Combination of Laparoscopic and Endoscopic Approaches to Neoplasia with Non-exposure Technique (CLEAN-NET) for GIST with Ulceration

Kazuhito NABESHIMA, Mifuji TOMIOKU, Kenji NAKAMURA and Seiei YASUDA

Department of Surgery, Tokai University School of Medicine

(Received June 15, 2015; Accepted July 1, 2015)

Combination of laparoscopic and endoscopic approaches to neoplasia with non-exposure technique (CLEAN-NET) was developed to avoid intraoperative tumor dissemination. We report two cases of gastric gastrointestinal stromal tumor (GIST) with ulceration surgically treated with CLEAN-NET at our institution. The first case was a 55-year-old male with hematemesis. Gastric endoscopy revealed a gastric GIST with ulceration of the fornix. CLEAN-NET was performed with the insertion of five trocars and a liver retractor. The operative time was 202 min (including cholecystectomy), with a perioperative blood loss volume of 29 ml; the postoperative hospital stay duration was 8 days. The second case was a 66-year-old male with a gastric submucosal tumor (SMT) with ulceration. CLEAN-NET was performed in a similar fashion to the first case. The operative time was 128 min, with a preoperative blood loss volume of 16 ml; the postoperative hospital stay duration was 9 days. In conclusion, CLEAN-NET was found to be safe and useful in the treatment of gastric GIST with ulceration.

Key words: CLEAN-NET, GIST, Laparoscopic surgery, LECS-related surgery

INTRODUCTION

According to National Comprehensive Cancer Network (NCCN) guidelines, a laparoscopic approach may be considered in selected cases of gastrointestinal stromal tumor (GIST) with favorable anatomic locations by surgeons with appropriate laparoscopic experience [1]. Laparoscopic-endoscopic cooperative surgery (LECS) for GIST was developed in 2008 [2]. Care must be taken to avoid tumor cell seeding into the peritoneal cavity during open gastric wall surgery for the treatment of gastric GIST with mucosal ulceration. To avoid this intraoperative tumoral dissemination, combination of laparoscopic and endoscopic approaches to neoplasia with non-exposure technique (CLEAN-NET) was developed by Inoue *et al*. [3].

Herein, we report two cases of GIST with ulceration surgically treated by CLEAN-NET at our institution.

PATIENT AND METHODS

Case 1

A 55-year-old male with hematemesis was admitted to our institution. Upper gastrointestinal endoscopy revealed a gastric submucosal tumor (SMT) (3.5 cm in size) with ulceration in the fornix. A diagnosis of GIST was made based on pathological findings of a biopsy specimen (Fig. 1A). Upper gastrointestinal radiography revealed an SMT located in the fornix (Fig. 1B). Abdominal contrast-enhanced computed tomography (CT) demonstrated an intraluminal gastric SMT with no evidence of lymph node or distant metastasis. The tumor was observed by conventional endoscopy under general anesthesia before surgical resection using CLEAN-NET with the insertion of five trocars and a liver retractor. Cholecystectomy due to the presence of gall stones was also performed. The postoperative course was uneventful.

Case 2

A 66-year-old male presented with gastric SMT identified during a routine medical checkup. Upper gastrointestinal endoscopy revealed a SMT (4 cm in size) with ulceration in the fornix (Fig. 2A). Pathological findings from an endoscopic biopsy specimen indicated GIST. Upper gastrointestinal radiography revealed a SMT in the fornix (Fig. 2B). Abdominal contrast-enhanced CT revealed an intraluminal gastric tumor. CLEAN-NET was performed in a similar fashion to Case 1. The postoperative course was uneventful.

THE CLEAN-NET SURGICAL PROCEDURE

The CLEAN-NET procedure involves the selective dissection of both the serosa and muscle layer using a laparoscopic electrocautery knife or scissors (Fig. 3A, Fig. 4A). The preserved mucosal layer provides a mechanical barrier between the gastric lumen and peritoneal cavity that aids in the prevention of peritoneal cavity contamination with gastric contents (Fig. 3B).

Tumors are observed with an upper gastrointestinal endoscope with the injection of indocyanine green (ICG) into peri-tumoral submucosal layers. Selective seromuscular dissection is performed using a laparoscopic electrocautery scissors (Fig. 4B).

The mucosa surrounding the GIST is then resected using a mechanical stapler (Fig. 3C, Fig. 4C) to prevent exposure of the gastric lumen to the peritoneal cavity (Fig. 3D, Fig. 4D) and peritoneal tumor cell seeding [3–5].

