A new breakthrough: ESD using a newly developed grasping type scissor forceps for early gastrointestinal tract neoplasms

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Key words: Endoscopic submucosal dissection; Novel device; Grasping type scissor forceps; Early gastrointestinal tract neoplasms; Endoscopic therapy

INTRODUCTION

The Endoscopic submucosal dissection (ESD) technique introduced by Hirao et al[1] has subsequently been modified by several investigators, allowing curative en bloc resection of broad superficial tumors with the use of special cutting knives. It has been reported that ESD improves the rate of successful en bloc resection in early stage gastrointestinal neoplasm as compared with endoscopic mucosal resection (EMR)[2,3]. However, ESD using knives is technically difficult and carries a high risk of perforation and bleeding. Complication rates with knives for the dissection of gastric tumor are reported to be 0% to 70%[4-8]. Incision using knife devices merely provides contact between the knife and the tissue and cuts using an electrosurgical current. These cutting processes do not fix the device to the targeted tissue, making it difficult to accurately place the knife during electrosurgical incision because of bodily motions such as cardiac or respiratory movement[9]. Lack of fixation and compression effects can cause unexpected incision and insufficient coagulation and result in major complications. Therefore, it is desirable to develop a new device to reduce such complications. We developed the grasping type scissor forceps (GSF) to resolve such ESD-related problems. Our animal and preliminary clinical studies showed that ESD using GSF is safe (no intraoperative complication) and technically efficient (curative en bloc resection rate 92%) method for dissection of early gastrointestinal tumors. The use of GSF is a promising option for performing ESD on early stage GI tract tumors both safely and effectively.
complications such as perforation and bleeding. We believe that the most effective and simplest way of avoiding such complications is to grasp and incise the targeted tissue using an electrosurgical current. We have therefore developed a new grasping type scissors forceps (GSF) which can grasp and incise the targeted tissue using an electrosurgical current. In this article we describe the concepts of development, clinical outcomes in ESD and future potential of this new device.

CLINICAL OUTCOMES OF ESD USING CONVENTIONAL KNIFE DEVICES

Recent results of en bloc resection rate of ESD for neoplasms in the esophagus, stomach and colorectum are 95%-100%, 76%-96% and 77%-98.6% respectively. On the other hand, reported bleeding and perforation rate of ESD for neoplasms in the esophagus, stomach and colorectum are 0% and 6.9%, 0%-40% and 0%-50%, and 0%-12% and 1.4%-10% respectively. Current ESD using knife devices shows high tumor eradication rates but substantial risks during the procedure.

THEORETICAL PROBLEMS OF ESD USING CONVENTIONAL KNIFE DEVICES

At present, numerous electrosurgical knives such as the diathermic needle knife, insulation-tipped electrosurgical knife (IT), hook knife, flex knife, triangle-tipped knife, flush knife, fork knife, and mucosectome are available for ESD (Figure 1). During ESD using conventional knife devices, problems may be encountered i.e. unintentional incision due to bodily motions, perforation due to thin gut wall and bleeding. Our proposed measures for each problem are shown in Table 1. We consider that the shortcomings of current knives are deficiency of fixing and lift up, compression to the targeted tissue and outside insulation. Therefore we developed a grasping type scissors forceps (Figures 1 and 2) to overcome the shortcomings of conventional knife devices.

NEWLY DEVELOPED GRASPING TYPE SCISSOR FORCEPS

The grasping type scissors forceps (GSF) (XDP2618DT, Fujifilm Corporation, Saitama, Japan) can grasp and cut a piece of tissue with an electrosurgical current. It has a 0.4 mm wide and 4 mm or 6 mm long serrated cutting edge to facilitate grasping the tissue. The outer side of the forceps is insulated so that electrosurgical current energy is concentrated at the blade to avoid burning the surrounding tissue. Furthermore, the forceps can be rotated to the desired orientation. The diameter of the forceps is 2.7 mm. The GSF is available for a standard endoscope with working channel width of 2.8 mm or over. This device is disposable and not reusable and is used for circumferential marginal incision, submucosal dissection and hemostatic treatment. The autocut mode (ICC 200; Erbe, Tübingen, Germany) 120W (effect 3) is used for cutting (circumferential incision and submucosal excision) and the soft coagulation mode 70W (effect 3) is used for hemostatic coagulation.

In our previous animal study (porcine stomach), we resected three specimens safely and easily with no unintentional incision by ESD using the GSF. The histological analysis of the ulcers due to the procedure showed shallow submucosal ulcers without perforation and excessive burning. All clinical studies described in this article were reviewed and approved by the ethics committee of Aso Iizuka Hospital.

