Video Article

Intraoperative Gastroscopy for Tumor Localization in Laparoscopic Surgery for Gastric Adenocarcinoma

Hoon Hur[1], Sang-Yong Son[1], Yong Kwan Cho[1], Sang-Uk Han[1]

[1]Department of Surgery, Ajou University, School of Medicine

Correspondence to: Hoon Hur at hhcmc75@naver.com

URL: https://www.jove.com/video/53170
DOI: doi:10.3791/53170

Keywords: Medicine, Issue 114, gastric adenocarcinoma, distal gastrectomy, early gastric cancer, tumor localization, laparoscopy, intraoperative gastroscopy

Date Published: 8/9/2016

Citation: Hur, H., Son, S.Y., Cho, Y.K., Han, S.U. Intraoperative Gastroscopy for Tumor Localization in Laparoscopic Surgery for Gastric Adenocarcinoma. *J. Vis. Exp.* (114), e53170, doi:10.3791/53170 (2016).

Abstract

Determining resection margins for gastric cancer, which are not exposed to the serosal surface of the stomach, is the most important procedure during totally laparoscopic gastrectomy (TLG). The aim of this protocol is to introduce a procedure for intraoperative gastroscopy, in order to directly mark tumors during TLG for gastric cancer in the middle third of the stomach. Patients who were diagnosed with adenocarcinoma in the middle third of the stomach were enrolled in this case series. Before surgery, additional gastroscopy for tumor localization is not performed. Under general anesthesia, laparoscopic mobilization of the stomach is performed first. After the first portion of the duodenum is mobilized from the pancreas and clamped, the surgeon moves to the other side for the gastroscopic procedure. On the insertion of a gastroscope through the oral cavity into the stomach, 2 - 3 cc of indigo carmine is administered via an endoscopic injector into the gastric muscle layer at the proximal margin of the stomach. The location of stained serosa in the laparoscopic view is used to guide distal subtotal gastrectomy, however, total gastrectomy is performed if the tumor is too close to the esophagogastric junction. A specimen is sampled after distal gastrectomy to confirm sufficient length from resection margin to tumor before reconstruction. In our case series, all patients had tumor-free margins and required no additional resection. There was no morbidity related to the gastroscopic procedure, and the time required for the procedure has gradually decreased to about five minutes. Intraoperative gastroscopy for tumor localization is an accurate and tolerated method for gastric cancer patients undergoing totally laparoscopic distal gastrectomy.

Video Link

The video component of this article can be found at https://www.jove.com/video/53170/

Introduction

Laparoscopic surgery has been become the treatment of choice for early gastric cancer in East Asian countries, including Korea and Japan.[1] The advantage of this surgery has been well demonstrated in several clinical trials for early gastric cancer (EGC).[2-4] Most of the procedures in these trials were accomplished by laparoscopy, but identification of the tumor location, resection of the stomach, including the primary tumor, and reconstruction were performed via minilaparotomy. Therefore, surgery requiring minilaparotomy has been labeled "laparoscopy-assisted gastrectomy."

Recently, however, surgical procedures have evolved to minimize trauma, improving the postoperative quality of life for patients. Since this concept has also been applied in laparoscopic surgery for gastric cancer, some experienced laparoscopic surgeons have tried to avoid minilaparotomy. Totally laparoscopic gastrectomy (TLG) for gastric cancer requires that all procedures are completed using only laparoscopic devices, without requiring an additional minilaparotomy for specimen resection and anastomosis. Since this type of surgery results in less pain and faster recovery relative to open or laparoscopy-assisted surgery, which require laparotomy, more surgeons prefer it.[5,6] However, an obstacle to TLG for gastric cancer is tumor localization without direct visualization or palpation to determine the area of stomach resection.

Tumor absence at the resection margin is very important to achieve success in gastric cancer surgery. If there is tumor involvement at the resection margin during distal gastrectomy for gastric cancer, additional resection is needed to avoid leaving tumor in the remaining stomach. In open and laparoscopy-assisted surgery, the primary tumor can be easily localized by palpation or direct visualization through a temporary gastrostomy. However, because the primary tumor is not easily detected in the laparoscopic view, determining resection margins for EGC in TLG may be difficult.

Several other methods requiring additional preoperative gastroscopy to determine resection margins have been proposed.[7-9] However, additional preoperative gastroscopy can be inconvenient for patients. We introduced a procedure for intraoperative gastroscopy to directly mark tumors during TLG for gastric cancer in the middle third of the stomach.

