

## Retrospective Study

## Early gastric cancer diagnostic ability of ultrathin endoscope loaded with laser light source

Takuto Suzuki, Yoshiyasu Kitagawa, Rino Nankinzan, Taketo Yamaguchi

**ORCID number:** Takuto Suzuki (0000-0002-2706-6734); Yoshiyasu Kitagawa (0000-0003-1374-2292); Rino Nankinzan (0000-0003-1775-7811); Taketo Yamaguchi (0000-0003-0232-2508).

**Author contributions:** Suzuki T designed the research; Suzuki T, Kitagawa Y, Nankinzan R and Yamaguchi T performed the research; Suzuki T, Kitagawa Y and Nankinzan R analyzed the data; Suzuki T wrote the paper.

**Institutional review board statement:** The study was reviewed and approved by the Chiba Cancer Center Institutional Review Board.

**Informed consent statement:** All study participants provided informed written consent prior to study enrollment.

**Conflict-of-interest statement:** The authors have no conflicts of interest to declare.

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**Manuscript source:** Unsolicited

**Takuto Suzuki, Yoshiyasu Kitagawa, Rino Nankinzan,** Department of Endoscopy, Chiba Cancer Center, Chiba 260-8717, Japan

**Taketo Yamaguchi,** Department of Gastroenterology, Chiba Cancer Center, Chiba 260-8717, Japan

**Corresponding author:** Takuto Suzuki, MD, PhD, Doctor, Department of Endoscopy, Chiba Cancer Center, 666-2 Nitonachou, Chuo-ku, Chiba 260-8717, Japan. [taksuzuki@chiba-cc.jp](mailto:taksuzuki@chiba-cc.jp)

**Telephone:** +81-43-2645431

**Fax:** +81-43-2628680

## Abstract

### BACKGROUND

Conventionally, the low luminous intensity, low image resolution, and difficulty in operation have been reported with the ultrathin endoscope. However, it has markedly advanced recently. The improvement of the diagnostic ability is expected.

### AIM

To compare the early gastric cancer diagnostic ability of an ultrathin endoscope loaded with a laser light source and that of the conventional endoscope.

### METHODS

The target subjects were 375 consecutive patients who underwent endoscopy at our hospital for post-endoscopic submucosal dissection follow-up of gastric cancer from January to August 2018. During endoscopy, the ultrathin endoscope was used in 140 patients (37.3%), and the conventional endoscope was used in 235 patients (62.7%). Patient background was adjusted using the propensity score matching method, and gastric cancer detection ability was evaluated in the two groups.

### RESULTS

The gastric cancer detection rate was 7.8% in the ultrathin endoscope group and 7.0% in the conventional endoscope group, and the mean intragastric observation time was  $4.1 \pm 1.7$  min in the ultrathin endoscope group and  $4.1 \pm 1.9$  min in the conventional endoscope group, showing no significant differences between the groups. Moreover, the biopsy implementation rate was 31.8% in the ultrathin endoscope group and 41.1% in the conventional endoscope group, and the biopsy prediction rate was 17.9% and 13.2%, respectively, showing no significant differences between the groups.

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**Received:** December 3, 2018**Peer-review started:** December 3, 2018**First decision:** January 30, 2019**Revised:** February 13, 2019**Accepted:** February 22, 2019**Article in press:** February 22, 2019**Published online:** March 21, 2019

## CONCLUSION

The gastric cancer diagnostic ability of the ultrathin endoscope loaded with a laser light source was comparable to that of the conventional endoscope. The observation time was also comparable. Thus, endoscopy using the ultrathin endoscope loaded with the laser light source would be the first option in screening examinations of gastric cancer due to its low invasion.

**Key words:** Conventional endoscope; Gastric cancer; Laser light source; Screening; Ultrathin endoscope

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**Core tip:** The gastric cancer diagnostic ability of the ultrathin endoscope loaded with a laser light source is comparable to that of the conventional endoscope. From the view of low invasion, the ultrathin endoscope is superior to the conventional endoscope. Thus, endoscopy using the ultrathin endoscope loaded with the laser light source would be the first option in screening examinations of gastric cancer.

