Technical Note

Non-exposed endoscopic wall-inversion surgery for gastrointestinal stromal tumor

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Abstract: Laparoscopic and endoscopic cooperative surgery (LECS) is an accepted method of laparoscopic wedge resection, which is minimally invasive, for gastrointestinal stromal tumors (GISTs). We established a type of LECS achieving a full-thickness resection, non-exposed endoscopic wall-inversion surgery (NEWS), in an effort to prevent exposure of the peritoneal cavity to gastric intraluminal contents. We employed this surgical technique in 28 gastric GIST patients. We failed to complete NEWS in the initial two patients and in one patient with a large tumor (40 mm × 35 mm), but otherwise carried out the procedure successfully. Although a learning effect is speculated to occur, based on a decreasing trend in the operation time, the median operation time was 184 minutes showing that NEWS is still a time-consuming method. No significant differences were recognized in tumor size or location, except near the esophagogastric junction (EGJ), nor in the cross-sectional circumference. NEWS is feasible and appears to be a good option, especially for small GISTs with mucosal ulceration rendering full-thickness enucleation by opening of the gastric wall unfeasible.

Keywords: Gastrointestinal stromal tumor (GIST); laparoscopic and endoscopic cooperative surgery (LECS); non-exposed technique

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Introduction

Gastrointestinal stromal tumor (GIST) is the most common mesenchymal neoplasm of the alimentary tract, and the stomach is the most frequently affected site, accounting for roughly of 60% of all patients with a GIST (1,2). Since gastric GIST rarely metastasizes to perigastric lymph nodes, gastric local resection without lymphadenectomy is accepted as a standard treatment. Laparoscopic local resection was thus introduced as a minimally-invasive approach and has achieved an acceptable outcome.

Tumor rupture is associated with a very high risk of recurrence (2), mainly within the peritoneal cavity (3). Therefore, preservation of the pseudocapsule and avoidance of tumor spillage resulting from rupture are the basic principles adhered to when resecting a GIST. Accordingly, laparotomy is basically employed for large GISTs to prevent unexpected tumor rupture during surgery, and a minimally-invasive approach is recommended only for smaller tumors (4). Furthermore, tumor ulceration is also considered to potentially be associated with tumor cell spillage. Local resection with intentional gastric perforation should be avoided in this situation because it results in a communication between the peritoneal cavity and the gastric intraluminal space.

With the aim of preventing exposure of the peritoneal cavity to gastric intraluminal contents, we established and reported a novel technique achieving full-thickness resection without the risk of gastric perforation; non-exposed endoscopic wall-inversion surgery (NEWS) (5-7). This is a form of laparoscopic and endoscopic cooperative

