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Image of the Month

En bloc resection of cardia cancer and lipoma with endoscopic submucosal dissection

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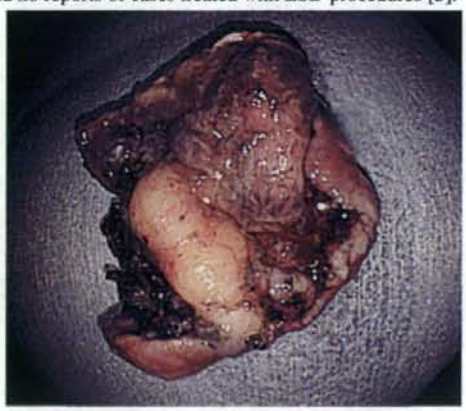
A 64-year-old gentleman was referred to our department for endoscopic submucosal dissection (ESD) of an early gastric cancer [1]. An upper-gastrointestinal endoscopy showed a superficial, shallow depression, 4 cm in diameter, from the lesser curvature to the anterior wall in the cardia. ESD was performed for this intramucosal adenocarcinoma (Fig. 1). Doing the submucosal dissection, we encountered with a yellowish-colored adipose tissue, 2 cm in diameter, beneath the cancerous mucosa unexpectedly. The capsulated adipose tissue was easily differentiated from extraluminal fat, because it was located over the muscularis propria in the submucosal layer and identified as a lipoma. So we carefully cut at the level of the deepest edge of the lipoma, and treated the feeding vessels. Injection agent with indigocarmine added was useful to discriminate the yellowish lipoma from blue-colored submucosa to dissect. Thus, the cancer with the lipoma was successfully resected in an en bloc fashion (Fig. 2). Histological assessment revealed a differentiated type intramucosal adenocarcinoma, 0-IIc, with curative resection and a well-differentiated adipose tumor covered by a fibrous capsule. The most recent endoscopy performed 8 weeks after ESD revealed no recurrence.

The stomach is a rare location for lipomas, and the lipomas represent about 3% of all benign gastric masses [2]. There are few reports of gastric lipoma with early gastric cancer, and no reports of cases treated with ESD procedures [3].



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GASTROENTEROLOGY

Multi-center survey regarding the management of anticoagulation and antiplatelet therapy for endoscopic procedures in Japan

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Key words
aspirin, endoscopic biopsy, endoscopic mucosal resection, endoscopic submucosal dissection, warfarin.

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The questionnaires were collected from participants at the meeting of Tokyo Gastrology Clinical Diagnosis Conference (TGCDC), supported by Eisai Co. and the contents were partially presented at the 7th TGCDC meeting, Tokyo, Japan, on 11 January, 2008.

Abstract

Background: A guideline on the management of anticoagulation and antiplatelet therapy for endoscopic procedures has been established from Japan Gastroenterological Endoscopy Society in 2005. However, it is unknown whether consensus on the management of these conditions is obtained among endoscopists in daily practice owing to the guideline.

Methods: To study the current practice on the management, survey questionnaires were sent to 13 representative endoscopists of 13 middle or high-volume hospitals in the Tokyo area.

Results: Responses were obtained from all 13 endoscopists. The results showed that only five (38%) and six (46%) hospitals had their own standard protocols regarding the management for endoscopic biopsy and endoscopic mucosal resection (EMR), respectively. There was a wide variation among endoscopists in terms of discontinuation of each agent. When the patients had a major risk of thromboembolism due to discontinuation of anticoagulants and antiplatelet agents, seven (54%) and five (38%) endoscopists, respectively, never took a biopsy. Similar numbers of endoscopists never carried out EMR. During discontinuation of anticoagulants or antiplatelet agents for biopsy and EMR, three (23%) and three (23%) endoscopists, respectively, experienced patients with thromboembolic events.

Conclusions: There is still a wide variation and confusion among endoscopists after establishment of our national guideline. A robust national guideline with clearer description based on the scientific evidence is needed.

Introduction

Increasing use of anticoagulants and antiplatelet agents in primary and secondary prophylaxis of cardiovascular, cerebrovascular and venous thromboembolic diseases, and in the status after implantation of a mechanical stent or valve/aortic prostheses, has raised a big management issue for patients with those agents during diagnostic and therapeutic endoscopy. From the standpoint of endoscopists, they should be stopped to lessen the risk of hemorrhage. However, the doctor who initially prescribed them would like to continue them because of a fear of thromboembolic events. Ideally, changes of treatment should be made with estimation of the risks and the benefits and be tailored to individual patients on a case-by-case basis. However, in fact, it is very difficult to estimate the risks of hemorrhage and thromboembolic events for each case. The dilemma has made a movement to establish a Japanese guideline on the management of anticoagulation and antiplatelet therapy for endoscopic procedures from Japan Gastroenterological Endoscopy Society in 2005 as well as in other countries (Tables 1,2).[1] Permeation of the guideline throughout our endoscopy society and the usefulness in daily practice should be validated after a few years of establishment and the guideline should be reformed according to the current inconsistency every few years. So, we conducted this pilot study using a survey questionnaire in the Tokyo area in order to determine the current daily practice regarding the

Table 1 Management of anticoagulant (warfarin) for endoscopic procedures

	Low-condition risk of thromboembolic event	High-condition risk of thromboembolic event
Low procedural risk	Discontinue 3–4 days before procedure Start at little rebleeding risk Check of INR ≤ 1.5 before procedure is desirable	Discontinue 3–4 days before procedure Start at little rebleeding risk Check of INR ≤ 1.5 before procedure is desirable Consider heparin
High procedural risk	Discontinue 3–4 days before procedure Start at little rebleeding risk Check of INR ≤ 1.5 is mandatory	Discontinue 3–4 days before procedure Start at little rebleeding risk Check of INR ≤ 1.5 before procedure is mandatory Consider heparin

INR, international normalized ratio.

Table 2 Management of antiplatelet agents for endoscopic procedures

	Low-condition risk of thromboembolic event	High-condition risk of thromboembolic event
Low and high procedural risk	Discontinue 3 days before procedure for aspirin alone Discontinue 5 days before procedure for ticlopidine alone Discontinue 7 days before procedure for aspirin and ticlopidine No description for start	Discontinue 3 days before procedure for aspirin alone Discontinue 5 days before procedure for ticlopidine alone Discontinue 7 days before procedure for aspirin and ticlopidine Consider heparin and hydration No description for start
Extremely high procedural risk	Discontinue 7 days before procedure for aspirin Discontinue 10–14 days before procedure for ticlopidine No description for start	Discontinue 7 days before procedure for aspirin Discontinue 10–14 days before procedure for ticlopidine Consider heparin and hydration No description for start

management of anticoagulation and antiplatelet therapy for endoscopic procedures.

Methods

From the participants' records of Tokyo Gastrology Clinical Diagnosis Conference (TGCDC) meetings held in Tokyo three times a year, survey questionnaires were sent between November 2007 and December 2007 to 13 endoscopists who identified themselves as representative endoscopists in middle or high-volume hospitals in the Tokyo area. Initial approval to collect the data was obtained from all the board members of TGCDC by email beforehand and final official approval to have collected the data and announce the results including publication was obtained at the board meeting held on 11 January, 2008.

The following 13 hospitals participated in the present survey: The University of Tokyo, Tokyo; National Cancer Center Hospital, Tokyo; Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo; International Medical Center of Japan, Tokyo; St Luke's International Hospital, Tokyo; Saitama Medical University International Medical Center, Saitama; Tokyo KoseiNenkin Hospital, Tokyo; Chofu Touzan Hospital, Tokyo; Tokyo Metropolitan Toshima Hospital, Tokyo; Tokyo Teishin Hospital, Tokyo; Mitsui Memorial Hospital, Tokyo; Toranomon Hospital, Tokyo; Tochigi Cancer Center, Tochigi, Japan.

