ORIGINAL RESEARCH

Endoscopic grading of gastric intestinal metaplasia on risk assessment for early gastric neoplasia: can we replace histology assessment also in the West?

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ABSTRACT

Objectives To assess the value of endoscopic grading of gastric intestinal metaplasia (EGGIM), operative link on gastritis assessment (OLGA) and operative link on gastric intestinal metaplasia (OLGIM) on risk stratification for early gastric neoplasia (EGN) and to investigate other factors possibly associated with its development.

Design Single centre, case–control study including 187 patients with EGN treated endoscopically and 187 age-matched and sex-matched control subjects. Individuals were classified according to EGGIM, OLGA and OLGIM systems. EGN risk according to gastritis stages and other clinical parameters was further evaluated.

Results More patients with EGN had EGGIM of ≥5 than control subjects (68.6% vs 13.3%, p<0.001). OLGA and OLGIM stages III/IV were more prevalent in patients with EGN than in control subjects (68% vs 11%, p<0.001, and 61% vs 3%, p<0.001, respectively). The three systems were the only parameters significantly related to the risk of EGN in multivariate analysis: for EGGIM 1–4 (adjusted OR (AOR) 12.9, 95% CI 1.4 to 118.6) and EGGIM 5–10 (AOR 21.2, 95% CI 5.0 to 90.2); for OLGA I/II (AOR 5.0, 95% CI 0.56 to 44.5) and OLGA III/IV (AOR 11.1, 95% CI 3.7 to 33.1); for OLGIM I/II (AOR 11.5, 95% CI 4.1 to 32.3) and OLGIM III/IV (AOR 16.0, 95% CI 7.6 to 33.4).

Conclusion This study confirms the role of histological assessment as an independent risk factor for gastric cancer (GC), but it is the first study to show that an endoscopic classification of gastric intestinal metaplasia is highly associated with that outcome. After further prospective validation, this classification may be appropriate for GC risk stratification and may simplify every day practice by reducing the need for biopsies.

Significance of this study

What is already known on this subject?

- Previous studies have shown that operative link on gastritis assessment and operative link on gastric intestinal metaplasia (OLGIM) systems are reliable predictors of the risk for gastric cancer (GC).
- An endoscopic grading of gastric intestinal metaplasia (EGGIM) was recently proposed and validated in individuals without GC using histology as gold standard.
- Although there is a strong correlation between the EGGIM and OLGIM stages, the independent value of EGGIM stages for GC risk assessment was not proven.

What are the new findings?

- For the first time, it is shown that an endoscopic score to assess the presence and extent of gastric intestinal metaplasia is associated with the risk of GC.
- The risk of GC increases with the stage of EGGIM.

How might it impact on clinical practice in the foreseeable future?

- Screening and surveillance programme including EGGIM staging is expected to be a practical approach that will help to achieve better risk stratification of gastritis in each individual.

INTRODUCTION

Gastric cancer (GC) remains a common malignancy and a leading cause of cancer mortality worldwide.[1] The 5-year survival rate of patients with GC is below 50%, whereas that of early GC can exceed 90%.[2–4] This means that early detection and treatment are crucial for the successful management of this disease. Screening and surveillance of people at risk are the best strategy for achieving those goals.[5–7]

Most GCs (typically intestinal type) occur as a result of progressive changes from chronic gastritis through gastric atrophy (GA), gastric intestinal metaplasia (GIM), dysplasia and ultimately invasive neoplasia.[8] *Helicobacter pylori* infection has been recognised as the main environmental promoter of this multistep carcinogenic process.[9] GA (defined as loss of pre-existent gastric glands) and GIM (defined as replacement of gastric epithelium by intestinal-type epithelium) are considered premalignant conditions because they confer risk for development of GC and the background in which dysplasia and adenocarcinoma may occur.[6 10 11] As the risk of GC increases in relation with the severity and extent of those preneoplastic changes, several systems for staging of gastritis have been proposed to rank the risk in each individual and to determine who should enter in endoscopic surveillance programmes.[12–14]

