Assessment of Gastritis Using Operative Link for Gastritis Assessment System

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Gastritis is an inflammatory condition of the gastric mucosa induced by Helicobacter pylori infection, autoimmunity and chemical agents. Although Sydney system was devised for semiquantitative methods of gastritis, most physicians and pathologists consider it to be too complex and bothersome to use for routine diagnosis. Moreover, Sydney system does not reflect the overall gastritis condition and it cannot directly predict increased gastric cancer risk. To overcome these limitations, a new gastritis staging method, called Operative Link for Gastritis Assessment (OLGA) system was designed by the international group of gastroenterologists and pathologists. This system may achieve simplification of reports for the gastritis condition and it can aid in predicting gastric cancer risk and planning patient surveillance. Herein, we reviewed the routine evaluation methods, clinical implication and advantage/limitations of the OLGA system.

Key Words: Gastritis; Helicobacter pylori; Atrophy; Metaplasia

INTRODUCTION

Gastritis is defined as an inflammatory condition occurred in gastric mucosa and it displays characteristic extent and distribution according to causal factors, severity or duration. Helicobacter pylori affected in about half of populations in the world, is the major cause of gastritis. Other sources include chemical agents and autoimmunity. Comprehensive assessment of clinical examination, serologic test (e.g., antibodies for infection or autoimmunity), endoscopy and histologic examination could be diagnostic tools for patients with gastritis. Typical histologic findings of gastritis are summarized as below: (1) chronic inflammatory infiltrates in lamina propria (lymphocytes, plasma cells and histiocytes), (2) active inflammatory infiltrates in lamina propria and gastric glands (neutrophils and eosinophils) and (3) loss of glandular units with replacement into fibrosis and smooth muscle proliferation, called as atrophy.

Gastritis is linked with development of gastric cancer. Previous epidemiologic and biologic studies investigated that intensity and distribution pattern of mucosal inflammation and atrophy are associated with carcinogenesis of gastric cancer and H. pylori are considered as a grade 1 carcinogen of gastric cancer. Extent of inflammation and atrophy has also relevance to gastric cancer occurrence. In despite of these results for the correlation of gastritis and gastric cancer, it is difficult to assess individual risk of gastric cancer development because accurate significance or relationship of environmental, biological and immunological factors has not yet been determined.

Sydney system is one of the most representative histologic methods for gastritis assessment adjusting semi-quantitative 4-tier scale. Sydney system was first established in 1990. Four years later, it was modified and updated into Houston-updated Sydney System. Sydney system recommends an itemized description of various microscopic findings including lymphoplasm cell infiltrates, neutrophilic infiltrates, intestinal metaplasia, mucosal atrophy and H. pylori. Severity/intensity of each factors is quantitatively expressed using 4 grading system, ranging from 0 (absence) to 3 (marked). After then, in April 2005, international group of gastroenterologists and pathologists (Operative Link for Gastritis Assessment, OLGA) held a meeting for reassessment of Sydney system and designa-
sted gastritis staging system such as hepatitis. OLGA system for gastritis was generated in this meeting.\textsuperscript{13}

OLGA system is based on the knowledge that atrophic change (severity and extent) is one of the most reliable factor of gastritis progression and prediction of gastric cancer development.\textsuperscript{13} Routine biopsy sampling can make a consistent and objective evaluation of mucosal atrophy and accurate mapping leading to staging of gastritis.\textsuperscript{13} OLGA system can be helpful to predict the risk of gastric cancer development and assume the causal factor in gastritis. Herein we described methods of OLGA staging system and their clinical significance depending on each stage.

