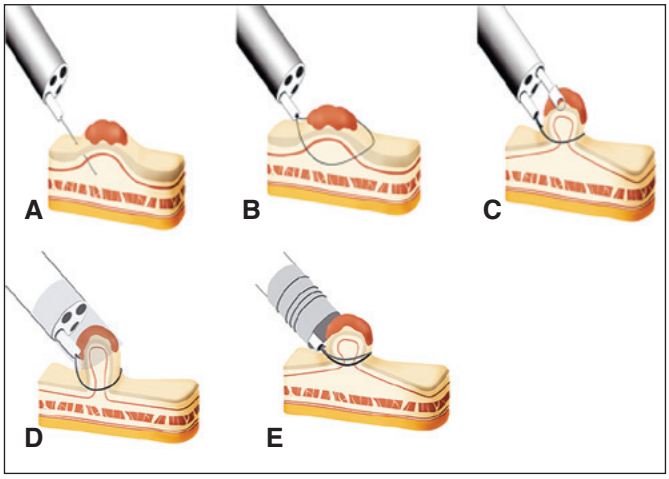

FIGURE 1. Endoscopic Mucosal Resection (EMR). **A-C.** Technique by *strip-biopsy* or lift and cut. **A.** Submucosal injection of saline solution. **B.** Polipectomy snare apreension. **C.** Alternative technique using double-channel endoscope, a special forceps and a polipectomy snare. **D-E.** EMR by *cap* or suck and cut. **D.** Use of cap in association of polipectomy snare. **E.** Technical adaptation using rubber band ligation and polipectomy snare to resected.

Mucins

The streptavidin-biotin-peroxidase method (DAKO) was done in 4-µm-sections of paraffin-embedded specimens for the immunohistochemical study of Muc-2 (Ccp58, Novocastra Laboratories, diluted 1:100, Newcastle, UK), Muc-5A (CLH2, Novocastra Laboratories, diluted 1:200), and CD-10 (56C6, Novocastra Laboratories, diluted 1:500). A search was performed for the staining of Muc-2 and Muc-5a in the cytoplasm of neoplastic cells. The CD-10 marker was considered positive when staining had a brush-border pattern on the luminal surface, which was then verified. Mucin cellular expression was considered positive when at least 5% of neoplastic cells expressed the marker per field of higher magnification (x40). Based on these markers, neoplasias were classified as gastric, intestinal, mixed, and indeterminate for mucins, shown in Table 1.

TABLE 1. Phenotypic Classifications of well differentiated adenocarcinoma

Phenotype	Muc2	Muc5A	CD-10
Gastric	-	+	-
Intestinal*	+	-	+
Mix**	+	+	+
Null	-	-	-

* Intestinal phenotype presents positive to marker Muc2 or CD-10. ** Mix phenotype presents positive to marker Muc2 and/or CD-10 associated to marker Muc5A positive.

Expression of p53 and Ki-67 monoclonal antibodies

The streptavidin-biotin-peroxidase method for LSAB+ (DAKO) was used in 4-µm-sections of paraffin-embedded specimens. Nuclear positivity of p53 markers was classified for intensity and distribution, whereas Ki-67 markers were classified for their distribution. The intensity of the p53 marker was stratified by: 0 – absence of staining; 1 – hardly visible staining; 2 – easily visible staining; 3 – intense staining in lesser degree than control; and 4 – as intense as control group.

The nuclear positivity of p53 and Ki-67 was evaluated for distribution pattern as: 0 – negative; 1– rare cells (less than 2%); 2 – small amount (2-20%); 3 – moderate amount (20-75%); and 4 – marked amount (more than 75%).

Expression of p53 was considered positive when nuclear positivity was stratified in grade 3 or 4, either for intensity or distribution. Ki-67 marker intensities for grade 3 or 4 were characterized as tumors with a high rate of proliferation.

Statistical analysis

Collected data were referred to as mean and standard deviation. Fisher's exact test was used to verify whether age, gender, lesion size, invasion level, macroscopic type, lesion location, endoscopic technique, number of fragments, and immunohistochemical markers (Muc5A, Muc2, CD-10, p53, and Ki-67) were also associated with a higher recurrence rate.

Statistical significance was used, and was established to be $P<0.05$.

RESULTS

Fifty-three patients underwent EMR for treatment of early gastric adenocarcinoma from June 1994 to December 2005. Recovered data existed from 46 of the total number of patients. Of 46 patients, 22 were identified to have a high likelihood of cure through EMR, as they presented differentiated histologic type, complete resection with free margins, no lymphatic or venous invasion, and tumoral invasion confined to the mucosal layer. Of the latter, 5 (22.7%) presented local recurrence within a mean of 5.8±4.16 months (range 1-18 months). All 5 patients with local recurrence were submitted to gastrectomy and have been cured, with no methastasis or recurrence.

