

## ORIGINAL ARTICLE OPEN ACCESS

# The Role of Endoscopic Grading of Gastric Intestinal Metaplasia (EGGIM) in Assessing the Extent and Degree of Gastric Intestinal Metaplasia

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## ABSTRACT

**Objectives:** We aimed to evaluate the consistency between endoscopic grading of gastric intestinal metaplasia (EGGIM) and the operative link on gastric intestinal metaplasia assessment (OLGIM) staging, as well as the value of endoscopic grading of gastric intestinal metaplasia (GIM) in early gastric cancer (EGC) risk.

**Methods:** The sample size was estimated to be at least 210 patients. To evaluate GIM, EGGIM staging was used during magnifying endoscopy with narrow-band imaging, while the OLGIM staging was carried out according to the updated Sydney system. The consistency between the two scoring systems and the accuracy of EGGIM in diagnosing OLGIM III/IV cases were evaluated. EGC risk was evaluated using the Kimura–Takemoto classification, the operative link on gastritis assessment (OLGA)/OLGIM, and EGGIM.

**Results:** Among the 210 patients, 68 (32.4%) had (previous) EGC and 142 (67.6%) had chronic atrophic gastritis (CAG). EGGIM and OLGIM staging showed good consistency ( $\kappa=0.805$ ,  $U=12.620$ ,  $p<0.001$ ) in diagnosing OLGIM III/IV GIM, with an area under the receiver operating characteristic curve for EGGIM of 0.95. Using a cut-off value of  $>4$ , the sensitivity and specificity were 95.7% and 91.4%, respectively. The EGGIM score was higher in the EGC group than in the CAG group (4.93 vs. 3.92,  $p<0.001$ ).

**Conclusions:** EGGIM shows good diagnostic performance and consistency with OLGIM, which can simplify endoscopic surveillance by reducing the need for biopsy. The EGGIM score is associated with EGC risk, and endoscopic surveillance is recommended for patients with EGGIM score  $>4$ .

## 1 | Introduction

Gastric cancer (GC) is one of the most common tumors in the gastrointestinal (GI) tract in China. It ranks as the fifth most common cancer and the third leading cancer-related cause of death globally in 2018 [1]. The 5-year survival rate of patients with GC has been estimated to be less than 50%; however, that of early gastric cancer (EGC) after resection is

$>90\%$  [2]. Therefore, early detection and treatment of GC is vital in clinical practice. Generally, the development of most GC tumors follows the Correa's sequence, from chronic non-atrophic gastritis (CNAG), chronic atrophic gastritis (CAG), gastric intestinal metaplasia (GIM), and hyperplasia to GC [3]. CAG and GIM are recognized as precancerous conditions of GC because the severity and extent of these conditions are associated with GC development [4]. The operative link for

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gastritis assessment (OLGA) [5] and the operative link on gastritis intestinal metaplasia assessment (OLGIM) [6] systems have been widely employed for evaluating the risks of GC development in CAG and GIM cases. Previous studies [7–9] have revealed that OLGA III/IV and OLGIM III/IV stages are significantly correlated with GC risk. Therefore, routine endoscopic examinations for patients with precancerous conditions can increase the detection rate of EGC.

Thanks to the advances in endoscopic technology, magnifying endoscopy (ME) now plays an important role in the screening and diagnosis of GIM. ME has been found to achieve a high accuracy and outperform white-light endoscopy (WLE) in detecting the precancerous conditions of GC [10–12]. Moreover, using ME with narrow-band imaging (ME-NBI), the appearance of light-blue crest (LBC), which shows as a thin light-blue linear structure in the ridge of the gyrus structure on the epithelial surface of gastric mucosa, is a characteristic manifestation of GIM [13]. In recent years, another endoscopic classification, namely the endoscopic grading of gastric intestinal metaplasia (EGGIM) [14], has been proposed to identify GIM on the basis of ME and evaluate its extent and severity quantitatively. A European multicenter study [15] showed that the area under the receiver operating characteristic (ROC) curve (AUROC) of EGGIM for the diagnosis of OLGIM III and IV stages was 0.96 (95% confidence interval [CI] 0.93–0.98), and the sensitivity and specificity reached 89% and 95%, respectively, with a cut-off value of  $> 4$ .