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The operative link on gastritis assessment (OLGA) and the operative link on gastric intestinal metaplasia (OLGIM) are histological staging systems based on the severity and topographic distribution of GA and GIM, respectively.[12 13] Both systems have stratified gastritis in five progressive stages from 0 to IV. Several studies have recognised OLGA and OLGIM stages III/IV as high risk for GC.[15–18]

Recently, a scale for endoscopic grading of gastric intestinal metaplasia (EGGIM) using high-definition, virtual chromoendoscopy with narrow-band imaging (NBI) was created and validated.[14 19] This classification rates the entire gastric mucosa according to the presence and extent of GIM from 0 to 10.[14] An EGGIM of ≥5 was found as the optimal cut-off to identify patients with OLGIM III/IV.[14] However, besides its strong relation with the advanced stages of GIM, the independent value of EGGIM as a risk classification for GC remains undetermined.[19]

This study aimed to assess the value of EGGIM, OLGA and OLGIM on risk stratification for early gastric neoplasia (EGN) and consequently for GC. We also analysed the role of other parameters for the risk of EGN and advanced stages of gastritis.

METHODS

Study design and patient selection

This was a case–control study conducted at a single centre (Portuguese Oncology Institute of Porto, Porto, Portugal). Patients with primary EGN who underwent endoscopic submucosal dissection from 2012 to 2017 were identified. EGN included low-grade dysplastic lesions, high-grade dysplastic lesions and early GC, all defined in accordance with the WHO classification of tumours of the stomach, which includes the Vienna system.[20 21] Patients with a history of gastric neoplasia, gastric resection or hereditary syndrome associated with increased risk of GC were excluded. There were 250 eligible patients.

Control subjects were selected from a cohort of patients followed up in the same centre who had undergone esophagogastroduodenoscopy (EGD) with random (more likely when no GIM was seen) or guided (more likely when GIM was seen), antrum and corpus gastric biopsies for staging of gastritis between years 2012 and 2017.[6] Subjects who underwent more than one EGD with gastric biopsies sampling during the assessed period were only considered once, giving preference for endoscopy and related pathology reports that stated simultaneously the EGGIM score or with more detailed description of the histological GA and GIM. Patients who had a history of gastric neoplasia, gastric resection and hereditary GI syndrome associated with increased risk of GC, or who were diagnosed with a gastric neoplastic lesion during the EGD under review were excluded. There were 281 eligible control subjects for inclusion.

An age-matched and sex-matched control was selected within a 3-year age range for each patient with EGN, resulting in 187 pairs for analysis (figure 1).[22 23]

Data collection

All data were collected from endoscopy and pathology reports, and electronic medical records. Family history of GC, smoking status, alcohol consumption, use of acetylsalicylic acid, use of proton pump inhibitors (PPIs), *H. pylori* infection status and gastritis staging according to EGGIM,[14] OLGA[24] and OLGIM[13] classifications were taken into account when comparing patients with EGN with control subjects. The family history was considered positive whenever there was at least one first-degree or second-degree relative with GC.[25] Smoking status (regarding

