

# Usefulness of an ultrathin endoscope in esophageal endoscopic submucosal dissection

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Daisuke Kikuchi<sup>1</sup>, Yugo Suzuki<sup>1</sup>, Yusuke Kawai<sup>1</sup>, Kosuke Nomura<sup>1</sup>, Yorinari Ochiai<sup>1</sup>, Junnosuke Hayasaka<sup>1</sup>, Yutaka Mitsunaga<sup>1</sup>, Takayuki Okamura<sup>1</sup>, Hiroyuki Odagiri<sup>1</sup>, Satoshi Yamashita<sup>1</sup>, Akira Matsui<sup>1</sup>, Masami Tanaka<sup>1</sup>, Shu Hoteya<sup>1</sup>

## Institutions

1 Gastroenterology, Toranomon Hospital, minato-ku, Japan

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## Corresponding author

Dr. Daisuke Kikuchi, Toranomon Hospital, Gastroenterology, minato-ku, Japan  
dkiku1230@gmail.com

## ABSTRACT

**Background and study aims** Endoscopic submucosal dissection (ESD) is sometimes challenging because of stenosis and scarring. We examined the use of an ultrathin endoscope for esophageal ESD, which is difficult using conventional endoscopes.

**Patients and methods** A designated transparent hood and ESD knife for ultrathin endoscopes have been developed and clinically introduced. Esophageal ESD was performed on 303 lesions in 220 patients in our hospital from February 2021 to February 2023. Of them, an ultrathin endoscope was used on 26 lesions in 23 cases. The safety and utility of an ultrathin endoscope in esophageal ESD were retrospectively verified.

**Results** All 26 lesions were resected en bloc, and serious complications such as perforation, massive bleeding, or pneumonia, were not observed. Lesions were found on the anal side of the stenosis and over the scarring in 38.6% (10/26) and 50% (13/26) of participants, respectively. Moreover, 46.2% of participants (12/26) had lesions on the cervical esophagus. The total procedure time was 64.1 ± 37.7 minutes, but the average time from oral incision to pocket creation was 121.2 ± 109.9 seconds.

**Conclusions** Ultrathin endoscopes may be useful for difficult esophageal ESD.

## Introduction

Endoscopic treatment is widely used for superficial esophageal cancer. Endoscopic treatment progressed from endoscopic mucosal resection to endoscopic submucosal dissection (ESD), drastically improving the en bloc resection rate [1, 2]. Intramucosal carcinoma, which has a low risk of lymph node metastasis, can be cured via endoscopic resection of the lesion, enabling treatment while maintaining the patient's quality of life. Stenosis, scarring, or lesions in the cervical esophagus are the major difficulties in esophageal ESD, among various difficulties that have been reported [3, 4, 5].

Owing to their minimal invasiveness, ultrathin endoscopes are primarily used for upper gastrointestinal endoscopy [6].

The image resolution is improved, and the lesion detection rate is comparable to conventional endoscopy [7]. Nevertheless, ultrathin endoscopes have not been used in therapeutic endoscopy because dedicated treatment devices are unavailable [8, 9]. However, ultrathin endoscopes have an advantage in therapeutic endoscopy as they can access narrow areas. This device is particularly advantageous in esophageal ESD, where a narrow visual field is associated with treatment difficulty due to stenosis or scarring. We collaborated with companies to develop two ultrathin endoscope devices to enable ESD and used them in clinical practice [10, 11]. This study retrospectively investigated the usefulness of ultrathin endoscopes in esophageal ESD.

## Patients and methods

We performed esophageal ESD on 220 patients with 303 lesions in Toranomon Hospital from February 2021 to February 2023. In these cases, ESD with a conventional endoscope was difficult. Ultrathin endoscopes were used for ESD in 26 lesions in 23 patients. An ultrathin endoscope was used when a conventional endoscope could not visualize the lesion or the site of dissection. Therefore, an ultrathin endoscope was used because starting with a conventional endoscope approach was impossible due to stenosis or curvature of the cervical esophagus.