However, the diagnostic performance of the EGGIM system has been less commonly studied in China. Therefore, we conducted this study aiming to verify the consistency in diagnostic accuracy of the EGGIM and OLGIM systems as well as the performance of the EGGIM in EGC.

## 2 | Participants and Methods

### 2.1 | Study Design and Participant Selection

Adult ( $\geq 18$  years) individuals who were scheduled to undergo endoscopic examination at the Endoscopy Center of the First Affiliated Hospital of Zhejiang Chinese Medicine University (Hangzhou, Zhejiang Province, China) from June 2022 to June 2023 were prospectively recruited. The diagnosis of CAG was made on the basis of histopathologic findings of the samples obtained from multi-site biopsy of the gastric antrum, incisura, and corpus under gastroscopy. The disease categories included CAG, EGC, and previous EGC that had been resected by endoscopic submucosal dissection (ESD) within 1 year before enrollment; cases with the latter two categories were classified into the EGC group. EGC was defined as GC limited to the mucosal or submucosal layer, with or without lymph node metastasis. Patients with known OLGIM stage who could not tolerate gastroscopy due to severe cardiopulmonary insufficiency or had a previous subtotal gastrectomy were excluded from the study.

The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Zhejiang Chinese Medicine University (no. 2023-KLS-352-01). Written informed consent was obtained from each participant before their enrollment.

### 2.2 | Endoscopic Procedures

The endoscopic procedures were carried out by three senior endoscopists who had performed endoscopic examinations for over 10 years and were proficient in WLE and ME-NBI. All of them were familiar with the EGGIM staging and were blinded to the pathologic findings of those who had undergone ESD within 1 year before enrollment. First, gastric mucosa was observed under WLE, and the endoscopic manifestations were evaluated by using the Kimura–Takemoto classification [16], which divided atrophy into the close (C-0, no atrophy; C-1, atrophy exclusively in the antrum; C-2, atrophy extending to the lesser curvature in the lower third of the corpus; and C-3, atrophy extending to the lesser curvature in the middle third of the corpus) and open types (O-1, border of atrophy lying between the lesser curvature and the anterior wall of the corpus; O-2, border of atrophy within the anterior wall of the corpus; and O-3, border of atrophy involving the posterior wall of the corpus and the greater curvature). ME-NBI was then performed to evaluate the mucosal features of the entire stomach and five areas of interest, i.e., the greater and lesser curvature of the antrum, the greater and lesser curvature of the corpus, and the gastric incisura. GIM was considered when LBC was observed under ME-NBI. The EGGIM scoring system was used to assess the range of GIM involved using the following scores: 0, no GIM; 1,  $\text{GIM} \leq 30\%$ ; and 2,  $\text{GIM} > 30\%$ . The total score of the EGGIM system ranged from 0 to 10 points [14]. During NBI examination, the EGGIM score was recorded and calculated by the endoscopist, after which targeted biopsy was performed where GIM was observed. When there was no GIM, random biopsy was performed according to the updated Sydney system [17]. The biopsy samples were then prepared in a standard manner for histopathologic evaluation, and the OLGA and OLGIM stages of the samples were determined.

### 2.3 | Data Collection

After the inclusion of the participants, their clinical characteristics and endoscopic and pathologic findings were recorded in the digital medical system of our hospital. Demographics including participants' age, sex, smoking status, alcohol consumption, and family history of GC, as well as the presence or absence of *Helicobacter pylori* (*H. pylori*) infection, EGGIM scores, the Kimura–Takemoto classification, and the OLGA and OLGIM stages of GIM were recorded. Smoking status was classified as never smoking, and past or current smoking. Alcohol consumption was divided into  $\geq 40$  g and  $< 40$  g daily [18]. A family history of GC was recorded when at least one first-degree or second-degree relative had GC. Positive *H. pylori* infection was confirmed based on the positivity of either one of the tests including rapid urease test (RUT), gastric mucosal tissue staining, or  $^{13}\text{C}$ - or  $^{14}\text{C}$ -urea breath test (UBT). Negative *H. pylori* infection was considered when there was no current infection or if the participant had undergone successful *H. pylori* eradication.