Several questions about management of patients on anticoagulants and antiplatelet agents undergoing esophagogastroduodenoscopy (EGD) with biopsy and endoscopic mucosal resection (EMR) including endoscopic submucosal dissection (ESD) for stomach neoplasms were asked of the endoscopists as follows: (i) Do you have a standard protocol at your hospital on the management of anticoagulation and antiplatelet therapy for endoscopic procedures? (ii) Do you feel the necessity for solid evidence on the management of anticoagulation and antiplatelet therapy for endoscopic procedures? (iii) How many days before and after the procedure is each agent stopped when it can be stopped? The agents asked about were warfarin, aspirin, ticlopidine, clopidogrel, cilostazol, ethyl icosapentate, beraprost sodium, sarpogrelate hydrochloride, dipyridamole, ozagrel sodium, trapidil and dilazep hydrochloride. (iv) How do you manage the patients with a major risk of thromboembolism? (v) Have you had patients with a bleeding complication due to insufficient discontinuation of anticoagulation and antiplatelet therapy? (vi) Have you had patients with a thromboembolic event during discontinuation of anticoagulation and antiplatelet therapy?

Results

Responses were obtained from all the endoscopists. In five (38%) and six (46%) hospitals, there were individual standard protocols for the management of anticoagulation and antiplatelet therapy for endoscopic biopsy and EMR, respectively, whereas, in the remainder of the hospitals, endoscopists themselves determined the protocol by referring to the Japanese guideline and/or the doctors who prescribed those agents. Twelve (92%) and 13 (100%) endoscopists desired solid evidence on the management of anticoagulation and antiplatelet therapy for EGD with biopsy and EMR, respectively.

Standard policy to stop and start agents

There were wide variations between endoscopists regarding consideration about discontinuation of anticoagulation and antiplatelet therapy to prevent bleeding complications from EGD with biopsy and EMR, although warfarin was stopped 4 days before the procedures, and aspirin, ticlopidine, and ethyl icosapentate were stopped 7 days before the procedures by most of the endoscopists (Fig. 1). The asked agents seemed to be divided into three groups, the agents with standard policy and consistency to some extent among endoscopists (warfarin, aspirin, ticlopidine, ethyl icosapentate), the agents with standard policy but inconsistency among endoscopists (clopidogrel, cilostazol, beraprost sodium, sarpogrelate hydrochloride, dipyridamole), and the agents without standard policy among endoscopists (ozagrel sodium, trapidil, dilazep hydrochloride).

No major differences were observed between EGD with biopsy and EMR regarding discontinuation before the procedures in any agents. In comparison with discontinuation before the procedures, more endoscopists had no standard policy regarding discontinuation after the procedures in any agents, especially after EMR.

Management of the patients with a major risk of thromboembolism

Seven (54%) endoscopists never took a biopsy and six (46%) endoscopists never performed EMR at their hospitals, if the patients had a major risk of thromboembolism with discontinuation of anticoagulants. Five (38%) endoscopists never took a biopsy and six (46%) endoscopists never performed EMR in their hospital, if the patients had major risk of thromboembolism with discontinuation of antiplatelet agents. The remainder of the endoscopists took a biopsy or carried out EMR after replacement by heparin for 3 to 7 days. The main protocol was withdrawal of the continuous perfusion of heparin 4–6 h before the procedures and resumption of heparin 6–8 h after the procedures with overlapping warfarin until adequate international normalized ratio (INR) was obtained.

Experience of bleeding complication and thromboembolic event

No endoscopists experienced patients with severe bleeding due to EGD with biopsy or EMR due to insufficient discontinuation of anticoagulation and antiplatelet therapy. On the contrary, two endoscopists (15%) and one endoscopist (8%) experienced a patient with cerebral infarction during discontinuation of aspirin and cilostazol, respectively, for EGD with biopsy. Two endoscopists (15%) and one endoscopist (8%) experienced a patient with cerebral infarction and mesenteric arterial thrombosis, respectively, during discontinuation of warfarin for EMR. The patient with mesenteric arterial thrombosis finally died after the event. Detail clinical course of each event was not obtained due to the nature of the survey with questionnaires.

Discussion

Several guidelines on the management of anticoagulation and antiplatelet therapy for endoscopic procedures including the Japanese guideline have gradually been established in the last decade.[1–7] A common feature of these guidelines is to classify the procedural risks into low and high and the condition risks for thromboembolism into low and high. In terms of the procedural risks, EGD with biopsy is considered to be a low-risk procedure and EMR including ESD is considered to be a high-risk procedure. However, how to manage the patients with different procedural risks is inconsistent between Western guidelines and the Japanese guideline. If the procedure is classified as a low-risk procedure, the risk of hemorrhage is very low and no change in medication may be acceptable in the Western guidelines. On the contrary, even when the endoscopic procedures are classified into a low-risk group, it is recommended to stop anticoagulants and antiplatelet agents for a considerable duration in the Japanese guideline. Although it is difficult to conclude the superiority of each standpoint, we have to keep in mind the facts that some endoscopists experienced major thromboembolic events during discontinuation of those agents and considerable percentages of endoscopists declared that they never took a biopsy at their hospital from patients with high-condition risk for thromboembolism.

In the literature, as far as we are aware, there are only a few reports on thromboembolic events during discontinuation of anticoagulants or antiplatelet agents.[8–11] However, this does not mean that the agents are safely ceased in any occasion as shown in this study. Recent small surveys from Korea and Japan revealed that six of 81 endoscopists 7.4%)[12] and seven of 81 endoscopists (8.6%),[13] respectively, experienced an embolism in their patients after cessation of these agents, similar to our survey. It should be stressed again that induced thromboembolic events during discontinuation of the agents may result in fatalities.

Racial differences in susceptibility to thromboembolism are sometimes used to establish different guidelines between countries, especially between the West and the East, because it is believed, without solid evidence, that Caucasians are potentially more susceptible to thromboembolism than Asians. A recent international survey conducted by Eastern and Western endoscopists on the issue supported a wide difference in the management between the two groups, which revealed that Eastern endoscopists were more concerned about an increased risk of bleeding.[14] However, we have to mention that this opinion is not obtained by the clinical data in the literature that compares the different rates of complications in gastrointestinal endoscopy between the East and the West. Furthermore, the survey also revealed, interestingly, that personal experience seemed to be a more powerful driver of practice than was the published literature even among Western endoscopists with the American Society for Gastrointestinal Endoscopy (ASGE) guidelines.[14]

Another large issue revealed by the present study is that there were several antiplatelet agents showing inconsistencies among endoscopists or without a standard policy regarding their managements. The major reason may be limited evidence on antiplatelet agents. However, in the Japanese guideline, the duration of discontinuation before procedures for aspirin and ticlopidine is only described from the data based on the quantitative bleeding time test and the platelet aggregation test in healthy Japanese.[15,16] Even when referring to Western guidelines, a clear description of the management of antiplatelet agents is also not made; the possibility of aspirin, ticlopidine, clopidogrel and dipyridamole interfering with platelet aggregation is only mentioned.[2–7] From this