Kazuhito NABESHIMA, Department of Surgery, Tokai University School of Medicine, 143 Shimokasuya, Isehara, Kanagawa 259-1193, Japan
Tel: +81-463-93-1121 Fax: +81-463-95-6491 E-mail: nabesima@is.icc.u-tokai.ac.jp

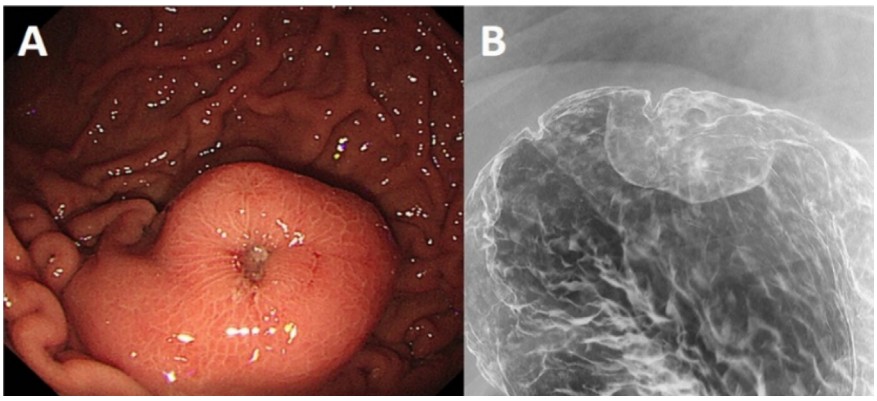

Fig. 1 Case 1. **A.** Endoscopic findings demonstrated an ulcerated SMT. **B.** UGIs revealed a SMT located at the fornix.

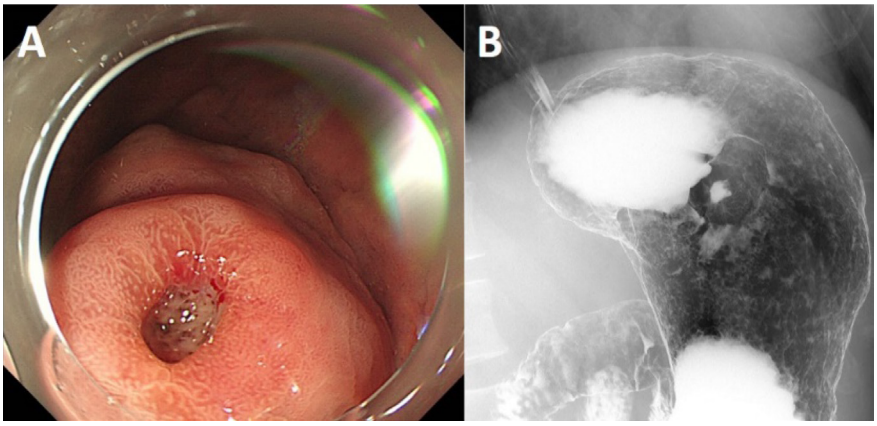

Fig. 2 Case 2. **A.** Endoscopic findings demonstrated an ulcerated SMT. **B.** UGIs revealed a SMT located at the fornix.