### 2.4 | Outcomes

The consistency between the EGGIM and OLGIM staging of GIM (OLGIM III/IV) was evaluated using histopathologic evidence obtained by gastric biopsy as the gold standard, and the optimal cut-off values for EGGIM were determined.

The proportions of individuals with EGGIM score 5–10 in the EGC group, including patients with newly diagnosed EGC and those who underwent ESD for EGC within 1 year before enrollment, and the CAG group, as well as the differences in their Kimura–Takemoto classification and OLGA/OLGIM staging between these two groups were evaluated.

## 2.5 | Statistical Analysis

In the absence of relevant studies, we used a higher  $\kappa$  value of 0.8 (highly consistent) to calculate the sample size of this study, which resulted in at least 160 cases required for analysis. Moreover, as this was a prospective study, the number of cases in different OLGIM stages was difficult to predict. Therefore, we increased the sample size to at least 210 cases.

Normal distribution of continuous variables was determined by using the Kolmogorov–Smirnov test. Continuous variables with normal distribution were expressed as mean  $\pm$  standard deviation, whereas those with skewed distribution were expressed as median and range. Categorical variables were expressed in numbers and percentages or frequencies. The independent-sample *t*-test was used to compare the difference in continuous variable (participant's age) between the EGC group and the CAG group, and the  $\chi^2$  test was used to compare the differences in categorical variables between groups. The  $\kappa$  consistency test was applied to analyze the consistency between the EGGIM and OLGIM staging systems. Analysis of the ROC curve was used to determine the optimal cut-off value of EGGIM score, while the OLGIM score was used as a reference; the diagnostic accuracy of the EGGIM score for OLGIM III/IV stages was expressed in terms of sensitivity and specificity in the ROC curve. All the statistical analyses were performed by using the SPSS Software version 26.0 (IBM, Armonk, NY, USA). A *p* value of less than 0.05 was considered statistically significant.

## 3 | Results

### 3.1 | Characteristics of the Participants

Altogether 210 patients who underwent gastroscopy between June 2022 and June 2023 were enrolled, including 68 patients in the EGC group and 142 patients with CAG. The mean age of patients in the EGC group was (67.75  $\pm$  7.43) years, and 69.1% of them were men. The mean age of patients in the CAG group was (62.78  $\pm$  8.76) years, which was significantly younger than that of the EGC group (*p* < 0.001), and 55.6% of them were men. The characteristics of the participants are summarized in Table 1.

### 3.2 | Comparison of the Classification of GIM Between EGGIM and OLGIM Staging Systems

In one patient with an EGGIM score of 0, no GIM was observed (OLGIM 0). Among the 89 patients with focal or moderate GIM (EGGIM score 1–4), 76 patients were pathologically confirmed to have OLGIM I/II GIM, and another 5 patients had OLGIM III/IV GIM. However, the other eight cases were diagnosed to have no GIM (OLGIM 0) based on their histopathologic findings. Of

the remaining 120 patients with extensive GIM (EGGIM score 5–10), 112 were pathologically confirmed as having OLGIM III/IV GIM, 7 had OLGIM I/II GIM, and 1 patient was histopathologically confirmed to have no GIM (OLGIM 0). According to the consistency analysis, the EGGIM and OLGIM stages showed good consistency for the diagnosis of GIM ( $\kappa$  = 0.805, *U* = 12.620, *p* < 0.001) (Table 2).

Overall, the AUROC for the diagnosis of OLGIM III/IV GIM based on EGGIM score was 0.95 (95% CI 0.91–0.98) (Figure 1). While the AUROCs for the diagnosis of OLGIM III/IV GIM in the EGC and CAG patients were 0.94 (95% CI 0.87–1.00) and 0.95 (95% CI 0.91–0.99), respectively. Different cut-off values were used to determine the optimal sensitivity and specificity. When using an EGGIM score of > 4, the sensitivity was 95.7% and the specificity was 91.4% (Table 3).