When an adequate approach to the dissection area is impossible because of a condition such as scarring, treatment is usually performed with a conventional endoscope followed by an ultrathin endoscope. This study retrospectively investigated the safety and efficacy of ultrathin endoscopes in esophageal ESD. The Ethics Committee of Toranomon Hospital approved this study.

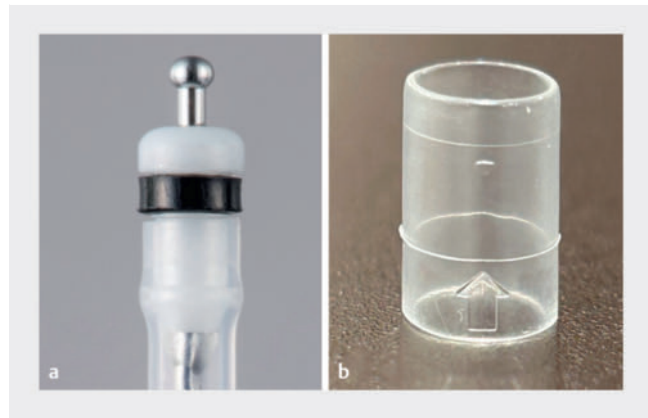
### Device

A transparent hood (Nichendo) for ultrathin endoscopes was jointly developed with Yasui Co., Ltd. (Miyazaki, Japan), and an ESD knife (Endosaber Fine) for ultrathin endoscopes was jointly developed with Yamashina Seiki Co., Ltd. (Shiga, Japan).

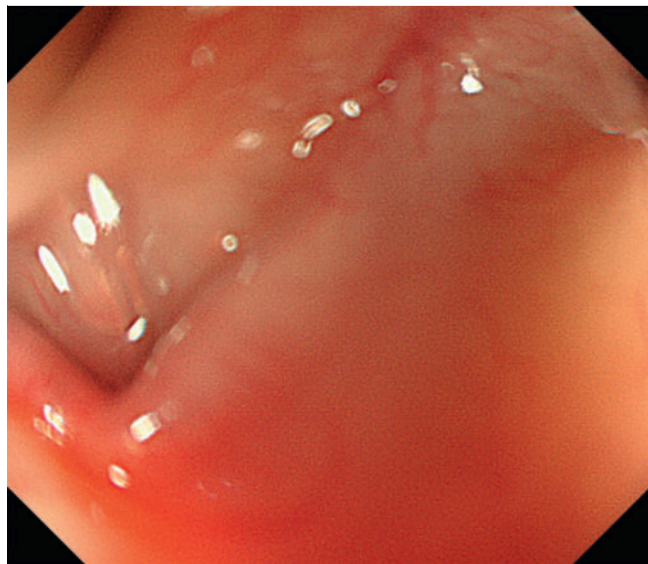
The cylindrical transparent hood has an outer diameter of 5.9 mm and is made of elastomer. The maximum outer diameter of the ESD knife was 1.95 mm. These devices were approved and clinically introduced in January 2021.

Conventional endoscopes include an Olympus GIF H290T (maximum diameter 11.8 mm) or a Fujifilm EG-L580RD7 (maximum diameter 11.8 mm). Ultrathin endoscopes include an Olympus GIF 1200N (maximum diameter 5.8 mm), an Olympus GIF 290N (maximum diameter 5.8 mm), or a Fujifilm EG-L580NW7 (maximum diameter 5.9 mm). ESD was performed beyond the stricture after pharyngeal chemoradiotherapy (▶ Fig. 1, ▶ Fig. 2, and ▶ Video 1).

Skilled endoscopists with board certification from the Japan Gastroenterological Endoscopy Society performed all ESD procedures in this study. Furthermore, the method of esophageal ESD was similar to the conventional method and is described briefly. First, iodine staining was used to diagnose the border (▶ Fig. 3). Then, markings were placed approximately 2 mm outside the lesions with a soft coagulation effect 4, 50W with a knife tip (▶ Fig. 4). Glycerol was injected outside the marking, and an incision was made with an endocut effect of 1, duration of 1, and interval of 1 (▶ Fig. 5). Afterward, dissection was performed with swift coagulation effect 3, 40W while observing the submucosal layer to be dissected with a transparent tip hood (▶ Fig. 6), and the lesion was resected en bloc (▶ Fig. 7, Fig. 8). Intraoperative hemorrhage was coagulated with a knife tip with swift coagulation effect 3, 40W. Hemostatic forceps were used (Pentax or Kaneka) with soft coagulation effect 4, 50W when hemostasis could not be obtained. This study used a VIO 300D high-frequency apparatus (ERBE, Tübingen, Germany).