GASTRITIS STAGING: THE OLGA SYSTEM

1. Biopsy sampling and processing

As mentioned above, it is important to define and clarify the extent and distribution of inflammatory and atrophic lesions for evaluation of cancer risk and causal factor of gastritis.\textsuperscript{10-12} Multi-regional, deep biopsy is necessary for mapping of gastric atrophy/inflammation and efficient evaluation for \textit{H. pylori}. Routine biopsy sampling has to be performed in oxyntic, antral and incisura angularis mucosa. Anterior and posterior walls of oxyntic and antral mucosa should be sampled. And then other additional focal lesions can be obtained.\textsuperscript{2,14,15} Specimen from antrum put into a bottle and specimens from oxyntic and incisura angularis mucosa put into another bottle, together. For more extensive examination of oxyntic mucosa, separate two regions of lesser and greater curvature may be biopsied and put into third sample bottle.\textsuperscript{5} Without tissue injury, materials should be fixed into formaldehyde as soon as possible.

2. Evaluation of gastric atrophy and gastritis staging

Ideally gastric atrophy should be evaluated in perpendicularly sectioned tissue exhibiting whole layers of gastric mucosa from foveolar epithelium to muscularis mucosa. International Group of Gastrointestinal Pathologists (Atrophy Club) made an algorithm for assessment of atrophic change: Absent: indefinite category causing to failure of valid assessment by severe inflammatory condition and shallow biopsy; Present (Fig. 1).\textsuperscript{1} Gastric atrophy is a loss of appropriate normal glandular unit and it is subdivided into two different phenotypes by metaplastic change. One type displays shrinkage and vanishing of glandular unit with proliferative fibrotic extension of lamina propria. Total area of glandular unit is lower, but remnant glandular units are normal in appearance. Another type of atrophy is accompanied with metaplastic change, such as intestinal or pseudopyloric metaplasia. Although total number of glands are not reduced, metaplastic change leads to loss of appropriate glands.\textsuperscript{16} Grading of atrophy in each biopsied specimen follows 4-tiered scale from 0 to 3 depending on percentage of atrophic glands (no atrophy, 0%, score=0; mild atrophy, 1~30%, score=1; moderate atrophy, 31~60%, score=2; severe atrophy, >60%, score=3). After then, the OLGA stage is set by combination of overall score of oxyntic and antral mucosa (Fig. 2).

3. Clinical implication of the OLGA system

1) Stage 0 gastritis

As Fig. 2, stage 0 represents the state of no atrophic change in five standardly biopsied (oxyntic, incisura angularis and antral) gastric mucosa. However, “indefinite for atrophy” should not be considered as stage 0 because the indefinite status means that it is impossible to make a definite diagnosis with given specimen and it is necessary for inflammation treatment and deep biopsy to appro-

![Fig. 1. Classification and grading of gastric atrophy proposed by International Group of Gastrointestinal Pathologists (Atrophy Club).](image-url)
2) Stage 1 gastritis

Stage 1 gastritis is the mildest and the most common atrophic condition and it shows focal atrophy, frequently confined to incisura angularis. Stage 1 gastritis includes so-called mild antrum-restricted or corpus predominant atrophic gastritis caused by *H. pylori* infection. However, detection of *H. pylori* may be difficult in stage 1 gastritis patient treated with proton pump inhibitor. The histologic evidence and possibility of *H. pylori* infection could be commented in pathologic report, such as coexisting inflammatory condition of lymphoplasmocytic or neutrophilic infiltrates. Almost patients suffered with dyspepsia have stage 0 or stage 1 gastritis lesion in endoscopic biopsy. Because these patients show no or minimal increased gastric cancer risk, the main treatment should be eradication of *H. pylori*.

3) Stage 2 gastritis

Stage 2 gastritis exhibits mild to moderate atrophic change in various foci. Nevertheless atrophy of antral mucosa tends to be predominant rather than that of oxyntic mucosa. Moderate corpus predominant atrophic gastritis, moderate antrum-restricted atrophic gastritis or mild multifocal atrophic gastritis can be belonged to this category. In also this stage, *H. pylori* infection is known as the most common causal factor. Stage 2 gastritis is epidemiologically associated with low risk gastric cancer risk and duodenal ulcer development rather than gastric ulcer.

4) Stage 3 gastritis

Stage 3 gastritis is a moderate to severe atrophic condition concurrently involved in both oxyntic and antral mucosa. Multifocal atrophic gastritis or corpus-restricted atrophic gastritis induced by autoimmunity should be considered in this condition. Stage 3 gastritis is classified as an increased gastric cancer risk groups and rarely intraepithelial neoplasm or invasive cancer may be coexist with this lesion.