### 3.3 | Risk Factors Related to EGC

As shown in Table 1, compared to the patients in the CAG group, those in the EGC group were older (*p* < 0.001). We also found that smoking was more common in patients with EGC (*p* = 0.034). While there were no significant differences in patients' sex, family history of GC, or alcohol consumption between the two groups (all *p* > 0.05), *H. pylori* infection had a trend to be related to EGC (*p* = 0.050).

The proportion of patients with Kimura–Takemoto classification O-2/O-3 in the EGC group was higher than in the CAG group (14.7% vs. 6.3%, *p* = 0.018). Both the OLGA III/IV (52.9% vs. 42.3%) and OLGIM III/IV stages (63.2% vs. 52.1%) tended to be more prevalent in patients in the EGC group than in the CAG group, although there were no statistically significant differences between the two groups. The mean EGGIM score in patients in the EGC group was higher than that in those with CAG (4.93  $\pm$  1.53 vs. 3.92  $\pm$  1.67, *p* < 0.001).

## 4 | Discussion

CAG and GIM are recognized as precancerous lesions of GC. *H. pylori* infection leads to the collapse of the normal mucinous gland, which is accompanied by GIM. When the degree and extent of CAG and GIM progress, GC risk increases; therefore, routine endoscopic surveillance is necessary for patients with CAG and GIM. Endoscopy is effective for the early detection of GI tumors. When combined endoscopic findings with pathologic evidence via biopsy, a definite diagnosis can be made for suspected lesions. OLGA and OLGIM systems have been used for risk stratification of GC. In particular, OLGA/OLGIM stages III/IV are independent risk factors for GC [19]. Compared with OLGA staging, OLGIM staging has higher interobserver consistency with the EGGIM system and repeatability, which can help identify patients at a high risk of developing GC. ME-NBI has a high accuracy in the diagnosis of GIM and dysplasia and is superior to WLE in the identification of GIM cases [20]. Observation of gastric mucosa under ME-NBI reveals LBC, a white opaque substance (WOS), and a marginal turbid band (MTB), indicating GIM at these sites [13, 21, 22]. Uedo et al. have demonstrated that combining NBI with ME could accurately identify the presence

**TABLE 1** | Clinicopathologic features of patients with early gastric cancer (EGC) and chronic atrophic gastritis (CAG).

| Variables                                   | EGC group (n = 68) | CAG group (n = 142) | p value |
|---------------------------------------------|--------------------|---------------------|---------|
| Male sex, n (%)                             | 47 (69.1)          | 79 (55.6)           | 0.062   |
| Age, years (mean ± SD)                      | 67.75 ± 7.43       | 62.78 ± 8.76        | < 0.001 |
| Current smoker, n (%)                       | 9 (13.2)           | 7 (4.9)             | 0.034   |
| Alcohol consumption, n (%)                  | 1 (1.5)            | 4 (2.8)             | 0.549   |
| Family history of GC, n (%)                 | 2 (2.9)            | 3 (2.1)             | 0.712   |
| <i>Helicobacter pylori</i> infection, n (%) | 1 (1.5)            | 12 (8.5)            | 0.050   |
| Kimura–Takemoto classification, n (%)       |                    |                     |         |
| C-1/C-2                                     | 9 (13.2)           | 33 (23.2)           | 0.061   |
| C-3/O-1                                     | 49 (72.1)          | 100 (70.4)          | 0.157   |
| O-2/O-3                                     | 10 (14.7)          | 9 (6.3)             | 0.018   |
| OLGA staging, n (%)                         |                    |                     |         |
| 0                                           | 14 (20.6)          | 30 (21.1)           | 0.279   |
| I/II                                        | 18 (26.5)          | 52 (36.6)           | 0.481   |
| III/IV                                      | 36 (52.9)          | 60 (42.3)           | 0.515   |
| OLGIM staging, n (%)                        |                    |                     |         |
| 0                                           | 2 (2.9)            | 8 (5.6)             | 0.285   |
| I/II                                        | 23 (33.8)          | 60 (42.3)           | 0.606   |
| III/IV                                      | 43 (63.2)          | 74 (52.1)           | 0.300   |
| EGGIM staging, n (%)                        |                    |                     |         |
| 0                                           | 0 (0)              | 1 (0.7)             | 0.209   |
| 1–4                                         | 23 (33.8)          | 66 (46.5)           | 1.000   |
| 5–10                                        | 45 (66.2)          | 75 (52.8)           | 1.000   |
| EGGIM score (mean ± SD)                     | 4.93 ± 1.53        | 3.92 ± 1.67         | < 0.001 |

