Su1115

THE STAGING OF GASTRITIS WITH THE OLGA SYSTEM IN THE ITALIAN SETTING: HISTOLOGICAL FEATURES AND GASTRIC CANCER RISK

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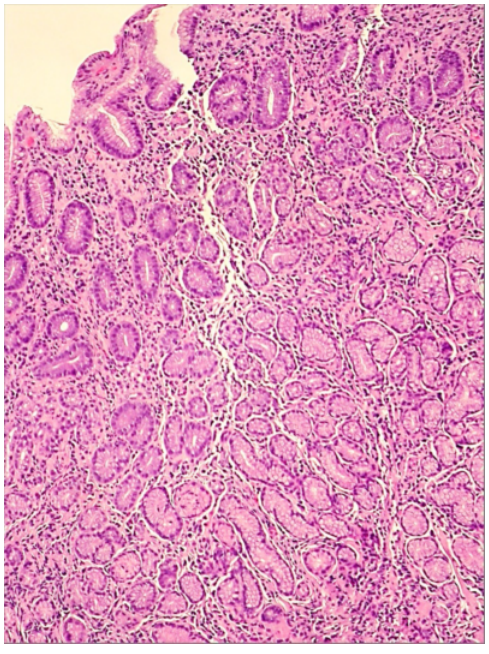
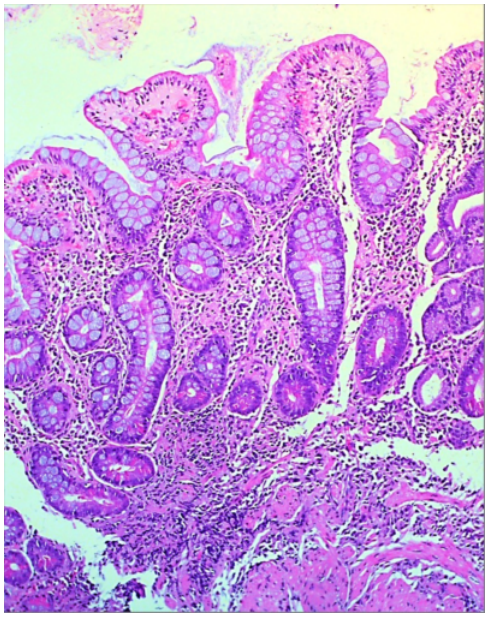
BACKGROUND: Recently OLGA (Operative Link on Gastritis Assessment) classification has been proposed to identify high-risk forms of gastritis that can evolve in gastric cancer (stages III and IV). Helicobacter pylori infection and age older than 40 have been considered as independent risk factor for high-risk OLGA stages. OBJECTIVE: The aim of this study was to confirm the role of OLGA staging in identifying patients at risk. METHODS: This is a retrospective study. Data were collected from records of endoscopy unit database. SPSS statistical software was used for all computations. PATIENTS: We analyzed 520 gastric biopsies from patients who underwent esophagogastroduodenoscopy for gastric cancer screening. Patients were subsequently classified as stage I-IV according to OLGA system and they were also clustered according to age, complete and incomplete metaplasia and atrophy. RESULTS: 156 M/354F, age 62.4±12.6 were included in the study. The distribution of histological features of gastric biopsies are reported in table 1. Complete metaplasia (269/284, p 0.01), gastric atrophy (343/367, p 0.005) and a grade of OLGA staging ≥ II (335/356, p 0.009) were prevalent in subjects older than 40 years old, as well as Helicobacter pylori infection tended to be higher (136/149 p ns). CONCLUSION: High-risk forms of gastritis according to OLGA staging system are significantly associated not only to H. pylori infection, but also to older age, gastric atrophy and complete metaplasia. That results can confirm the importance of OLGA system in order to identify patients at risk, requiring more surveillance.



OLGA 0: well visible glands, occupying the entire mucosal layer



OLGA IV: glands are totally disappeared; we can also observe diffuse intestinal complete metaplasia and hypertrophic muscolaris mucosae.

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GASTRIC INTESTINAL METAPLASIA TYPE III AND PROSPECTIVE RISK OF GASTRIC CANCER IN COLOMBIA

