ORIGINAL ARTICLE

Effectiveness of endoscopic clipping and computed tomography gastroscopy for the preoperative localization of gastric cancer

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Purpose: Before laparoscopic gastrectomy for gastric cancer can be planned, it is very important to know the precise location of the tumor. The aim of this study was to evaluate 3 methods of predicting the exact location of the tumor: preoperative gastrofibroscopy (GFS), preoperative computed tomography gastroscopy (CT), and intraoperative gastroscopy-guided laparoscopy (Lap). **Methods:** In this study, 15 patients were prospectively identified, and endoscopic clips were preoperatively placed on the proximal 1 cm of the tumor, at the angle on the greater curvature and opposite the angle on the greater curvature. The distances between the pylorus and the proximal tumor clip (PT), the angle clip (PA), the greater curvature clip (PG), and the gastroesophageal junction were measured by preoperative GFS, preoperative CT, intraoperative Lap, and visual inspection (Vis). **Results:** PT, PA, and PG values measured by preoperative GFS differed significantly from the Vis values (P < 0.01). However, preoperative CT measurements of PT, PA, and PG did not differ from the Vis values (P = 0.78, P = 0.48, and P = 0.53, respectively). Intraoperative Lap and Vis PT values differed by only 1.1 cm on an average (P = 0.10), but PA and PG values varied by 1.9 and 3.4 cm, respectively (P = 0.01 for both). **Conclusion:** Endoscopic clipping combined with preoperative CT gastroscopy is more useful than preoperative GFS for preoperatively predicting the location of early gastric cancers and will be helpful for planning laparoscopic gastrectomy.

Key Words: Stomach neoplasms, Laparoscopy, Gastrectomy, X-ray computed tomography, Gastroscopy

INTRODUCTION

Gastric cancer is the fourth−most common type of cancer and the second−leading cause of death in the world. Nearly 1 million new cases are diagnosed each year [1].

Although the incidence of gastric cancer and mortality due to this disease have decreased gradually in Japan and Korea, it remains the second-most frequent cause of death in Korea [2].

Laparoscopic surgery is associated with significantly

better quality of life compared to open surgery; patients have less pain and recover faster, their hospital stay is shorter, and their cosmetic outcome is better [3,4]. Consequently, in the Republic of Korea and Japan, laparoscopic surgery is often used to treat early gastric cancer.

Before laparoscopic gastrectomy can be planned, it is very important to know the precise location of the tumor. This is because decisions regarding surgical strategy (subtotal, proximal, or total gastrectomy) and the resection area of the lymph nodes depend on the location of the tumor. However, to our knowledge, studies determining the accuracy of various preoperative methods of locating early gastric cancers have not yet been reported. The aim of this study was to evaluate 3 such methods: preoperative gastrofibroscopy (preop GFS), preoperative computed tomography gastroscopy (preop CT), and intraoperative gastroscopy-guided laparoscopy (intraop Lap).

METHODS

We prospectively selected 15 patients with early gastric cancer who underwent laparoscopic gastrectomy between January 2010 and June 2010. The study was approved by the local Institutional Review Board. Patients were included in the trial if 1) they had histologically proven primary gastric adenocarcinoma; 2) the tumor was diagnosed as T1a or T1b gastric cancer; 3) they had no history of abdominal operations; 4) they had no history of treatment for gastric cancer, including endoscopic mucosal resection; and 5) they provided written informed consent.