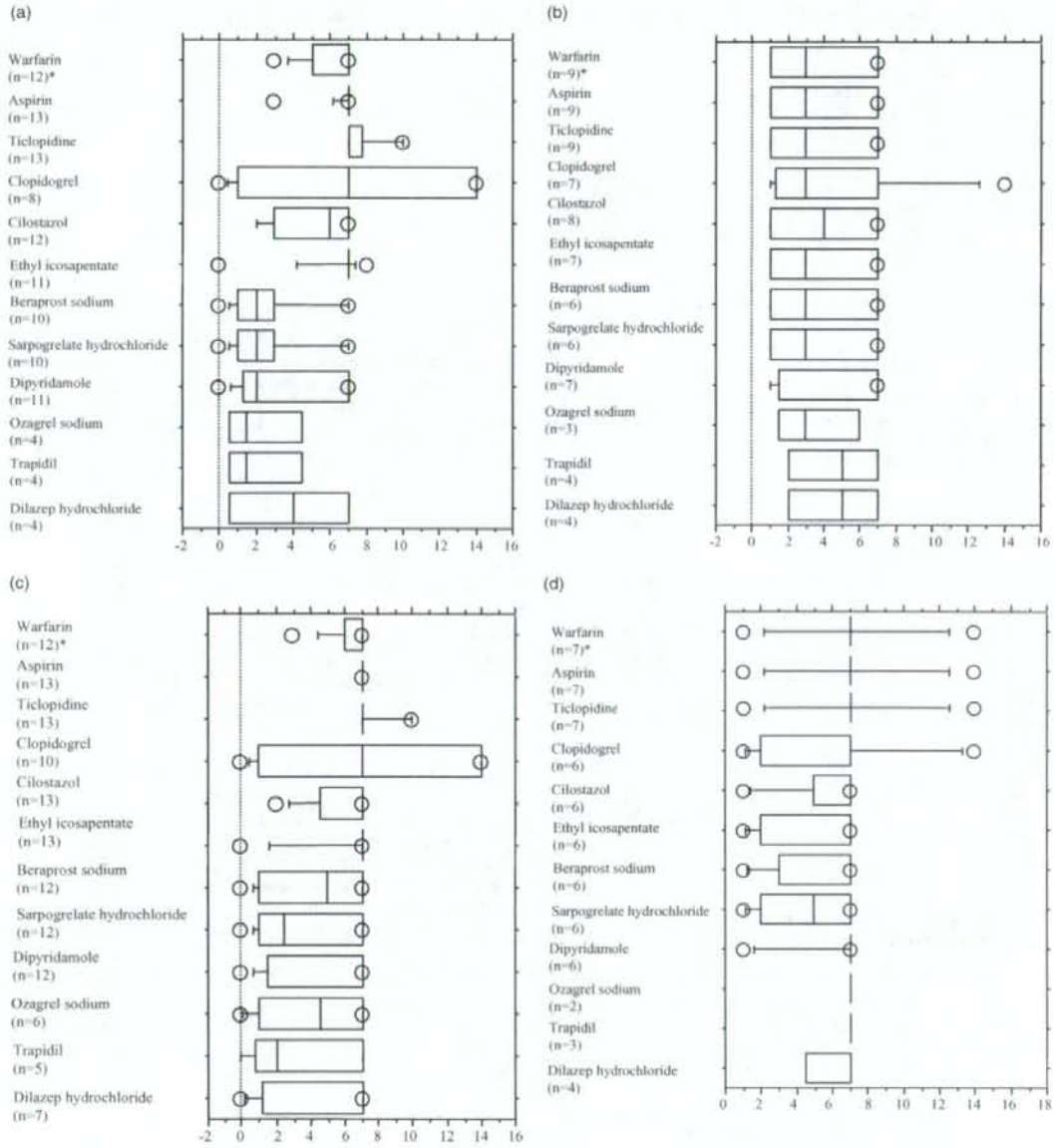

Figure 1 Duration of discontinuation for endoscopic procedures in anticoagulation and antiplatelet therapy. (a) Duration of discontinuation before endoscopic biopsy. (b) Duration of discontinuation after endoscopic biopsy. (c) Duration of discontinuation before endoscopic mucosal resection. (d) Duration of discontinuation after endoscopic mucosal resection. *The number is that of endoscopists who described the exact days. The others of 13 endoscopists did not have their standard policy in their hospitals.

information, it may not be necessary to discontinue the other agents nominated in the present study as antiplatelet agents before endoscopic procedures; however, the legitimacy to neglect these agents because of a risk of hemorrhage cannot be judged from the guidelines. Furthermore, regarding all the antiplatelet agents, a recommended duration of discontinuation after the procedures is very obscure.

Ido *et al.* reported their own efforts to establish provisional rules concerning management of anticoagulation and antiplatelet therapy for endoscopic procedures in cooperation with related departments in their hospital.[17] The description about the duration of discontinuation before and after endoscopic procedures for each disease is very concrete for each agent, although a recent agent, clopidogrel, and a few other antiplatelet agents are not described. We are convinced that most endoscopists prefer more practical guidelines authorized by our endoscopy society similar to the report by Ido *et al.* Further innovation of the guidelines on antiplatelet agents in more detail is warranted.

Limitations of the present study may be the small number of participating hospitals and questionnaire surveys, which results in the possibility of recall bias. However, even with these limitations, the tendency for different management for patients with anticoagulation and antiplatelet therapy among different hospitals was clearly recognized and the problems that should be solved on this topic were clarified. Additionally, we recognize the importance of this type of survey, because, in the past, these surveys drove the proposal for the establishment and refinement of guidelines for managing patients taking these agents in Western countries.[18–20]

In summary, the present study revealed that there was little consensus in our daily practice regarding the management of anticoagulation and antiplatelet therapy for endoscopic procedures even after a few years have passed since the establishment of the Japanese guideline. A reference guideline with clearer descriptions based on solid evidence that can be updated at least every few years should be established in the near future to prevent unnecessary anxiety of endoscopists and inappropriate management of patients.

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Digestive Endoscopy

Feasibility of electrocautery snaring as the final step of endoscopic submucosal dissection for stomach epithelial neoplasms

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Abstract

Background. Endoscopic submucosal dissection (ESD) is a novel endoluminal technique that permits the resection of gastric neoplasms.
Aim. To analyse the feasibility of snaring as the final step of ESD.
Patients and methods. One hundred and ninety-nine consecutive gastric neoplasms resected by four ESD experts from January 2004 to May 2007 were investigated. Forty-five (22.6%) were finally resected finally using a snare. Rates of *en bloc* resection, complete (R0 plus *en bloc*) resection, mean operation time, and complications were assessed between the snaring and the non-snaring groups.
Results. *En bloc* resection rate was significantly lower and delayed bleeding rate was significantly higher in the snaring group than in the non-snaring group (91.1% [41/45] vs. 100% [154/154], 11.1% [5/45] vs. 1.9% [3/154], respectively), although complete resection rate (86.7% [39/45] vs. 92.9% [143/154]) and mean operation time (70.2 min vs. 75.8 min) were not significantly different between the two groups. Six perforation cases (3 [6.7%] in the snaring group, 3 [1.9%] in the non-snaring group) were observed, but snaring did not lead to perforation in any case. When the subjects were divided into small (≤2 cm) and large (>2 cm) tumours, *en bloc* resection rate in large tumours was still significantly different between the groups (76.9% [10/13] vs. 100% [67/67]), whereas in small tumours it was no longer significantly different (96.9% [31/32] vs. 100% [87/87]).
Conclusions. Snaring may facilitate successful ESD for smaller tumours, but multiple-piece resection should be taken into account especially for larger tumours.

Keywords: Endoscopic submucosal dissection; Piecemeal resection; Snaring resection; Stomach neoplasm

1. Introduction

Endoscopic submucosal dissection (ESD) is a recently developed endoscopic treatment used mainly for intramucosal neoplasms of the gastrointestinal tract. It is characterised by a circumferential mucosal incision and submucosal dissection beneath the lesion. ESD has an invaluable advantage over the other treatment modalities, because the target lesion can be endoluminally resected in one piece without organ resection, even if the lesion is large or associated with submucosal fibrosis [1,2]. However, ESD is a highly advanced technique among the various endoscopic treatments, and special expertise in addition to training under the supervision of experienced hands is preferable.

Among the several steps involved in ESD, the most difficult step is considered to be submucosal dissection, that, if it does not go as planned, may result in active bleeding or perforation. In the clinical scene of ESD, snaring in a half way, where *en bloc* resection may be possible after circumferential mucosal incision and an appropriate amount of submucosal dissection, can be performed as a substitute for completion of submucosal dissection. Otherwise, in the case of difficulty in continuing the submucosal dissection due to technical problems, we are unwilling to use a snare after proceeding with submucosal dissection as much as possible. It is thought that using a snare may shorten operation time spent on submucosal dissection or rescue the patient from a difficult situation, but it may lead to uncertainty for *en bloc* resection or to the possibility of an increased tumour-positive margin. So, we retrospectively analysed differences in the outcomes of ESD for stomach epithelial neoplasms between the groups with

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Table 1
Clinicopathological features of 199 gastric lesions in the snaring and the non-snaring groups

	Snaring ($N=45$)	Non-snaring ($N=154$)	p-Value
Age (y.o.) (mean ± S.D.)	68.5 ± 9.0	68.1 ± 8.5	0.825
Sex (male/female)	37/8	118/36	0.541
Location (U/M/L)[a]	15/20/10	43/47/64	0.054
Circumference (LC/GC/AW/PW)[b]	13/9/9/14	66/19/29/40	0.317
Gross type (elevated/depressed/combined)	19/25/1	58/87/9	0.577
Histology type (intestinal/diffuse/adenoma)	38/3/4	123/11/20	0.746
Submucosal fibrosis (presence/absence)	8/37	25/129	0.821
Depth of invasion (mucosa/submucosa)	35/10	122/32	0.837
Tumour size (mm) (mean ± S.D.)	17.8 ± 10.2	22.6 ± 15.7	0.056

[a] U, upper third; M, middle third; L, lower third of the stomach.
[b] LC, lesser curve; GC, greater curve; AW, anterior wall; PW, posterior wall of the stomach.

and without electrocautery snaring as the final step of ESD, in order to find out whether snaring has been beneficial or not in our case series.

