Diseases of the Esophagus (2009) **22**, 439–446
DOI: 10.1111/j.1442-2050.2008.00925.x

DISEASES OF THE ESOPHAGUS

Original article

Assessment of novel endoscopic techniques for visualizing superficial esophageal squamous cell carcinoma: autofluorescence and narrow-band imaging

Y. Yoshida,[1] K. Goda,[1] H. Tajiri,[1,2] M. Urashima,[3] N. Yoshimura,[1] T. Kato[2]

[1]*Departments of Endoscopy and* [2]*Gastroenterology and Hepatology, and* [3]*Division of Clinical Research & Development, The Jikei University School of Medicine, Tokyo, Japan*

SUMMARY. **Lugol chromoendoscopy (LCE) is a useful technique for visualizing superficial esophageal squamous cell carcinoma (SESCC), but the stimulating effect of the Lugol solution can sometimes cause clinical problems. Newly developed techniques such as narrow-band imaging (NBI) and autofluorescence imaging (AFI) enable SESCC to be easily visualized without LCE. This study aimed to assess the visualizing power of white-light imaging (WLI), NBI, and AFI, compared with LCE. Sixteen patients with 16 SESCCs underwent LCE and endoscopy with NBI and AFI before endoscopic or surgical treatment. Twenty sets of endoscopic SESCC images were prepared, each of which contained still images from WLI, NBI, AFI, and LCE. The image sets were shown to 25 endoscopists, who then each completed a questionnaire about the ease-of-detection of the SESCCs, scoring WLI, NBI, and AFI images with reference to a perfect score for LCE; mean scores were compared. Overall, significantly higher scores were given for NBI than for WLI and AFI, with no significant difference between WLI and AFI. Stratification by endoscopist characteristics indicated that younger or less experienced endoscopists gave significantly higher scores for AFI than WLI. Stratification by lesion characteristics revealed that AFI had significantly higher scores than WLI for flat/elevated lesions or those with diameter ≥20 mm; scores were significantly lower for depressed lesions or those with diameter <20 mm. For SESCC, the visualizing power of NBI seems more similar to that of LCE than AFI or WLI: NBI might be more useful than AFI or WLI in detecting SESCC. AFI seems to have both superior and inferior visualizing power to WLI depending on characteristics of endoscopists or SESCC lesions.**

KEY WORDS: **autofluorescence imaging, endoscopy, narrow-band imaging, squamous cell carcinoma, superficial esophageal cancer.**

INTRODUCTION

The prognosis of squamous cell carcinoma (SCC) of the esophagus, if detected at an advanced stage, is poor, worse than that of Barrett's adenocarcinoma.[1,2] Superficial esophageal squamous cell carcinoma (SESCC), in which the infiltration is confined to the mucosa or submucosa, has a better prognosis than advanced SCC.[3] Mucosal SCC, which is highly likely to be indicated for endoscopic mucosal resection (EMR), has the best prognosis.[3,4] Consequently, early detection is very important.

Lugol chromoendoscopy (LCE) is useful for the early detection of esophageal SCC because SESCC is clearly visible as an unstained area.[5,6] A large prospective study recently revealed LCE to increase the sensitivity of esophageal endoscopy for the detection of high-grade squamous dysplasia and SCC.[7] However, due to the stimulus of Lugol solution, LCE occasionally causes agitation, heartburn, or severe cough, and it also carries a risk of allergic reaction. Moreover, a major disadvantage of LCE is the increased duration of the endoscopic examination.[7]

The incidence of esophageal cancer has been reported to be much lower than that of stomach and colon cancer both in Japan and worldwide.[8] Therefore, as the incidence of SESCC must be even lower, ordinary endoscopists take a long time to gain adequate experience in its diagnosis and treatment.

Address correspondence to: Dr Kenichi Goda, MD, PhD, Department of Endoscopy, The Jikei University School of Medicine, Nishi-shimbashi 3-25-8, Minato-ku, Tokyo 105-8461, Japan. Email: kengoendoscopy@hotmail.co.jp
Contribution to the paper: Y. Y., 2/10; K. G., 3/10; H. T., 1/10; M. U., 2/10; N. Y., 1/10; T. K., 1/10.