5) Stage 4 gastritis

Severe atrophic change in whole gastric walls is noted in stage 4 gastritis, which is epidemiologically correlated with progressive phases of multiple atrophic gastritis. Gastric carcinogenesis (both invasive and non-invasive lesions) could be likely to be occurred in diffusely atrophic area. The extent of atrophic area has a positive correlation with gastric cancer risk and atrophic area with metaplastic change also displays genetic and morphologic alterations resulting in cancer development. Therefore patients with OLGA stage 3 and 4 gastritis are increased risk group of gastric cancer and should be fulfilled with careful follow up study.

### Application of OLGA system

Atrophic status of gastric mucosa (extent and severity) and *H. pylori* infection are most reliable factors for gastric cancer prediction. Using routine biopsy protocol and histologic evaluation by OLGA system allow reasonable and beneficent management for gastritis patients. Graham and Asaka classified patients as four gastric cancer risk groups using OLGA system and they also provided a new

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<th>Moderate atrophy (grade 2)</th>
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Fig. 2. Operative Link for Gastritis Assessment staging system frame presenting with severity and distribution of gastric atrophy.
strategy for assessment of gastritis patients reflecting the individual possibility of cancer development risk (Table 1 and Fig. 3). According to their proposal, *H. pylori* infection is first evaluated. If *H. pylori* are infected, eradication of this organism is followed. And then surveillance plan of patients can be established by atrophic status (OLGA stage).3

5. Advantage and limitation of OLGA system

The Houston-updated Sydney System’s guideline has been commonly used for gastritis grading.14 It contains a variety of pathologic information about inflammation, atrophy, metaplasia as well as *H. pylori* infection and regarded as a useful research tool.14 However, simple arrangement of information prevents physicians from assessment of comprehensive gastric condition and cancer risk. Moreover, interobserver disagreement between pathologists induces a reduction of reliability and a confusion of relationship between gastritis and gastric cancer.1 In this aspect, OLGA system contains simple, useful histologic information and it is also able to predict cancer risk by mapping atrophic status of stomach. And more simple and decreased assessment items can increase the reproducibility and concordance rate in microscopic evaluation.1 Additionally comprehensive understanding on gastritis and cancer can lead to make effective and valuable clinical strategies. However, some limitations of OLGA system are expected in biopsy sampling and interpretation in practical area. First, in biopsy, deep sampling including muscularis mucosa must be done for atrophy evaluation. Because atrophy is the nearly only measurement unit in OLGA system, shallow biopsy could not give any information into pathologists and clinicians. Second, categorization and simplification of disease could make doctors to neglect the mild form of disease. For example, early autoimmune gastritis, corpus-restricted atrophic gastritis, initially represents as OLGA stage 1 or stage 2 gastritis lesion considered as minimal to modest risk group. However, corpus-restricted autoimmune gastritis is known to increase gastric cancer risk. Mistaken relief and neglect depending on OLGA system let the disease grow or progress. Third, OLGA system is newly designed gastritis evaluation methods, so that cancer risk in accordance with OLGA stage groups has not yet been established. Further evaluation for delicate strategy, such as follow up period and risk assessment should be investigated with more cases and times. Fourth, in Korea, low medical costs in pathology prohibits precise diagnosis based on thorough pathologic examination of “each five” biopsy materials. Moreover, much efforts including massive education for pathologists, who are unfamiliar even to Houston-updated Sydney System is strongly recommended.

The new OLGA system could be an effective and facile method for understanding the cause of gastritis and prediction of gastric cancer. Even though its limitations and unfamiliarity, further practical application and investigation are needed for improving the methods of gastritis evaluation and gastric cancer prediction.

![Fig. 3. Schema for surveillance of gastritis patients based on *Helicobacter pylori* infection and atrophic gastritis, all of both known as reliable factors of gastric cancer development.](image-url)
REFERENCES