2. Patients and methods

One hundred and ninety-nine consecutive lesions with a diagnosis of early gastric cancer (EGC) or gastric adenoma (GA) between January 2004 and May 2007 were retrospectively investigated. These cases had all been resected by four, very experienced ESD experts, each of whom had performed ESD on more than 30 cases of EGC or GA. Lesions in a remnant stomach after gastrectomy or in a gastric tube after oesophagectomy were excluded, because the number was small and the specific conditions might affect subsequent analysis. Cases whose medical records were insufficient for retrospective analysis were also excluded. Clinicopathological features of 199 lesions were divided into two groups, the snaring group ($n=45$) and the non-snaring group ($n=154$), according to the requirement of an electrocautery snare for tumour resection (Table 1). Age, sex, location and circumference of the tumour, gross type, histology type, coexistence of submucosal fibrosis, depth of invasion, and mean tumour size (the greatest diameter of the lesion on actual measurement) were not significantly different between the two groups, although the cases in the non-snaring group tended to be located predominantly in the lower third and be larger in comparison with those in the snaring group.

The indication for ESD was determined by preoperative prediction of GA or EGC without nodal metastases described by the previous study [3] from thorough endoscopic examinations with endoscopic biopsy. The ESD technique has been described elsewhere [4,5]. In brief, a flex-knife (KD-630L; Olympus, Tokyo, Japan) [6,7] was used as the main electrosurgical knife, and other knives, such as an insulation-tipped diathermic knife (IT knife) [8] and a hook-knife [9], were used when required by the lesion. These knives were used for mucosal cutting to isolate the lesion from surrounding non-neoplastic mucosa, and for submucosal dissection to detach the lesion from the muscle layer. A mixture of 10% glycerin plus 5% fructose and 0.9% saline preparation (Glyceol, Chugai Pharmaceutical Co., Tokyo, Japan) containing 0.005% indigo carmine and 0.0005% epinephrine was used to make a submucosal fluid cushion [10]. Hyaluronic acid was added to the injection solution when the lesion had ulcerative findings or when it was in a difficult location, such as the cardia [11]. Haemostatic forceps (HDB2422W; Pentax, Tokyo, Japan) were used for reduction in bleeding during the procedure or for the treatment of visible vessels on the mucosal defect after resection. During submucosal dissection, an electrosurgical snare 15 mm (SD-210L-15, Olympus) or 25 mm (SD-210L-25, Olympus) in diameter was used when the operator required. The decision as to whether a snare was used or not was completely left to the judgment of the operator in consideration of several factors, e.g., operation time, technical difficulty, encountering complications, patient's comorbidity (Table 2).

We investigated the differences between the snaring and the non-snaring groups in rates of *en bloc* resection and complete resection (the rate of cases revealing no tumour on the edge of the one-piece resected specimen), mean operation time and complications in an overall analysis. Moreover, as shown in Tables 3 and 4, all the subjects were divided into two groups according to tumour size (small [≤2 cm] or large

Table 2
The main indications for snaring

	$N=45$
Positive indication of snaring for faster resection[a]	20
Passive indication of snaring to end up resection	25
Because of poor conditions during the operation[b]	11
Massive bleeding during the operation	5
Perforation during the operation	3
Poor condition of the patient	3
Because of difficulties in the lesion itself[c]	14
The location of the tumour made ESD difficult	11
Submucosal fibrosis made ESD difficult	3

[a] Submucosal dissection would be easy to continue, but snaring was done only for the reason of saving time.
[b] Submucosal dissection would be unfavourable to continue, so snaring was done.
[c] Submucosal dissection would be difficult to continue, so snaring was done.

Table 3
Clinicopathological features of 80 gastric lesions >2 cm in size in the snaring and the non-snaring groups

	Snaring ($N=13$)	Non-snaring ($N=67$)	p-Value
Age (y.o.) (mean ± S.D.)	70.6 ± 8.1	68.5 ± 8.2	0.403
Sex (male/female)	13/0	52/15	0.113
Location (U/M/L)[a]	6/5/2	23/19/25	0.310
Circumference (LC/GC/AW/PW)[b]	2/2/3/6	32/6/14/15	0.139
Gross type (elevated/depressed/combined)	9/4/0	30/33/4	0.233
Histology type (intestinal/diffuse/adenoma)	12/1/0	52/8/7	0.401
Submucosal fibrosis (presence/absence)	2/11	11/56	>0.999
Depth of invasion (mucosa/submucosa)	8/5	47/20	0.531

[a] U, upper third; M, middle third; L, lower third of the stomach.
[b] LC, lesser curve; GC, greater curve; AW, anterior wall; PW, posterior wall of the stomach.

Table 4
Clinicopathological features of 119 gastric lesions ≤2 cm in size in the snaring and the non-snaring groups

	Snaring ($N=32$)	Non-snaring ($N=87$)	p-Value
Age (y.o.) (mean ± S.D.)	67.6 ± 9.3	67.9 ± 8.8	0.889
Sex (male/female)	24/8	66/21	>0.999
Location (U/M/L)[a]	9/15/8	20/28/39	0.137
Circumference (LC/GC/AW/PW)[b]	11/7/6/8	34/13/15/25	0.812
Gross type (elevated/depressed/combined)	10/21/1	28/54/5	0.830
Histology type (intestinal/diffuse/adenoma)	26/2/4	71/3/13	0.765
Submucosal fibrosis (presence/absence)	6/26	14/73	0.784
Depth of invasion (mucosa/submucosa)	27/5	75/12	0.774

[a] U, upper third; M, middle third; L, lower third of the stomach.
[b] LC, lesser curve; GC, greater curve; AW, anterior wall; PW, posterior wall of the stomach.

[>2 cm]), to compare the outcomes of the two groups for a sub-analysis, because the tumour size might affect the results. This was of particular concern in the snaring group because a snare might limit the ability to resect in terms of its size.

For the statistical analyses, Student's t-test for age, operation time and tumour size, Chi-square test for location, circumference, gross type and histology type and Fisher's exact probability test for the other variables were used. A p-value < 0.05 in each analysis was considered to be statistically significant.

3. Results

The overall results for using a snare in the ESD procedure are summarised in Table 5. *En bloc* resection rate was significantly lower in the snaring group than in the non-snaring group (91.1% vs. 100%). There were no significant differences in complete resection rate and mean operation time between the two groups. One of the major complications, delayed bleeding rate, was significantly higher in the snaring group than in the non-snaring group (11.1% vs. 1.9%). In all six cases, perforation was occurred during direct submucosal dissection and were not due to snaring.

Table 6 shows the results of the sub-analysis between the snaring and the non-snaring groups according to tumour size. In large tumours, *en bloc* resection rate in the snaring group was still significantly lower (76.9%) than in the non-snaring group (100%), whereas in small tumours, it was not significantly different between the two groups. In terms of operation time, there was no significant difference between the snaring and the non-snaring groups regardless of small or large tumour, although large tumours needed significantly longer time than small tumours in both groups. It was no longer significantly different in major two complications between the snaring and the non-snaring groups in this sub-analysis.

Table 5
Overall outcomes between the snaring and the non-snaring groups

	Snaring ($N=45$)	Non-snaring ($N=154$)	p-Value
En bloc resection rate (%)	**91.1**	**100**	**0.002***
Complete resection rate[a] (%)	86.7	92.9	0.225
Operation time (min) (mean ± S.D.)	70.2 ± 58.4	75.8 ± 58.6	0.574
Delayed bleeding rate[b] (%)	**11.1**	**1.9**	**0.016***
Perforation rate[c] (%)	6.7	1.9	0.130

[a] The rate of cases revealing no tumour on the edge of the resected specimen.
[b] The rate of cases needing emergency endoscopy due to hematemesis or melena.
[c] All cases were snared after perforation during submucosal dissection (perforation is not directly due to snaring).
* Statistically significant.