In this protocol, we applied the laparoscopic surgery for patients with early gastric cancers at the preoperative studies, which are not included in absolute indication for endoscopic submucosal dissection.

Protocol

Ethics Statement: This procedure involving human subjects has been approved by the Institutional Review Board (IRB) at Ajou University Hospital.

1. Preparation for Surgery

1. Allow a soft diet one day before surgery, with nothing by mouth after midnight before the surgery.
   Note: Do not insert a nasogastric tube before and during the surgery. This protocol does not use any tube to deflate the stomach. Instead of that, the intra-gastric gas can be aspirated by laparoscopic puncture needle if the stomach is distended causing limited view for laparoscopic surgery.
2. After placing the patient on the operating table, administer the induction agent (Thiopental Sodium, 100 mg).
3. After intravenous injection of a muscle relaxant (Rocuronium bromide, 1.0 mg/kg), insert the endotracheal tube through the oral cavity.
4. Start the anesthetic gas (Sevoflurane, 2 - 3%) via the endotracheal tube, then monitor the patient for stability during surgery.

2. Surgical Procedure before Intraoperative Gastroscopy

1. Place the patient in reverse Trendelenburg position, and stand at the right side of the patient.
2. Make 10 mm incision at the infraumbilical area, and insert the first trocar into the abdominal cavity.
3. As soon as the trocar is inserted, connect the gas tube for carbon dioxide with the trocar to create a pneumoperitoneum of 15 - 18 mm Hg.
4. Insert a rigid 30° laparoscope through the trocar, and explore the abdominal cavity on a monitor connected with the laparoscopic system.
5. Insert 4 additional trocars (one 12 mm and three 5 mm) as working ports. Insert 12 mm trocar at the right upper side of the umbilicus. Insert other three 5 mm trocars at left upper side of the umbilicus and both upper outer quadrants of the abdomen.
6. Dissect the gastrocolic ligament along the transverse colon toward the inferior pole of the spleen using ultrasonic endoscopic scissors.
7. Ligate the left gastroepiploic artery and vein originating from splenic vessels at the root with a laparoscopic clip and resect them using ultrasonic endoscopic scissors, after exposure of the superior border of the pancreatic tail.
8. Using ultrasonic endoscopic scissors, dissect the peripyloric lymph nodes around the pylorus and the head of the pancreas, and resect the right gastroepiploic vessels at their origin.
9. Before resection of the first portion of the duodenum, clamp the duodenum with a laparoscopic clamp to prevent migration of gas into the small bowel during the gastroscopic procedure (**Figure 1**).

3. Intraoperative Gastroscopy

1. Move to the left side of the patient's head to perform intraoperative gastroscopy.
2. Insert a gum shield to protect the teeth and gums during intraoperative gastroscopy.
3. Turn the head of the patient to the left side for insertion of the gastroscope.
4. Insert the gastroscope into the stomach carefully through the mouth and the esophagus, to avoid injury to the mucosa of the oral cavity, the esophagus, and the stomach.
5. Insufflate the stomach by injecting gas through the gastroscope to locate the primary lesion.
   Note: Most gastroscopes have a specific button to inject gas into the bowel during the procedure.
6. Approximate the distance between the proximal margin of the tumor and the esophagogastric junction using the scale marked on the gastroscope (**Figure 2**), and perform total gastrectomy (as described previously) if the distance is too short to salvage the proximal stomach.[10]
7. If total gastrectomy is not necessary, insert an endoscopic injector through a small hole of the gastroscope, and inject 2 - 3 cc of indigo carmine into the gastric wall using an endoscopic injector at an area 2 - 3 cm proximal from the tumor margin, avoiding intra- or extraluminal leakage (**Figure 3A**).
   1. Insert the needle of the injector into the gastric wall obliquely to avoid the perforation of gastric wall by the needle. In addition, inject indigo carmine very slowly to identify intraluminal leakage during injection.
8. After dye injection, aspirate inflation gas through the gastroscope to make the laparoscopic procedure easier.
   Note: Most gastroscopes have a specific button to aspirate inflation gas during the procedure.