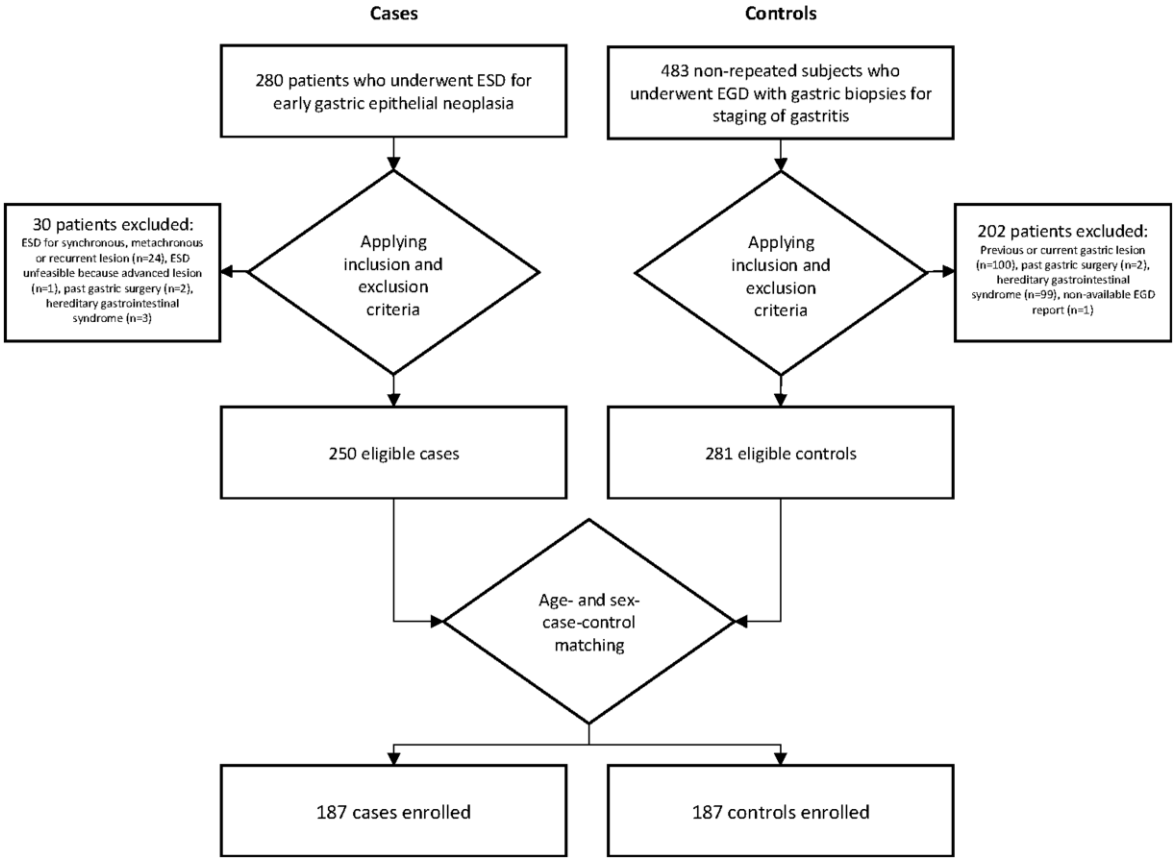

Figure 1 Flowchart of study patient enrolment. EGD, esophagogastroduodenoscopy; ESD, endoscopic submucosal dissection.

tobacco) was classified into never-smokers and current/ex-smokers.[26 27] Alcohol use was divided into drinking more than or equal to 40 g and less than 40 g of alcohol per day.[28] *H. pylori* status was considered negative if there was no current or past evidence of infection.[29] Maintenance use of acetylsalicylic acid or PPI was considered when the drug was part of the patient usual medication.[30 31] The EGN locations were classified by dividing the stomach into three segments: upper third (fundus and upper body and middle body); middle third (lower body, body–antrum transition and angular incisura); and lower third (antrum). The early GC differentiation was divided into well and moderately differentiated, and undifferentiated. In the EGN group, for gastritis staging, data from the therapeutic endoscopy or from a previous or follow-up endoscopy up to 1-year interval were considered. In the control group, no distinction was done between random and guided biopsy sampling for staging of gastritis; however, it is likely that biopsies were random when no GIM was seen and guided when GIM was seen. GA and GIM were classified according to the updated Sydney System.[32] Based on these data, OLGA and OLGIM were calculated.[13 33] EGGIM data were collected from patients' endoscopy reports. EGGIM is a scale for EGGIM using high-resolution endoscopy with NBI, which evaluates the extent of GIM in five different areas of the stomach (lesser and greater curvature of the antrum, lesser and greater curvature of the corpus, and incisura). Each one is scored 0 (no GIM), 1 (focal GIM) or 2 points (extensive GIM), giving a maximum score of 10 points.[14] This was always calculated using Olympus HQ-190 scopes. Since this classification was only created in 2015, EGGIM data were collected from the first endoscopy report that stated this classification (when available) or when the endoscopic description/images in the report allowed EGGIM calculation (in both groups).