Table 6
The outcomes between the snaring and the non-snaring groups according to tumour size

	Tumour >2 cm			Tumour ≤2 cm		
	Snaring ($N=13$)	Non-snaring ($N=67$)	p-Value	Snaring ($N=32$)	Non-snaring ($N=87$)	p-Value
En bloc resection rate (%)	**76.9**	**100**	**0.004**[*]	96.9	100	0.269
Complete resection rate[a] (%)	69.2	88.1	0.099	93.8	96.6	0.610
Mean operation time (min) (mean ± S.D.)	103.1 ± 67.1	103.7 ± 67.1	0.976	56.9 ± 49.6	54.3 ± 39.7	0.773
Delayed bleeding rate[b] (%)	15.4	1.5	0.067	9.4	2.3	0.120
Perforation rate[c] (%)	0	3.1	>0.999	9.4	1.1	0.059

[a] The rate of cases revealing no tumour on the edge of the resected specimen.
[b] The rate of cases needing emergency endoscopy due to hematemesis, melena.
[c] All cases were snared after perforation during submucosal dissection (perforation is not directly due to snaring).
[*] Statistically significant.

4. Discussion

As tips and tricks for ESD have accumulated, performing ESD has gradually permeated into the repertoire of surgical techniques, especially in Japan [12]. The technique has significant advantages over other endoscopic treatments in the areas of controlling the shape and size of the resected specimen and the high probability of *en bloc* resection of an entire lesion. However, ESD is sometimes very difficult to perform and the operator must overcome many hurdles during the procedure.

The snaring technique is a basic one used in polypectomy or endoscopic mucosal resection (EMR) for pedunculated or small flat lesions [13]. Although snaring is easily performed and considered to save time, the disadvantage is uncertainty of *en bloc* resection [1,14]. When snaring is applied during ESD procedure, we should always consider this disadvantage; if snaring causes multiple-piece resection, the original advantage of ESD, the precise histopathological evaluation of an entire lesion, will be lost.

Why, then, is a snare used as the final step in ESD? There are various reasons. The most frequent one may be its time-saving advantage. However, Table 5 shows that snaring did not shorten operation time in our case series. Then, considering these results, does snaring actually shorten the operation time? The answer should be absolutely "yes". In some cases, a snare was used because it took an unexpectedly long time to dissect the submucosal layer beneath the tumour. In other cases, it was used because continuation of the submucosal dissection until complete detachment of the lesion from the muscle layer was impossible. So, when the results obtained from the overall analysis are considered in their clinical context, we are convinced that snaring absolutely shortens the procedure. If snaring had been planned beforehand for time-saving purposes, then normal operations that had not involved these extenuating circumstances would have been finished in much shorter time.

Although the overall analysis shows that *en bloc* resection rate was significantly lower in the snaring group than in the non-snaring group, the sub-analysis according to tumour size yielded quite important evidence for us. The results indicated that almost all small tumours (2 cm as a cut-off line between small and large tumours) could be removed in *en bloc* fashion. On the other hand, the rate of *en bloc* resection of large tumours in the snaring group was significantly lower than that in the non-snaring group. Furthermore, the larger the tumour size is, the longer operation time is. A dilemma emerges in the tradeoff between operation time and possibility of *en bloc* resection, especially for large tumours. It is reported that piecemeal resection leads to non-curative treatment, causing non-evaluable histopathology of the tumour and potentially local recurrence [1]. Even though it takes longer time to resect, the first priority should be curative resection of the tumour for the cases of no complications. So, in conditions where long operation time does not become a disadvantage for patients, such as under general anaesthesia, we recommend to accomplish complete submucosal dissection by an electrosurgical knife instead of using a snare. However, this consideration should be withdrawn when poor conditions during the operation occurred, and snaring should be used as a salvage technique, considering risks and benefits of the patient. Another possible point at issue of increasing the number of incomplete resections due to a burning effect of snaring for margins of resected specimens was not observed in our case series, which may surely encourage us to use a snare when *en bloc* resection is undoubtedly possible, in order to shorten operation time.

In terms of complications, delayed bleeding frequently occurred when a snare was used. In the "snaring" series, a snare was used in some cases of declared technical difficulties, presence of comorbidity or occurrence of complications. These variables might have determined the higher rate of delayed bleeding observed in this subgroup of patients, although the reason for this is still unclear. Another explanation is that snaring might cause insufficient coagulation of submucosal vessels, which implies that non-bleeding visible vessels should be more intensively treated after resection of the tumour with a snare, especially in the area detached by a snare. Although perforation occurred in six cases, the causes for perforation were not related to snaring, but were

due to inappropriate submucosal dissection by electrosurgical knives in all cases. On the contrary, an appropriate use of a snare may decrease perforation rate owing to reduction in time spent on direct submucosal dissection.

In summary, we suggest that lesions >2 cm in size should be resected in complete submucosal dissection style without snaring, in order to avoid multiple-piece resection, and that lesions ≤2 cm in size may be treatable through snaring in order to reduce operation time. However, the shortcoming of this report was a retrospective, non-controlled setting, even though the results were obtained from the consecutive data. A prospective, randomised controlled study about the feasibility of "planned" snaring is desirable to confirm our results, especially for smaller tumours.

Practice points

- Snaring resection may be acceptable for small lesions (≤2 cm) as the final step of endoscopic submucosal dissection (ESD) for stomach epithelial neoplasms to save operation time.
- Complete submucosal dissection by an electrosurgical knife is recommendable for large tumours (>2 cm) to avoid multiple-piece resection.

Research agenda

- A prospective, randomised trial is favourable to elucidate the feasibility of snaring as the final step of ESD, especially for small lesions.

Conflict of interest

None declared.

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DISEASES OF THE ESOPHAGUS

Case report

Detailed comparison between endocytoscopy and horizontal histology of an esophageal intraepithelial squamous cell carcinoma

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SUMMARY. **Endocytoscopy allows the real-time microscopic observation of living cells. Unlike the cross-sectional images obtained by conventional histology, endocytoscopy provides cellular images in a plane parallel to the surface of the mucosa. However, there is little knowledge about the endocytoscopic diagnosis of carcinomas. Using a specimen obtained by the endoscopic submucosal dissection of an intraepithelial esophageal squamous cell carcinoma, a detailed comparison between endocytoscopic and horizontal histological images was made, revealing the similarity between the images. Sharp lateral borders between atypical and normal epithelium and differences in cellularity and the sizes and shapes of the nuclei were clearly identified by endocytoscopy. Further horizontal histological investigations of this case also showed the variety of endocytoscopic images in non-cancerous and cancerous epithelia.**

KEY WORDS: **endocytoscope, esophageal neoplasm, histology, ultra-high magnification.**

INTRODUCTION

Endocytoscopy enables a real-time microscopic observation of living cells[1–4] and has the potential to guide endoscopic biopsy. However, it is not known what the endocytoscopic images represent in relation to standard cross-sectional histopathological images. A more appropriate evaluation would correlate the endocytoscopic images to that of histological images obtained in a plane parallel to the tissue surface. Increased cellularity, uneven sizes and shapes of nuclei and a distinct border interface between atypical and normal epithelium are likely to be the minimum essential findings to make an endocytoscopic diagnosis of malignancy. We here describe a case of an esophageal intraepithelial squamous cell carcinoma analyzed *in vivo* with endocytoscopy and correlate it with a corresponding horizontal histological examination in order to confirm the feasibility of an endocytoscopic diagnosis of carcinoma or a normal epithelium in the esophagus.

CASE REPORT

A 82-year-old man with three esophageal squamous cell carcinomas (two intraepithelial and one invasive) underwent endoscopic submucosal dissection (ESD) of these lesions, as described elsewhere.[5] All the lesions were completely resected *en bloc*, and a conventional histopathological assessment was performed for the invasive carcinoma and the larger intraepithelial carcinoma to make a final histological decision of curability. Because the remaining smaller intraepithelial carcinoma (7 mm in size), resected with a tumor-free margin confirmed by iodine staining (Fig. 1) had little influence on further management, the lesion was investigated for a detailed comparison between the endocytoscopy and horizontal histology after informed consent was obtained from the patient.