Immunohistochemical studies were performed in 18 (78.2%) resected specimens, since analysis of the remaining specimens was not possible due to the loss of resected material. Therefore, 18 patients were stratified according to recurrence, and paired for demographic data (age and gender) (Table 2), histopathologic data, and endoscopic features (endoscopic technique applied for resection, macroscopic type, number of resected fragments, and location) (Figure 2) (Table 3). There was no statistical difference in the studied clinicopathologic factors.

TABLE 2. Demographic parameters of recurrence and no recurrence subgroups in patients with high probability of cure

Demographic parameters	No recurrence	Recurrence	*P*
Gender			
Female	02 (15.4%)	01 (20%)	0.308
Male	11 (84.6%)	04 (80%)	
Age			
< 60 years	07 (53.8%)	04 (80%)	0.814
≥ 60 years	06 (46.2%)	02 (20%)	
Ethnicity			
Caucasian	09 (69.2%)	02 (40%)	
Afro-American	02 (15.4%)	0	0.145
Asian	02 (15.4%)	03 (60%)	

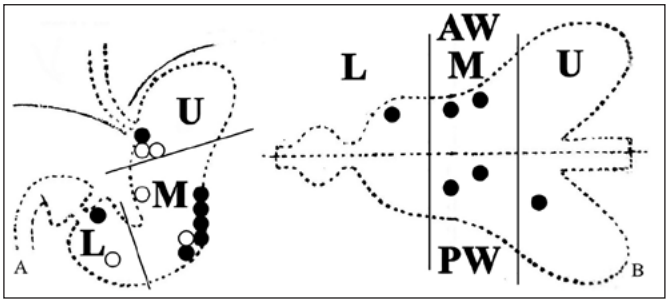

FIGURE 2. Localization of Early Gastric Cancer resected with high probability of cure with and without reccurrence. **A.** Localization of the cases at lesser or greater curvature in upper, middle and lower segments of stomach. **B.** Localization in upper, middle and lower segments at anterior or posterior stomach wall. ● No recurrence and ○ Recurrence. U: upper, M: middle, L: lower, LC: lesser curvature, GC: greater curvature, AW: anterior wall, PW: posterior wall.

TABLE 3. Parameters of recurrence and no recurrence subgroups in patients with high probability of cure after EMR of early gastric cancer

Parameters	No recurrence (n=13)	Recurrence (n=5)	*P*
Technique			
"CAP"	01 (7.7%%)	02 (40%)	0.099
"Strip biospy"	12 (92.3%)	03 (60%)	
Macroscopic Type			
IIa	09 (69.2%)	02 (40%)	
IIc	02 (15.4%)	03 (60%)	0.145
IIa+IIc	02 (15.4%)	0	
Number of fragment			
1	08 (61.5%)	03 (60%)	0.767
≥2	05 (38.5%)	02 (40%)	
Invasion depht			
m1	01 (7.7%)	01 (20%)	
m2	06 (46.2%)	02 (40%)	0.758
m3	06 (46.2%)	02 (40%)	

Immunohistochemical study revealed that tumoral expression of Muc5A-type mucin was associated with a higher recurrence rate (Table 4) (Figure 3).

TABLE 4. Mucin marker expression, p53 and Ki-67 in intramucosal tumours in recurrence and no recurrence subgroups after EMR of early gastric cancer

Markers	No recurrence (n=13)	Recurrence (n=5)	*P**
Muc2	10 (76.9%)	5 (100%)	0.239
Muc5A	2 (15.4%)	4 (80%)	**0.026**
CD10	3 (23%)	0	0.239
p53	2 (15.4%)	2 (40%)	0.261
Ki-67	5 (38.4%)	2 (40%)	0.952

