Editorial

Grading of gastritis: an impossible dream?

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The stomach is a complex organ, carrying out diverse functions, such as the reception and grinding of ingested food; the secretion of acid, digestive enzymes, intrinsic factors, and mucus; and the transfer of the processed food into the intestine. These functions are integrated by a complex array of neural and peripheral control mechanisms that regulate gastric activity in concert with that of the entire digestive system, as well as other organs. To perform such complex activities, the mucosal lining of the stomach varies, and the mucosa is generally classified as cardiac, fundic, or antral, according to the anatomical location. The mucosal glands of these regions contain specialized cells that play key regulatory functions. For instance, gastrin, secreted from G cells in the antrum, regulates acid secretion and controls proliferation of the gastric mucosa, and the recently identified ghrelin, which is secreted from X-like cells in the fundic gland, seems to be involved in controlling appetite, as well as in gut motility. However, under normal conditions, the endoscopic differentiation of these specialized mucosal areas is difficult, even by an experienced hand.

A number of exogenous and endogenous factors, such as infection (most notably with *Helicobacter pylori*); chemical injury, such as that caused by nonsteroidal anti-inflammatory drugs or bile acid; autoimmunity; and circulatory changes are known to affect the macroscopic appearance of the gastric mucosa. The clinical diagnosis of gastritis is based on endoscopically detectable mucosal changes, although the diagnostic sensitivity and accuracy depends on the observer. Therefore, the sensitivity and reproducibility are generally considered to be rather poor for differentiating subtle alterations such as these seen in gastritis [1]. In order to overcome this problem, an attempt to semi-quantitatively score the mucosal appearance, to facilitate objective assessment, has been proposed, in line

with the histological grading of gastritis [2,3]. Although the initially proposed histological grading system has been revised to improve objectivity [4], there are some problems inherent with any classification based on biopsy specimens. For example, the grading of atrophy is reported to have a high rate of discordance between observers [5,6]. Moreover, the macroscopic extent of atrophy in the whole stomach may be more easily diagnosed by endoscopy rather than by biopsy [7]. Even the presence of intestinal metaplasia, which can be diagnosed with less discordance, may not be accurately determined by histology, because of the patchy nature of the lesion, which gives different results even within a single biopsy specimen [8]. Despite these limitations, the Updated Sydney System for the histological classification and grading of gastritis [3] has been internationally accepted, and is instrumental in helping to assess various treatment effects. In contrast, endoscopic versions of classification and grading systems for gastritis have gathered much less attention. This lack of utilization of an endoscopic grading system for gastritis may be explained in terms of the difficulty in performing the observations under uniform, reproducible conditions, and the difficulty in carrying out repeated observations. Various forms of image recording may not adequately circumvent these difficulties, because of a variety of factors, such as the distance between the scope and the mucosa, air insufflation, light intensity, color balance, and patient preparation, and the performance of endoscopy that can influence images captured by gastroscopy cannot be adequately controlled.

In this issue of *Gastric Cancer*, Kubo et al. [9] propose an endoscopic scoring system for the evaluation of the gastric mucosa of the remnant stomach. This seems to be a bold and formidable attempt, considering the problems mentioned above. Furthermore, the remnant stomach has additional characteristics that give rise to complex changes, because a part vital for the integrity of its function is lost, and various changes associated with

the disease process that caused the surgical intervention could be present. In their proposal, Kubo et al. [9] advocate the use of three simple indices Residual food, Gastritis and Bile reflux, that they term the RGB classification, to evaluate the gastric mucosa. After confirming excellent results for interobserver variation, they found a statistically significant difference between operative procedures with these indices, indicating that this scoring system may be useful for assessing the reconstruction procedure after gastrectomy. Although this classification system is promising, we must be careful in accepting its validity, because there are a number of weaknesses in this study. First of all, comparative studies between their institution and others that may be different not only in regard to patient preparation and observation procedures but also in regard to surgical skills, as well as postoperative management, will be required to test the interobserver variation and surgical reconstruction results. In addition, the reproducibility or consistency of the data between examinations performed on different occasions in the same patient has to be examined. Secondly, their study design may not be appropriate for precise comparisons between reconstruction procedures. The demographic features (age, sex, *H. pylori* status, medication, and associated diseases, such as hepatitis) of the patients in each group have not been analyzed. These possible confounding factors, when skewed between the groups, may compromise their results. Moreover, the food taken the day before examination was not properly standardized. This may cause a possible bias, because food restriction, or the avoidance of food that tends to be retained in the stomach, may depend on the daily condition of the patient. Therefore, their data on the degree of food residue must be tested with a standardized diet and supported by other indices of gastric emptying. Thirdly, the term “gastritis”, as used in their study, seems to be a misnomer, because previous studies, using similar endoscopic grading systems for assessing mucosal changes in the remnant stomach, have pointed out that there is a poor correlation between endoscopic inflammation, such as mucosal redness, and histological inflammation [3,10–12]. A good example of this is the discrepancy shown between the macroscopic findings and those of histological inflammation after Roux-en-Y biliary diversion [13]. Therefore, the term “gastropathy”, would be better suited than “gastritis” for the purpose of endoscopic grading [1]. Fourthly, bile reflux, assessed by visual observation during endoscopic observation, has been shown to be unreliable for evaluating the actual bile reflux measured quantitatively during daily life [10]. This may explain the poor correlation between the bile reflux score and the “gastritis” score in the study of Kubo et al. [9], because the endoscopic “gastritis” scores used in previous studies seemed to reflect the

extent of bile reflux [10–13]. These apparent problems will hamper fair comparisons between the operative procedures.