Preoperative clipping and measurements

The proximal tumor clip, the angle clip, and the greater curvature clip (Fig. 1A) were placed preoperatively. One experienced endoscopist used preop GFS (Fig. 1B) to
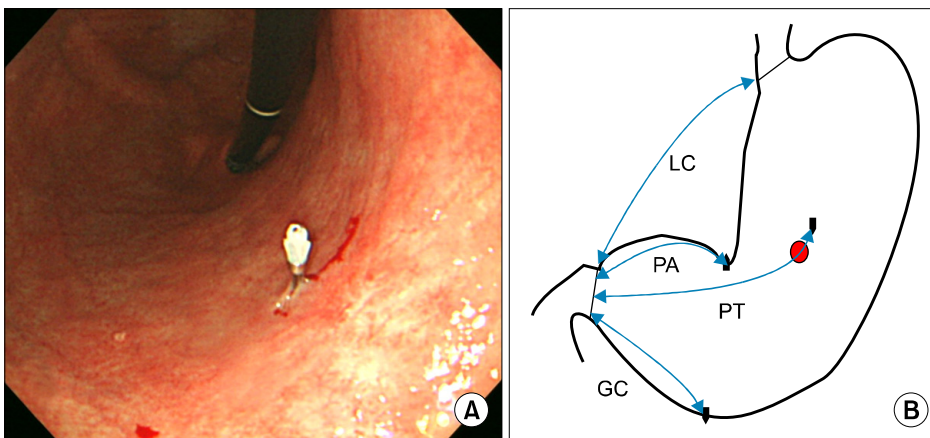

Fig. 1. Preoperative clipping and preoperative measurements using a gastrofibroscope. (A) An endoscopic clip was placed proximal to the tumor. (B) The distances between the pylorus and the proximal tumor clip (PT), the angle clip (PA), the clip opposite the angle on the greater curvature and the gastroesophageal junction (lesser curvature, LC) were measured. GC, greater curvature.
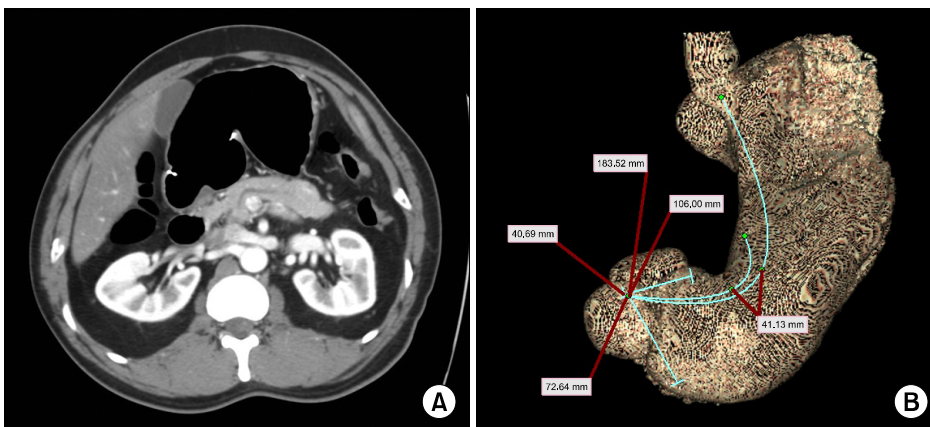

Fig. 2. Preoperative measurements using a computed tomography (CT) scan. The endoscopic clips were readily detected by CT scans (A), which allowed the 3-dimensional image to be reconstructed. Distances between the pylorus and the clip proximal to the tumor, the angle clip, the clip placed opposite the angle on the greater curvature, and the gastroesophageal junction were measured (B).

Fig. 3. Intraoperative measurements with laparoscopy. The endoscopic clip on the serosa side was marked with Gentian Violet stain by a laparoscopic surgeon using a gastrofibroscope, and an operator using a Nelaton ruler measured the distances between the pylorus and the clip proximal to the tumor, the angle clip, the clip opposite the angle on the greater curvature, and the gastroesophageal junction.
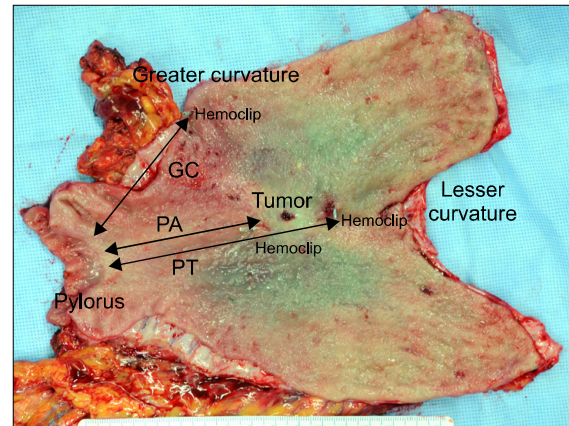