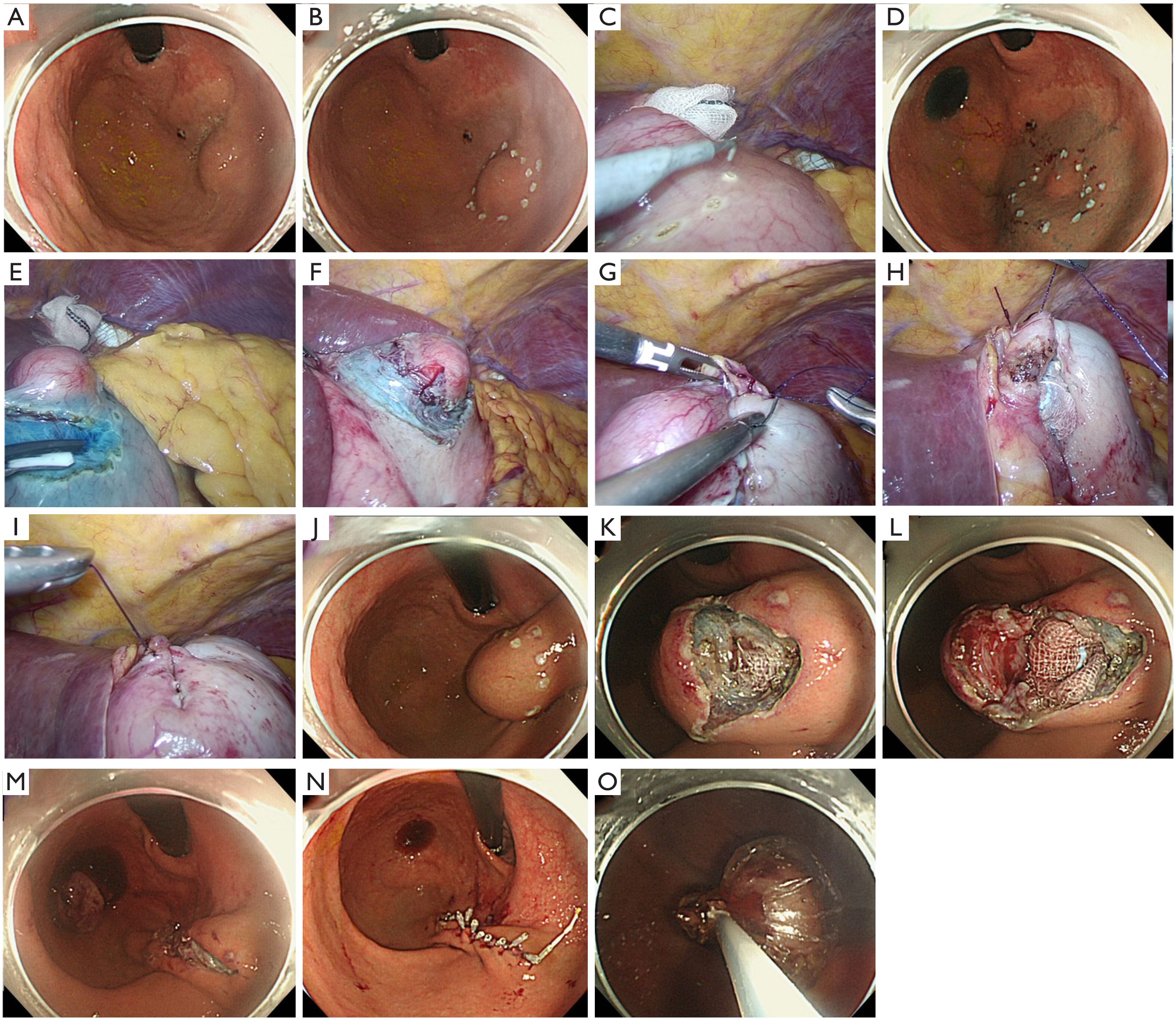

Figure 1 Technical detail of non-exposed endoscopic wall-inversion surgery for gastric gastrointestinal stromal tumor. (A) Identification of the tumor location; (B) markings on the mucosa around the lesion; (C) markings on the serosa; (D) injection into the submucosal layer; (E,F) circumferential seromuscular layer cutting; (G-I) seromuscular suturing with inversion of the lesion with a gauze spacer; (J) extensive protrusion of the gastric mucosa due to the inverted tissue; (K-M) incision of the muco-submucosal layer; (N) endoscopic clips placement to close an artificial linear ulcer; (O) oral extraction using an endoscopic retrieval device.

surgery (LECS). The concept of this technique was initially described based on results obtained with *ex vivo* experimentation (5), and the first application to clinical practice was reported in 2014 (7). We herein describe the technical details and also the short-term results obtained with this procedure.

Procedure of NEWS

Technical procedures are detailed in the images presented as *Figure 1* and illustrated in *Figure 2*. A 12-mm camera port is inserted via the umbilicus and pneumoperitoneum is then established. Three 5-mm trocars are placed in the left upper, left lower, and right upper quadrants, and one 12-