4. Procedure after Intraoperative Gastroscopy

1. Return to the right side of the patient after the gastroscopic procedure.
2. In the laparoscopic view, confirm the proximal portion of the tumor by identifying serosal staining by blue dye (**Figure 3B**).
3. Mark the stained portion to be resected with an endoscopic clip, avoiding involvement of tumor at the resection margin (**Figure 4A**).
   Note: We recommend performing this procedure within 5 - 10 min after surgery begins, because the dye can sometimes be washed out during subsequent procedures.
4. If the dye cannot be detected in the serosa, immediately re-inject the dye under gastroscopic visualization.

5. Procedure after Intraoperative Gastroscopy

1. Resect the duodenum, and perform other procedures for lymph node dissection according to the Japanese treatment guidelines.[11]

2. After lymph node dissection, resect the stomach at the proper location at least 3 cm proximal from the tumor margin, guided by the marking clip, using 2 endoscopic staplers.
3. As soon as the distal stomach is resected, insert the specimen into an endoscopic bag and withdraw it from the abdominal cavity through a 2 - 3 cm extension of the infraumbilical trocar site.
4. Send the tissue from the proximal margin to pathology for intraoperative histological evaluation.
5. After confirmation of tumor-free tissue in the proximal portion of the resected stomach, perform an anastomosis between the remaining stomach and the proximal jejunum with intracorporeal linear staplers (**Figure 4B**).

Representative Results

Of 20 patients who underwent intraoperative gastroscopy, 18 underwent distal subtotal gastrectomy, guided by findings at gastroscopy. However, we performed total gastrectomy on two patients, because the proximal tumor margin was too close to the esophagogastric junction, as determined on intraoperative gastroscopy. The distance from the tumor to the proximal resection margin was 3.5 cm and 2.5 cm in these two patients, respectively (**Table 1**).

Total mean operative time for distal gastrectomy was 188 min. The mean time for tumor localization with intraoperative gastroscopy was 8.4 min, and it gradually decreased from 11.8 min (initial 5 cases) to 4.6 min (last 5 cases) (**Figure 5**). Intracorporeal reconstruction with Billroth II anastomosis followed distal gastrectomy in all patients. There was no morbidity, except for gastric stasis and adhesive ileus in two patients. Finally, there were no complications related to intraoperative gastroscopy.

Mean tumor size in patients who underwent distal gastrectomy was 2.89 (range: 0.5 - 3.2) cm. EGC was the final diagnosis in 16 patients, but one exhibited muscle invasion and another exhibited serosal invasion. The mean distance from tumor to resection margin was 3.3 (range: 0.5 - 6.7) cm. Most common histologic type was signet ring cell carcinoma (**Table 1**).

No.	Age, y	Sex	LN[a] dissect-ion	Resect-ion	Recon-struction	Op[b] time, min	GFS[c] time, min	Location	Frozen for PRM[d]	Histo-logy	Stage	Tumor size, cm	Proximal length from tumor, cm
1	57	male	D1+	Subtotal	Billroth-II	235	15	Posterior	Tumor free	signet ring cell	Ia	2.5	2.7
2	44	female	D2	Subtotal	Billroth-II	140	12	Greater	Tumor free	signet ring cell	Ia	1	6
3	51	female	D2	Subtotal	Billroth-II	195	10	Posterior	Tumor free	signet ring cell	Ia	1	7
4	34	female	D2	Subtotal	Billroth-II	235	10	Anterior	Tumor free	Pooly differen-tiated	Ia	1.5	6.7
5	56	male	D2	Subtotal	Billroth-II	225	12	Greater	Tumor free	signet ring cell	Ia	1.5	3
6	51	male	D1+	Subtotal	Billroth-II	200	13	Lesser	Tumor free	Moderatly differen-tiated	Ia	2	4.1
7	46	female	D1+	Subtotal	Billroth-II	110	8	Greater	Tumor free	signet ring cell	Ia	2	4
8	68	female	D2	Subtotal	Billroth-II	200	7	Lesser	Tumor free	Pooly differen-tiated	Ib	5	2
9	42	female	D1+	Subtotal	Billroth-II	170	9	Lesser	Tumor free	signet ring cell	Ib	3.2	3.6
10	50	male	D1+	Subtotal	Billroth-II	200	12	Lesser	Tumor free	signet ring cell	Ia	2.5	0.5
11	31	female	D1+	Subtotal	Billroth-II	210	8	Greater	Tumor free	signet ring cell	Ia	1.2	1.3
12	56	female	D2	Subtotal	Billroth-II	175	7	Lesser	Tumor free	signet ring cell	IIIa	2.5	0.5
13	65	male	D1+	Subtotal	Billroth-II	150	5	Lesser	Tumor free	Undiffer-entiated	Ia	0.5	5
14	36	female	D1+	Total	Roux-en-Y	180	Conver-sion	Lesser	Tumor free	signet ring cell	IIa	1.5	3.5
15	71	female	D1+	Subtotal	Billroth-II	190	5	Greater	Tumor free	signet ring cell	Ia	11	2.6
16	48	female	D2	Subtotal	Billroth-II	185	4	Anterior	Tumor free	signet ring cell	Ia	6	1.3
17	36	female	D1+	Total	Roux-en-Y	305	Conver-sion	Greater	Tumor free	Pooly differen-tiated	Ia	7	2.5
18	46	male	D1+	Subtotal	Billroth-II	180	4	Posterior	Tumor free	Pooly differen-tiated	Ia	0.5	3
19	51	male	D1+	Subtotal	Billroth-II	180	6	Anterior	Tumor free	Well differen-taited	Ia	2	2.5
20	43	female	D1+	Subtotal	Billroth-II	120	5	Greater	Tumor free	signet ring cell	Ia	0.6	7