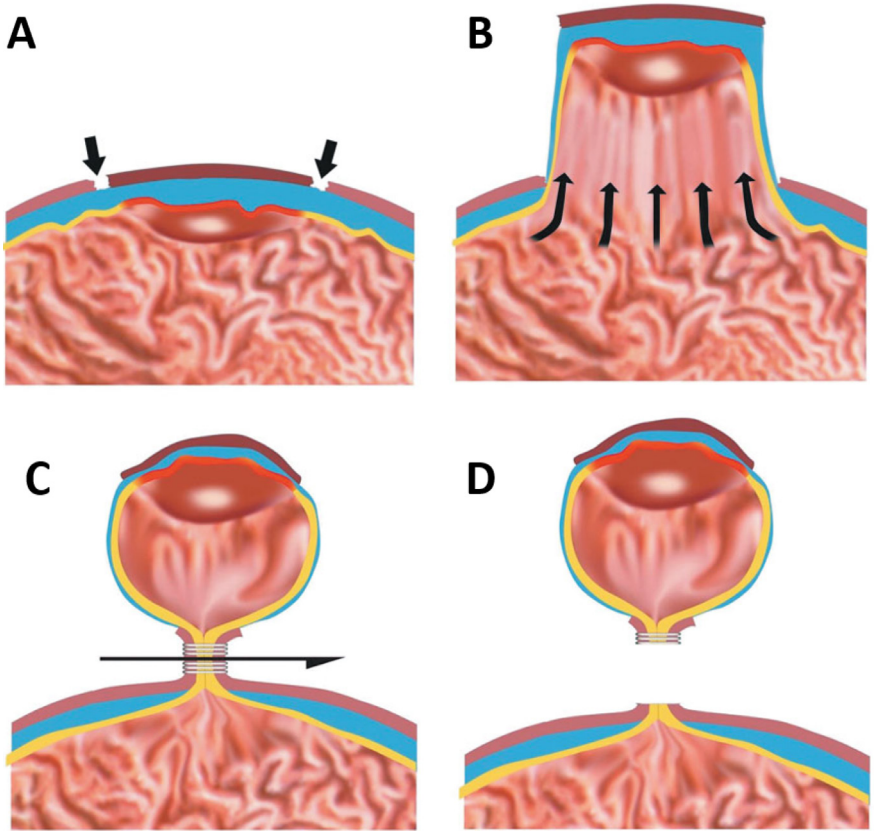

Fig. 3 Schema of the procedure. **A.** Seromuscular layer cutting. **B.** Preserved mucosal layer pulled out toward the outside of the stomach. **C.** Resected mucosal layer using a mechanical stapler. **D.** Mechanical barrier between gastric lumen and peritoneal cavity [4].

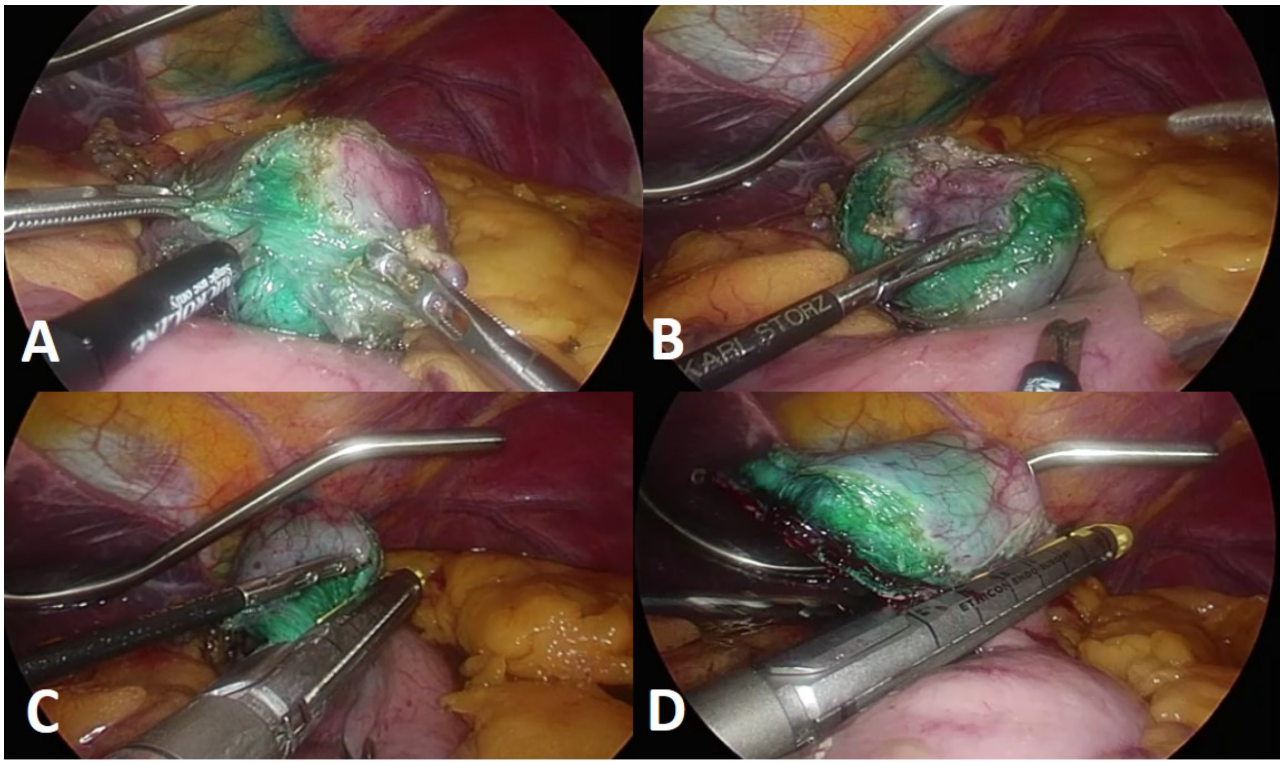

Fig. 4 Procedure of Combination of laparoscopic and endoscopic approaches to neoplasia with non-exposure technique (Case 1). **A.** Seromuscular dissection layer by laparoscopic devices following submucosal injection of ICG with saline. **B.** Entire dissection circumference. **C.** Full-layer resection using a mechanical stapler. **D.** Two staples applied using a laparoscopic liner stapler.