Statistical analysis

Continuous variables were reported as mean with SD. Categorical variables were expressed as absolute frequency and percentage. Student's t-test was applied to compare the unique continuous variable (age) between patients with EGN and control subjects. χ^2 test was applied to compare categorical variables between the analysed groups. Unadjusted ORs and 95% CIs were calculated from cross-tabulations. Binary logistic regression models (forward stepwise method) were used to estimate adjusted ORs (AORs) and the related 95% CI. Only variables with a p value of <0.10 on univariate analysis were included in multivariate analysis. EGGIM, OLGA and OLGIM stages were not included in the same regression model because they are closely related to each other and to avoid collinearity. Receiver operating characteristic (ROC) curve analysis was performed to compare the accuracy of the different gastritis staging systems for EGN.[34]

A two-sided p value of <0.05 was regarded as statistically significant. All statistical analyses were performed using the Statistical Package for Social Sciences software for Windows V.22.

RESULTS

Patients clinicopathological characteristics

This study compared 187 patients with EGN with 187 control patients without gastric neoplasia, matched for age and gender. The EGN group had a total of 90 (48%) intraepitelial neoplasms (13 (7%) low-grade dysplastic lesions and 77 (41%) high-grade dysplastic lesions) and 97 (52%) early GCs (74 (40%) invading the lamina propria or muscularis mucosae and 23 (12%) invading the submucosa). Of the 97 early GCs, 90 (93%) were well/moderately differentiated and 7 (7%) were undifferentiated. Endoscopically, the topographic location of the EGNs was as follows: 32 (17%) in the upper third, 52 (28%) in the middle third and 103 (55%) in the lower third. Indications for EGD in the control group included dyspepsia, reflux, anaemia and gastritis surveillance.

Table 1 Clinicopathological characteristics of patients with early gastric neoplasia and control subjects

	Patients with early gastric neoplasiapatients n=187	Control subjects without gastric neoplasia n=187	P value
Age, mean±SD	65.2±9.2	64.9±9.2	0.775
Gender (male), n (%)	104 (55.6)	104 (55.6)	1
History of *Helicobacter pylori* infection, n (%)	73 (44.2)	85 (45.5)	0.82
Smoking (current/ex-smoker), n (%)	64 (43.5)	39 (39.0)	0.478
Alcohol consumption (≥40 g/day), n (%)	43 (37.4)	25 (29.4)	0.239
Acetylsalicylic acid, n (%)	23 (12.6)	23 (14.2)	0.671
PPI, n (%)	109 (59.9)	66 (40.5)	<0.001
Family history of GC, n (%)	38 (29.7)	17 (16.7)	0.021
Gastric atrophy (moderate to severe), n (%)			
Corpus	97 (61.0)	32 (18.1)	<0.001
Antrum	142 (85.5)	46 (27.2)	<0.001
ntestinal metaplasia (moderate to severe), n (%)			
Corpus	77 (47.5)	9 (5.1)	<0.001
Antrum	121 (72.5)	16 (9.5)	<0.001

EGN, early gastric neoplasia; GC, gastric cancer; PPI, proton pump inhibitor.

The demographic and underlying gastritis features of patients are shown in table 1. PPI use and family history of GC were more common among patients with EGN than among control subjects (p<0.05). The proportions of patients with *H. pylori* infection, smoking habits, alcohol consumption and acetylsalicylic acid use were not significantly different between groups (p≥0.05). At both sites of the stomach, the prevalence of moderate-to-severe GA and GIM was significantly higher in the EGN group than in the non-EGN group (p<0.001).

Gastritis staging using EGGIM, OLGA and OLGIM

As shown in table 2, patients with EGN had higher EGGIM, OLGA and OLGIM stages than control subjects. There were 0.6% of patients with EGN and 30% of control subjects with EGGIM 0, 0.6% patients with EGN and 16% of control subjects with OLGA 0, and 3% of patients with EGN and 67% of control subjects with OLGIM 0. Subjects with OLGA I/II were more common in the control group than in the EGN group (74% vs 32%, p<0.05). In contrast, the absolute number of subjects with EGGIM 1–4 and OLGIM I/II were more common in the EGN group than in the control group (48 vs 17, p<0.001 and 60 vs 52, p<0.001, respectively). Subjects with EGGIM ≥5 were more prevalent in the EGN group than in the control group (69% vs 13%, p<0.001). Stages III/IV were more common in the EGN group than in control subjects for both OLGA (68% vs 11%, p<0.001) and OLGIM (61% vs 3%, p<0.001; table 2).

