New method of endoscopic full-thickness resection: a pilot study of non-exposed endoscopic wall-inversion surgery in an ex vivo porcine model

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Abstract The indications for endoscopic full-thickness resection (EFTR) are limited because transmural communication during the entire procedure, causing tumor dissemination into the abdominal space, is inevitable. We invented a new method of EFTR without transmural communication, and explored its feasibility in an ex vivo porcine model. Three explanted porcine stomachs were used. First, markings around a model lesion were made with a flexible endoscope, and 0.9% normal saline with indigocarmine was injected into the submucosa around the markings. Second, a circumferential sero-muscular incision was made from the outside with an electrocautery knife, guided by the color of the submucosal injection and intragastric navigation with the endoscope. Third, the muscle layer was linearly sutured with the lesion inverted into the inside. Finally, a circumferential muco-submucosal incision was made with an electrocautery knife employed with the endoscope. The method was performed for 3 lesions (1 anterior wall, 1 lesser curve, and 1 posterior wall of the gastric body), and all lesions were successfully resected in en-bloc fashion. The mean size of the resected

specimen was 4.5 cm in diameter. Neither perforation nor apparent air leakage was seen during or after the resection. Non-exposed endoscopic wall-inversion surgery (NEWS) is thought to be effective as a minimally invasive, and minimal-size endoluminal surgery for gastric submucosal tumors with or without ulceration, or even node-negative early gastric cancer that is difficult to resect by endoscopic submucosal dissection.

Keywords Endoscopic full-thickness resection · Gastric neoplasm · Endoscopic submucosal dissection

Introduction

Endoscopic full-thickness resection (EFTR) has been invented as a minimally invasive endoluminal surgery for gastrointestinal tumors [1–3]. The important characteristic of EFTR is that the margin of the tumor can be definitely checked from the inside with a flexible endoscope and the full layer of the tract is resected, so the resection size can be made smaller and a lesion that has penetrated into the deeper layer of the wall can be resected. But this method has the potential to cause tumor dissemination into the abdominal space, because perforation of the wall is inevitable in resecting the lesion. If the concept of a “no-touch isolation” technique is applied, it is thought that the endoluminal space where the tumor’s surface is exposed should not lead to the intraabdominal space during the operation [4, 5]. Therefore, the indication for EFTR has been limited mainly to submucosal tumors (SMTs) without ulceration. Laparoscopic and endoscopic cooperative surgery (LECS) has also been invented as one of the minimally invasive surgeries mainly for gastric SMTs [6], and has gradually gained acceptance in Japan. LECS is thought

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to be acceptable because minimal sized local resection is achieved, and a lesion that is technically difficult to resect with a laparoscopic linear stapler can be resected. But this technique also creates a hole in the gastric wall from which the stomach contents may flow into the abdominal space.

In the clinical setting, laparoscopic wedge resection has been performed for gastric SMTs as minimally invasive surgery [7, 8]. This method is technically less challenging than the methods described above and has no possibility of dissemination because there is no access between the inside and outside of the wall. The margin of the tumor, however, cannot be clearly recognized because laparoscopic linear staplers have to be used, and, consequently, the resection size is large.

On the other hand, endoscopic submucosal dissection (ESD), characterized by a circumferential mucosal incision and submucosal dissection, has been established as an alternative method to open surgery for node-negative gastrointestinal epithelial neoplasms [9–13]. The ESD technique has enabled larger lesions or tumors with ulceration to be resected in en-bloc fashion and in an optimal size. But ESD needs very experienced hands and is still one of the most difficult endoluminal surgeries. Thus, for example, a lesion with fibrosis that is firmly attached to the muscular layer, which, theoretically, can be resected, may not actually be resected by ESD.

To avoid the possibility of dissemination and to resect the full layer with an optimal resection size, the concept of EFTR, without communication between the intraabdominal space and the intragastric space during the entire procedure, using an ESD technique is warranted. If such a technique is feasible, the indications for local resection as minimally invasive endoluminal surgery may, consequently, be expanded to tumors exposed on the surface of gastric mucosa. We invented a new method of laparoscopy-assisted EFTR without transmural communication, and explored its feasibility in an ex vivo porcine model.

Methods

Three whole stomachs harvested from freshly slaughtered pigs were used. After thawing with flowing water at room temperature and repeated irrigation with water and 20,000 units of pronase, each stomach was set on a ESD training model.

First, markings around a model lesion were made with the tip of a Flexknife (KD-630L; Olympus, Tokyo, Japan) operated from a flexible endoscope (GIF-XQ230; Olympus) in swift coagulation mode (effect 4, 40 W) used with a VIO300D device (ERBE, Tübingen, Germany), and 0.9% normal saline with indigocarmine was injected into the submucosa around the markings with an injection needle (Fig. 1a). Second, a

Fig. 1 Schemes of non-exposed endoscopic wall-inversion surgery (NEWS). **a** Making markings around the lesion with the tip of an electrocautery knife employed with a flexible endoscope. **b** Sero-muscular incision from the outside of the stomach. **c** Linear suturing of muscular layers after inversion of the lesion. **d** Muco-submucosal incision from the inside of the stomach

Fig. 2 Procedures of non-exposed endoscopic wall-inversion surgery (NEWS). **a** Sero-muscular incision from the outside of the stomach. **b** Linear suturing of muscular layers. **c** Endoscopic view of the inverted lesion. **d** The resected specimen and the defect after full-thickness resection

Table 1 Outcomes of non-exposed endoscopic wall-inversion surgery (NEWS) in an ex vivo porcine model