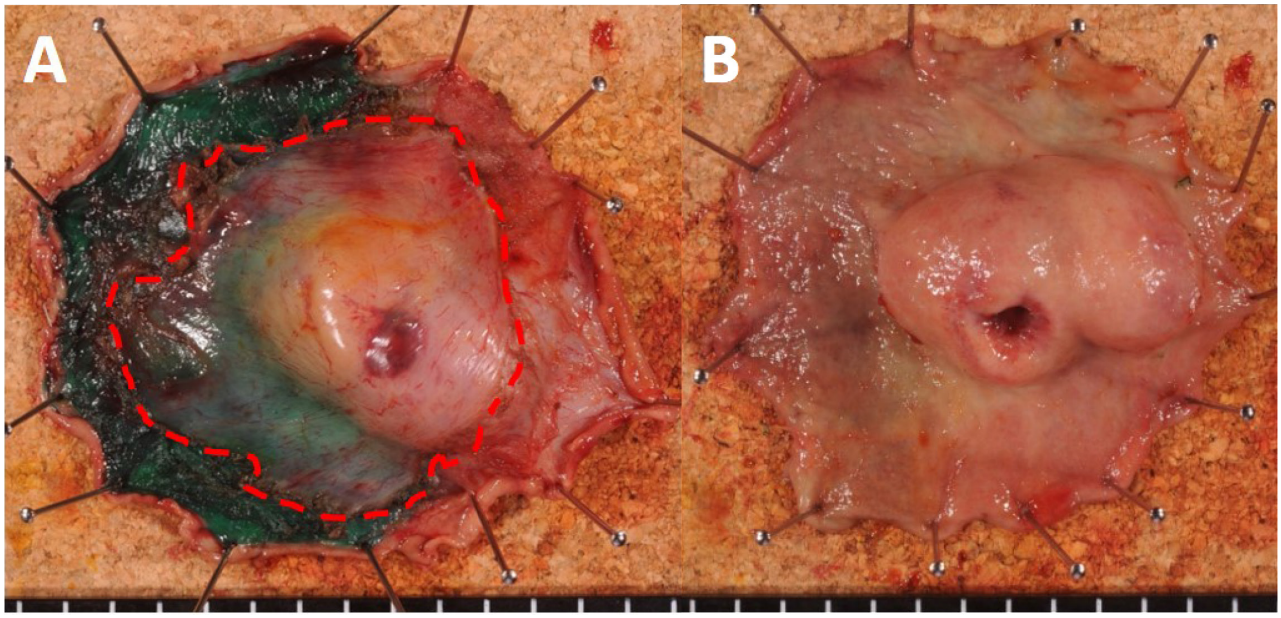

Fig. 5 Case 1. Resected specimens. **A,** Serosal surface of the tumor (red line indicates the serosal surgical margin) and **B,** mucosal side.

RESULT

Case1

The resected specimen was minimal resection of serosal surface (Fig. 5A), the tumor was approximately 3.5 × 2.5 cm in size (Fig. 5B), the operative time was 202 min (including cholecystectomy for gall stones), the estimated intraoperative blood loss volume was 29 ml, and the patient was discharged on postoperative day 8.

Case2

The resected specimen was also minimal serosal surface (Fig. 6A) the tumor was approximately 4.0 × 2.5 cm in size (Fig. 6B), the operative time was 128 min, the estimated intraoperative blood loss volume was 16 ml, and the patient was discharged on postoperative day 9.