For the presence of EGN, the areas under the curve (AUCs) ROC for EGGIM, OLGA and OLGIM systems were 0.84 (95% CI 0.70 to 0.99), 0.80 (95% CI 0.68 to 0.92) and 0.84 (95% CI 0.71 to 0.98), respectively (p<0.001, figure 2).

Table 2 Univariate and multivariate analyses of the risk of early gastric neoplasia in subjects according to the analysed variables

	Patients with early gastric neoplasia	Control subjects without gastric neoplasia	Univariate analysis			Multivariate analysis		
	n=187	n=187	OR	95% CI	P value	OR	95% CI	P value
History of *Helicobacter pylori* infection, n (%)								
No	92 (55.8)	102 (54.5)	1					
Yes	73 (44.2)	85 (45.5)	0.95	0.63 to 1.45	0.82	–	–	–
Smoking, n (%)								
Never-smoker	83 (56.5)	61 (61.0)	1					
Current/ex-smoker	64 (43.5)	39 (39.0)	1.21	0.72 to 2.02	0.478	–	–	–
Alcohol consumption, n (%)								
<40 g/day	72 (62.6)	60 (70.6)	1					
≥40 g/day	43 (37.4)	25 (29.4)	1.43	0.79 to 2.61	0.239	–	–	–
Acetylsalicylic acid, n (%)								
No	159 (87.4)	139 (85.8)	1					
Yes	23 (12.6)	23 (14.2)	0.87	0.47 to 1.63	0.671	–	–	–
PPI, n (%)								
No	73 (40.1)	97 (59.5)	1			1		
Yes	109 (59.9)	66 (40.5)	2.19	1.43 to 3.38	<0.001	2.12	0.93 to 4.81*	0.073
Family history of GC, n (%)								
No	90 (70.3)	85 (83.3)	1			1		
Yes	38 (29.7)	17 (16.7)	2.11	1.11 to 4.02	0.021	1.73	0.65 to 4.57*	0.271
OLGA, n (%)								
0	1 (0.6)	26 (15.5)	1			1		
I/II	50 (31.8)	124 (73.8)	10.48	1.39 to 79.36	0.005	5	0.56 to 44.47†	0.149
III/IV	106 (67.5)	18 (10.7)	153.11	19.54 to 1199.9	<0.001	11.07	3.71 to 33.07†	<0.001
OLGIM, n (%)								
0	5 (3.0)	115 (66.9)	1			1		
I/II	60 (36.1)	52 (30.2)	26.54	10.07 to 69.96	<0.001	11.48	4.08 to 32.29*	<0.001
III/IV	101 (60.8)	5 (2.9)	464.6	130.73 to 1651.1	<0.001	15.97	7.64 to 33.38*	<0.001
EGGIM, n (%)								
0	1 (0.6)	9 (30.0)	1			1		
1–4	48 (30.8)	17 (56.7)	25.41	2.99 to 215,72	<0.001	12.92	1.41 to 118.61‡	0.024
5–10	107 (68.6)	4 (13.3)	240.75	24.27 to 2388.0	<0.001	21.21	4.99 to 90.16‡	<0.001

*Adjusted for family history of GC, PPI and OLGIM stage
†Adjusted for family history of GC, PPI and OLGA stage.
‡Adjusted for family history of GC, PPI and EGGIM stage.
EGGIM, endoscopic grading of gastric intestinal metaplasia; GC, gastric cancer; OLGA, operative link on gastritis assessment; OLGIM, operative link on gastric intestinal metaplasia; PPI, proton pump inhibitor.

Risk of early gastric neoplasia

Multivariate analysis did not show that *H. pylori* infection, family history of GC, smoking habits, alcohol consumption, acetylsalicylic acid use, and PPI use were significantly associated with the risk of EGN. For the EGGIM classification, both stages EGGIM 1–4 (AOR 12.9, 95% CI 1.4 to 118.6) and EGGIM 5–10 (AOR 21.2, 95% CI 5.0 to 90.2) were significantly associated with higher risk of EGN (table 2).

On comparison of OLGA III/IV with OLGA 0, the OLGA stage III/IV was associated with higher risk of EGN (AOR 11.1, 95% CI 3.7 to 33.1). In contrast, the lower association between OLGA I/II and EGN did not meet statistical significance in the multivariate analysis (table 2).