Immediately after ESD, the resected specimen was evaluated by endocytoscopy to assess the cancerous region, normal epithelium and the interface between carcinoma and normal epithelium following staining

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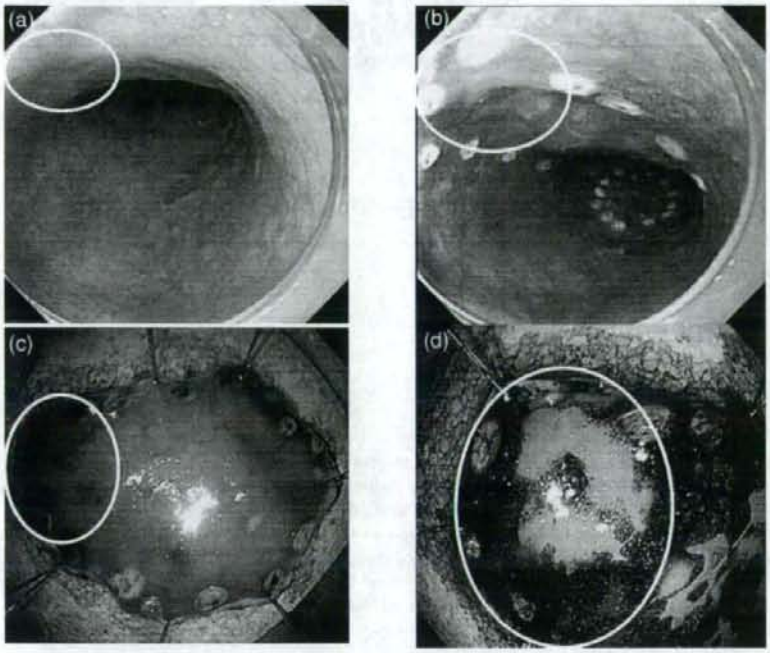

Fig. 1 Intra-epithelial esophageal carcinoma with endocytoscopic and horizontal histological observations, (a) ordinal endoscopic view, (b) iodine-staining endoscopic view with marking around it (the marking is to encircle a coexisting intra-epithelial carcinoma), (c) resected specimen by endoscopic submucosal dissection (a single resection is made with a coexisting intra-epithelial carcinoma), (d) close-up image of the resected specimen with iodine staining. *The circle in each figure shows the same area in both endocytoscopic and horizontal histological observations.

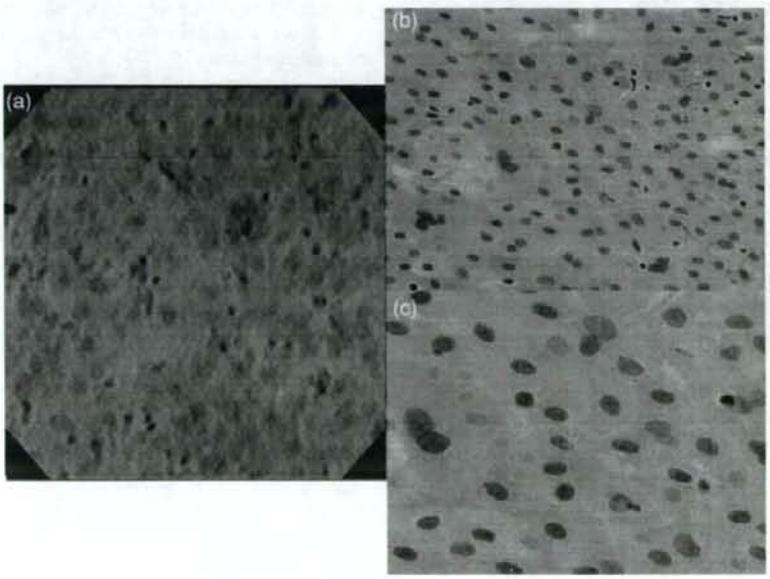

Fig. 2 Endocytoscopic and horizontal histological images of the intra-epithelial carcinoma showing the increased cellular density and the irregular arrangement and uneven sizes and shapes of the nuclei, (a) endocytoscopic image (1% methylene blue staining, original magnification 450× on a 35-cm monitor), (b) histological image (hematoxylin and eosin staining, original magnification 200×), (c) histological image (hematoxylin and eosin staining, original magnification 400×).

with 1% methylene blue.[6] A prototype endocytoscopy system, which consisted of a 3.2-mm diameter soft-catheter-type endocytoscope (XEC-300-2, Olympus Medical Systems Co., Tokyo, Japan), VISEA video system center (OTV-S7V, Olympus Medical Systems Co., Tokyo, Japan), and high-brightness light source (CLH-SC, Olympus Medical Systems Co. Tokyo, Japan), was used. The endocytoscope provides a fixed magnification of 450× (on a 36-cm monitor), which covers a 300 × 300-μm area of tissue. After observation, the specimen containing the entire lesion with surrounding normal epithelium was fixed with formalin and embedded in paraffin. Horizontal histological sections of the carcinoma, normal epithelium and normal–cancer border were made from each block and stained with hematoxylin and eosin.

A comparison of the endocytoscopic and histological images was performed. The endocytoscopic images bore a close resemblance to the surface horizontal histological images. The carcinoma showed increased cellular density with a completely irregular arrangement and uneven-sized and -shaped nuclei (Fig. 2), whereas the normal epithelium showed a regular cellular arrangement and even-sized and -shaped nuclei (Fig. 3). The tissue interface between the carcinoma and the normal epithelium was clearly identified in the endocytoscopic image as well as in the histological image (Fig. 4).

DISCUSSION

Endocytoscopy enables cells at the luminal surface to be viewed in their natural living state. In the attempt to obtain a real-time histological analysis at endoscopy (an optical biopsy), several methods, including endocytoscopy, have proved promising for potential clinical use.[7] Natural images can be obtained using endocytoscopy alone, because this system uses white light and is similar to an optical microscope, conferring a great advantage over other techniques in the application of histopathological knowledge to interpret the images. As shown in this case, it was possible to distinguish between the carcinoma and the normal epithelium endocytoscopically and to correlate these findings with a histologic diagnosis obtained at a plane similar to that of endocytoscopy. Key findings such as the degree of cellularity, nuclear size and shape, and a distinct normal–neoplastic interface could be clearly identified by endocytoscopy in order to identify the presence of a neoplastic lesion.

Inoue *et al.*[8] recently reported on their excellent progress in establishing a preliminary classification with five grades of endocytoscopic atypia. The classification corresponded well with the Vienna histological classification[9] and the overall accuracy was 82%. However, there are still limited data of the characteristics of endocytoscopic images of various

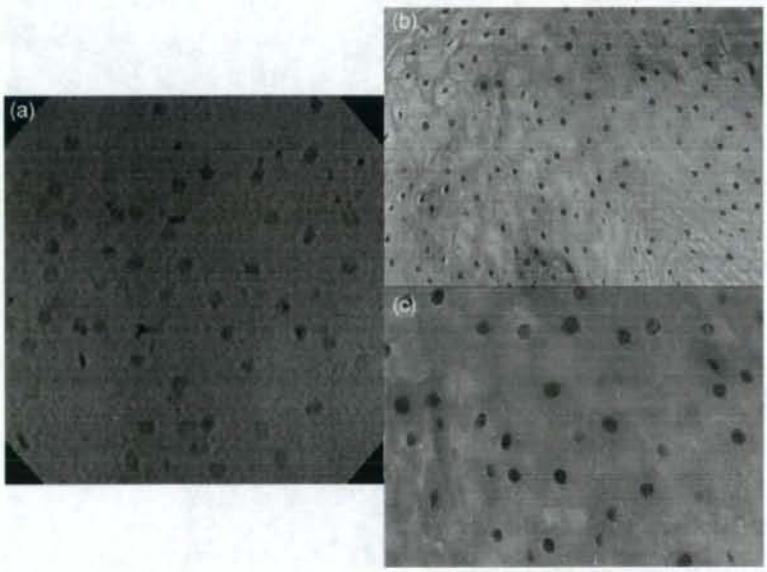

Fig. 3 Endocytoscopic and horizontal histological images of the normal epithelium showing the regular cellular arrangement and even sizes and shapes of nuclei, (a) endocytoscopic image (1% methylene blue staining, original magnification 450× on a 35-mm monitor), (b) histological image (hematoxylin and eosin staining, original magnification 200×) and (c) histological image (hematoxylin and eosin staining, original magnification 400×).