**Citation:** Suzuki T, Kitagawa Y, Nankinzan R, Yamaguchi T. Early gastric cancer diagnostic ability of ultrathin endoscope loaded with laser light source. *World J Gastroenterol* 2019; 25(11): 1378-1386

**URL:** <https://www.wjgnet.com/1007-9327/full/v25/i11/1378.htm>

**DOI:** <https://dx.doi.org/10.3748/wjg.v25.i11.1378>

## INTRODUCTION

Barium x-ray with photofluorography has been widely used in screening examinations including health checkups because it has the effect of decreasing gastric cancer fatality rate<sup>[1-3]</sup>. However, the sensitivity of this examination method was reportedly limited to 39% in the case of early gastric cancer<sup>[4]</sup>. In order to overcome this drawback, esophagogastroduodenoscopy (EGD) has adopted instead. Since the marked effect of EGD to suppress gastric cancer fatality rate was demonstrated recently, EGD has been widely used in gastric cancer diagnosis<sup>[5,6]</sup>. However, for the patients EGD is an unpleasant examination accompanied by afflictions such as nausea, gag reflex, and choking, and there are also cardiovascular loads<sup>[7-9]</sup>. Thus, diameter thinning has advanced in the evolution of endoscope, and even an examination using an ultrathin endoscope such as transnasal endoscopy has been promoted<sup>[10]</sup>.

It was reported that less problems, higher patient acceptability, and lower loads would accompany an ultrathin endoscope to the heart and lung than those with the conventional endoscope<sup>[11-15]</sup>. In disseminating endoscopy, an ultrathin endoscope is highly needed. In contrast, the low luminous intensity, low image resolution, and difficulty in operation were reported with the ultrathin endoscope in comparison with the conventional endoscope, and it was also pointed out that the examination time would be longer with the ultrathin endoscope due to the dark field of vision and lower absorption capacity (small channel diameter)<sup>[16]</sup>. At present, an endoscope using a laser light source has been developed. In comparison with the conventional endoscope using the xenon light source, the field of vision is bright and broad, and high image quality has been achieved with a laser light source. Furthermore, operation has also been improved by expansion of the channel diameter (forceps diameter).

Some studies reported that the early gastric cancer diagnostic ability is comparable between the ultrathin and conventional endoscopes, but in other reports the inferiority of the ultrathin endoscope to the conventional endoscope was reported<sup>[17-21]</sup>. In such reports, the low diagnostic capacity of the ultrathin endoscope was pointed out, particularly in the case of small early gastric cancer or gastric cancer in the U region<sup>[22]</sup>. At this time, the aim was to compare the early gastric cancer diagnostic ability between the ultrathin endoscope and the conventional endoscope loaded with the laser light source.

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## MATERIALS AND METHODS

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### Study design

This retrospective analysis of database on EGD was conducted at the Chiba Cancer Center, Japan. This was approved by the ethics committee of Chiba Cancer Center, and the contents were displayed on the notice board for in- and outpatients. The study was conducted in accordance with the World Medical Association's Declaration of Helsinki. All patients provided informed consent to undergo EGD. All authors had access to the study data and approved the final manuscript.

### Patients

The target patients were those who underwent endoscopic submucosal dissection (ESD) for gastric cancer at this hospital and were periodically undergoing endoscopy thereafter. At this hospital, post-ESD endoscopy is performed initially at 3 mo after ESD, at 1 yr after ESD, and thereafter once a year. Because gastric cancer develops metachronously, patients with a history of ESD have a high risk for gastric cancer. In this study, such patients were targeted. In addition, patients infected with *Helicobacter pylori* (*H. pylori*) must receive eradication therapy. There were 375 consecutive patients who underwent endoscopy at this hospital from January to August 2018 and were enrolled in this study. Patients with postoperative gastric remnant were excluded. At this hospital, the ultrathin endoscope was being used in the same manner as the conventional endoscope, and in the patients who prefer transnasal endoscopy, the ultrathin endoscope was used. In this study, the ultrathin endoscope was used in 140 patients (37.3%), and the conventional endoscope was used in 235 patients (62.7%). The endoscopists in charge were five specialists authorized by the Japan Gastroenterological Endoscopy Society and four non-specialists.