Fig. 4. Postoperative measurement by visual inspection. The distances between the pylorus and the clip proximal to the tumor (PT), the angle clip (PA), and the clip opposite the angle on the greater curvature (GC), were measured after the operation.

measure the distances between the pylorus and the clip proximal to the tumor (PT), the angle clip (PA), the greater curvature clip (PG), and the gastroesophageal junction (LC). The patients, who had fasted for at least 8 hours, were then subjected to preop CT with a 64-channel CT scanner (Brilliance 64, Philips Medical Systems, Haifa, Israel). Before preop CT, each patient received 10 mg of butyl scopolamine (Buscopan, Boehringer Ingelheim, Seoul, Korea) intravenously to minimize bowel peristalsis and to facilitate hypotonia. They also received 2 packs (8 g) of gas-producing granules (Robas granules, Dong In Dang, Siheung, Korea) with 10 mL of water to achieve gastric distension. The following scanning parameters were used: 64 × 0.625 mm collimation, a pitch of 1.172, and a rotation time of 0.75 seconds. The tube voltage was set to 120 kVp and the milliamperage was 200 mA. All images were entered into a workstation for 3-dimensional (3D) imaging (Rapidia 2.8, Infinitt, Seoul, Korea), after which PT, PA, PG, and LC were determined (Fig. 2). Finally, after the proximal jejunum was clamped, intraoperative gastrofibroscopy was performed. An operator laparoscopically marked the serosa side of the endoscopic clip with Gentian Violet stain, and an operator using a handmade Nelaton ruler measured PT, PA, PG, and LC (Fig. 3). After the oper-

ation, the distances between the pylorus and each clip and between the pylorus and the gastroesophageal junction were measured by visual inspection (Vis) of the resected specimen (Fig. 4).

To evaluate the accuracy of preop GFS, we corrected the preop GFS values by dividing preop CT LC by preop GFS LC. The preop GFS values were then multiplied by this preop CT: preop GFS ratio, thus yielding the corrected preop GFS values (corrected GFS value = preop GFS value × preop CT LC ÷ preop GFS LC). For example, when preop GFS PT, preop CT LC, and preop GFS LC were 24 cm, 18 cm, and 36 cm, respectively, the preop CT: preop GFS ratio was 18:36, which equals 0.5. The corrected GFS PT value (24 cm) was then multiplied by 0.5, yielding 12 cm (24 × 18 ÷ 36 = 12).

Statistical analyses

Statistical analyses were performed with SPSS ver. 12.0 (SPSS Inc., Chicago, IL, USA). The data are presented as means standard deviation (±standard deviaion). To determine the statistical significance of differences, 1-way analysis of variance (ANOVA) with *post hoc* (Tukey) test and the paired samples t-test were used. A P-value of < 0.05 was considered statistically significant.

Table 1. The distances between the pylorus to the proximal tumor clip, the angle clip, the greater curvature side clip and to the gastroesophageal junction (lesser curvature) were measured by preoperative gastrofibroscopy (preop GFS), preoperative computed tomography (preop CT), intraoperative gastrofibroscopy-guided laparoscopy (intraop Lap) and visual inspection (Vis)

	Preop GFS	Preop CT	Intraop Lap	Vis	Correct GFS[a]
PT	15.8 ± 9.2	7.1 ± 4.1	8.4 ± 4.1	7.3 ± 3.7	7.5 ± 4.9
PA	16.2 ± 6.7	6.0 ± 2.1	8.3 ± 2.6	6.4 ± 1.1	6.4 ± 3.0
PG	14.8 ± 5.0	7.6 ± 2.8	10.6 ± 4.6	7.2 ± 1.9	8.2 ± 4.4
LC	31.7 ± 8.4	16.5 ± 4.3	17.1 ± 4.8		

Values are presented as mean ± standard deviation.
PT, distance between pyloric canal to tumor clip; PA, distance between pyloric canal to angle clip; PG, distance between pyloric canal to greater curvature clip; LC, distance between pyloric canal to gastroesophageal junction.
[a]Correct GFS, corrected preop GFS, correct GFS value = preop GFS value × (preop CT LC/ preop GFS LC).