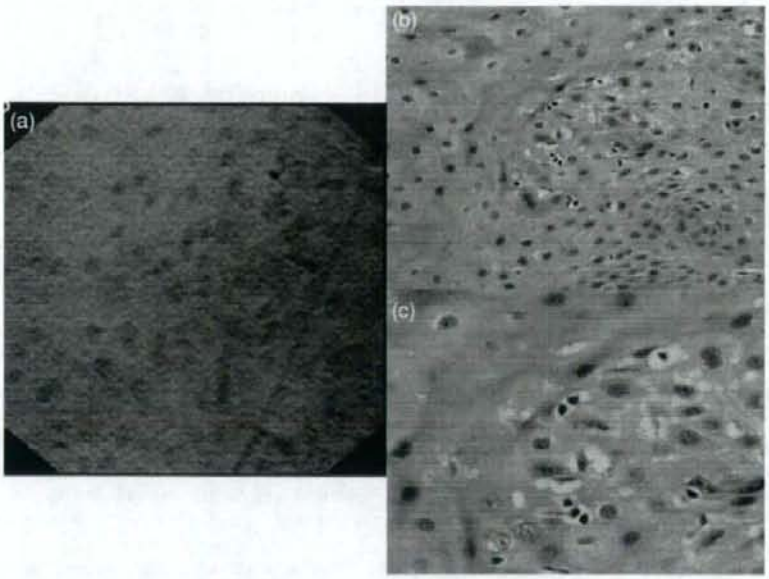

Fig. 4 Endocytoscopic and horizontal histological images of the border of intraepithelial carcinoma and normal epithelium. The lateral border is clearly identified by both the (a) endocytoscopic image (1% methylene blue staining, original magnification 450× on the 35-mm monitor), and (b) the horizontal histological images (hematoxylin and eosin staining, original magnification 200×) and (c) histological image (hematoxylin and eosin, original magnification 400×).

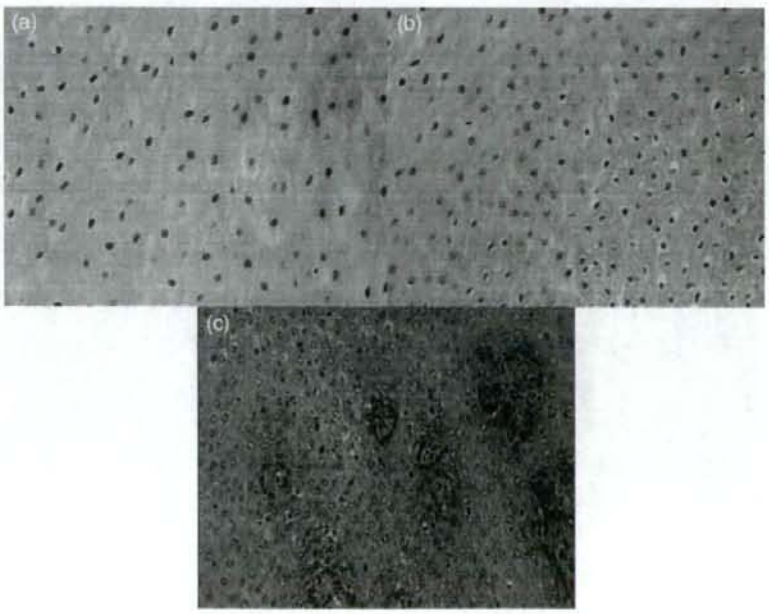

Fig. 5 Horizontal histological images from (a) the surface, (b) the middle and (c) the deepest image in the normal epithelium (hematoxylin and eosin staining, original magnification 200×). The cellular density and size of nuclei gradually increase from the surface to the deepest in a normal stratified squamous epithelium. Intra-papillary capillary vessels and light nuclei can be observed in the deepest part.

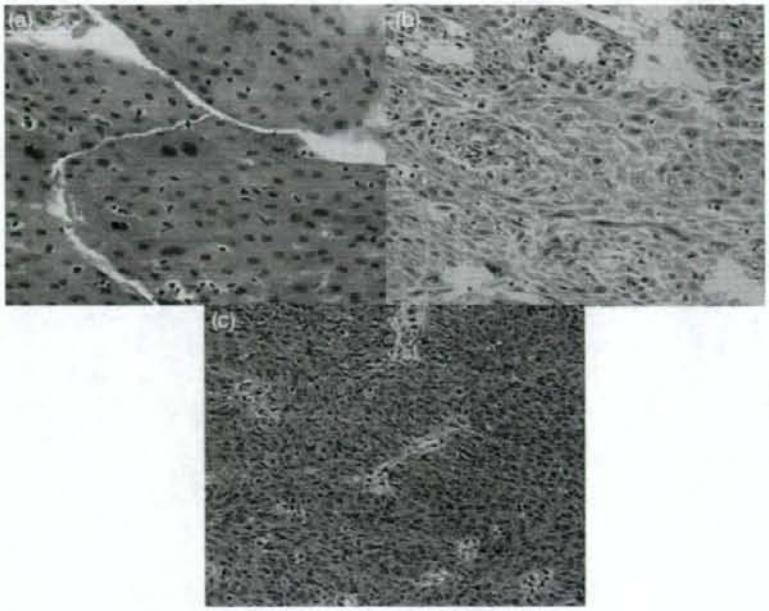

Fig. 6 Horizontal histological images from (a) the surface, (b) the middle, (c) the deepest surface image (hematoxylin and eosin, original magnification 200×) in the intraepithelial carcinoma. The cellular density and size of the nuclei are high, even on the surface and the cellular arrangement and shape of the nuclei are irregular in each part of the intraepithelial carcinoma. The images look quite different according to their depth.

conditions. Some observations can be made from this case study, which may lead to further progress in the knowledge of endocytoscopic images. Cellular density and the size of nuclei gradually decrease from the stratum basale epidermis to the surface in the normal stratified squamous epithelium. Thus, when erosion occurs, one may expect that the endocytoscopic images will show increased cellular density without showing the irregularity of size and shape of the nuclei (Fig. 5). On the other hand, the cellular density and size of nuclei are high even at the surface and the cellular arrangement and shape of the nuclei are irregular in intraepithelial carcinoma (Fig. 6).

From this case study, we also recognized the disadvantages of endocytoscopy. A major limitation is that critical factors such as the depth of the invasion cannot be assessed by endocytoscopy. This requires another imaging modality, such as confocal endoscopy or optical coherence tomography.[10,11] However, there is no doubt that endocytoscopy represents a powerful tool that enables the observation of living cells *in vivo* at the mucosal surface and the diagnosis of neoplastic lesion based on differences in cellular characteristics. The establishment of endocytosocopic diagnosis is promising, but needs further study in a larger cohort, including comparisons of *in vivo* endocytoscopy with biopsy or a histology of endoscopically or surgically resected specimens.

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Endoscopic Submucosal Dissection for Gastric Cancer

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Opinion statement

Endoscopic submucosal dissection (ESD) is a novel endoscopic treatment that enables a clinician to resect an early-stage gastric cancer in en bloc fashion. ESD is indicated for those cancers in which there is a high probability of en bloc resection and low probability of lymph node metastasis. The latter may be the limiting factor at institutions skilled at ESD. Several ESD techniques are available with similar outcomes. Thus, selection depends on operator preference and expertise. Gastrectomy with lymphadenectomy should be applied initially to those early gastric cancers with high probability of positive lymph nodes or as an additional treatment after ESD. Endoscopic mucosal resection (EMR) should be reserved for small, nonulcerated, intramucosal, differentiated cancers. Disadvantages of ESD in comparison with EMR are longer operation times and higher incidences of intraoperative bleeding and perforation, but the indication for ESD includes larger and ulcerative lesions not amenable to EMR.

Introduction

Endoscopic resection is possible for localized gastric epithelial neoplasms without lymph node metastases. Because it may not be able to discern the latter preoperatively, the neoplasm should be resected en bloc to best evaluate the risk. Until recently, resection by endoscopic mucosal resection (EMR) was limited to small lesions (ie, < 2 cm) [1,2]. Endoscopic submucosal dissection (ESD) is a new technique that uses a cutting device to permit a larger resection and resection of ulcerative neoplasms. First, fluid is injected into the submucosa to elevate the lesion from the muscle layer. Next, the mucosa surrounding the lesion is precut. Finally, the connective tissue of the submucosa beneath the lesion is dissected.

INDICATIONS FOR ESD

Based upon large numbers of surgically treated cases with and without lymph node metastasis, the following types of early gastric cancers may benefit from ESD: 1) intramucosal, differentiated adenocarcinoma with presence of ulcer when the lesion is less than or equal to 3 cm; 2) intramucosal, differentiated adenocarcinoma without ulceration of any size; 3) intramucosal, undifferentiated adenocarcinoma without ulceration when the lesion is less than or equal to 2 cm; and 4) differentiated adenocarcinoma with minute submucosal penetration (≤ 500 μm) when the lesion is less than or equal to 3 cm [3]. Also, the endoscopist's technical skill must be taken into consideration. For cases in which endoscopic ultrasonography reveals fusion of the muscle layer and the mucosal layer, which may occur in cancers that previously had a deep ulcer extending into the proper muscle layer, it is difficult to identify the gastric wall plane during submucosal dissection. Thus, in our opinion, these patients should not undergo ESD. Also, most Japanese investigators would not endoscopically resect an undifferentiated adenocarcinoma, as these lesions' margins are often indistinct, and even the small, undifferentiated carcinoma with ulcer finding has potential to spread to the regional lymph nodes.