Case no.	Location	Circumference	Maximal diameter (mm)	Time to endoscopic resection (min)	En-bloc resection	Perforation	Air leakage
1	Middle body	Anterior wall	45	40	Yes	No	No
2	Middle body	Lesser curve	50	90	Yes	No	No
3	Middle body	Posterior wall	40	35	Yes	No	No

circumferential sero-muscular incision was made from the outside with the Flexknife in dry cut mode (effect 4, 60 W), guided by the color of the indigocarmine injected into the submucosa and intragastric navigation with the endoscope (Fig. 1b). Third, the muscle layer was linearly sutured with 3-0 vicryl at approximately 5 mm intervals with the lesion inverted into the inside (Fig. 1c). Finally, a circumferential muco-submucosal incision was performed from the inside with the Flexknife operated from the endoscope (Fig. 1d). After the operation, the stomachs were opened and closely inspected, and the resected specimens were also inspected.

The parameters of en-bloc resection, complete resection (en-bloc resection with all markings), perforation, and air leakage during the operation were investigated, as well as the maximal resection size and procedure time of endoscopic resection. Perforation was defined as creating a hole with the Flexknife during endoscopic resection, and air leakage was defined as emerging air bubbles on the suture line during endoscopic resection.

Results

The method was performed for 3 lesions (1 anterior wall, 1 lesser curve, and 1 posterior wall of the gastric body). All lesions were successfully resected in en-bloc fashion, and also complete resection was achieved for all lesions (Fig. 2; Table 1). Neither perforation nor apparent air leakage was seen during the operation. The maximal sizes of the resected specimens and the procedure times for endoscopic resection were 45 mm and 40 min; 50 mm and 90 min; and 40 mm and 35 min, respectively. In the resected specimens, there was no apparent displacement between the muco-submucosal and sero-muscular layers.

Discussion

In this ex vivo experiment, we demonstrated the feasibility of a new method, called non-exposed endoscopic wall-inversion surgery (NEWS). This method could be also be

feasible clinically if the procedure of linear suturing from the outside was done laparoscopically.

The most important advantage of this method is that, theoretically, no transmural communication is made despite the full-thickness resection. No transmural communication means no dissemination of tumor during the procedure, which also implies that the indications for this technique could be expanded to tumors exposed on the surface of the gastric mucosa. Therefore, this technique, as a minimally invasive, and minimal sized endoluminal surgery, may be feasible not only for gastric SMTs without ulceration, but also for gastric SMTs with ulceration or node-negative early gastric cancer (EGC) that is difficult to resect by ESD. Furthermore, theoretically, this method enables any lesion located in the stomach to be resected with suitable margins. SMT in the gastric fundus, for example, is difficult to treat by laparoscopic local resection because a linear stapler cannot reach a suitable position, as Hiki et al. [6] have mentioned, but the present method would make it possible to treat SMT in the gastric fundus.

There have been some previous studies of EFTR without transmural communication [14–16]. In these techniques, a pseudopolyp is first created by using a grasping or lifting device, and fixed with or without an endoloop, and finally resected with an electrocautery snare or specialized equipment such as a flexible stapling device. The intrinsic drawbacks of these methods are that the resection margins cannot be confirmed in creating a pseudopolyp, and the resection size is limited by the devices used. In contrast, NEWS can determine the resection area firmly and optimally. Therefore, the present method is thought to be more advantageous than these previous methods.

If the NEWS method is indicated for possible node-negative EGC that is technically difficult to resect by ESD and is not suitable for resection by EFTR or LECS because of possible dissemination, this method is thought to be less invasive than laparoscopic resection or open surgery in terms of preservation of the whole stomach. Although adequate skill and experience are needed, time will solve the technical problems. Furthermore, there is another advantage with NEWS, in that less intraoperative bleeding may occur than with conventional ESD. This is because NEWS does not require submucosal dissection, in which intraoperative bleeding would be easily induced. Furthermore, the possibility of postoperative bleeding, which is one of the major complications of ESD and occurs in approximately 5% of gastric ESD cases [17], may be also decreased because the defect of the lesion is linear, which would make closure by clipping easy.

The concept of sero-muscular incision was introduced by Inoue et al. [18], who invented the combination of laparoscopic and endoscopic approaches to neoplasia with a non-exposure technique (CLEAN-NET). With this

method the lesion is finally resected with laparoscopic linear staplers after sero-muscular incision and the resected specimen is extracted via the abdominal wall. Although full-thickness gastric wall resection without perforation could also be possible with CLEAN-NET, the margin of the lesion cannot be confirmed when the lesion is resected with staplers, which may therefore finish with tumor-positive surgical margins or may make the resection area too large. In terms of the ideal resection area, we think that NEWS would be superior to CLEAN-NET, because with our technique a more flexible resection area can be created that is optimal for the target lesion, and this would ensure resection in an en-bloc fashion without any apparent discrepancy between the muco-submucosal layer and the sero-muscular layer.

The limitation of the present study is that it is an ex vivo, small-number pilot study using porcine stomach. Various factors such as the whole procedure time, intra-operative bleeding, and the technical difficulty of the laparoscopic approach remain unclear. Therefore, the feasibility of this method has to be validated in an in vivo animal study.

In conclusion, we have invented a new method of EFTR, called non-exposed endoscopic wall-inversion surgery (NEWS), which enabled full-thickness resection of the gastric wall without transmural communication, and we validated its feasibility in an ex vivo porcine model. The indications for EFTR could be expanded by this method.

Conflict of interest None.

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