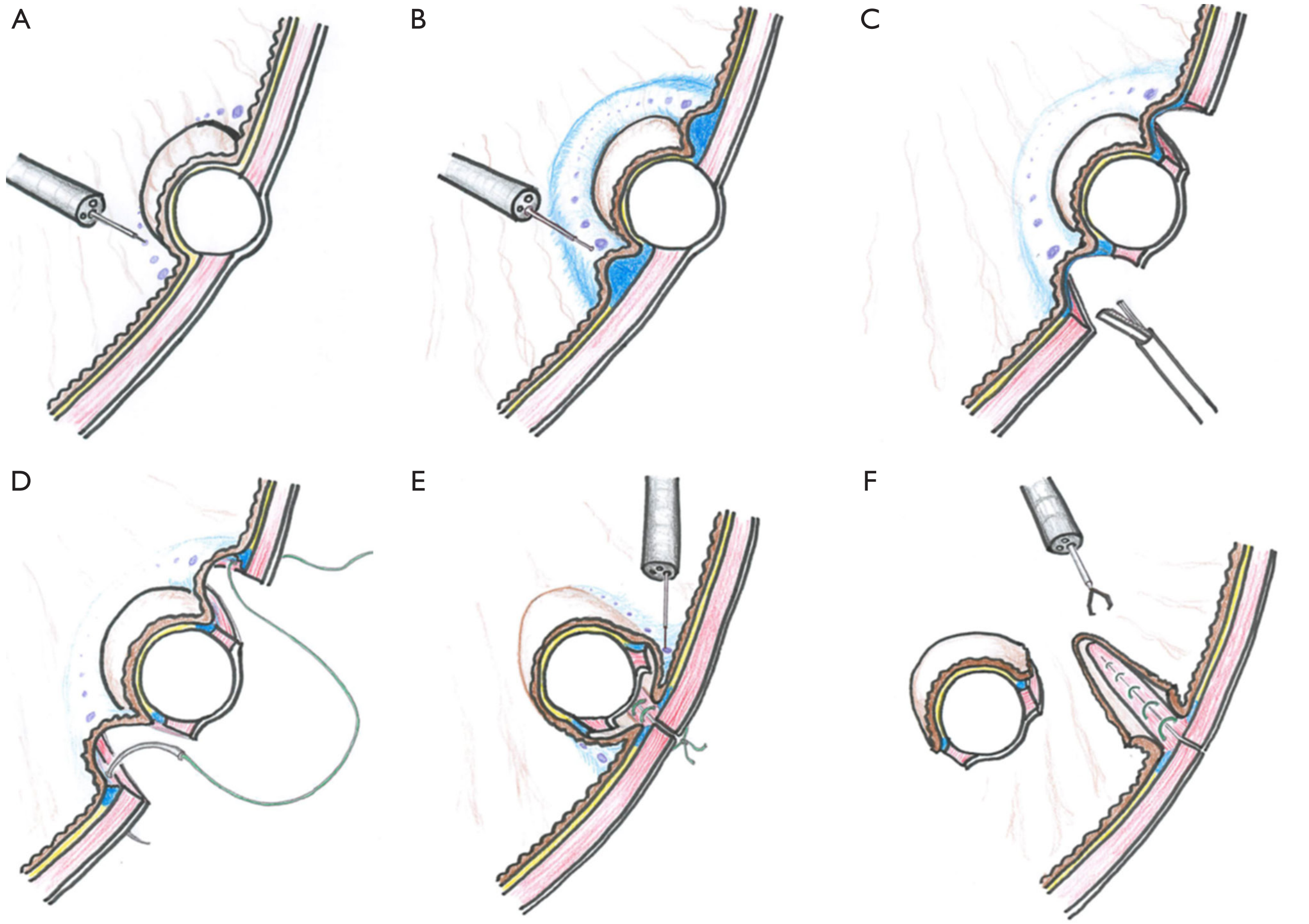

Figure 2 Illustrations to explain the procedures. (A) Markings on the mucosa around the lesion; (B) injection into the submucosal layer; (C) circumferential seromuscular layer cutting; (D) seromuscular suturing; (E) incision of the muco-submucosal layer after inversion of the lesion; (F) loss of continuity between the lesion and gastric wall.

mm trocar in the right lower quadrant. The tumor location is confirmed employing an endoscope with a carbon dioxide supplier (*Figure 1A*). Markings are made by electrocautery on the mucosa around the lesion under endoscopic vision (*Figures 1B* and *2A*) as well as laparoscopically on the serosa just opposite the mucosal markings, guided by pressing the gastric wall using the endoscopic device, or the fiber-optic probe of a diode laser system (*Figure 1C*). A 0.4% sodium hyaluronate solution with a small amount of indigo carmine dye is endoscopically injected into the submucosal layer circumferentially around the mucosal markings with a standard injection needle, of the type used during endoscopic submucosal dissection (*Figure 1D* and *2B*). The seromuscular layer is then incised circumferentially around the serosal markings (*Figures 1E,F* and *2C*). The seromuscular layer is linearly sutured using 3-0 absorbable thread (*Figures 1G* and *2D*). The lesion is naturally inverted into the stomach (*Figure 2E*), and a gauze spacer is inserted between the seromuscular suture plane and the seromuscular surface of the inverted tissue which facilitates the subsequent muco-submucosal incision (*Figure 1H,I*). Endoscopy shows extensive protrusion of the gastric mucosa due to the inverted tissue (*Figure 1J*). The muco-submucosal layer is circumferentially incised outside the mucosal markings, using an endoscopic submucosal dissection technique, until the gauze spacer is found (*Figure 1K,L*). After removal of the gauze spacer, the muco-submucosal incision is completed (*Figures 1M* and *2F*). The resulting artificial linear ulcer is closed using endoscopic clips to promote mucosal healing (*Figure 1N*). The specimen is extracted orally using an endoscopic retrieval device (*Figure 1O*).