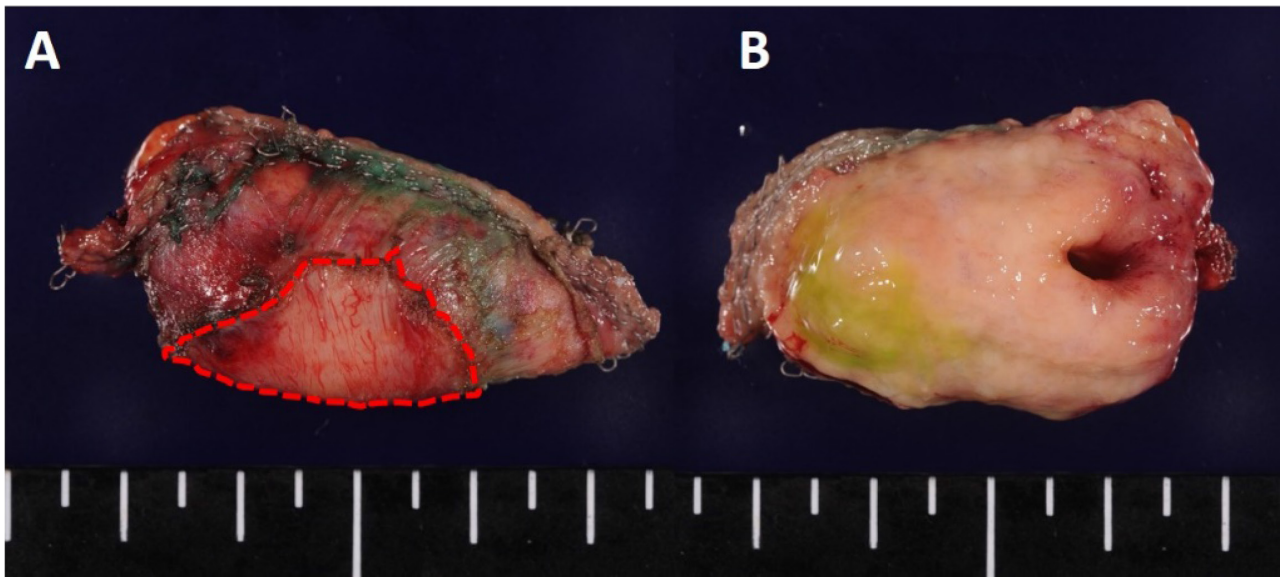

Fig. 6 Case 2. **A,** Serosal surface of the tumor (red line indicates the serosal surgical margin) and **B,** mucosal side.

Pathological findings

The final pathological diagnosis of two cases were low-risk GISTs, based on histopathological identification of spindle-shaped cells, c-kit and CD34 positive on immunohistochemical staining, and 5 mitotic counts or less per 50 high-power field in both cases.

DISCUSSION

Laparoscopic wedge resection of the stomach was developed by Ohgami *et al.* in 1994 as a method of laparoscopic resection of early gastric cancer [6, 7]. The principles have been applied to other gastric tumor types.

According to NCCN guidelines [1], laparoscopic approach may be considered for selected GISTs in favorable anastomotic locations. The same surgical principles of complete macroscopic resection including the prevention of the pseudocapsule and avoidance of tumor rupture should be followed laparoscopy. The Japanese clinical guideline for GIST [8] recommended laparoscopic surgery by an experienced surgeon in cases of GIST less than 5 cm in size. Substantially more of the normal gastric wall is retained with these approaches compared to conventional laparoscopic wedge resection of the stomach for gastric GISTs.

In 2008, Hiki *et al.* described the use of LECS for the treatment of GIST, with the advantage of reduced area of resected gastric wall [2]. However, LECS also carry risks of peritoneal infection because of the necessity of full-thickness gastric layer resection. To avoid gastric perforation, some modified LECS procedures have been developed such as CLEAN-NET [3] and non-exposed endoscopic wall-inversion surgery (NEWS) to allow non-exposure full-thickness gastric wall resection [9, 11]. CLEAN-NET uses a seromuscular incision by laparoscopic electrocautery knife or scissors to preserve the continuity of the mucosa, which works as stretched a barrier of 'CLEAN-NET'. The mucosal tissue is pulled out toward the outside of the stomach and the stretched mucosa is dissected together with minimal area of full-thickness stomach wall. And procedure of NEWS is mucosal marking placed after precise observation of demarcation line under endoscopy, circumferential seromuscular incision with suturing under laparoscopy, and circumferential mucosal incision under endoscopy. The resected specimen collected per orally. Therefore, CLEAN-NET is limited tumor size in 3 cm or less to avoid the mucosal laceration, a limitation of NEWS is also 3 cm or less in tumor size because of large size of resected specimen cannot retrieved per orally [3, 5, 9].

In our two cases, tumor size were more than 3cm, but the operation succeeded because we performed carefully seromuscular dissection.