Table 1: Surgical and Pathologic Outcomes of Patients who Underwent Intraoperative Gastroscope to Identify Tumor Location. Please click here to download this table.

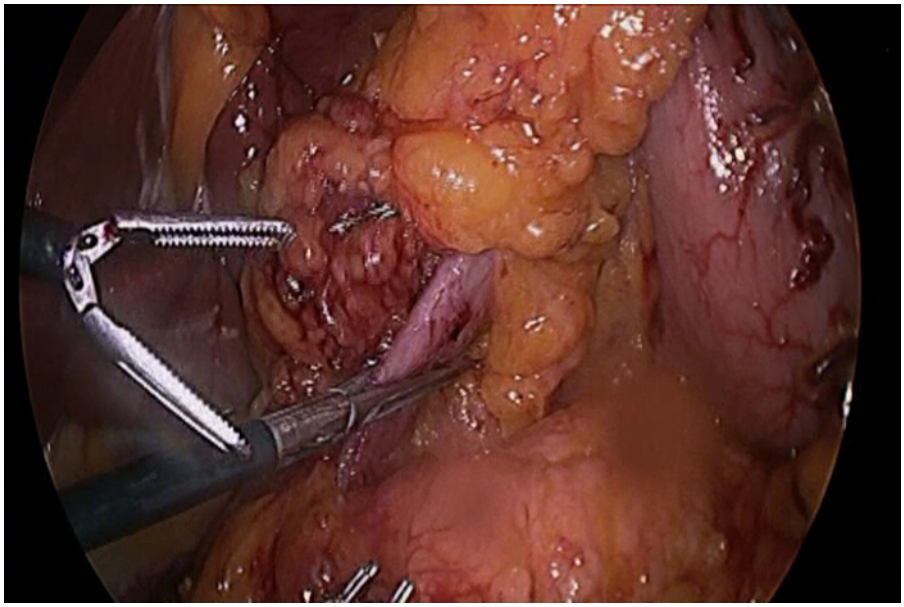

Figure 1: Laparoscopic Clamp to Prevent Gas Passage into the Small Bowel. Before insertion of the gastroscope during surgery, the duodenum or jejunum should be clamped with a laparoscopic instrument. Gastroscopic procedures inevitably require the insufflation of gas into the lumen of the bowel to precisely visualize the lesions, and gas that has passed into the small bowel cannot be easily aspirated when the gastroscopic procedure finishes. Consequently, inflated small bowel can interfere with the laparoscopic procedure. Please click here to view a larger version of this figure.