Abbreviations: CG, chronic gastritis; EGGIM, endoscopic grading of gastric intestinal metaplasia; GC, gastric cancer; OLGA, operative link on gastritis assessment; OLGIM, operative link on gastric intestinal metaplasia assessment; SD, standard deviation.

**TABLE 2** | Consistency of endoscopic grading of gastric intestinal metaplasia (EGGIM) and the operative link on gastric intestinal metaplasia assessment (OLGIM) in the diagnosis of gastric intestinal metaplasia.

| OLGIM staging (n) | EGGIM score |     |      | Total (n) | $\kappa$ | U      | p value |
|-------------------|-------------|-----|------|-----------|----------|--------|---------|
|                   | 0           | 1–4 | 5–10 |           |          |        |         |
| 0                 | 1           | 8   | 1    | 10        | 0.805    | 12.620 | < 0.001 |
| I/II              | 0           | 76  | 7    | 83        |          |        |         |
| III/IV            | 0           | 5   | 112  | 117       |          |        |         |
| Total             | 1           | 89  | 120  | 210       |          |        |         |

of histologic GIM when LBC on the epithelial surface was observed [13]. However, a major limitation of previous studies is that only patients with a known diagnosis of GIM, dysplasia, GC, or those at a high risk for GC were included [23, 24]. A previous study investigated the predictive value of ME-NBI for GIM identification and showed that ME-NBI achieved a sensitivity, specificity, accuracy, positive predictive value, and negative

predictive value of 80%, 96%, 93%, 84%, and 95%, respectively, indicating that it could be used for target biopsy in clinical practice [25]. Meanwhile, the EGGIM system focuses on the use of ME-NBI to identify GIM and its distribution in the stomach. Esposito et al. confirmed that EGGIM could determine a high risk of GC (OLGIM III/IV) without histopathologic evidence compared with OLGA [15]. In addition, a case–control study evaluated the

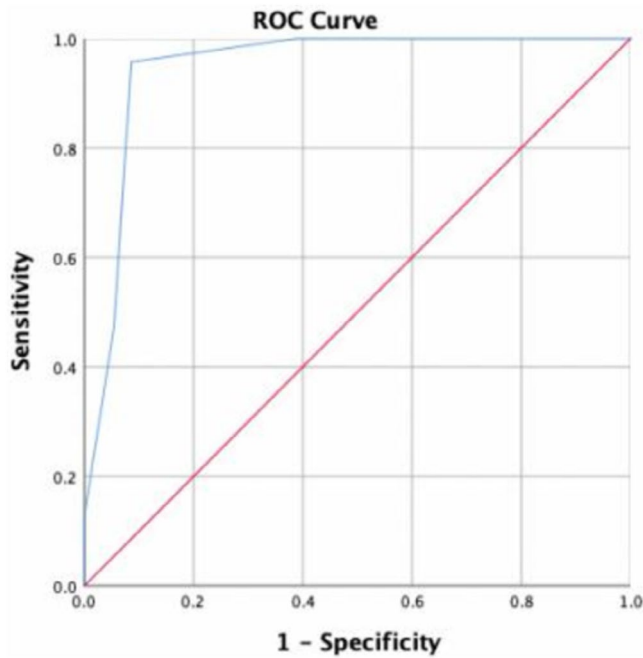


**FIGURE 1** | Receiver operating characteristic (ROC) curve analysis of the endoscopic grading of gastric intestinal metaplasia for the operative link on gastric intestinal metaplasia assessment III/IV gastric intestinal metaplasia. The area under the ROC curve is 0.95.