In consideration of all of these difficulties in evaluating the functional state of the residual stomach by endoscopy alone, it seems that any attempt to determine the grade of gastritis with visual indices alone is an impossible dream. Nevertheless, an attempt to establish an objective endoscopic grading system will be the first step to take in making comparisons between operative procedures that may eventually lead to improvements in the quality of life of patients after gastrectomy. This leads to the last criticism of the study of Kubo et al. [9]. As mentioned by themselves, they had no intention of assessing patient complaints in this study. However, the assessment of patients’ symptoms and satisfaction is most important when the improvement of operative procedures is being considered. However, it would be difficult to tackle this issue by relying only on gastroscopic grading, because post-gastrectomy symptoms may have many other causes, such as reflux esophagitis, Roux-en-Y stasis syndrome, dumping, and so on.

In Japan, a large number of patients are still operated on for gastric cancer and must live with a remnant stomach. Therefore, this type of study, intended to compare reconstruction procedures after gastrectomy, is keenly needed. Moreover, the remnant stomach operated for gastric cancer tends to have a high risk of developing secondary cancer [14,15]. For earlier and more accurate detection of heterochronous cancer arising in the remnant stomach, more precise and detailed endoscopic surveillance is essential. A grading system may be revised to incorporate this purpose, and this may better guide the endoscopic surveillance. Thus, let us hope that the effort by Kubo and colleagues revitalizes the old issue of endoscopic assessment of the remnant stomach. The marked progress in endoscopy and image analysis, together with progress in various functional analyses, could mean that the impossible dream, of an endoscopic scoring system that leads to improved patient care after gastrectomy, may come true in the future.

References

1. Carpenter HA, Tally NJ. Gastroscopy is incomplete without biopsy: clinical relevance of distinguishing gastropathy from gastritis. *Gastroenterology* 1995;108:917–24.
2. Tytgat GNJ. The Sydney System: endoscopic division. Endoscopic appearances in gastritis/duodenitis. *J Gastroenterol Hepatol* 1991;6:223–34.
3. Price AB. The Sydney System: histologic division. *J Gastroenterol Hepatol* 1991;6:209–22.
4. Dixon MF, Genta RM, Yardley JH, Correa P, and the participants in the International Workshop on the Histopathology of Gastritis, Houston 1994. Classification and grading of gastritis. The Updated Sydney System. *Am J Surg Pathol* 1996;20:1161–81.

5. El-Zimaity HM, Graham DY, al-Assi MT, Malaty H, Karttunen TJ, Graham DP, et al. Interobserver variation in the histopathological assessment of *Helicobacter pylori* gastritis. *Hum Pathol* 1996;27:35–41.
6. Chen XY, van der Hulst RW, Bruno MJ, van der Ende A, Xiao SD, Tytgat GN, Ten Kate FJ. Interobserver variation in the histopathological scoring of *Helicobacter pylori* related gastritis. *J Clin Pathol* 1999;52:612–15.
7. Kimura K, Satoh K, Taniguchi Y, Ido K, Kihira K, Ohata Y, Yoshida Y. Some personal comments on the Sydney system for the classification of chronic gastritis. *J Gastroenterol* 1994; 29(Suppl VII):114–19.
8. Cassaro M, DiMario F, Leandro G, Genta RM, Rugge M. The dark side of the gastric biopsy. *Hum Pathol* 1999;30:741–4.
9. Kubo M, Sasako M, Gotoda T, Ono H, Fujishiro M, Saito D, et al. Endoscopic evaluation of the remnant stomach after gastrectomy: proposal for a new classification. *Gastric Cancer* 2002;5:83–9.
10. Richie WP. Alkaline reflux gastritis. An objective assessment of its diagnosis and treatment. *Ann Surg* 1980;192:288–98.
11. Malgerada JR, Philips SF, Shorter RG, Higgins JA, Magrina C, van Heerden JA, Adson MA. Postoperative reflux gastritis: pathophysiology and long-term outcome after Roux-en-Y diversion. *Ann Intern Med* 1985;103:178–83.
12. Dixon MF, O'Conner HJ, Axon A, King RFJG, Johnston D. Reflux gastritis: distinct histopathological entity? *J Clin Pathol* 1986;39:524–30.
13. O'Conner HJ, Newbold KM, Alexander-Williams J, Thompson H, Drumm J, Donovan IA. Effect of Roux-en-Y biliary diversion on *Campylobacter pylori*. *Gastroenterology* 1989;97:958–64.
14. Offerhaus GJA, Stadt JVD, Hubregtse K, Tersmette AC, Tytgat GN. The mucosa of the gastric remnant harboring malignancy. *Cancer* 1989;64:698–703.
15. Sowa M, Kato Y, Onoda N, Kubo T, Maekawa H, Nishimura M, et al. Early cancer of the gastric remnant — with special emphasis on the importance of follow-up of gastrectomized patients. *Hepato-gastroenterology* 1992;39:400–4.