Usefulness of transnasal endoscopy where endoscopic submucosal dissection is difficult

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Abstract

Background Early gastric cancer located from the pyloric ring to inside the duodenal bulb (DB) is not easily treated by endoscopic submucosal dissection (ESD). The endoscope needs to be reversed inside the DB to set the resection line at a safe distance from the anal side. Because of the space limitations and limited flexibility of conventional endoscopy (CE), there have been increasing possibilities of complications. Here we report a new ESD technique using a transnasal endoscope (TN-E) that is reversed inside the DB. **Methods** The subjects were 5 patients with early gastric cancer or adenoma, at locations ranging from the pyloric ring to inside the DB, who were all treated by ESD. We compared results in these patients (TN-E group) with results in five patients with similar disease characteristics who were treated by ESD before July 2008, when the TN-E treatment method was introduced (CE group). In the TN-E group, after marking by CE, we switched the endoscope to the TN-E, and performed the reversing procedure inside the DB, and cut the anal side of the lesion in a semicircle. We switched back to CE to dissect the remaining half on the oral side. We compared the average resection time, en-bloc resection rate, and safety margin between the TN-E and CE groups. **Results** Reversing inside the DB and the anal-side procedures proved easy and there were no complications. No

bleeding or perforation occurred. The average resection times and en-bloc resection rates were not different between the two groups. All the resections by the TN-E were more than 5 mm away from the tumor margin, whereas a resection rate with a safety margin of more than 5 mm was 80% by CE. **Conclusions** In conclusion, the TN-E was safe and effective for use inside the DB. ESD using the TN-E contributed to accurate pathological diagnosis, because the size of the resected specimen was sufficient to prevent the burning effect caused by the ESD.

Keywords Endoscopic submucosal dissection · Gastric cancer · Transnasal endoscopy · Duodenal bulb

Introduction

The introduction of a new technique called endoscopic submucosal dissection (ESD) has led to remarkable progress in the endoscopic treatment of early gastric cancer [1–3]. However, performing ESD is difficult in some cases when the location of the lesion poses problems. In particular, lesions extending (a) in the part of the antrum near the pyloric ring, (b) onto the pyloric ring, and (c) from the pyloric ring to the inside of the duodenal bulb pose technical difficulties.

For the en-bloc resection of the tumor with an adequate safety margin, the lines of resection should clear the tumor by 3–5 mm or more in consideration of the burning effect caused by the ESD; this makes an accurate pathological diagnosis feasible. Thus, the endoscope needs to be rotated through 180° in order to maintain an adequate safe distance between the lines of resection on the anal side and the tumor. However, because the duodenal bulb is a hollow organ 25–30 mm in diameter, it is generally not feasible to rotate the endoscope within the organ to accomplish the task.

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Moreover, even if the endoscope can be rotated, operational difficulties are encountered due to the limited range of motion, bleeding from forcible operation of the endoscope, complications such as perforations, and the necessity for piecemeal resection instead of en-bloc resection [4]. In particular, lesions on the posterior wall cannot be viewed in their entirety even if the endoscope is rotated because the shaft of the endoscope obstructs the view. In order to cope with these problems we used a transnasal endoscope (TN-E) EG-530N2 (Fujifilm, Tokyo, Japan) whose width when the shaft was bent at the most acute angle was smaller than that of the XQ-240 endoscope (Olympus, Tokyo Japan), which has been considered to have the smallest width. The XQ-240 has an outer diameter smaller than that of the H-260Z endoscope

(Olympus), which is usually used in ESD (Fig. 1a–c). The EG-530N2 TN-E has a non-metal tip and, therefore, is the only commercially available endoscope that can be used with high-frequency electrosurgery devices in ESD. This report examines cases in which we used this TN-E to treat lesions where ESD was difficult.

Methods

Patients

ESDs were conducted from August to December 2008, using the TN-E in five patients with early gastric cancer or

Fig. 1 **a** Image showing side views comparing the sizes of the H-260Z endoscope, which has water delivery capability; the XQ-240 endoscope, which has the smallest width when the shaft is bent at the most acute angle; and the EG-530N2 transnasal endoscope. **b** Image showing side views comparing the widths when the shaft is bent at the most acute angle with respect to the H-260Z endoscope, which has water delivery capability; the XQ-240 endoscope, which has the

smallest width when the shaft is bent at the most acute angle; and the EG-530N2 transnasal endoscope. **c** Image showing front views comparing the sizes of the H-260Z endoscope, which has water delivery capability; the XQ-240 endoscope, which has the smallest width when the shaft is bent at the most acute angle; and the EG-530N2 transnasal endoscope. *FTS* fujinon toshiba system

Table 1 List of 5 patients with early gastric cancer or adenoma that developed from the vicinity of the pyloric ring to the duodenal bulb, in whom ESD treatments were conducted using a transnasal endoscope