In order to investigate the diagnostic ability of the ultrathin endoscope, the backgrounds were adjusted with the group using the conventional endoscope by the propensity score (PS) matching method to compare gastric cancer detection rate as the primary evaluation item and intragastric observation time, biopsy implementation rate, biopsy prediction rate, and details of detected gastric cancers as the secondary evaluation items.

### Ultrathin endoscope using laser light source

An endoscopic system using a laser light source (LASEREO, Fujifilm, Japan) was used. This system has two lasers with different wavelengths. One is a white light laser (wavelength  $450 \pm 10$  nm) providing wide-spectrum white light illumination suitable for general observation. The other is a blue laser imaging mode laser (wavelength  $410 \pm 10$  nm) with characteristics of short wavelength and narrowband. Therefore, in comparison with the endoscope system using the conventional xenon light source, it is feasible to visualize a brighter and higher-resolution image. The ultrathin endoscope (EG-L580NW) used in this system is 5.8 mm in scope outside diameter, 2.4 mm in forceps diameter, and  $140^\circ$  in viewing angle showing markedly improved performance as compared with the previous ultrathin endoscope. It can be used in not only the transoral but also transnasal route. As the conventional endoscope, EG-L590WR, EG-L590ZW, or EG-L600ZW was used.

### Propensity score matching

We created a PS-matched cohort by attempting to match a patient who underwent the examination with an ultrathin endoscope with a patient who underwent the examination with a conventional endoscope (1:1 match) using a greedy nearest neighbor-matching technique. A caliper width of 0.05 of the standard deviation for the logit of the PS was used for the developed PS. After matching, crude comparisons of the matched cohorts were made. Upon matching, four covariates that could possibly influence the detection of gastric cancer were used, namely age, sex, degree of gastric mucosa atrophy, and endoscopist.

### Statistical analysis

The clinical data were calculated as mean value with standard deviation, median value with range, and rate with 95% confidence interval (CI). In comparison between the two groups, Student's *t*-test was used to analyze numerical values. Chi-square and Fisher's exact tests were used to analyze rate values. A *P*-value  $< 0.05$  was considered to indicate statistical significance. Statistical analyses were performed using SPSS version 23.0 for Windows (IBM Japan, Ltd., Japan).

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## RESULTS

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The ultrathin endoscope was used via the transnasal route in 41 patients (29.3%) and transoral route in 99 patients (70.7%). In the conventional endoscope group, a sedative agent was used in 74 patients (31.5%). Due to being post-ESD, the patients were supposed to have undergone *H. pylori* eradication therapy. *H. pylori*-positive patients accounted for only 3.7% of the whole. **Table 1** shows the patient backgrounds and results of the two groups before matching. After matching 140 patients of the ultrathin endoscope group and 235 patients of the conventional endoscope group, 129 patients in each group were adopted for analysis. The C-statistic of PS score was 0.557. **Table 2** shows the matching results and balances. **Table 3** shows the patient backgrounds of the two groups after matching. Gastric cancer was detected in 10 patients (7.8%, 95%CI 3.1%-12.4%) of the ultrathin endoscope group and 9 patients (7.0%, 95%CI 2.6%-11.4%) of the conventional endoscope group, showing no significant difference between the two groups ( $P = 0.81$ ). All detected gastric cancers were in the early stage, and the median tumor size (range) was 7.5 mm (3-30 mm) in the ultrathin endoscope group and 6.0 mm (3-15 mm) in the conventional endoscope group, showing no significant difference between the two groups ( $P = 0.42$ ). The region (U/M+L) of detected gastric cancer was 4/6 in the ultrathin endoscope group and 2/7 in the conventional endoscope group, showing no significant difference ( $P = 0.41$ ) (**Table 4**). In addition, the mean intragastric observation time was  $4.1 \pm 1.7$  min in the ultrathin endoscope group and  $4.1 \pm 1.9$  min in the conventional endoscope group, showing no significant difference ( $P = 0.96$ ). The biopsy implementation rate was 31.8% (95%CI 23.8%-39.8%) in the ultrathin endoscope group and 41.1% (95%CI 32.6%-49.6%) in the conventional endoscope group, showing no significant difference ( $P = 0.12$ ) but a tendency to be lower in the former. The biopsy prediction rate was 17.9% (95%CI 7.9%-27.9%) and 13.2% (95%CI 5.2%-21.2%) in the ultrathin and conventional endoscope groups, respectively, showing no significant difference ( $P = 0.48$ ) but a tendency to be lower also in the latter (**Table 5**). **Figures 1 and 2** show the patients in whom gastric cancer was actually detected.