▶ **Fig. 1** Images of devices that have been developed and clinically introduced. **a** Transparent hood for ultrathin endoscope (Nichendo). **b** Endoscopic submucosal dissection knife for ultrathin endoscope (Endosaber Fine).



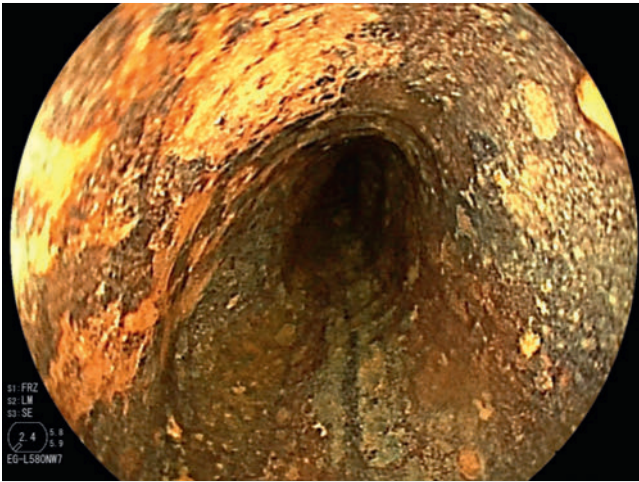
▶ **Fig. 2** A conventional endoscope could not pass through the stenosis after CRT.

### ▶ VIDEO

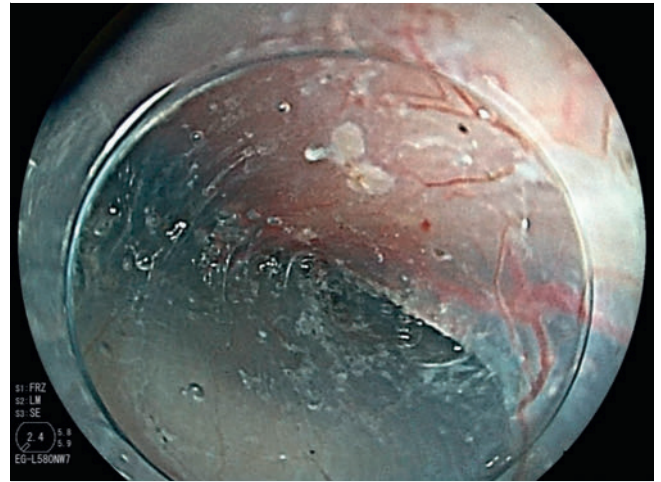


▶ **Video 1** ESD procedure using an ultrathin endoscope on a lesion with a pharyngeal stricture.