RESULTS

Patient characteristics

The mean age of the patients was 60.9 years old. Out of 15 patients, 11 were men and 4 women. The most frequent tumor location was the lower body (n = 12, 80%), followed by the upper body (n = 2, 13.3%), and then the midbody (n = 1, 6.7%). The mean tumor size was 2.3 cm (median, 1.3 cm). Regarding tumor-node-metastasis stage, 12 patients (80%) had stage I tumors and the remaining 3 (20%) had stage II tumors. The mean operation time was 317 minutes. The mean postoperative hospital stay was 15.2 days (median, 13 days).

Comparison of preop GFS and Vis

The distances between the pylorus and the proximal tumor clip, the angle clip, the greater curvature clip, and the gastroesophageal junction were measured by preop GFS, preop CT, intraop Lap, and Vis (Table 1). One-way ANOVA with *post hoc* test revealed significant differences between the mean distance from the pylorus to the clip proximal to the tumor (PT) measured by preop GFS (15.8 cm), preop CT (7.1 cm), intraop Lap (8.4 cm), and Vis (7.3 cm) (P < 0.01). Similarly, mean measurements of the distance from the pylorus to the angle clip (PA) differed significantly between preop GFS (16.2 cm), preop CT (6.0 cm), intraop Lap (8.3 cm), and Vis (6.4 cm) (P < 0.01), and the distance between the pylorus and the greater curvature differed significantly between preop GFS (16.2 cm), preop CT (7.6 cm), intraop Lap (10.6 cm), and Vis (7.2 cm) (P < 0.01). Preop GFS also overestimated the distance from

Table 2. Statistical analysis by analysis of variance and poststatistical analysis by Tukey's analysis of the mean preop GFS, preop CT, intraop Lap and Vis values

Group		Mean (subgroup by P = 0.05)	
		1.00	2.00
PT	Preop CT	7.1	
	Vis	7.3	
	Intraop Lap	8.4	
	Preop GFS		15.8
PA	Preop CT	6.0	
	Vis	6.4	
	Intraop Lap	8.3	
	Preop GFS		16.2
PG	Preop CT	7.6	
	Vis	7.2	
	Intraop Lap	10.6	
	Preop GFS		16.2
LC	Preop CT	16.5	
	Intraop Lap	17.1	
	Preop GFS		31.3

Preop GFS, preoperative gastrofibroscopy; Preop CT, preoperative 3-dimensional multidetector-row computed tomography; Intraop Lap, intraoperative gastrofibroscopy-guided laparoscopy; Vis, visual inspection; PT, distance between pyloric canal to tumor clip; PA, distance between pyloric canal to angle clip; PG, distance between pyloric canal to greater curvature clip; LC, distance between pyloric canal to gastroesophageal junction.

the pylorus to the gastroesophageal junction: the preop GFS value for LC was 31.7 cm, and the preop CT and intraop Lap values were 16.5 and 17.1 cm, respectively (P < 0.01) (Table 2).

Comparison of Vis, preop GFS, preop CT, and intraop Lap

Table 3 summarizes the paired samples t-test results,

Table 3. Analysis of preop GFS, preop CT, intraop Lap, correct GFS and Vis values by paired sample t-test

	Mean	SD	SE	95% CI	P-value[a]
Preop GFS PT–Vis PT	8.5	7.5	1.9	4.3–12.6	<0.01
Preop GFS PA–Vis PA	9.8	6.8	1.8	6.1–13.6	<0.01
Preop GFS PG–Vis PG	7.6	5.5	1.4	4.5–10.6	<0.01
Preop CT PT–Vis PT	-0.2	2.9	0.8	-1.9–1.4	0.78
Preop CT PA–Vis PA	-0.4	2.2	0.6	-1.6–0.8	0.48
Preop CT PG–Vis PG	0.4	2.4	0.6	-0.9–1.7	0.53
Intraop Lap PT–Vis PT	1.1	2.5	0.7	-0.3–2.5	0.10
Intraop Lap PA–Vis PA	1.9	2.3	0.6	0.6–3.2	0.01
Intraop Lap PG–Vis PG	3.4	4	1.0	1.2–5.6	0.01
Correct GFS PT–Vis PT	1.4	3.6	0.9	-0.6–3.4	0.15
Correct GFS PA–Vis PA	2.0	3.6	0.9	0.1–4.0	0.04
Correct GFS PG–Vis PG	0.8	4.5	1.2	-1.6–3.3	0.48