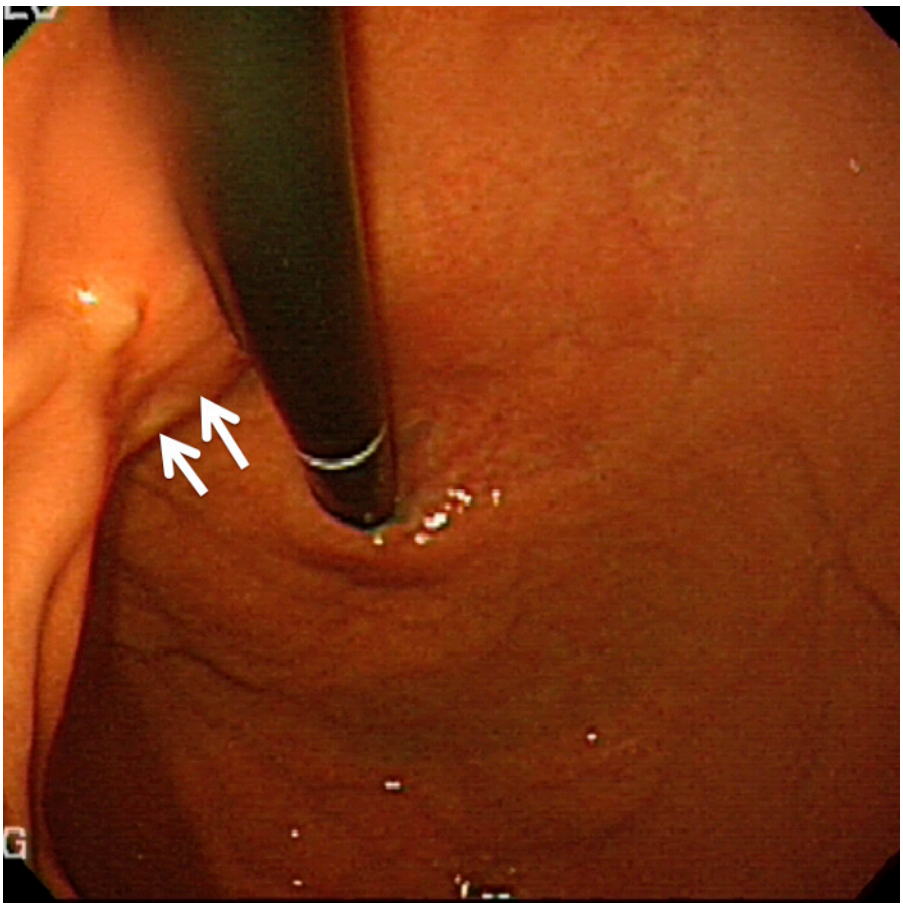

Figure 2: Measurement of the Distance between the Tumor and Esophagogastric Junction. Most gastroscopes have a scale with approximate 5 cm gradations. If the distance between the margin of tumor and esophagogastric junction is 5 cm or less, it is too difficult to retain the proximal part of the stomach and the surgeon should perform a total gastrectomy for gastric cancer. Please click here to view a larger version of this figure.

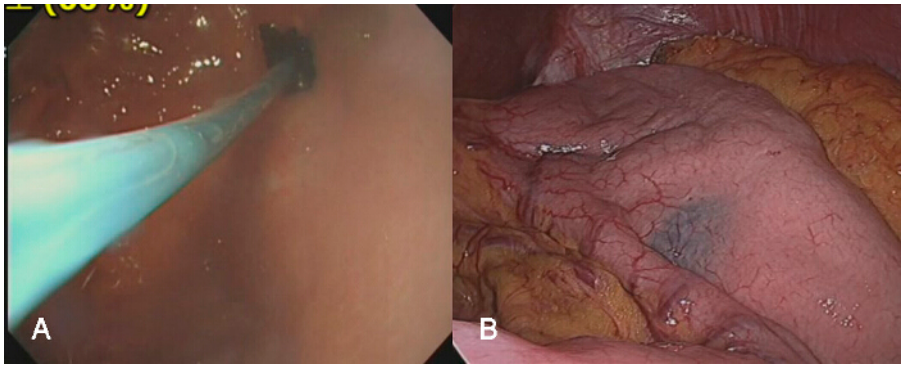

Figure 3: Injection of Blue Dye into the Gastric Wall. A) An endoscopic injector can be introduced through a small channel on the gastroscope. The needle of the endoscopic injector is exposed, and injected into the gastric wall at an area 2 - 3 cm proximal from the tumor margin. If the needle is inserted into the gastric wall forcefully, it can penetrate the gastric wall, and the dye will be injected into the peritoneal cavity. **B)** This would make identification of the precise location of the tumor difficult in the laparoscopic view. Therefore, this injection procedure should be performed carefully. Please click here to view a larger version of this figure.