For the OLGIM staging system, the AORs were statistically significant in stages OLGIM I/II (AOR 11.5, 95% CI 4.1 to 32.3) and OLGIM III/IV (AOR 16.0, 95% CI 7.6 to 33.4; table 2).

Analysis for the risk of advanced stages of gastritis

An additional analysis was performed to identify parameters associated with EGGIM of ≥5, OLGA III/IV and OLGIM III/IV (online supplementary tables 1–3). Male gender was the only parameter significantly associated with higher risk of EGGIM of ≥5 in multivariate analysis (AOR 3.1, 95% CI 1.5 to 6.4). By univariate analysis the current/ex-smoker status was marginally associated with EGGIM ≥5; however, the association did not reveal statistical significance in the multivariate analysis (online supplementary table 1).

Current/ex-smoker status was the only parameter significantly associated with the risk of OLGA III/IV (AOR 2.3, 95% CI 1.2 to 4.5). Family history of GC showed a significant association with OLGA III/IV in univariate analysis, although it was not significant after adjustment for other parameters (online supplementary table 2).

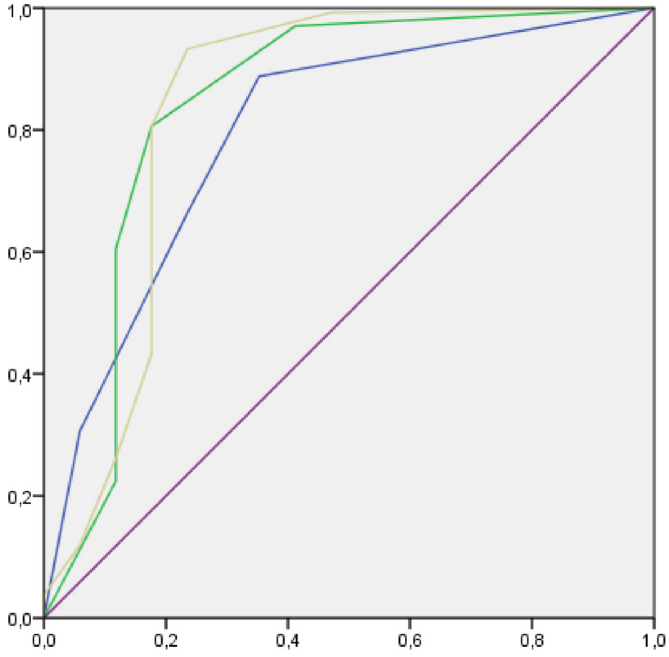

Figure 2 The yellow, blue and green lines represent the receiver operating characteristic curves for endoscopic grading of gastric intestinal metaplasia, operative link on gastric atrophy and operative link on gastric intestinal metaplasia scores compared with the diagnosis of early gastric neoplasia, giving areas under the curve of 0.84 (95% CI 0.70 to 0.99), 0.80 (95% CI 0.68 to 0.92) and 0.84 (95% CI 0.71 to 0.98), respectively.

Multivariate analysis showed that high alcohol consumption was associated with higher risk of OLGIM III/IV (AOR 2.8, 95% CI 1.4 to 5.8). Although family history of GC and current/ex-smoker status were marginally associated with higher risk of OLGIM III/IV in univariate analysis, these tendencies did not achieve statistical significance in the multivariate testing (online supplementary table 3).

DISCUSSION

To the best of our knowledge, this is the first study to show that an endoscopic classification of GIM can be a useful tool for risk assessment of EGN and consequently of GC. We found that histologically, GIM (OLGIM I/II and III/IV) and advanced GA (OLGA III/IV), but also endoscopic GIM (EGGIM 1–4 and 5–10), were the only parameters independently associated with the risk of EGN development. Male gender, alcohol use and current/ex-smoker status were identified as risk factors for advanced stages of gastritis. In contrast, *H. pylori* infection, acid acetylsalicylic use, PPI use and family history of GC were not associated with increased incidence of EGN nor late-stages of GA/GIM.