*Fischer's exact test

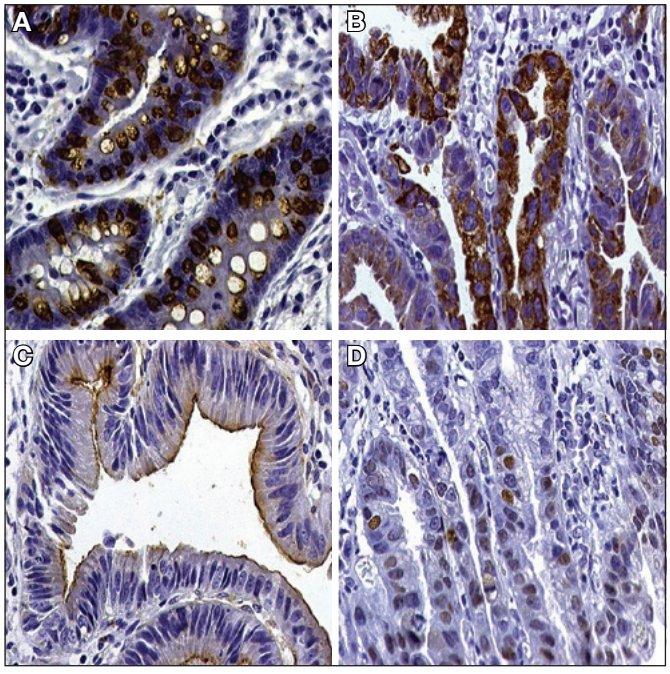

FIGURE 3. A. Cytoplasmic coloration of gastric cancer cells with expression of Muc2 marker in a case classified as mixed type (40X magnification). **B.** Cytoplasmic coloration of gastric cancer cells with expression of Muc5a marker in case classified as gastric type (40X magnification). **C.** Coloration of the brush border of the gastric cancer cells demonstrating the expression of the CD-10 mucinic marker in case classified as intestinal type (40X magnification). **D.** Positive staining of p53 marker (40X magnification).

In the recurrence group, four (80%) patients had the mixed type, and one (20%) had the intestinal type. In the group without recurrence, no patient had the mixed type, but 10 (76.9%) had the intestinal type, 2 (11.1%) had the gastric type, and 1 (7.7%) had the indeterminate type (Table 5).

TABLE 5. Phenotypic type distribution of well differentiated adenocarcinoma in patients with high probability ou cure after EMR of EGC among the recurrence and no recurrence subgroups

Phenotype	No recurrence (n = 13)	Recurrence (n = 5)	*P**
Gastric	02 (15.4%)	0	0.004**
Intestinal	10 (76.9%)	01 (20%)	
Mix	0	04 (80%)	
Null	01 (7.7%)	0	

*Fischer's exact test. ** Statistic difference between intestinal and mix types and groups with and without recurrence. There wasn't difference between the other phenotypes.

DISCUSSION

The classification of gastric cancer in two broad categories, along with different histogenesis and biological behavior, has been well established[27,31,36]. Gastric cancers are classified as intestinal, expanding, or differentiated, as well as diffuse, infiltrative, or undifferentiated. The first type is characterized by expanding growth and liver metastasis, occurring in elderly male patients. The second type presents infiltrative growth and peritoneal dissemination, with a higher incidence in young women[39]. Regarding carcinogenesis, the well-differentiated type originates in the atrophic gastric mucosa with intestinal metaplasia, while the undifferentiated type originates in the trophic gastric mucosa[27,36,45,55]. Undifferentiated carcinoma can spread towards the submucosa with an increase in size, as well as presenting a higher risk of lymph node metastasis[62]. Patients with differentiated gastric carcinoma present a higher 5-year survival rate, compared to those with undifferentiated gastric carcinoma; the former may be an independent prognostic factor[17,34]. However, patients with differentiated tumors without serosa involvement, but with lymph node metastasis, are recognized to present a worse prognosis, compared to those with undifferentiated tumors[1]. Therefore, confounding situations of histogenesis and biological behavior, using this classification, can often be identified[34-36].

Moreover, cases of differentiated type carcinoma with a pronounced trend toward invasion and metastasis, even in the early stage, have been observed[50]. In these cases, endoscopic resection is hindered by the likelihood of local recurrence or metastasis. In order to explain this unexpected biological behavior, immunohistochemical evaluations have acquired greater relevance.

Up to 50% of human cancers are estimated to present some mutation of the p53 gene[4,25,26]. This alteration is involved in the carcinogenesis of gastric cancer, although this is not an independent factor[44]. Some authors suggest its relation to late events of gastric cancer[8,15]. Conversely, Ki-67 is a marker of cell proliferation and related to the prognosis of gastric cancer[70]. Higher rates of the Ki-67 marker, associated with p53, are found to be useful markers for lymph node metastasis in patients with early gastric carcinoma[48]. In this study, p53 and Ki-67 markers were not found to be associated with tumor recurrence[15].

Other markers are used to understand tumor biological behavior, e.g., mucin expression, through which subclassification of gastric cancer in phenotypes was established[2,7,14,19,49,64,66,69]. Thus, gastric tumors may express mucin phenotypes of gastric, intestinal, and mixed intestinal and gastric, or indeterminate types[10,50].