No.	Sex	Age (years)	Part	Shape	Size (mm)	Resection size (mm)	Histologic diagnosis	Operation time (min)
1	M	73	P-ring (PW)—Duodenal Bulb	Protruded	10 × 12	30 × 20	High-grade dysplasia, m	81
2	M	60	Antrum (LC)—P-ring	Superficial depressed scar	20 × 8	50 × 40	Well-differentiated adenocarcinoma, m	79
3	M	67	Antrum (AW)—P-ring	Superficial depressed scar	20 × 15	50 × 40	Well-differentiated adenocarcinoma, m	74
4	M	71	P-ring (PW)—Duodenal Bulb	Protruded	15 × 8	36 × 36	Well-differentiated adenocarcinoma, m	62
5	M	71	Antrum (GC)—P-ring	Superficial elevated	27 × 17	45 × 40	Well-differentiated adenocarcinoma, m	88

P-ring pyloric ring, *AW* anterior wall, *PW* posterior wall, *LC* lesser curvature, *GC* greater curvature, *m* mucosal invasion

Table 2 List of 5 patients with early gastric cancer or adenoma that developed from the vicinity of the pyloric ring to the duodenal bulb, in whom ESD treatments were conducted using a conventional endoscope

No.	Sex	Age (years)	Part	Shape	Size (mm)	Resection size (mm)	Histologic diagnosis	Operation time (min)
1	M	77	Antrum (AW)—P-ring	Superficial depressed	17 × 12	45 × 35	Moderately differentiated adenocarcinoma, m	72
2	M	54	Antrum (AW)—P-ring	Superficial elevated	10 × 8	35 × 32	High-grade dysplasia, m	79
3	M	74	Antrum (LC)—P-ring	Superficial depressed	18 × 18	40 × 40	Well-differentiated adenocarcinoma, m	73
4	M	57	P-ring (PW)—P-ring	Superficial depressed	18 × 16	40 × 40	Well-differentiated adenocarcinoma, m	91
5	M	63	P-ring (LC)	Superficial elevated	10 × 8	35 × 35	Well-differentiated adenocarcinoma, m	61

Fig. 2 **a** Image showing a lesion extending from the pyloric ring to the inside of the duodenal bulb, as viewed from the oral side. *Arrowheads* indicate boundaries of the tumor, and *black arrows* indicate scars that were created in biopsy to confirm the safety margin

and serve as reference for dissection. **b** Image showing the marking procedure on the scars created in the biopsy to confirm the safety margin. **c** Image showing markings on the oral side

adenoma that developed from the antrum of the pyloric ring to the duodenal bulb (Table 1). These patients were compared with patients whose lesions were smaller than 30 mm, in the same locations as those described above who were treated by ESD before July 2008 when the above-mentioned treatment method was introduced (Table 2).

Pretreatment evaluation

Biopsies were conducted one week before ESD treatment for the preoperative assessment of safety margins. The extent of the tumors was diagnosed by magnifying endoscopy using narrow band imaging (NBI), as well as by

visually identifying the extent using 0.2% indigo carmine solution [5, 6]. Samples were collected from four sites around the tumor site about 3 mm away from the tumor to confirm the absence of atypical cells at these sites. Based on the overall results of the above assessments, lesions falling within the criteria (including the expanded criteria [7]) for the indications of ESD were identified.

Premedication

Premedication consisted of 25 mg pentazocine, 5 mg diazepam, and 35 mg pethidine hydrochloride injected intravenously. In elderly patients or patients with underlying diseases, the dose of diazepam was reduced to 2.5 mg. Because propofol must be administered by an anesthesiologist in Japan, we avoided using this agent and used the above-mentioned combination of sedatives and analgesics as premedication [8].

ESD technique with the TN-E

A high-frequency electrosurgery device, the ICC200 (ERBE, Elektromedizin, Tübingen, Germany), was used in the following setting: argon plasma coagulation (APC) at 40 W [9] or coagulation at 30 W for marking, endo cut effect 3 at 80 W for dissection, and endo cut effect 3 at 80 W or coagulation at 50 W for abrasion.

The solution to be used for local injection was prepared by mixing 2 g of glycerin (20 ml), 80 mg of 0.4% sodium hyaluronate (20 ml), and 2 ml of indigo carmine solution [10].

At the beginning of the ESD treatment, the usual observations were made using the H-260Z. The oral side

was marked about 3 mm away from the tumor (Fig. 2a–c) with reference to the four biopsy scars, using our self-made pre-cutting knife, which is 2 mm in length (Fig. 3; this custom-made knife can be inserted into a biopsy channel of 2 mm). The viewing monitor was then switched from that of the Olympus scope to that of the Fujifilm scope, and subsequently the EG-530N2 TN-E fitted with an end hood of our own manufacture (Fig. 4) was used for the operation. The TN-E is about 6 mm in diameter, and an end hood adjusted to the dimension must be manufactured in order to maintain an adequate distance from the mucosal membrane and to ensure safe dissection and abrasion [11]. Then, through a special mouthpiece for use with the TN-E (Endo Leader; Top, Tokyo, Japan) (Fig. 5), the TN-E was inserted transorally and rotated 180° in the duodenal bulb. After the rotation, the anal side was marked using our self-