**TABLE 3** | The accuracy of the operative link on gastric intestinal metaplasia assessment (OLGIM) for the diagnosis of stages III/IV gastric intestinal metaplasia evaluated according to different cut-off values of the endoscopic grading of gastric intestinal metaplasia (EGGIM) staging system.

| Cut-off values | Sensitivity (%) | Jorden index | Specificity (%) |
|----------------|-----------------|--------------|-----------------|
| > 0            | 100             | 0.011        | 1.1             |
| > 1            | 100             | 0.022        | 2.2             |
| > 2            | 100             | 0.237        | 23.7            |
| > 3            | 100             | 0.613        | 61.3            |
| > 4            | 95.7            | 0.871        | 91.4            |
| > 5            | 47.0            | 0.416        | 94.6            |
| > 6            | 12.8            | 0.128        | 100             |
| > 7            | 3.4             | 0.034        | 100             |
| > 8            | 1.7             | 0.017        | 100             |
| > 9            | 0               | 0            | 100             |

values of EGGIM, OLGA, and OLGIM in the risk stratification of early gastric neoplasia (EGN). The authors demonstrated that EGGIM (adjusted OR 21.2, 95% CI 5.0–90.2 for EGGIM  $\geq 5$ ), OLGA, and OLGIM systems were all associated with EGN risk and that there were more patients with EGN having EGGIM  $\geq 5$  compared with those without (68.6% vs. 13.3%,  $p < 0.001$ ) [26]. In addition, OLGA (68% vs. 11%,  $p < 0.001$ ) and OLGIM III/IV (61% vs. 3%,  $p < 0.001$ ) were more prevalent in patients with

EGN than in subjects without EGN. In the current study, we also confirmed that there was consistency between the EGGIM and OLGIM systems for the diagnosis of GIM, with an AUROC of 0.95 (95% CI 0.91–0.98) when using EGGIM  $\geq 5$  for the diagnosis of OLGIM III/IV among patients with EGC or CAG.

According to the MAPS II guideline [4], biopsy is recommended for the first-time diagnostic upper GI endoscopy for staging gastric precancerous conditions, while additional biopsy may not be necessary during the follow-up period [27]. EGGIM system is a simple, intuitive, real-time tool that can be used to evaluate the entire stomach, allowing accurate surveillance recommendations to be made immediately after endoscopy, without the need for biopsy. When suspicious gastric mucosal lesions are observed, targeted biopsy can be performed under the guidance of NBI.

The Kimura–Takemoto classification is widely applied in clinical practice, which evaluates endoscopic atrophy and the severity of CAG. The EGGIM system, as a relatively novel endoscopic classification for the staging of GIM, is rarely used in Asia. A number of studies have confirmed that the Kimura–Takemoto classification has good consistency with the OLGA staging system. Our study confirms that EGGIM and OLGIM staging have good consistency. With the development of endoscopic technology and artificial intelligence, we believe EGGIM can be widely used in a clinical setting to stage the severity of GIM.

There were some limitations to our study. This was a single-center case–control study, which might have led to selection bias. Because of the need to take five biopsy samples of gastric mucosa, to reduce the damage to normal gastric mucosa, patients with CAG had more severe atrophy under endoscopy; therefore, there was no significant difference in OLGA/OLGIM stage between the EGC group and the CAG group. Nevertheless, the mean EGGIM score in patients in the EGC group was higher than that in patients with CAG (4.93 vs. 3.92,  $p < 0.001$ ), and endoscopic surveillance should be intensive for patients with EGGIM  $> 4$ . Finally, the application of EGGIM requires experienced endoscopists with NBI, which has limited its use in primary healthcare hospitals.

In conclusion, we found that the EGGIM system could evaluate the extent and degree of GIM and exhibited good diagnostic consistency with OLGIM staging in clinical practice. Moreover, EGGIM scores in patients with an EGC history or who were detected to have EGC were higher than in those with CAG. Therefore, it is expected to be a useful tool for the risk stratification of GC. During endoscopic follow-up, the EGGIM system may simplify endoscopic surveillance by decreasing the need for biopsy.

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#### Conflicts of Interest

Bin Lyu is an Editorial Board Member for the *Journal of Digestive Diseases* and was not involved in the editorial review or the decision to publish this article. All authors declare that there are no competing interests.

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