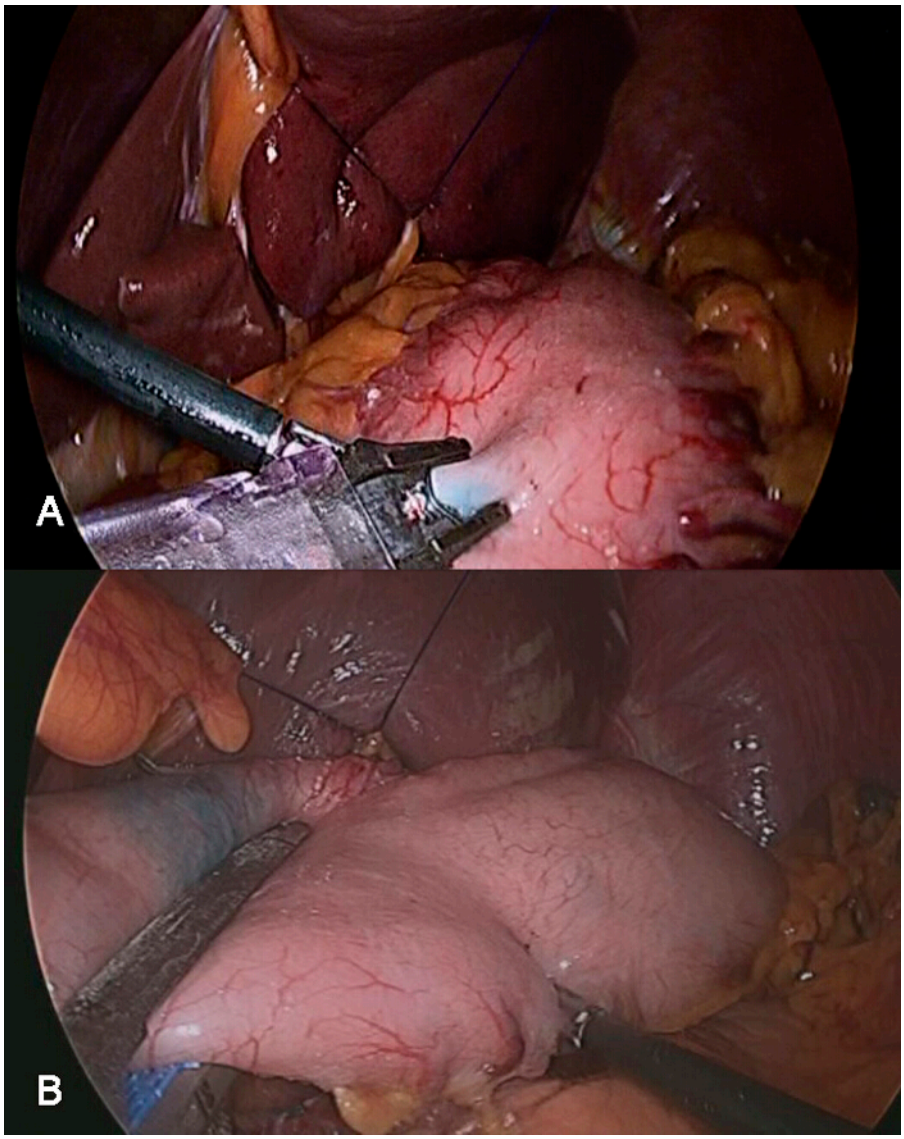

Figure 4: Laparoscopic Resection Guided by the Stained Surface of the Stomach. After lymph node dissection, the stomach should be resected at the proper area to completely remove the primary tumor. **A)** A marker made with a laparoscopic clip, which can be useful in determining the portion for resection, should be applied 5 to 10 min after gastroscopic injection of the dye. **B)** Laparoscopic resection can be completed with two or three laparoscopic linear staplers. Please click here to view a larger version of this figure.