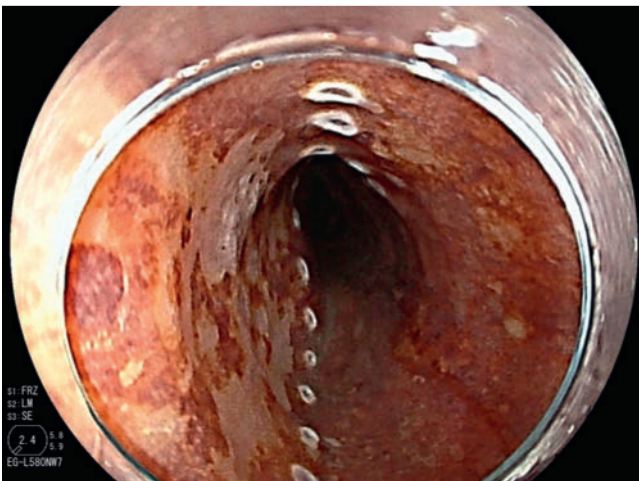




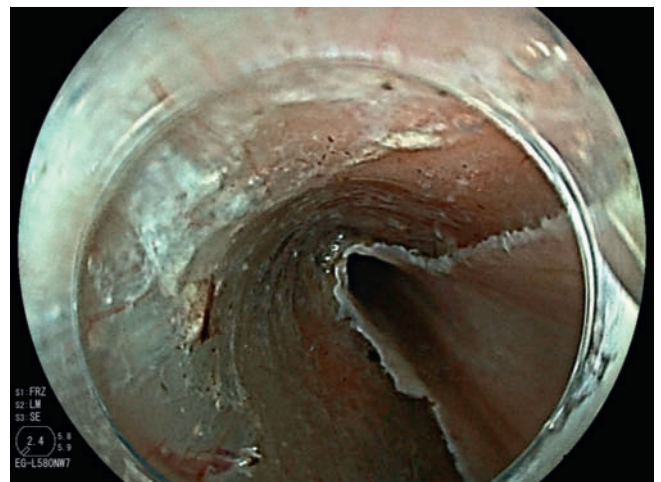
► **Fig. 3** A lesion was identified as an iodine-unstained area.



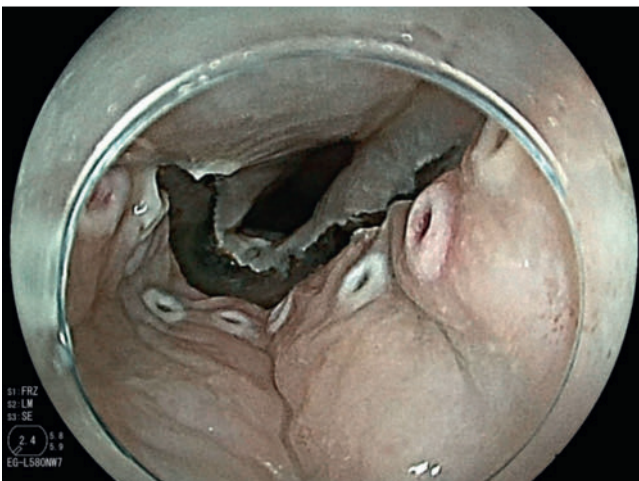
► **Fig. 6** The submucosal layer was dissected using the pocket creation method.



► **Fig. 4** A marking was placed 2 mm outside the lesion.



► **Fig. 7** The lesion was resected en bloc.



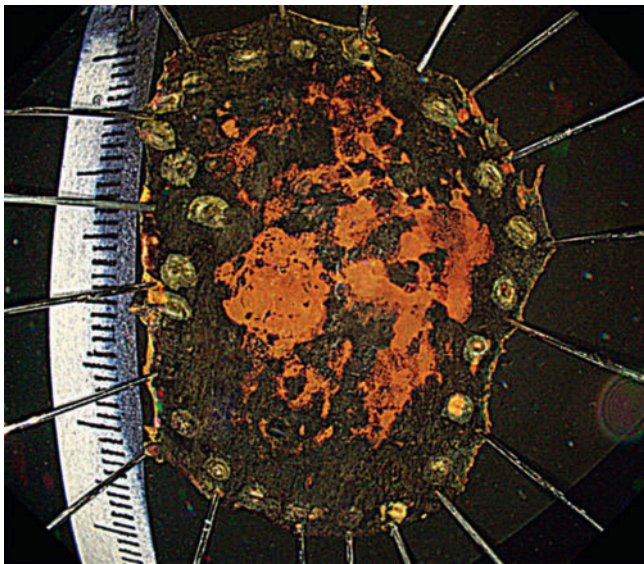
► **Fig. 5** An anal side incision was performed.

ESD was initiated with an ultrathin endoscope for lesions on the anal side of the stenosis or the cervical esophagus when a lesion could not be approached with a conventional endoscope. Furthermore, ESD with a conventional endoscope was combined with an ultrathin endoscope when the dissected layer could not be visualized due to fibrosis during dissection.

A local injection or an oral steroid was administered at operator discretion to prevent postoperative stenosis. Fluid replacement was performed while the patient was fasting on the day of ESD. Examination, x-ray, and blood testing were performed the day after ESD and meals were started at operator discretion.