## DISCUSSION

In this study it was shown that the ultrathin endoscope loaded with a laser light source can detect gastric cancer at the same rate as the conventional endoscope. Until recently, the problems with the ultrathin endoscope were dark images, low image quality, and weak absorption power. The inferiority of the ultrathin endoscope to the conventional endoscope in gastric cancer detection rate has been reported<sup>[17-21]</sup>. However, the ultrathin endoscope loaded with the laser light source is markedly different from the conventional endoscope system using the xenon light source, and the image quality and brightness have been remarkably improved. In this study, patients with a history of ESD for gastric cancer were enrolled. Gastric cancer tends to multiply metachronously. In addition, according to the World Health Organization, *H. pylori* is the definite carcinogen of gastric cancer, and the majority of patients targeted in this study received *H. pylori* eradication therapy. The onset rate of gastric cancer is reduced by *H. pylori* eradication therapy, but a certain risk of gastric cancer remains even after eradication. Therefore, such patients have a higher risk of gastric cancer than the general population<sup>[23]</sup>. The ultrathin endoscope showed a diagnostic ability that was not inferior to that in the conventional endoscope even in such patients.

It was thus far unavoidable to extend the examination time due to the poor absorption capacity, dark image, and narrow viewing angle, but in the case of the ultrathin endoscope loaded with the laser light source, the examination time was comparable to the conventional endoscope, due to the improvement of absorption capacity brought about by expansion of the forceps diameter and the expansion of observation range brought about by the improvement of viewing angle and brightness. As one of the factors, it is estimated that the amount of highly viscous gastric mucosa was small after the aforementioned *H. pylori* eradication therapy and the time required for mucosa washing and accompanying absorption could be shortened. However, because the number of *H. pylori*-negative patients is expected to increase hereafter, the situation was considered to reflect the current status.

Detected gastric cancers were not different between the two groups in lesion site and size. The lower diagnostic ability of the ultrathin endoscope was pointed out in the previous studies in the diagnosis of small gastric cancers < 20 mm in the U region, but such tendency was not seen in this study<sup>[21,22]</sup>. Furthermore, the biopsy implementation and prediction rates were not significantly different between the two groups. There was rather a tendency of the biopsy implementation rate to be lower and the biopsy prediction rate to be higher in the ultrathin endoscope group. The