Preop GFS, preoperative gastrofibroscopy; Preop CT, preoperative 3-dimensional multidetector-row computed tomography; Intraop Lap, intraoperative gastrofibroscopy-guided laparoscopy; Correct GFS, corrected preop GFS; Vis, visual inspection; SD, standard deviation; SE, standard error; CI, confidence interval; PT, distance between pyloric canal to tumor clip; PA, distance between pyloric canal to angle clip; PG, distance between pyloric canal to greater curvature clip.
[a]Two-sided t-test.

where a Vis value was compared to the corresponding value measured by another method. For the comparison of preop GFS with Vis, the PT, PA, and PG values all differed significantly (P < 0.01 for all). However, the PT, PA, and PG values measured by preop CT did not differ from those measured by Vis: the mean difference in PT was only -0.2 cm (P = 0.78), while the mean differences in PA and greater curvature were -0.4 and 0.4 cm, respectively (P = 0.48 and P = 0.53, respectively). When intraop Lap and Vis were compared, the difference between PT values (1.1 cm, P = 0.10) was not significant, but the PA and PG values were statistically different (1.9 and 3.4 cm, respectively; P = 0.01 for both).

Comparison of preop GFS, Vis, and corrected GFS values

Because of the significant differences between preop GFS values and those of all the other methods, we corrected the preop GFS values by multiplying them by the preop CT: preop GFS ratio (Table 1). The mean preop CT: preop GFS ratio was 0.58 (0.25), and the corrected GFS values for PT, PA, and PG were 8.7, 8.4, and 8.0 cm, respectively. Comparison of corrected GFS and Vis revealed no significant differences for PT (1.4 cm) and PG (0.8 cm) values (P = 0.15 andP = 0.48, respectively), but the difference in PA was statistically significant (2.0 cm, P =

0.04) (Table 3).

DISCUSSION

The aim of this study was to evaluate 3 methods of predicting exact tumor location: preop GFS, preop CT, and intraop Lap. We found that preop GFS measurements differed significantly from preop CT and intraop Lap measurements. We conclude that endoscopic clipping combined with preoperative CT is most useful for preoperatively predicting the location of early gastric cancers, and intraoperative gastroscopy-guided laparoscopy is also useful. However, preoperative GFS is not helpful because of the distension of the stomach during GFS.

Kitano et al. [5] first described laparoscopy-assisted distal gastrectomy, in 1994, and this procedure is now frequently used to treat early gastric cancer in Japan and Korea. Kanaya et al. [6] later reported delta-shaped anastomosis during Billroth type I totally laparoscopic distal gastrectomy (TLDG), and Takaori et al. [7] described the successful use of intracorporeal Roux-Y reconstruction after TLDG. Two studies have reported that compared to laparoscopy-assisted distal gastrectomy, TLDG results in a superior postoperative recovery and shorter hospital stay, although it is more costly [8,9]. However, a dis-

advantage of TLDG is that the operator can only assess the margins after resection. This means that if the resection margin is very short and/or positive for malignant cells, the operation may not only be longer, with increased risk and cost, it may also have to be converted from subtotal to total gastrectomy. For this reason, it is very important that the tumor site be precisely known, allowing for accurate planning of the operation.

We usually perform preop GFS to examine both the location of cancer and to confirm the results of the biopsy. We perform preop CT for staging purposes before routine preoperative examination. Intraoperative GFS frequently reveals that preoperative GFS data are inaccurate when the tumor is located on the side of the lesser curvature, or in the middle or upper part of the body. This is true even when the preop GFS measurements are made by an experienced endoscopist. In contrast, when the tumor is located in the lower body, the preop GFS data are usually quite accurate. This is because of the distension of the stomach during GFS. Supporting this interpretation is our finding that preop GFS values were about twice as great as Vis values.