### Evaluation items

Short-term outcomes evaluated included intraoperative perforation, muscle layer injury, procedure time, intraoperative bleeding, postoperative bleeding, pneumonia, and fever. Outcomes such as postoperative stenosis and recurrence were evaluated as long-term factors. The procedure time required



► **Fig. 8** The pathological diagnosis was squamous cell carcinoma, pT1a-LPM, 25 × 18 mm, Iy0, v0, margin negative.

from the start of the oral side incision to pocket creation in cases using the pocket creation method was measured by analyzing video images.

## Results

This study included 23 patients (19 males and four females, ► **Table 1**). Ultrathin endoscopes were used in 8.6% (26/303) of all esophageal ESD procedures during the same period. The average age of the patients was  $72.8 \pm 8.0$  years. Eight of the 26 ESD procedures were completed with an ultrathin endoscope and 18 with an ultrathin and a conventional endoscope. In nine of those 18 cases, ultrathin endoscopes were used first due to the stenosis, and then conventional endoscopes were used in combination with an ultrathin endoscope. In the remaining nine cases, conventional endoscopes were used first, and then ultrathin endoscopes were used due to scarring. ESD procedures were performed under general anesthesia in 18 cases and under conscious sedation with sedatives and analgesics in eight.

Lesions were found on the anal side of the stenosis in 38.6% (10/26) and with scarring in 50% (13/26). Furthermore, 46.2% of patients (12/26) had lesions in the cervical esophagus (► **Table 2**).

En bloc resection was possible for all 26 lesions. Serious complications, such as intraoperative perforation, pneumonia, and intraoperative bleeding, were not observed. Muscle layer damage was observed in seven lesions, but all could be followed up conservatively. Stenosis was prevented with corticosteroids in three cases. These patients only had mild stenosis and balloon dilatation was not required. Balloon dilatation was required in one patient with stenosis in whom steroids were not used.

► **Table 1** Patient characteristics.

|                                       |                |
|---------------------------------------|----------------|
| Number of patients                    | 23 cases       |
| Age, years ( $\pm$ SD)                | $72.8 \pm 8.0$ |
| Gender (male:female)                  | 19:4           |
| History of pharyngeal cancer, % (n/n) | 56.5 (13/23)   |
| History of esophageal cancer, % (n/n) | 90.0 (21/23)   |

SD, standard deviation.

► **Table 2** Lesion characteristics.

|                                                   |                 |
|---------------------------------------------------|-----------------|
| Number of lesions                                 | 26              |
| Tumor size (mm $\pm$ SD)                          | $18.8 \pm 14.1$ |
| Specimen size (mm $\pm$ SD)                       | $32.6 \pm 13.2$ |
| Lesions on the anal side of the stenosis, % (n/n) | 38.6 (10/26)    |
| Lesions with scarring, % (n/n)                    | 50 (13/26)      |
| Lesions on the cervical esophagus, % (n/n)        | 46.2 (12/26)    |

SD, standard deviation.

► **Table 3** Study results.

|                                 |                 |
|---------------------------------|-----------------|
| En bloc resection rate, % (n/n) | 100 (26/26)     |
| R0 resection rate, % (n/n)      | 80.8 (21/26)    |
| Procedure time (min $\pm$ SD)   | $62.2 \pm 36.7$ |
| Perforation, % (n/n)            | 0 (0/26)        |
| Muscle injury, % (n/n)          | 26.9 (7/26)     |
| Massive bleeding, % (n/n)       | 0 (0/23)        |
| Delayed bleeding, % (n/n)       | 0 (0/23)        |
| Pneumonia, % (n/n)              | 0 (0/23)        |
| Stenosis after ESD, % (n/n)     | 4.3 (1/23)      |

ESD, endoscopic submucosal dissection; SD, standard deviation.

The average size of the specimens was  $32.6 \pm 13.2$  mm and the invasion depth was T1a-MM in one lesion; all others were T1a-epithelial or lamina propria. Five lesions had positive or ambiguous lateral margins and all had negative vertical margins. Total procedure time was  $64.1 \pm 37.7$  minutes. The pocket creation method was used in 53.8% of cases (14/26). The average time required from the start of oral incision to pocket creation was  $121.2 \pm 109.9$  seconds (► **Table 3**).