Our study has some limitations. We only included patients with EGNs resected endoscopically; therefore, our results are more legitimate for the intestinal type of GC, which typically follows the Correa precancerous cascade of changes initiated by a non-self-limiting inflammation.[8] As some evidence has shown that GA and GIM might have a role (still uncertain) in pathogenesis of diffuse-type GC,[11 23] there are motifs to believe that EGGIM may be a useful tool to analyse the background mucosa of patients who develop this Lauren type of GC. In this study, we could not distinguish when random or guided biopsy strategies were used for staging of gastritis, even though it is likely that biopsies were random when no GIM was seen and guided when GIM was seen. This would be particularly relevant, because we may argue that for staging of gastritis, guided biopsies by virtual chromoendoscopy can upgrade OLGA and OLGIM stages (and vice-versa when considering random/non-guided biopsies). Indeed, this might strengthen our results since by overstaging gastritis, the risk of cancer would be lower in those patients. Besides that, biopsy samples of the incisura angularis were not available in all the patients, which could have downgraded the stage of OLGA/OLGIM in some cases.[23 35] However, it is expected that biopsy strategies were not different applied for both groups. Also, during the data collection, there were missing data and the investigators were unblinded to the different cohort groups, which may have introduced a potential classification bias but presumably non-differential between both groups. In addition, the study was developed in a centre where endoscopists have significant experience in virtual chromoendoscopy, namely, in NBI, which means that EGGIM study outcomes cannot be generalised to non-expert settings. Nevertheless, we have previously described the reliability and feasibility of its use.[36 37] Regarding *H. pylori*, the observed prevalence was lower than expected for this population (in particular for the EGN group), which most likely reflects some limitations introduced by the study design, such as unreported past eradications by patients, the use of different methods to confirm eradication and the impossibility to confirm the conditions in which these tests were performed (ie, with timely withdrawal of PPIs and antibiotics). However, this was not differently determined for both groups.

Curiously, we found a non-significant trend for possible increased risk of EGN in PPIs users. This result should be interpreted with caution, because no causal link between PPIs and GC has been proven. Indeed, cumulative evidence coming from observational studies, reviews and a recent meta-analysis have showed that long-term use of PPIs can possibly increase the risk of GC.[31 38–41] However, given that PPIs are commonly taken without prescription, we speculate that some patients may have started taking these medications only at the time of the diagnosis, what may overestimate this tendency. Further well-designed prospective studies are needed to clarify this subject matter.

Several studies have described an increased prevalence of premalignant conditions and GC in first-degree and second-degree relatives of patients with GC, and suggested that GIM in relatives of patients with GC may progress more frequently and rapidly to cancer than in other patients.[25 35 42 43] In this study, a positive family history of GC showed a trend for increased risk of EGN and advanced stages of gastritis, which did not meet statistical significance in the multivariate analysis. The sample size may have limited the results. However, as family history (especially in first-degree relatives) appears to be a strong and consistent risk factor for GC in the published literature, endoscopic screening and surveillance according to the underlying gastritis should be offered to these patients.[42]

In this study, the three stratification systems used to evaluate GA and GIM were all significantly related to the risk of EGN, consequently of GC. However, they have different characteristics. OLGA and OLGIM focus on the recognition of GA and GIM in biopsy samples to rank the individual risk of GC. Regarding formulation, OLGA and OLGIM are comparable, but it is recognised that the interobserver agreement between pathologists for scoring GIM has been superior to GA.[13] Multiple studies and a recent meta-analysis have established an association between advanced (III/IV) OLGA or OLGIM stages with increased incidence of GC.[17 18 23 33 44–46] In our study, stage III/IV

defined in both systems had a marked association with EGN risk, highlighting the clinical priority of offering endoscopic surveillance to these patients. In contrast, while OLGA stage I/II was not significantly associated with the risk of EGN, OLGIM stage I/II was (despite in lower degree than OLGIM III/IV), which underlines the importance of GIM by itself as a precancerous condition.