Two-dimensional CT detects early gastric cancer at very low sensitivity, 20% to 53% [10,11]. However, 3D CT, which permits fast scanning, the rapid infusion of intravenous contrast medium, and gastric wall filling, is associated with a markedly increased tumor detection rate, as high as 80% to 88% [12-14]. This is because it images 2 or 3 layers of the enhanced gastric wall [15]. In the Republic of Korea, the incidence of early gastric cancer is much higher than it was 10 years ago [16]. This means that it is very important to precisely locate early gastric cancer before the operation, especially in cases of laparoscopic gastrectomy. However, the ability of CT to predict the location of early gastric cancer is limited, particularly if the cancer is located on the horizontally oriented portion of the gastric wall, such as the lesser or greater curvature; this is because of poor z-axis resolution and a partial volume averaging effect [17,18]. In addition, CT detects flat and depressed or excavated tumors with more difficulty than protruding-type tumors, and it rarely detects tumors that are located in the gastric angle [15,19].

We found that preoperative endoscopic clipping followed by CT scan was very useful for accurately predicting the tumor site. Indeed, while endoscopic clipping was initially developed to facilitate hemostasis during gastrointestinal bleeding, now it is also widely used as a marker for radiotherapy or for closing gastrointestinal perforations [20-22]. Ryu et al. [23] have also reported the usefulness of preoperative endoscopic clipping for predicting the location of early gastric tumors before open surgery. In addition, Hyung et al. [24] have reported that placing an endoscopic clip proximal to the tumor is also useful for detecting the tumor intraoperatively by laparoscopic ultrasonography. Thus, preoperative endoscopic clipping is a very simple and useful method. However, if the tumor is located in the posterior of the stomach, the intragastric air can distort preoperative measurements of tumor location, in which case clipping should be accompanied by laparoscopic ultrasonography.

Preoperative clipping has also been reported to be useful for intraoperative gastroscopy [8,25]. Tumor site can be readily detected by intraoperative endoscopy under laparoscopic guidance, and indeed, in our hospital, we intraoperatively confirm tumor site using this method. Although endoscopy is time consuming, the surgeon can easily perform it, and we have the endoscope in the operation room itself. However, because the tumor can be difficult to identify with an endoscope, an experienced endoscopist should be enlisted to perform preoperative endoscopic clipping. Other investigators preoperatively marked the location of the gastric tumor in the submucosal layer of the stomach with an India ink tattoo [7,26]. However, while endoscopic tattooing with dye yields good results for colonic lesions, it has been associated with several complications, such as fat necrosis with inflammatory pseudotumoral formation or colonic abscess with localized peritonitis [23,27,28]. Phlegmonous gastritis has also been reported after Indian ink marking in early gastric cancer, and the ink can also disappear [29].

Before this study, we suspected that intraoperative laparoscopy would locate early gastric cancers preoperatively more accurately than either preoperative CT or preoperative GFS. However, we found that preoperative CT with endoscopic clipping was in fact the most accurate way to predict cancer location. The relative inaccuracy of

intraop Lap can be attributed to gastric contraction and folding. Errors in intraop Lap cannot be avoided since it is difficult to obtain precise measurements by intraop Lap when the stomach is distended. This is why we endoscopically remove intragastric gas before making the intraop Lap measurements. We believe another cause is the rigidity of the handmade Nelaton ruler, which is problematic when measuring distances that include the curved stomach wall. However, intraop Lap remains highly useful for detecting tumors and determining resection margins.

Despite recent technological developments, preoperative endoscopic clipping, 3D reconstruction, and measurement of the distance of a tumor from the pylorus or gastroesophageal junction remains a complex and time-consuming procedure. We recommend limiting this method to early gastric cancers located in the middle body, especially those that are proximal to the angle on the side of the lesser curvature.

In conclusion, endoscopic clipping combined with CT gastroscopy is very useful for preoperatively measuring the location of early gastric cancers, which is helpful for planning laparoscopic gastrectomy.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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