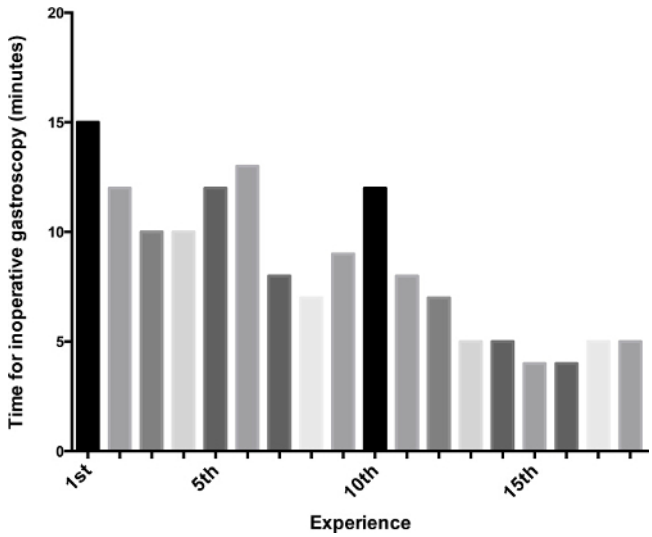

Figure 5: Change in Time Required for Intraoperative Gastroscopy and Tumor Localization. The mean time for tumor localization with intraoperative gastroscopy (8.4 min) gradually decreased from 11.8 min (initial 5 cases) to 4.6 min (last 5 cases).

Discussion

In this protocol, we introduced a procedure for intraoperative gastroscopy to accurately and reliably identify tumor location in the middle third of the stomach. We were able to successfully perform distal subtotal gastrectomy based on the findings of intraoperative gastroscopy.

To date, various methods have been applied to identify the location of early gastric cancer in the laparoscopic view. Most common methods used preoperative gastroscopic clipping, and surgeons could detect the location of clips using laparoscopic ultrasonography or portable plain radiography.[7,9] These techniques required additional preoperative gastroscopy one or two days before surgery. Laparoscopic ultrasonography for intraoperative detection of clips requires specific instruments and skills and involves subjective interpretation. Another option, intraoperative portable radiology, can show only a two-dimensional view; additional exposure to radiation can be harmful to patients. Recently, Jeong and colleague reported gastroscopic autologous blood tattooing before surgery.[8] They reported that this procedure also requires preoperative gastroscopy one day before surgery, and consequently is inconvenient for patients. Another disadvantage of this procedure is that it is impossible to recognize incorrect injection into the gastric wall before surgery.

Unlike other procedures, we performed additional gastroscopy while patients were under general anesthesia during surgery. Therefore, patients enrolled in the present study avoided the inconvenience of additional preoperative gastroscopy. The dye injected into the muscle layer was easily detected during surgery, because we examined the serosa within 5 to 10 min after injection, and immediately clipped the center of the stained serosa before the dye spread. The exact tumor location was detected in all patients with our procedure.

The critical step of our procedure is injection of the blue dye into the gastric wall without leakage into the extraluminal area. When more commonly used dyes, such as methylene blue, leak into the intraperitoneal region, there is concern for the occurrence of postoperative adhesions, methemoglobinemia, and pulmonary edema by chromopertubation. In our protocol, indigo carmine is used instead of methylene blue, because it is a relatively nontoxic, inexpensive dye. Even so, the leakage of dye can make precise localization of tumors difficult. Therefore, it is recommended that a surgeon experienced in gastroscopic procedures, such as endoscopic injection, perform this procedure.

When blue dye and a specific instrument like an endoscopic injector are not available, our procedure can be modified. As soon as the operating surgeon inserts the gastroscope and inflates the stomach, the assistant surgeon compresses the area where the primary tumor is expected to be located, enabling the operating surgeon to identify the distance between the location of the primary tumor and the compressed lesion. Through communication between the operating and the assistant surgeon, the tumor can be precisely localized.

Several limitations of our technique for tumor localization should be considered. First, intraoperative gastroscopy may require a learning curve for specific endoscopic skills. One report suggested that surgeons would overcome the learning curve of gastroscopic procedures after about 80-90 cases.[12] The surgeon who participated in this study had sufficient experience (more than 400 cases) to overcome the learning curve. Sometimes, intraoperative gastroscopy may be difficult due to the positioning of patients under general anesthesia. If the anesthesiologist extends the jaw of the patient, the gastroscope can be easily passed through the throat and into the esophagus. Second, specific devices for this procedure, like the gastroscopic system, should be ready in the operating room. However, several recently suggested procedures for gastric resection also require use of an intraoperative gastroscope.[13,14] In the future, intraoperative gastroscopy will be more common in gastric surgery, and the gastroscopic system will be essential in the operating room Third, tumor margins were only determined by endoscopic findings in this protocol. Sometimes, the margin of superficial spreading tumors can be unclear, even though an elevated and discolored lesion can be assumed to be a tumor. Recent evolving techniques, such as infrared endoscopy or molecular *in vivo* imaging, may verify the tumor margin; if applied to intraoperative gastroscopy,[15,16] the procedure in this protocol can be more accurate and useful.