The majority of differentiated adenocarcinomas are known to originate from intestinal metaplasia, presenting an intestinal phenotype[7,27,36]. However, some originate from gastric mucosa without intestinal metaplasia, and were named as the gastric phenotype. Some studies demonstrated that this phenotype determines a higher potential of invasion and metastasis than the intestinal type, which resulted in a worse prognosis[23,37,50,56]. Early-stage cancer, with a gastric phenotype, demonstrated aggressive biological behavior, in comparison to the undifferentiated type[50]. The mixed phenotype presented intermediate aggressiveness[23,50,56].

Encouraging results from immunohistochemical studies of gastric cancer show an increased understanding of gastric tumor carcinogenesis. Of note, differentiated adenocarcinoma with a gastric phenotype had results similar to those of undifferentiated adenocarcinoma, regarding prognosis and tumor biological behavior[23,30,50,56]. Other authors consider the gastric phenotype of well-differentiated cancer an independent factor for lymph node metastasis, even at an early stage[19,23,50].

In this study, 22.7% of patients with differentiated intramucosal gastric cancer (totally resected with EMR) presented with local recurrence. In the literature, these rates usually range from 2.8% to 5.7%, given this situation. The extremely high recurrence rate motivated the search for recurrence risk factors, including demographic, clinical, endoscopic, and immunohistochemical aspects. In the recurrence group, 2/5 (40%) of patients were found to have piecemeal resection, while the remaining patients had *en bloc* resec-

tion. Of these, the M3 layer was found to be involved in 3/5 (60%) cases. However, neither the occurrence of piecemeal resection nor the depth of infiltration into the mucosa predicted local recurrence in our study. With known factors for local recurrence, piecemeal resection was brought to our attention. In the study conducted by Miyata et al.[32], a larger lesion size was associated with a higher number of resected fragments, showing a significant difference but no relation to lesion location. Other studies demonstrated a larger lesion size, a lower rate of *en bloc* resection, even with different techniques and similar local recurrence rates of 1.7% and 2.3%, respectively[11,58]. In this study, all 5 recurrences occurred with lesions smaller than 20 mm, while 3 of them were resected *en bloc*, so that local recurrence could not be attributed to these risk factors. However, p53 and Ki-67 markers were not found to be related to local recurrence, likely confirming the fact that such markers are more strongly expressed in advanced gastric cancer, compared to early gastric cancer[15].

The only predictive factor for local recurrence was a mixed phenotype, demonstrating the usefulness of immunohistochemical study for selection of patients for EMR. In the recurrence group, four (80%) patients had mixed type and one (20%) had intestinal type recurrence. Corroborating our data, Tajima et al.[49] analyzed 63 gastric adenomas and 133 differentiated early gastric cancers, with 24 cases of gastric adenomas in a 2-year follow-up, presenting five cases of malignant transformation. The authors associated cases of malignant transformation to gastric and mixed phenotypes, characterized by HGM (human gastric mucin), MUC6, MUC2, and CD10 mucin markers. Kabashima et al.[20] analyzed the expression of CD10, MUC2, HGM, and concanavalin, to be intramucosal differentiated tumors. By assessing these markers, they found the gastric phenotype in 36.8% (42/114). They demonstrated that the gastric phenotype group had more activity involving metalloproteinase[20], which is associated with degradation of the extracellular matrix and facilitating tumor invasion and dissemination[6,31]. It is important to emphasize that some studies demonstrated how the biological behavior of a tumor with a gastric phenotype was comparable to an undifferentiated tumor[19,50,56].

There is no consensus on the nature and number of antibodies that might be used to define a mucin phenotype of gastric carcinoma, or what percentage of positive tumor cells in each staining section must be used[3,19,21,22,23,24,28,42,51,56,63,67]. Shiroshita et al.[52] suggested that to define a gastric phenotype, MUC5AC mucin or HGM must present in foveolar cells and MUC6 mucin, as well as in cells of the pyloric gland, which are part of the minimal panel to be investigated. For the intestinal phenotype, MUC2 mucins and CD10 must also be investigated. This research suggests that the immunohistochemical profile of mucin expression is a prognostic factor (after EMR of differentiated intramucosal early gastric cancer), as an integral part of the investigation for selected cases (before referral for minimally invasive therapy). In cases already submitted for treatment, in which the immunohistochemical profile of mucin expression was only possible after endoscopic treatment, the finding of mixed phenotype indicates a need for close follow-up or complementary therapy, plus a larger endoscopic or surgical resection, especially with a high risk of local recurrence.