TECHNIQUES OF ESD USING GSF

ESD technique using GSF is as follows (Figure 3). Circumferential markings are made by using a hook knife (KD-620LR, Olympus) with coagulation current 20-40W created by an electrosurgical generator (ICC 200; Erbe, Tübingen, Germany) (Figure 4A). Next, 10% glycerin with 0.9% NaCl and 5% fructose (Glycol; Chugai Pharmaceutical Co., Tokyo, Japan) or hyaluronic acid solution (MucoUp; Johnson and Johnson Co., Tokyo, Japan) is injected into the submucosal layer to lift up the lesion. The lesion is separated from the surrounding normal mucosa following complete incision around the lesion using the GSF (Figure 4B and C). A piece of submucosal tissue is grasped, lifted up and cut with the GSF using electrosurgical current to achieve submucosal excision (Figure 4D). Finally, the lesion is completely resected (en bloc resection) by GSF (Figure 4E and F). Treatment of bleeding during the procedure is done by coagulation with the GSF (Soft coagulation mode 70W, effect 3). Prophylactic coagulation of visible vessels is carried out using GSF (Soft coagulation mode 70W, effect 3).

CLINICAL OUTCOMES OF ESD USING GSF IN OUR PRELIMINARY STUDIES

Clinicopathological characteristics of the lesions treated by ESD using GSF are summarized in Table

| Problems                  | Proposed measures                                      |
|---------------------------|--------------------------------------------------------|
| Unintentional incision    | Device fixation to the targeted tissue                 |
| Perforation               | Outside insulation                                     |
| Bleeding                  | Lift up the targeted tissue by device                  |
|                           | Good visualization of the targeted area                |
|                           | Compression of the blood vessel by device              |

ESD: Endoscopic submucosal dissection.
Akahoshi K et al. ESD using grasping type scissor forceps

2. All lesions were treated simply and safely with no unexpected incision by a beginner endoscopist in ESD. The grasping and lift up steps before cutting the targeted tissue provided good visualization of the interest and allowed the use of sufficient pre-cut coagulation. The technical outcome\cite{17,18} is summarized in Table 3. The mean size of the epithelial tumors and resected specimens was 16.6 ± 9.0 mm and 33.0 ± 10.5 mm respectively. The curative en bloc resection rates according to tumor location were 100% (3/3) in the esophagus, 97% (34/35) in the stomach\cite{17}, 80% (8/10) in the colon and rectum\cite{18} and 92% (45/49) overall. All lesions were resected in en bloc fashion endoscopically. Four cases (8%) were judged as histologically positive margin of the tumor cells due to burning effect. The mean operating time according to tumor location was 74.7 ± 26.3 min in the esophagus, 104.1 ± 54.4 min in the stomach\cite{17}, 154.9 ± 83.6 min in the colon and rectum\cite{18} and 114.0 ± 63.4 min overall.

No intra-operative severe complications (perforation or uncontrollable bleeding) occurred and post-operative bleeding was seen in 2% (1 of 49) of cases.

**THEORETICAL ADVANTAGES OF GSF AS COMPARED TO CONVENTIONAL KNIFE DEVICES**

**Safety**

GSF can grasp the targeted tissue. The grasping step has three safe effects: (1) fixation, (2) lift-up effect and (3) compression effect (Table 4, Figure 5). (1) The grasping step prior to electrosurgical incision provides fixation of the device to the targeted tissue to avoid unintentional incision\cite{13-18}. GSF has a thin serrated cutting edge and an insulated coating of the outer side of the forceps. These characteristics facilitate grasping the targeted tissue and concentrate electrosurgical current energy.
Akahoshi K et al. ESD using grasping type scissor forceps

reduce the chance of unintentional incisions, bleeding and other severe complications.

**Simplicity**

Each step of ESD (circumferential incision, submucosal excision, hemostatic treatment) can be achieved by the following three operations: (1) grasping the targeted tissue (fixation), (2) lifting up the grasped tissue (separation from the underlying proper muscle layer to prevent perforation) and (3) cutting the grasped tissue (or coagulating the blood vessel) using an electrosurgical current. These operations are simple and as easy as a bite biopsy technique.

**Facility for training of ESD**

ESD using GSF is safe and simple. In our preliminary studies, all cases were safely and effectively resected using this method by a beginner endoscopist in ESD. Furthermore, in the grasping confirmation step we could sufficiently discuss the adequacy of the grasped tissue with the attending endoscopist prior to incision using electrosurgical current. This precut confirmation step is the greatest advantage of our method and is useful for safety and for training in ESD.