**Table 1 Clinical background, gastric cancer detection rates, and the details of the two groups before matching**

	Ultrathin endoscope	Conventional endoscope	P value
Number of screened subjects	140	235	
Transnasal	41 (29.3%)	0 (0%)	-
Sedation	16 (11.4%)	74 (31.5%)	< 0.001
Age in yr, median (range)	74 (43-89)	73 (43-93)	0.49
Gender, male	99 (70.7%)	187 (79.6%)	0.05
<i>Helicobacter pylori</i> positive	6 (4.3%)	9 (3.8%)	0.83
Atrophy, open type	108 (77.1%)	197 (83.8%)	0.11
Operator (expert/nonexpert)	99/41	178/57	0.28
Number of gastric cancer	12	20	
Number of subjects with gastric cancer/detection rate	12 (8.6%)	18 (7.7%)	0.75
Location (U/M, L)	4/4, 4	3/11, 6	0.22
Size in mm, median (range)	5 (3-30)	6.5 (3-18)	0.37
Morphological type (I, IIa/IIb, IIc)	0, 6/0, 6	2, 6/0, 12	0.09
Depth of invasion (m/sm)	10/2	20/0	0.06

reason for such tendency was not clear, but it was suggested that the ultrathin endoscope would be able to provide appropriate findings.

There are limitations in this study. First, this was a retrospective study, but the bias could be minimized in the investigation by matching the backgrounds using the PS matching method. Next, the ultrathin endoscope was used via not only the transnasal but also the transoral route in this study for pooled analysis, and a sedative agent was frequently used in the conventional endoscope group. Therefore, the influence of these factors on the analysis cannot be negated. Lastly, this study was performed in a limited number of patients at a single medical institution. It is therefore desired to perform a prospective multicenter study hereafter.

As EGD becomes widely known as a gastric cancer diagnostic procedure, the ultrathin endoscope may become the first-choice screening examination in gastric cancer diagnosis due to its low invasion.

**Table 2 Confirmation of propensity score matching results and balances**

	Full cohort			Propensity score-matched cohort		
	Conventional	Ultrathin	ASD, %	Conventional	Ultrathin	ASD, %
<i>n</i>	235	140		129	129	
Age in yr	73.1 ± 7.6	73.2 ± 7.6	1.9	73.2 ± 7.6	73.4 ± 7.1	2.7
Male	187, 79.6	99, 70.7	20.6	98, 76.0	97, 75.2	1.8
Specialist	178, 75.7	99, 70.7	11.4	95, 73.6	92, 71.3	5.2
Atrophy	198, 84.3	108, 77.1	18.1	103, 79.8	107, 82.9	8.0

Data: mean ± SD or *n*, %. ASD: Absolute standardized difference.

**Table 3 Clinical background of the two groups after matching**

	Ultrathin endoscope	Conventional endoscope	<i>P</i> value
Number of screened subjects	129	129	
Age in yr, median (range)	74 (52-89)	74 (47-87)	0.46
Gender, males	108 (77.1%)	99 (76.7%)	0.16
<i>Helicobacter pylori</i> positive	5 (3.9%)	4 (3.1%)	0.73
Atrophy, open type	107 (82.9%)	103 (79.8%)	0.52
Operator, expert/nonexpert	92/37	95/34	0.68