## Discussion

Squamous cell carcinoma (SCC) has been identified as cancer with a high metachronous carcinogenesis rate. The incidence of metachronous carcinogenesis 5 years after ESD for pharyngeal and esophageal SCC is approximately 20% [12, 13]. Careful endoscopic follow-up is important, but patient prognosis is excellent if the disease is detected early. We usually perform follow-up endoscopies twice a year in patients with a history of SCC. All of the patients in this study had a history of pharyngeal or esophageal SCC that was discovered during follow-up endoscopy.

Esophageal stenosis and narrowing of the lumen occasionally is seen in patients and the causes are various. Stenosis is a major clinical problem, especially after extensive ESD, and various methods to prevent stenosis have been reported [14, 15, 16, 17, 18]. Among them, steroids are currently the most widely used. Nevertheless, we have often seen patients for whom balloon dilatation was required. Stenosis also can occur after radiation therapy for esophageal and pharyngeal cancer. Radiation-induced stenosis is more severe than post-ESD stenosis, and dilation may not resolve the stenosis.

Esophageal ESD can be complicated by various factors, one of which is stenosis, which is the major factor impacting procedure success. Furthermore, lesions from post-ESD scarring and cervical esophageal lesions are sometimes difficult to treat with normal ESD. All of our patients had at least one of these complications. An ultrathin endoscope may not be necessary when balloon dilatation is performed, and treatment with a conventional endoscope is possible. However, the lesion will be damaged if balloon dilation is performed on the anal side of the stenosis with a normal diameter device. An ultrathin endoscope has great advantages if a conventional endoscope cannot pass through the balloon dilation because of severe stenosis.

Moreover, dissecting the scar under direct vision using a conventional endoscope is sometimes difficult. Even in such a case, an ultrathin endoscope can be used in a narrow space in the scar to perform dissection under direct vision. Furthermore, lesions in the cervical esophagus are sometimes difficult to approach using a conventional endoscope. An ultrathin endoscope approach is possible in such cases. Subsequent treatment is relatively easy if the submucosal space can be entered using an ultrathin endoscope using the pocket creation method [19]. Approximately half of the patients in this study underwent ESD of the cervical esophagus. Ultrathin endoscopes are useful for ESD in the narrow and curved cervical esophagus.

This study has some limitations, as does ESD with an ultrathin endoscope. First, this study was not a comparison study with a conventional endoscope. ESD with conventional endoscopes was performed as much as possible and ultrathin endoscopes were used only when treatment with conventional endoscopes was challenging. In the future, we will further clarify the criteria for using ultrathin endoscopes and conduct randomized controlled trials to verify the usefulness of ultrathin endoscopes. An ultrathin endoscope is more unstable than a conventional endoscope because of its thinness and softness.

However, the pocket creation method was used as much as possible because the endoscope provides stability when entering the narrow submucosal space. A pocket can be created quickly using an ultrathin endoscope, which is considered a great advantage.

Furthermore, an ultrathin endoscope in an ESD procedure is difficult to aspirate and waterjets cannot be used. ESD using an ultrathin endoscope is more difficult than with a conventional endoscope. Massive bleeding during an ESD procedure can be a difficult complication. Hence, we attempted to perform ESD with a conventional endoscope as much as possible. Operators who perform ESD with an ultrathin endoscope must have a higher level of skill. Using an ultrathin endoscope does not eliminate all complications. Ultrathin endoscopes are considered suitable for ESD because the procedure causes relatively little bleeding. An ultrathin endoscope with a large forceps diameter and a waterjet function should be developed.

## Conclusions

We developed two devices that enable ESD with an ultrathin endoscope and introduced them for clinical use. They were used for esophageal ESD 2 years after their introduction. ESD is usually difficult to perform with a conventional endoscope. The ultrathin endoscope was used for 8.6% of all esophageal ESDs. The procedure took a long time, but en bloc resection was safely performed in all cases. Ultrathin endoscopes may be useful for difficult cases of esophageal ESD.

## Conflict of Interest

The authors declare that they have no conflict of interest.

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