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Background: In the Correa model of gastric carcinogenesis, *Helicobacter pylori* causes chronic gastritis, which over time may progress through the premalignant stages of atrophic gastritis, intestinal metaplasia (IM), and dysplasia, to finally gastric cancer (GC). Extension and types of IM have been associated with differential GC risk. Our study evaluated the association between type III IM (a subtype of incomplete IM with sulfomucin-positive columnar cells) and prospective risk of GC in a cohort of individuals from a high-risk area in Colombia. **Methods:** 795 subjects with gastric precancerous lesions were randomized to anti-*H. pylori* treatment or placebo at enrollment. Gastric biopsies at baseline were scored according to our validated histopathology scoring system. Ten individuals developed GC during 16 years of follow-up (median time to GC, 8 years, interquartile range, 3-12). Three controls were selected for each GC case, matched for age, sex, histopathology score at baseline, anti-*H. pylori* treatment at baseline, and length of follow-up. Sections from all biopsies with IM were stained with high-iron diamine/Alcian blue (HID-AB). IM was initially classified into complete and incomplete types, assessing percentages of epithelium replaced with either IM type. The percentage of epithelium containing sulfomucin-positive columnar cells was assessed in HID-AB sections. All evaluations were performed semiquantitatively by a pathologist blinded to clinical information. The maximum value obtained in a single biopsy across the set of biopsies for each subject was considered for the analyses comparing GC cases and controls. To assess differences in anatomic location of IM, biopsies were grouped into antrum (including incisura) and corpus. Conditional logistic regression models were used to estimate odds ratios (OR). **Results:** All individuals who developed GC had IM at baseline. As a result of the case-control matching, there were no statistically significant differences in extension of complete-type (p=0.86) or incomplete-type (p=0.43) IM. Notably, greater expression of sulfomucins at baseline, was associated with increased GC risk (adjusted OR= 1.29, 95% CI, 1.02-1.63 for each increment in 5% on the expression of sulfomucins). In anatomic location-specific analyses, mean extensions of sulfomucins, total and subtype IM were greater in the antrum as compared to the corpus: 6% vs. 1% for sulfomucins (p= 0.003), 53% vs. 22% (p<0.001) for total 7% vs. 19% for complete-type (p=0.01), and 17% vs. 3% for incomplete-type (p<0.001), regardless of case-control status. **Conclusions:** All IM lesions were more extensive in the antrum. Assessment of sulfomucin expression in gastric IM is useful for the identification of patients at higher risk of GC. This strategy could prove useful to determine which individuals with IM may benefit from closer endoscopic surveillance.

Su1117

AUTOPHAGIC PROTEINS AS MARKERS OF DYSPLASTIC CHANGES IN GASTRIC MUCOSA

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Gastric adenocarcinomas remain a difficult disease to treat, and early recognition remains a key. Early detection of low-grade dysplasia (LGD) and risk stratification of LGD cases becomes important for improved management, considering the relatively rapid progression of high-grade dysplasia (HGD) to carcinoma. Metabolic dysregulation, including autophagy, is a phenomenon with well-recognized contribution to carcinogenesis, and we aimed to examine autophagy by examining the level and distribution of p62, LC3B and LAMP2A. We examined a total of 36 cases of gastric mucosa (biopsy and resection) by immunohistochemistry (IHC). The obtained staining intensity and staining patterns were compared between gastric specimens with histologically confirmed cases of normal, dysplasia and adenocarcinoma. p62 and LC3 proteins could be readily detected in the cytoplasm in the gastric mucosa by IHC. Cytoplasmic p62 staining intensity was higher in the specimens with dysplasia (33.3-40% with 3+ staining *vs.* 0% in intestinal metaplasia and normal mucosa). This trend was not observed with cytoplasmic LC3 staining intensity. LAMP2A staining exhibited mostly punctate pattern, and the staining intensity was not discriminating between the different histological categories. Nucleocytoplasmic shuttling of p62 and LC3 has been previously described, and we observed nuclear staining in the gastric mucosa. Lower nuclear p62 was seen in adenocarcinoma in comparison to cases with dysplasia (66.7% with 0+ staining in adenocarcinoma *vs.* 10% in dysplasia). A similar but less dramatic trend was observed with nuclear LC3 (25% with 0+ staining in adenocarcinoma *vs.* 0-9.1% in other categories). *in vitro* works have placed ErbB family members, including EGFR and ErbB2/HER2, as upstream modulators of autophagy. In our cohort, 2/6 cases of adenocarcinoma were positive for *ERBB2* amplification, and these cases concordantly exhibited highest cytoplasmic p62 staining compared to other adenocarcinoma cases. When we examined the mRNA levels in gastric adenocarcinoma cases from The Cancer Genome Atlas (TCGA), we found an interesting series of positive correlations between *ERBB2* mRNA levels and a number of autophagy-related genes, including *BECN1* (Spearman rho = 0.2449, $p < 0.0001$) and *p62/SQSTM1* (rho = 0.1329, $p = 0.0067$), while correlating negatively with *MAP1LC3A* (rho = -0.1079, $p = 0.0279$). This pattern of correlations was not observed with *EGFR* mRNA levels. Taken together, an interesting role for autophagy in gastric adenocarcinoma pathogenesis is suggested by the combined IHC and mRNA data. As in cases of HER2-positive breast cancers, p62 levels appear to be higher in HER2-positive gastric adenocarcinoma. It is unclear whether the cytoplasmic accumulation of p62 can be equated with decreased autophagy, and further work is underway to tease out the clinical significance of our findings.