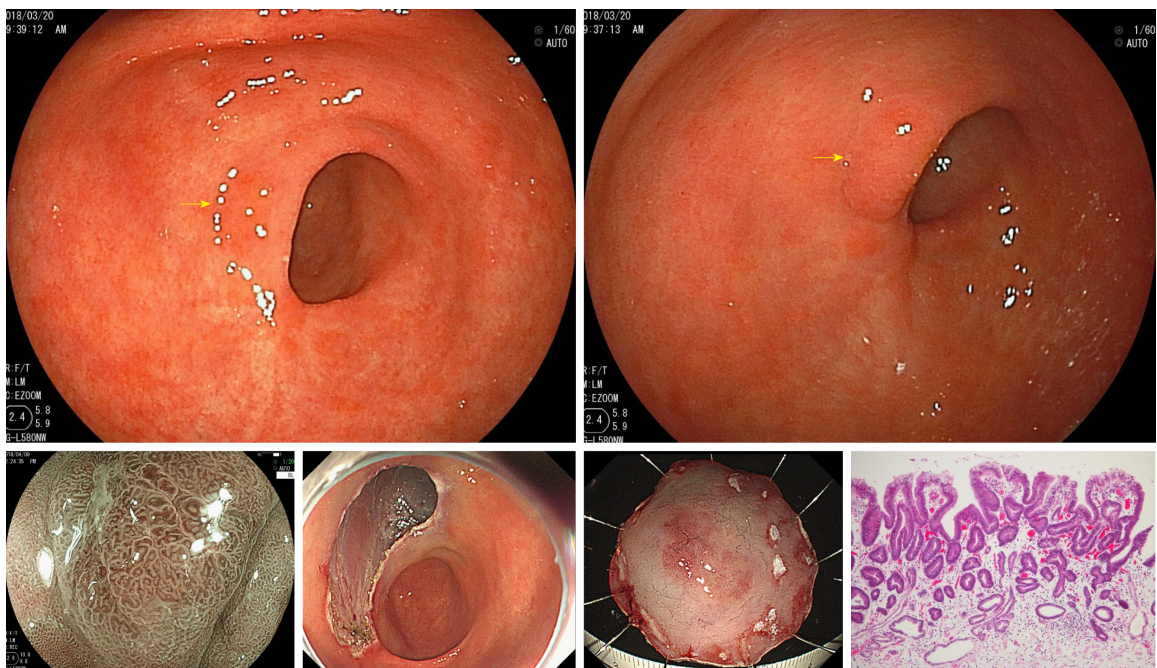
**Table 4 Gastric cancer detection rates and details of detected gastric cancers in the two groups after matching**

	Ultrathin endoscope	Conventional endoscope	<i>P</i> value
Number of gastric cancer	10	9	
Number of subjects with gastric cancer/detection rate	10 (7.8%)	9 (7.0%)	0.81
Location (U/M + L)	4/4 + 2	2/6 + 1	0.41
Size in mm, median (range)	7.5 (3-30)	6.0 (3-15)	0.42
Morphological type (I, IIa/IIb, IIc)	0, 6/0, 4	0, 2/0, 7	0.10
Depth of invasion (m/sm)	8/2	9/0	0.16

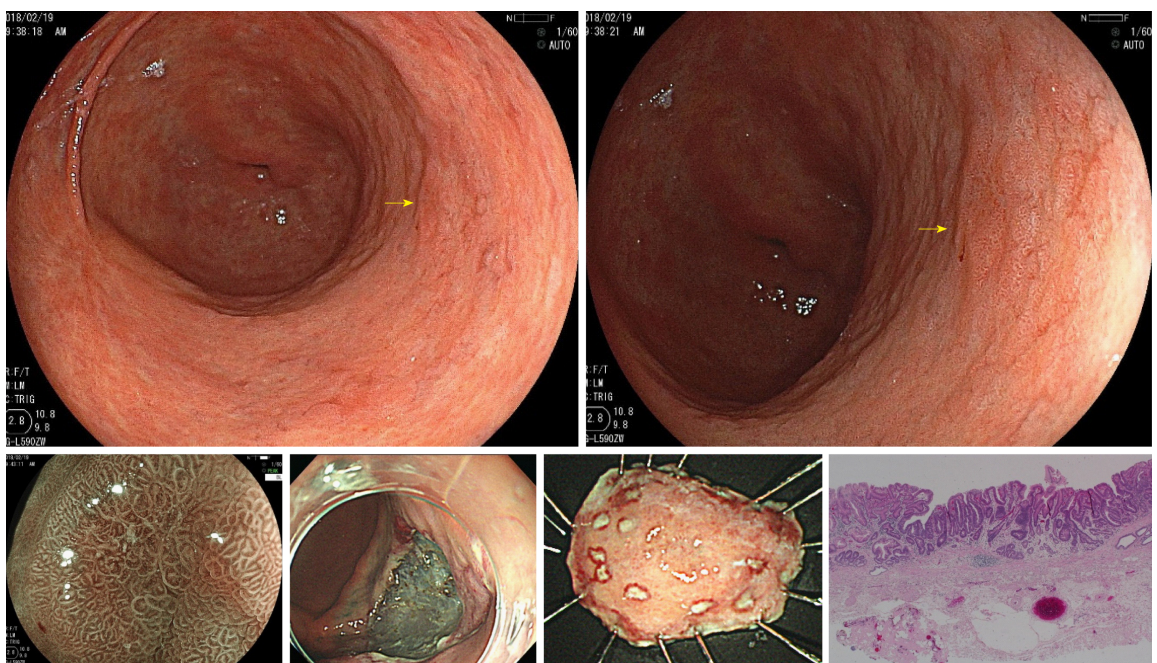
**Table 5 Comparison of intragastric observation time, biopsy implementation rate, and biopsy prediction rate between the two groups**