Results

We employed NEWS in 28 patients with a GIST between January 2012 and August 2017. The clinicopathological characteristics and operative data of our series are presented in *Table 1*. In the first case, the procedure had to be converted to classical LECS because the tumor was of the totally intraluminal growth type and the tumor margin was poorly recognized on the laparoscopic view. Mucosal injury with a small perforation occurred during the laparoscopic seromuscular cutting phase in case 2. We therefore made two modifications to our technique; employment of the optical fiber system to identify the tumor border clearly from the serosal side and doubling the amount of hyaluronate solution to be injected into the submucosal layer before the laparoscopic seromuscular cutting phase. After these modifications, the full NEWS process was successfully carried out in 25 patients. In case 25, the resected tissue could not be retrieved through the esophagus due to the short axis diameter of the resected GIST being 35 mm, and it was extracted via the gastric window and a small laparotomy incision.

Excluding this patient, case 25, the tumor diameter ranges were 10–45 mm for the long axis and 9–26 mm for the short axis. The only postoperative complication was a fever of unknown origin in one case (Clavien-Dindo grade II), with postoperative courses otherwise being uneventful. Neither conversion of the retrieval route nor unexpected gastric perforation during the procedure was associated with negative postoperative outcomes.

The median operation time was 184 minutes. The operation time gradually decreased during the study period and was within 3 hours for most patients managed during the later part of this study, the exception being one patient with a tumor near the esophagogastric junction (EGJ) (327 min). No significant differences were recognized in tumor size or location, except near the EGJ, nor in the cross-sectional circumference.

Discussion

LECS has now become accepted as a minimally invasive surgical technique for gastric GIST, having gained widespread acceptance since the first report of classical LECS in 2008 (8). Extra-gastric growth type GISTs can easily be identified solely based on a laparoscopic view and laparoscopic wedge resection can be achieved even without support from an endoscopist. However, endoscopy does indeed facilitate identifying the exact tumor location, especially for intraluminal growth type GIST with no significant serosal distortion. Furthermore, it allows the boundary of the GIST to be recognized by endoscopy, while also offering the essential negative margin and minimizing the resected gastric tissues thereafter. However, classical LECS has an innate flaw due to the deliberate gastric perforation that is potentially associated with the risks of bacterial infection and/or tumor cell implantation to the peritoneal surface when gastric juice contains tumor cells dispersed from the primary GIST. Therefore, we hesitate to employ the original LECS procedure with intentional gastric perforation for GISTs with either ulceration or delle formation, or even an artificial ulcer after an extensive biopsy procedure, due to possible tumor cell spillage into the peritoneal cavity.

Employing a non-exposed technique for the digestive tract theoretically reduces the surgical site infection rate and, thereby, postoperative inflammatory responses as well. Although this overcomes the flaw of classical LECS and appears to be an ideal method, NEWS has a major limitation in terms of tumor size due to the tumor retrieval route. The esophageal orifice and EGJ are both among the most inherently narrow areas in the human body. In our series, the maximum tumor size which could be extracted orally was 45 mm in the longest axis and 26 mm in the shortest axis. One tumor, 40 mm × 35 mm in size, could not be retrieved orally and had to be extracted via the abdominal wall. NEWS can be employed basically for small GIST. Based on our experience, the short axis diameter of the tumor is the determinant of NEWS feasibility. With a short axis diameter of less than 30 mm, NEWS is feasible. Therefore, meticulous evaluation of tumor size prior to performing NEWS appears to be essential. Endoscopic ultrasound sonography and computed tomography are recommended for evaluating the exact tumor size.