Fig. 4 Image of the attachment hood of our own manufacture. Top, Japan

Fig. 3 Image showing side views of our self-made pre-cutting knives (2.0 and 2.5 mm in length) and a needle knife

Fig. 5 Image of the mouthpiece for the transnasal endoscope

Fig. 6 **a** Image showing the marking procedure on the anal side using our self-made pre-cutting knife (2 mm in length). **b** Image showing a local injection procedure in the locations around the markings to elevate the mucosal membrane. **c** Image of the pre-cutting procedure on the anal side of a lesion using our self-made pre-cutting knife (2.5 mm in length). **d** Image of dissection of a lesion halfway around on the anal side. **e** Image of abrasion of a lesion from the anal side using our self-made pre-cutting knife (2.5 mm in length). **f** Image of a lesion spontaneously shifting toward the oral side due to tension

toward the gastric antrum. **g** Image of a lesion completely shifted into the gastric antrum. **h–j** Images showing the remaining dissection halfway around the lesion on the oral side made using the IT knife 2 in combination with the usual H-260Z endoscope, thereby completing the dissection of the whole circumference. **k** Image of complete abrasion using the IT knife 2. **l** Image of the abrasion area after dissection as viewed from the oral side. **m** Image of the abrasion area after dissection as viewed from the anal side. **n** Image of a resected sample

made pre-cutting knife (2 mm in length; Fig. 6a). The solution prepared as stated above was then locally injected around the marking dots to elevate the mucosal membrane (Fig. 6b), and after the pre-cutting of the lesions on the anal side using our self-made pre-cutting knife (2.5 mm in length; Fig. 6c), dissection was made halfway around the lesion while maintaining the depth of the dissection at the appropriate level (Fig. 6d). Then, another submucosal local injection was performed, and abrasion was conducted from the anal side using our self-made pre-cutting knife (2.5 mm in length; Fig. 6e). This procedure created tension toward the gastric antrum, and the lesion spontaneously shifted to the oral side (Fig. 6f). When the lesion had shifted completely into the gastric antrum (Fig. 6g), the viewing monitor was switched again to that of the Olympus scope, and the remaining dissection around the lesion on the oral side was performed using an IT knife 2 (Olympus) with the usual H-260Z endoscope, thereby completing the dissection of the whole circumference (Fig. 6h–j). After the dissection, local injection was performed again to elevate the tumor. Finally, abrasion of the whole tumor was performed to resect the tumor (Fig. 6k–n). Written informed consent was obtained from all patients who received this procedure.

Surgical time and resection rate

The time required for the resection and the rate of en-bloc resection in patients treated with the above-described method were compared with those of patients with tumors smaller than 30 mm in problematic locations who were treated before July 2008.

Statistical analysis

Statistical analyses were performed by the Mann–Whitney *U*-test. A probability value of less than 0.05 was considered to indicate statistical significance.

Results

Rotation in the duodenal bulb was sufficiently easy so as to facilitate the treatment of the anal side with an ample safety margin. Traction of the lesion onto the antrum was also easily performed without creating excessive tension. The average time for resection in patients treated before the introduction of the TN-E was 75.2 min and that in patients treated after the introduction of the TN-E was 76.8 min. No significant differences in resection time were found between the patient groups. The en-bloc resection rate in patients treated before the introduction of the TN-E was 80% and the rate in patients treated after its introduction

was 100% (4/5 vs. 5/5, respectively). All the resections by the TN-E were more than 5 mm away from the tumor margin, whereas a resection rate with a safety margin of more than 5 mm by conventional endoscopy was 80%.

Discussion

In the treatment of early gastric cancer in locations where ESD is difficult, the TN-E is considered to be a safe and extremely useful method of resection with an ample safety margin. Remarkably, even in cases in which the duodenal bulb is deformed or narrowed due to ulcer scars and rotation within the duodenal bulb is not feasible, a TN-E can be inserted into the second portion of the duodenum, rotated safely in that location, and then pulled up into the duodenal bulb for ESD in the narrow lumen. The small diameter of the scope provides a large motion space, which enables easy dissection on the pyloric ring with either a downward or an upward view. These features ensure the performance of an en-bloc resection, and the possibility of perforation and bleeding during rotation is considered to be extremely low. However, there are various points that can be improved. For instance, only a small number of attachment devices are available for the TN-E, because the biopsy channel of the TN-E is smaller than the typical biopsy channels. So physicians must manufacture their own devices appropriate for the size of such a channel. Moreover, the image resolution of the TN-E is inherently low. The lack of significant differences in mean resection time between the two patient groups in our study was due to the time consumption in the TN-E group for changing devices, such as switching monitors, changing endoscopes, and changing mouthpieces. This point may be addressed in the future. Future improvements will open the possibilities for ESD using a TN-E.

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