	Ultrathin endoscope	Conventional endoscope	<i>P</i> value
Observation time of stomach in min	4.1 ± 1.7	4.1 ± 1.9	0.96
Biopsy implementation rate	31.8% (41/129) (95%CI 23.8-39.8)	41.1% (53/129) (95%CI 32.6-49.6)	0.12
Biopsy prediction rate	17.9% (10/56) (95%CI 7.9-27.9)	13.2% (9/68) (95%CI 5.2-21.2)	0.48

CI: Confidence interval.



**Figure 1** A patient with gastric cancer detected through the ultrathin endoscope. Ila lesion in the vicinity of previous endoscopic submucosal dissection scar on the anterior wall of the antrum. Results of endoscopic submucosal dissection: 10 mm × 10 mm, tubular adenocarcinoma, well-differentiated type, pT1a (M).



**Figure 2** A patient with gastric cancer detected through the conventional endoscope. Endoscopic submucosal dissection scar on the anterior wall of the antrum and IIc lesion on the posterior wall. Results of endoscopic submucosal dissection: 5 mm × 5 mm, tubular adenocarcinoma, well-differentiated type, pT1a (M).

## ARTICLE HIGHLIGHTS

### Research background

An ultrathin endoscope has low luminous intensity, low image resolution, and difficulty in operation. However, the ultrathin endoscopy is a useful tool for screening endoscopy because of its low invasion.

### Research motivation

Recently endoscopic technology has markedly advanced. The improvement of the diagnostic ability of ultrathin endoscope has also improved. Evaluating the diagnostic ability of the ultrathin endoscope is warranted.



### Research objectives

In this study, early gastric cancer diagnostic ability of an ultrathin endoscope loaded with a laser light source was compared with that of the conventional endoscope.

### Research methods

The study subjects were 375 consecutive patients who underwent endoscopy at our hospital for post-endoscopic submucosal dissection follow-up of gastric cancer from January to August 2018. During endoscopy, the ultrathin endoscope was used in 140 patients (37.3%), and the conventional endoscope was used in 235 patients (62.7%). Patient background was adjusted using the propensity score matching method, and gastric cancer detection ability was evaluated in the two groups.

### Research results

The gastric cancer detection rate was 7.8% in the ultrathin endoscope group and 7.0% in the conventional endoscope group, and the mean intragastric observation time was  $4.1 \pm 1.7$  min in the ultrathin endoscope group and  $4.1 \pm 1.9$  min in the conventional endoscope group, showing no significant differences between the groups. Moreover, the biopsy implementation rate was 31.8% in the ultrathin endoscope group and 41.1% in the conventional endoscope group, and the biopsy prediction rate was 17.9% and 13.2%, respectively, showing no significant differences between the groups.

### Research conclusions

The gastric cancer diagnostic ability of the ultrathin endoscope loaded with a laser light source was comparable to that of the conventional endoscope. The observation time was also comparable. Thus, endoscopy using the ultrathin endoscope loaded with the laser light source would be the first option in screening examinations of gastric cancer due to its low invasion.

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**P- Reviewer:** Christodoulidis G, Sitkin S

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