The procedure is still time-consuming though a learning effect, as indicated by the decreasing trend in operation time, is speculated to be present. Insertion of a gauze spacer accompanied by wall inversion after seromuscular cutting has been employed in recent cases. This maneuver reduces the operation time by facilitating the muco-submucosal incision phase owing to the creation of a wider space between the closed seromuscular plane and the tissue to be resected. Given that seromuscular layer suturing alone is acceptable for alimentary tract anastomosis, endoscopic clipping of the artificial linear ulcer might be optional. Further time reduction might thus be achieved by omitting

Table 1 Characteristics of 28 consecutive patients with gastric GIST

Case No.	Age (years)	Sex	Location	Cross-sectional circumference	Maximum diameter of resected specimen, mm	Tumor size (long axis), mm	Tumor size (short axis), mm	Mucosal ulceration	Mitotic index (Mitoses/hpf)	Malignant risk	Retrieval route	Operation time, min	Perforation	Complication (Clavien-Dindo classification)
1	59	M	U	Post	45	19	16	No	>10/50 hpf	High	Transabdominal	292	Yes	None
2	61	M	U	Post	33	26	26	No	≤5/50 hpf	Low	Transoral	357	Yes	None
3	71	F	U	Ant	38	25	23	No	≤5/50 hpf	Low	Transoral	265	No	None
4	79	F	U	Ant	35	25	20	No	≤5/50 hpf	Low	Transoral	190	No	None
5	49	M	U	Ant	28	17	17	No	≤5/50 hpf	Very low	Transoral	140	No	None
6	58	F	M	Post	48	30	23	No	≤5/50 hpf	Low	Transoral	191	No	None
7	61	M	M	Ant	30	25	20	No	≤5/50 hpf	Low	Transoral	162	No	None
8	71	M	U	Ant	50	45	25	Yes	≤5/50 hpf	Low	Transoral	263	No	None
9	64	F	M	Post	36	18	18	No	≤5/50 hpf	Very low	Transoral	183	No	None
10	76	M	M	Post	24	24	20	No	≤5/50 hpf	Low	Transoral	175	No	None
11	65	M	L	Post	30	10	9	No	≤5/50 hpf	Very low	Transoral	217	No	None
12	76	F	U	Post	25	18	18	Yes	≤5/50 hpf	Very low	Transoral	214	No	None
13	77	M	M	Post	40	40	20	No	≤5/50 hpf	Low	Transoral	194	No	None
14	70	F	U	Post	20	17	14	No	6-10/50 hpf	Low	Transoral	191	No	None
15	52	M	U	Post	30	22	17	No	≤5/50 hpf	Low	Transoral	159	No	None
16	67	M	U	Post	20	20	18	No	≤5/50 hpf	Very low	Transoral	148	No	None
17	68	F	U	Less	38	30	20	No	≤5/50 hpf	Low	Transoral	156	No	Grade II
18	67	M	U	Less	28	22	19	No	6–10/50 hpf	Intermediate	Transoral	200	No	None
19	50	F	EGJ	Gre	37	34	23	No	6–10/50 hpf	Intermediate	Transoral	327	No	None
20	65	M	M	Less	22	12	9	No	≤5/50 hpf	Very low	Transoral	98	No	None
21	85	M	U	Ant	45	30	26	No	≤5/50 hpf	Low	Transoral	185	No	None
22	54	M	U	Post	27	25	20	Yes	≤5/50 hpf	Low	Transoral	189	No	None
23	55	M	U	Ant	35	24	22	No	≤5/50 hpf	Low	Transoral	176	No	None
24	76	M	U	Ant	38	15	14	No	≤5/50 hpf	Very low	Transoral	132	No	None
25	82	M	M	Ant	40	40	35	No	≤5/50 hpf	Low	Transabdominal	161	Yes	None
26	72	M	U	Ant	30	17	14	No	≤5/50 hpf	Very low	Transoral	146	No	None
27	53	F	U	Post	18	15	12	No	≤5/50 hpf	Very low	Transoral	122	No	None
28	76	M	U	Ant	37	30	22	No	≤5/50 hpf	Low	Transoral	174	No	None

GIST, gastrointestinal stromal tumor; M, male; F, female; U, upper third; M, middle third; L, lower third; EGJ, esophagogastric junction; Post, posterior wall; Ant, anterior wall; hpf, high power fields.

endoscopic clipping.

Local resection with complete preservation of the vagal nerve system, minimal resected volume of the unaffected stomach wall and the least possible deformation of the stomach is ideal for preserving inherent gastric function to the maximum extent possible. Given that gastric GISTs 5 cm or smaller can potentially be removed through laparoscopic wedge resection (9), a non-exposed LECS technique appears to be the best current option for small GISTs with mucosal ulceration rendering full-thickness enucleation by opening of the gastric wall unfeasible. It is not clear that the same concept can be employed for GISTs in other organs such as the esophagus, duodenum, and colon. We hope the unique concept of this technique might promote a discussion about establishing and offering a new treatment modality for alimentary neoplasms, especially given the risk of peritoneal seeding when techniques with exposure are applied.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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