On the other hand, considering from the oncological point of view, combined laparoscopic and endoscopic surgery has substantial utility in cases of GIST without ulceration; however, GIST with ulceration has a higher potential to disseminate into the peritoneal cavity, following open gastric wall incision. The major limitation of the original LECS procedure, termed "classical LECS," and other combined laparoscopic endoscopic full-layer resection techniques is the potential for gastric content to enter the peritoneal cavity through the open gastric wall incision [5], there is a risk of causing even leading to tumor cell seeding, but also bacterial contamination of the abdominal cavity.

It may be the same as the rupture of GIST to expose GIST with ulceration in peritoneal cavity. GIST with presence of rupture was prognostic factor [12], even if there is difference in a spontaneous rupture and the iatrogenic rupture, the careful operation for the GIST is necessary.

In conclusion, CLEAN-NET was found to be safe and useful for the treatment of gastric GIST with ulceration. This procedure is useful for gastric epithelial tumors and GISTs, especially GISTs with ulceration.

STATEMENT OF CONFLICT

The authors have no conflicts of interest or financial disclosures.

REFERENCES

1) NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Soft tissue sarcoma, http://www.nccn.org/professionals/physician_gls/f_guidelines.asp#sarcoma
2) Hiki N, Yamamoto Y, Fukunaga T, Yamaguchi T, Nunobe S, Tokunaga M, Miki A, Ohyama S, Seto Y. Laparoscopic and endoscopic cooperative surgery for gastrointestinal stromal tumor dissection, Surg Endosc 2008; 22: 1729–35.
3) Inoue H, Ikeda H, Hosoya T, Yoshida A, Onimaru M, Suzuki M, Kudo SE. Endoscopical Mucosal Resection, Endoscopic Submucosal Dissection, and Beyond: Full-Layer Resction for Gastric Cancer with Nonexposure Technique (CLEAN-NET), Surg Oncol Clin N Am 2012; 21, 129–140.
4) Shiwaku H, Inoue H, Satodate H, Odaka N, Ito H, Kudo S. Clinical experience of full thickness resection of early gastric cancer with severe scar: CLEAN-NET (Combination of Lparoscopic and Endoscopic Approaches to Neoplasia with Non Exposure Technique), J. Jpn. Soc. Endosc. Surg. 2011; 11: 291–298.
5) Hiki N, Nunobe S, Matsuda T, Hirasawa T, Yamamoto Y, Yamaguchi T. Laparoscopic endoscopic cooperative surgery. Dig Endosc. 2015; 27: 197–204.
6) Ohgami M. · Kumai K. · Otani Y. · Wakabayashi G. · Kubota T. · Kitajima M. Laparoscopic Wedge Resection of the Stomach for Early Gastric Cancer Using a Lesion-Lifting Method, Dig Surg 1994; 11: 64–67.
7) Ohgami M, Otani Y, Kumai K, Kubota T, Kim YI, Kitajima M. Curative laparoscopic surgery for early gastric cancer: Five years experience World J. Surg. 1999; 23; 187–193.
8) The Japanese clinical guideline of GIST, Apr. 2014, (3rd edition). Kanehara & CO., LTD.
9) Goto O, Mitsui T, Fujishiro M, Ikuo Wada, Nobuyuki Shimizu, Yasuyuki Seto, Kazuhiko Koike. New method of endoscopic full-thickness resection: a pilot study of non-exposed endoscopic wall-inversion surgery in an ex vivo porcine model. Gastric Cancer 2011; 14: 183–187.
10) Abe N, Mori T, Takeuchi H, Ueki H, Yanagida O, Masaki T, Sugiyama M, Atomi Y. Successful treatment of early gastric cancer by laparoscopy-assisted endoscopic full-thickness resection with lymphadenectomy. Gastrointest Endosc 2008; 68; 1220–4.
11) Mitsui T, Niimi K, Yamashita H, Goto O, Aikou S, Hatao F, Wada I, Shimizu N, Fujishiro M, Koike K, Seto Y. Non-exposed endoscopic wall-inversion surgery as a novel partial gastrectomy technique. Gastric Cancer. 2014; 17: 594–9.
12) Joensuu. H, Vehtari. A, Rilhimaki. J, Nishida. T, Steigen. S. E, Brabec. O, Plank. L, Nilsson. B, Cirilli. C, Braconi. C, Bordoni. A, Magnusson. M. K, Linke. Z, Sufliarsky. J, Federico. M, Jonasson. J. G, A. Paolo. S. T, Rutkiwski. P, Risk of recurrence of gastrointestinal stromal tumour after surgery: an analysis of pooled population-based cohorts. Lancet Oncology 2012; 13; 265–274.