In conclusion, intraoperative gastroscopy for tumor localization is an accurate and tolerated method for gastric cancer patients undergoing totally laparoscopic distal gastrectomy.

Disclosures

The authors have no conflicts of interest or financial ties to disclose.

Acknowledgements

This study was supported by a grant from the National R&D Program for Cancer Control, Ministry of Health & Welfare, Republic of Korea (1320270).

References

1. Kim, Y. W., Yoon, H. M., Eom, B. W., & Park, J. Y. History of minimally invasive surgery for gastric cancer in Korea. *J Gastric Cancer.* **12**, 13-17 (2012).
2. Kim, H. H. *et al.* Morbidity and mortality of laparoscopic gastrectomy versus open gastrectomy for gastric cancer: an interim report--a phase III multicenter, prospective, randomized Trial (KLASS Trial). *Ann Surg.* **251**, 417-420 (2010).
3. Kim, M. C., Kim, K. H., Kim, H. H., & Jung, G. J. Comparison of laparoscopy-assisted by conventional open distal gastrectomy and extraperigastric lymph node dissection in early gastric cancer. *J Surg Oncol.* **91**, 90-94 (2005).
4. Kim, Y. W. *et al.* Improved quality of life outcomes after laparoscopy-assisted distal gastrectomy for early gastric cancer: results of a prospective randomized clinical trial. *Ann Surg.* **248**, 721-727 (2008).
5. Kinoshita, T. *et al.* Comparison of laparoscopy-assisted and total laparoscopic Billroth-I gastrectomy for gastric cancer: a report of short-term outcomes. *Surg Endosc.* **25**, 1395-1401 (2011).
6. Song, K. Y. *et al.* Is totally laparoscopic gastrectomy less invasive than laparoscopy-assisted gastrectomy?: prospective, multicenter study. *J Gastrointest Surg.* **12**, 1015-1021 (2008).
7. Hyung, W. J. *et al.* Intraoperative tumor localization using laparoscopic ultrasonography in laparoscopic-assisted gastrectomy. *Surg Endosc.* **19**, 1353-1357 (2005).
8. Jeong, O., Cho, S. B., Joo, Y. E., Ryu, S. Y., & Park, Y. K. Novel technique for intraoperative tumor localization during totally laparoscopic distal gastrectomy: endoscopic autologous blood tattooing. *Surg Endosc.* **26**, 1778-1783 (2012).
9. Kim, H. I. *et al.* Intraoperative portable abdominal radiograph for tumor localization: a simple and accurate method for laparoscopic gastrectomy. *Surg Endosc.* **25**, 958-963 (2011).
10. Kim, H. I., Cho, I., Jang, D. S., & Hyung, W. J. Intracorporeal esophagojejunostomy using a circular stapler with a new purse-string suture technique during laparoscopic total gastrectomy. *J Am Coll Surg.* **216**, e11-16 (2013).
11. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2010 (ver. 3). *Gast Can.* **14**, 113-123 (2011).
12. Lee, H. H., Song, K. Y., Park, C. H., & Jeon, H. M. Training of surgical endoscopists in Korea: assessment of the learning curve using a cumulative sum model. *J Surg Educ.* **69**, 559-563 (2012).
13. Cho, W. Y. *et al.* Hybrid natural orifice transluminal endoscopic surgery: endoscopic full-thickness resection of early gastric cancer and laparoscopic regional lymph node dissection--14 human cases. *Endoscopy.* **43**, 134-139 (2011).
14. Abe, N. *et al.* Endoscopic full-thickness resection with laparoscopic assistance as hybrid NOTES for gastric submucosal tumor. *Surg Endosc.* **23**, 1908-1913 (2009).
15. Hoetker, M. S. *et al.* Molecular in vivo imaging of gastric cancer in a human-murine xenograft model: targeting epidermal growth factor receptor. *Gastrointest Endosc.* **76**, 612-620 (2012).
16. Ishihara, R. Infrared endoscopy in the diagnosis and treatment of early gastric cancer. *Endoscopy.* **42**, 672-676 (2010).