With the development of a new mucosectomy technique, endoscopic submucosal dissection (ESD)[40], *en bloc* resection rates were found to be 98% to 100% for lesions smaller than 2 cm[13,41,68], and 79% to 97% for those larger than 2 cm[11,13,41], along with local recurrence rates of 0 to 1%[11,61,68]. In the present study, none of the 18 lesions was resected by ESD technique, since this technique had barely been introduced in Brazil at the time. Resections with larger safe margins and resection *en bloc* are believed to have curative capacity for lesions with more aggressive biological behavior. When compared to EMR, ESD is considered to be a more complex technique, with a longer learning curve. It is related to more complications, though, specifically perforation and bleeding[9]. It is possible that some centers will continue EMR for treatment of early gastric cancers, measuring up to 15 mm. In this setting, we believe that mucin expression is useful to stratify risk for local cancer recurrence. We also believe that mucin expression should be studied to better stratify risk for local cancer recurrence, after expanded indication in ESD cases[12].

In conclusion, our results suggest that mucin expression predicts local recurrence of early gastric cancers, after being treated with EMR. Moreover, gastric adenocarcinoma with mixed mucin phenotype expression was found to be a risk factor for local recurrence, in cases in which a high likelihood of cure was fulfilled.

Authors' contributions

Hondo FY performed the majority of experiments; Kishi H, Safatle-Ribeiro AV and Ribeiro-Jr U provided analytical tools and were involved in manuscript editing; Pessorrusso FCS was in charge of data acquisition, and also involved in manuscript editing; Hondo FY performed the analysis and interpretation of data; Maluf-Filho F revised the article and approved the final version for publication.

Ethical standards

All procedures were in accordance with the ethical standards of the Committee on Human Experimentation (institutional and national), as well as with the Helsinki Declaration of 1964 and its later versions.

Disclosure

This study is part of a master's degree thesis at University of São Paulo Medical School. The main text can be found at [http://www.teses.usp.br/teses/disponiveis/5/5154/tde-20062007-161637/pt-br.php]. Text in Portuguese (Br).

Hondo FY, Kishi H, Safatle-Ribeiro AV, Pessorrusso FCS, Ribeiro Jr U, Maluf-Filho F. Caracterização dos fenótipos de mucina podem prever a recorrência do câncer gástrico precoce após a mucosectomia endoscópica. Arq Gastroenterol. 2017;54(4):308-14.

RESUMO – Contexto – A ressecção endoscópica da mucosa é tratamento aceito para o tratamento do câncer gástrico precoce em casos selecionados. Os critérios histopatológicos favoráveis à ressecção endoscópica curativa são adenocarcinomas intramucosos, bem diferenciados, com margens lateral e profunda livres, ausência de ulceração ou de embolização angiolinfática. Taxas de recorrência local próximas a 5% têm sido descritas mesmo quando se cumprem tais critérios. Por outro lado, a expressão antigênica por células tumorais tem sido relacionada com o comportamento biológico de diversos tumores. **Objetivo –** Avaliar se a imunoexpressão de mucinas, p53 e Ki-67 podem predizer a recorrência tumoral após mucosectomia endoscópica no câncer gástrico precoce, mesmo se critérios de cura histopatológicos forem atingidos. **Métodos** – Vinte e dois pacientes com critérios de cura para ressecção endoscópica e sumetidos a mucosectomia foram selecionados. A recorrência local ocorreu em 5/22 (22,7%). O estudo imunohistoquímico foi realizado em 18 (81,8%) espécimens. Os pacientes foram divididos em grupos com e sem recorrência local. Foram comparados quanto a dados demográficos, endoscópicos, histológicos e fatores imunohistoquímicos para MUC2, MUC5A, CD10, p53, e Ki-67. **Resultados** – A imunoexpressão de mucinas permitiu a reclassificação dos adenocarcinomas gástricos em intestinal (10), gástrico (2), e de fenótipo misto (4) e nulo (2). Os fenótipos mistos (positivos tanto para MUC2 quanto para MUC5A) foram encontrados em 80% dos casos no grupo de recorrência local, enquanto tipos intestinais (MUC2 positivo e MUC5A negativo) foram identificados em 76,9% dos casos sem recorrência (*P*=0,004). Os outros fatores observados não se relacionaram com a recorrência tumoral. **Conclusão** – O fenótipo misto do câncer gástrico precoce está associado a maior probabilidade de recorrência local após a mucosectomia.

DESCRITORES – Neoplasias gástricas. Ressecção endoscópica de mucosa. Mucinas gástricas.

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