On the other hand, EGGIM focuses on the recognition of endoscopic GIM and its distribution in the stomach using NBI.[14] This endoscopic GIM assessment was first applied in a multicentre prospective study and returned an AUC of 0.98 (95% CI 0.97 to 0.99) for extensive GIM.[14] Recently, it was externally validated and showed an AUC of 0.96 (95% CI 0.93 to 0.98) for the diagnosis of OLGIM III/IV. By using the cut-off score of ≥ 5, the sensitivity and specificity to identify patients with OLGIM III/IV were 89% and 95%, respectively.[19] Although EGGIM correlates very well with histology, the value of EGGIM for risk assessment of GC was not yet proven. In the current study, we confirmed that EGGIM≥ 5 had a remarkable association with EGN. As observed with OLGIM, the risk of EGN was increased in patients with less advanced stages of EGGIM (score 1–4), even to a lower degree. The AUCs in EGGIM, OLGA and OLGIM for EGN were similar. However, the AOR magnitude of high-risk EGGIM, OLGA and OLGIM suggest that endoscopic GIM classification, which considers visualisation of all the gastric mucosa and do not rely only on small histological fragments of the mucosa, may be more appropriate for risk stratification than histological systems.

Indeed, owing to the patchy and multifocal distribution of premalignant conditions in gastric mucosa, non-guided gastric biopsies for staging of gastritis may miss these lesions, downgrade OLGA and OLGIM stages, and thus miss patients with extensive GA or GIM who would require surveillance.[37] In contrast, patients with mild/focal GIM submitted to guided biopsies for staging of gastritis targeted to areas of GIM may have their OLGIM upgraded and underwent unnecessary oversurveillance. Therefore, as shown in a recent study of den Hollander *et al* there are reasons to believe that a risk stratification tool solely based on histopathology might not be sufficient.[47]

Several studies have confirmed that in expert hands high-definition endoscopy with NBI is highly accurate for the diagnosis of GIM and dysplasia and superior to white-light endoscopy in identifying patients with GIM.[37 48 49] In this context, EGGIM has emerged as a simple, intuitive, real-time tool that, considering the entire gastric mucosa, instead of small histological snapshots of gastric tissue, and using NBI, can allow a better staging of gastritis, help in the identification of EGN, target biopsies, and ultimately improve the diagnostic yield of endoscopy and risk stratification of each individual. Furthermore, this endoscopic classification for staging GIM may allow offering of a correct proposal for surveillance immediately after the endoscopy without the need of biopsies and to give a better insight into dynamic changes of GIM during follow-up EGD (progressive, static or regression).

Obviously, the application of EGGIM should be restricted to endoscopists with proper training in NBI. Nevertheless, the learning process of the gastric NBI patterns does not seem to be long nor complex, but as all techniques there is a learning curve that should be respected before starting to use this classification in endoscopy reports.[36] Despite this system opening fantastic opportunities, its widespread use faces three more additional issues that need to be taken into account. First, EGGIM is only studied and validated for NBI, but as already mentioned in previous papers, it is not expected that its outcomes would be restricted to Olympus and this type of virtual chromoendoscopy. However, its extension to other providers and their modes of virtual chromoendoscopy needs to be investigated in future studies. Second, across Europe (and elsewhere), there are still many departments in which virtual chromoendoscopy and high-definition processors and screens are not routinely available, which may hinder the general roll-out of the system as a new standard. Third, the time needed for more detailed inspection of the gastric lining compared with standardised evaluation with white-light and biopsy sampling may increase time constraints, depending on the department setting, which might make adequate and appropriate use of EGGIM more difficult. Despite these issues, this work further strengthens the potentialities of EGGIM, reason why we admit that after proper training, endoscopists might start to introduce this grading in their clinical practice (in combination with the recommended gastric biopsy sampling in an index endoscopy), since it may help to stratify more properly the individual risk of each patient than histology alone. The reproducibility of this tool has to be further validated in large prospective studies.

In summary, this is the first study to show that an endoscopic score to assess the presence and extent of GIM (EGGIM) is a useful tool to assess the risk of GC. Our results indicate the most advanced stages of GIM (EGGIM≥ 5 and OLGIM III/IV) as the most relevant risk factors for EGN. This study provides another perspective about the importance of the gastritis staging systems for the prediction of gastric neoplasms and highlights that patients at risk need a careful follow-up. Screening and surveillance programmes including EGGIM staging are expected to be a practical approach that, by adding a whole vision of the gastric mucosa, will help to achieve better risk stratification in each individual and reduce the need for biopsies.

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