**CURRENT DISADVANTAGES OF ESD USING GSF**

The procedure time of ESD using GSF was longer than the reported times using knife devices. The main reasons were (1) these clinical trials were performed by a beginner in ESD (The endoscopist was the inventor of GSF with prior experience of only seven cases of conventional ESD) and (2) the frequent difficulties in rotating the GSF to the desired orientation during ESD.

| Table 2 Clinicopathological characteristics (n = 49) |
|-----------------------------------------------|
| Gender, male/female | 32/17 |
| Mean age years (range) | 69 (31-87) |
| Location, n |  |
| Esophagus | 3 |
| Middle | 1 |
| Lower | 2 |
| Stomach | 35 |
| Upper | 9 |
| Middle | 8 |
| Lower | 18 |
| Duodenum |  |
| Bulbus | 1 |
| Colorectum | 10 |
| Cecum | 2 |
| Ascending | 1 |
| Transverse | 2 |
| Descending | 2 |
| Rectum | 3 |
| Histologic type and depth of invasion, n |  |
| Carcinoma | 27 |
| Mucoza | 24 |
| Superficial submucosa | 2 |
| Deep submucosa | 1 |
| Adenoma |  |
| Mucosa | 20 |
| Carcinoid tumor |  |
| Deep submucosa | 1 |
| Granular cell tumor |  |
| Deep submucosa | 1 |

| Table 3 Technical results of ESD using GSF (n = 49) |
|-----------------------------------------------|
| Curative en-bloc resection rate, Total | 92% (45/49) |
| Esophagus | 100% (3/3) |
| Stomach | 97% (34/35) |
| Duodenum | 100% (1/1) |
| Colon and rectum | 80% (8/10) |
| Mean ± SD operating time, minutes (Range), Total | 114.0 ± 63.4 (33-337) |
| Esophagus | 74.7 ± 26.3 (59-105) |
| Stomach | 104.1 ± 54.4 (33-264) |
| Duodenum | 172 |
| Colon and rectum | 154.9 ± 83.6 (70-337) |
| Mean ± SD size of tumor size, mm (Range) | 16.6 ± 9.0 (5-43) |
| Mean ± SD size of resected specimen, mm (Range) | 35.0 ± 10.5 (15-60) |
| Intra-operative perforation rate | 0/49 (0%) |
| Intra-operative major bleeding rate | 0/49 (0%) |
| Postoperative bleeding rate | 1/49 (2%) |
| Postoperative perforation rate | 0/49 (0%) |

| Table 4 Theoretical advantages of GSF during ESD |
|-----------------------------------------------|
| Advantageous mechanism | Expected physical effects | Technical outcome |
| Grasp | Fix | (1) No unintentional incision |
| Lift-up | (2) Good visualization |
| (3) Sufficient separation from the underlying proper muscle layer to prevent perforation |
| Compress | (4) Hemostatic effect to prevent and treat bleeding |
| Outside insulation | Closed discharge | (5) Minimizing damage to the surrounding tissue to prevent perforation |
| Rotatable | Change the direction of grasping | (6) Facilitating accurate targeting |

GSF: Grasping type scissor forceps.
Akahoshi K et al. ESD using grasping type scissor forceps

Figure 3  Schematic shows ESD using GSF. Step 1: Marking dots are made on the circumference of the lesion to outline the incision line; Step 2: A concentrated glycerin solution mixed with a small volume of epinephrine and indigo carmine dye is injected into the submucosal layer around the target lesion to lift the entire lesion; Step 3: The lesion is separated from the surrounding normal mucosa by complete incision around the lesion using the GSF; Step 4: A piece of submucosal tissue is grasped by GSF; Step 5: A grasped tissue is lifted up and cut with the GSF using electrosurgical current to effect submucosal exfoliation; Step 6: The lesion is resected in one piece; m: Mucosa; sm: Submucosa; mp: Muscularis propria.

Figure 4  Endoscopic view of the procedure of ESD using GSF. A: Marks are made at several points along the outline of the lesion with a coagulation current; B: The mucosa is incised outside the marker dots to separate the lesion from the surrounding non-neoplastic mucosa using GSF; C: Completion of the GSF cutting around the lesion with a safe lateral margin; D: The submucosal connective tissue beneath the lesion is grasped and lifted up and excised using GSF from the underlying muscle layer; E: The lesion is cut completely from the muscle layer; F: The resected specimen showing en bloc resection of the lesion.
a retroflex approach. A significant learning curve is associated with achieving proficiency in ESD[31]. Probst et al[32] showed a learning curve resulting in a decreasing procedural duration and an increasing rate of complete en bloc resection over time. Procedure time will be shortened in the near future by the learning curve in ESD using GSF and a solution to the problem of rotating the GSF by further mechanical refinement.

**FUTURE POTENTIAL**

From recent studies, ESD shows a higher tumor eradication rate than conventional EMR irrespective of tumor size[4,12,21,26]. However, ESD using conventional knife devices requires highly skilled endoscopists and a sufficient training program is required for permeation of this technique[31,32]. At present because of this requirement, the merits of ESD can be obtained in only a few advanced institutions in Japan and several other Asian countries[4,12,21,26]. Because of its safety and simplicity, we believe that ESD using GSF will become widely accepted for use throughout the world[4,33-37]. We hope to expand the application of this procedure to decrease the complications associated with ESD. However, further refinements and experiences of this method are needed in order to more easily achieve the curative en bloc resection of early GI tract tumor. Furthermore, extensive controlled, randomized studies in controlling ESD-related complications e.g., vs IT knife, vs needle knife or vs other conventional devices are necessary to fully evaluate the usefulness of our new device.

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