VARIOUS TECHNIQUES OF ESD

ESD requires special cutting knives, such as the needle knife [4], the insulation-tipped electrosurgical (IT) knife [5], the hook knife [6], the flex knife [7,8•], and the triangle-tip (TT) knife [9]. It also requires submucosal injection to elevate the mucosa and separate it from the

Table 1. Recent outcomes for endoscopic submucosal dissection of early gastric cancer

Technique	En bloc resection rate	Local recurrence rate	Complication rate	
			Bleeding	Perforation
IT knife	93% (957/1033)	NA	6% (59/945)	4% (35/945)
Tip of thin snare/flex knife	95% (56/59)	NA	1.7% (1/59)	3.4% (2/59)
Sodium hyaluronate and small-caliber tip transparent hood	99% (69/70)	NA	1% (1/70)	0% (0/70)
Hook knife	95% (194/204)	0.5% (1/204)	NA	1.5% (3/204)
Hypertonic saline-epinephrine solution	79% (36/46)	0% (0/46)	4% (2/46)	8% (4/46)
Mixture of hyaluronic acid, glycerin, and sugar	100% (26/26)	0% (0/26)	3.8% (1/26)	0% (0/26)
TT knife	88% (14/16)	NA	NA	0% (0/16)
IT knife in the West	25% (6/24)	NA	12.5% (3/24)	0% (0/24)

IT—insulation-tipped electrosurgical; NA—not analyzed; TT—triangle-tip.

muscular layer. Although no one technique or injection solution has been shown to be superior to the others, hyaluronic acid alone or in combination with glycerin and sugar appears to make a longer-lasting cushion with less tissue damage [10–12,13•,14••] (Table 1). The less favorable results achieved in Western case series compared with Japanese case series may be due to different biological activities of early gastric cancers, less experience with the techniques, and insufficient information about the techniques in detail.

Treatment

Concomitant pharmacologic treatment

Antibiotics

- No evidence exists for the use of prophylactic antibiotics before, during, or after ESD.
- In case of perforation, standard doses of second-generation cephalosporins and fasting for 2 days may be sufficient if the perforation is closed immediately and completely with endoclips [15•].
- Although rare, aspiration pneumonia should be treated with broad-spectrum cephalosporin and clindamycin according to the pneumonia's severity and the antibiotic sensitivity of the organisms in the hospital.

Acid suppressant

- ESD-induced ulceration heals in most cases after 8 weeks of empiric proton pump inhibitor administration [16].
- A proton pump inhibitor prevents delayed bleeding more effectively than a histamine 2-receptor antagonist [17•].

Concomitant surgery

- Emergency surgery is rarely required to treat complications of ESD.
- Additional gastrectomy with lymphadenectomy is strongly recommended when histologic assessment reveals a high probability for lymph node metastasis as discussed previously.
- Histologic incomplete resection due to tumor extension into the lateral margin, or nonevaluable resection margin due to the effects of coagulation necrosis or multiple-piece resection does not always require additional surgery. These patients may be closely observed with endoscopy and biopsy, particularly if burn effect exists at the margin.

Selection of various ESD techniques

- Several ESD techniques are named by the electrosurgical knives applied or injection solution used. The results obtained by each technique are similar, as shown in Table 1. Selection depends mainly on each operator's preference and expertise.
- The needle knife enables a sharp cut. When applied vertically from the wall plane, the knife can easily pass through the stomach wall, resulting in perforation. To mitigate perforation, it is advisable to use a transparent endoscopic hood and to use hyaluronic acid as the injection solution [18,19].
- The IT knife has a ceramic ball at the top of a needle knife. The ceramic ball is placed within the submucosal layer so as to hook the mucosa or the submucosal connective tissue. Then the knife is pulled to cut the tissue at the needle blade [20•].
- The hook knife has a bending part at a right angle on the top of a needle knife. The tip of the bending is placed within the submucosal layer so as to hook the mucosa or the submucosal connective tissue that is to be cut. Then the knife is pulled into the direction of the lumen or scope [21•].
- The TT knife has a triangular-shaped metal plate attached to the tip of a needle knife. It is used in a way similar to the hook knife. The triangular shape obviates the need to rotate the tip to hook the tissue that is to be cut [9].
- The flex knife has a soft, thick, and looped tip. The knife's softness may prevent perforation, even when it is used vertical to the wall plane [8•].
- Although no study has compared the relative efficacy and safety of the various knives used for ESD, we prefer to start with a flex knife. An IT knife may be selected in cases of coexisting fibrosis because it is difficult to recognize the wall plane within the fibrotic tissue under direct visualization but easy to recognize it from the plane of the exposed proper muscle layer [22]. We prefer a mixture of high–molecular weight hyaluronic acid, glycerin, and sugar as the submucosal injection solution [13•].

Chemotherapy

- There is no evidence that chemotherapy is an efficient treatment for early gastric cancer.
- There is no evidence that chemotherapeutic agents used in the neoadjuvant or adjuvant setting lead to better survival than surgery or endoscopic treatment alone for early gastric cancer.

Surgery

Laparoscopic surgery

- Laparoscopic wedge resection, laparoscopic intragastric mucosal resection, and laparoscopic gastrectomy may be used to treat early gastric cancer [23].
- The first two techniques can be applied to treat node-negative cancers.
- Laparoscopic gastrectomy enables partial or total stomach resection and resection of perigastric lymph nodes. It can be used to treat all early gastric cancers, with or without lymph node metastases.
- Using laparoscopic surgery to cure early gastric cancer remains controversial. For node-negative cancers, ESD may be preferred. For the rest of early gastric cancers, laparoscopic surgery may be minimally beneficial over open surgery in terms of short-term outcomes and cosmesis [23].

Open surgery

- Open surgery is the gold standard for treating early gastric cancers not amenable to endoscopic resection.
- Most surgeons in Japan consider extended lymphadenectomy (D2 dissection) essential to remove possible lymph node metastases. However, several prospective studies conducted outside Japan have not reported any therapeutic benefit from a D2 over a D1 dissection [24].
- Less invasive surgical strategies, which consist of a reduced scope of lymphadenectomy and a reduced resection of the stomach, such as modified D1 dissection, modified D2 dissection, local resection with adjacent lymphadenectomy, pylorus-preserving gastrectomy, segmental gastrectomy, and proximal gastrectomy, are also treatment options for early gastric cancer [24].

Other endoscopic modalities

Tissue obliteration technique

- Laser vaporization [25,26], photodynamic therapy [27], microwave coagulation [28], argon plasma coagulation [29,30], and injection of anticancer agents [31] or ethanol [32] have been used.
- Tissue obliteration techniques should be applied only as palliative treatment in patients who cannot undergo endoscopic resection or surgery, because histology of the entire lesion, which is essential to judge curability, cannot be obtained.

Polypectomy

- Polypectomy is applied to the resection of protruding intramucosal cancers with a narrow base or stalk. The technique is the easiest to perform, but only a few cancers are amenable.
- Because the resected margin is burned with thermocoagulation, protruding cancers suspicious for submucosal invasion should be resected by EMR or other appropriate resection techniques.

EMR

- EMR can be accomplished by the inject, lift, and cut technique (eg, strip biopsy [1]) or by the inject, suck, and cut technique (eg, EMR with cap [2]).
- Indications for EMR include differentiated mucosal adenocarcinoma with elevation and size less than 2 cm and flat or depressed differentiated mucosal adenocarcinoma without ulcer and size less than 1 cm [33••].
- The inject, suck, and cut technique may obtain a large section more easily than the inject, lift, and cut technique [34].
- Retrospective analyses of the comparison between ESD and EMR showed that ESD increased en bloc and histologically complete resection rates compared with EMR but was associated with longer average operation times and a higher incidence of intraoperative bleeding and perforation [35,36•].

Disclosure

No potential conflict of interest relevant to this article was reported.