In recent years, the novel imaging techniques of narrow-band imaging (NBI) and autofluorescence imaging (AFI) have been developed and their clinical usefulness in visualizing SESCC without LCE is now being reported.[9,10] Until recently, the AFI endoscopy system used a fiber optic endoscope, which provided an image of insufficient quality.[11] Newly developed AFI technology is now incorporated in video endoscopy systems, and the image quality has improved remarkably.[12] Most studies of this AFI system have looked at diagnosing dysplasia or adenocarcinoma in Barrett's esophagus,[13,14] but there have been quite few reports for SESCC also.[9] For NBI, there have been studies involving many cases of pharyngeal and esophageal SCC.[10,15,16]

To the best of our knowledge, there have been no reports comparing NBI and AFI with LCE in visualizing SESCC; the clinical usefulness of AFI in SESCC remains largely unknown, and it is not known whether NBI or AFI is more suitable for detecting SESCC. Here, we carried out a questionnaire survey to assess the visualizing power of conventional white-light imaging (WLI), NBI, and AFI, compared with LCE.

MATERIALS AND METHODS

Between September 2005 and October 2006, 24 consecutive patients with 25 lesions of esophageal SCC underwent work-up endoscopy with NBI, AFI, and Lugol staining at the Jikei University Hospital. Of the 25 lesions, 16 lesions in 16 patients were endoscopically or surgically treated and confirmed histologically as SESCC. All of the nine excluded lesions showed large fungating or ulcerating tumor. Five of the nine lesions were surgically treated and histologically determined as advanced SCC that had invaded the muscularis propria or deeper. Four of the nine lesions were suspected to be advanced SCC by endoscopic ultrasonography or computed tomography and treated by radiochemotherapy. Written informed consent was obtained from all patients before examination and treatment.

Histopathologic findings were evaluated according to the Guideline for the Clinical and Pathological Studies in Carcinoma of the Esophagus.[17]

Endoscopy imaging system

We used a prototype endoscopy system (XGIF-Q240FZ, Olympus Medical Systems Corp., Tokyo, Japan) comprising a high-resolution white-light video endoscope equipped with NBI and AFI systems. The light source unit (XCLV-260LIP, Olympus Medical Systems Corp.) has two sets of rotary filters in front of a xenon bulb: one for WLI and NBI, and the other for AFI. The prototype endoscope was equipped with two separate high-quality monochromatic charge-coupled devices (CCDs): one for high-resolution WLI and NBI, and the other for AFI. It is easy to switch from WLI mode to NBI or AFI mode in a few seconds by pushing the control knob on the endoscope.

NBI

An NBI system has a high-resolution mode in which the WLI is composed of sequential images taken through red, green, and blue (RGB) band-pass filters. In NBI mode, the central wavelengths of the RGB filters (445 nm [blue], 540 nm [green], and 620 nm [red]) are narrowed to 415 nm (blue) and 540 nm (green). Using the wavelength dependence of the light penetration depth into the mucosa and the hemoglobin absorption characteristics in the surface layer, NBI technology allows the mucosal surface layer to be displayed in high contrast and enhances hemoglobin-rich areas such as blood vessels.

AFI

White light from a xenon lamp is divided using an AFI-dedicated optical filter into blue excitation light (390–470 nm) and green reflected light (540–560 nm). The blue excitation light causes living tissue to autofluoresce. A barrier filter installed in front of the CCD allows passage of autofluorescence with a wavelength between 470 and 690 nm only, cutting the blue excitation light and detecting weak autofluorescence. These two types of light are captured by the CCD at the distal end of the scope and converted to an electrical signal. In the video processor, the light signals of autofluorescence and the green-reflected light are converted into green and red/blue data, respectively, then synthesized into the AFI color image that is displayed on the monitor.

Endoscopic procedures

Patients underwent upper endoscopy under conscious sedation with intravenous pethidine hydrochloride (35–70 mg; Opystan, Mitsubishi Tanabe Pharma Corporation, Osaka, Japan) supplemented with flunitrazepam (0.3–0.6 mg; Rohypnol, Chugai Pharmaceutical Co. Ltd., Tokyo, Japan). In order to suppress esophageal peristalsis, either scopolamine butylbromide (20–40 mg; Buscopan, Boehringer Ingelheim GmbH, Ingelheim, Germany) or Glucagon (1–2 mg; Glucagon G Novo, Novo Nordisk, Bagsværd, Denmark) was also administered intravenously.

All endoscopic procedures were carried out by an endoscopist (K.G.) proficient in both NBI and AFI endoscopy. All four endoscopic procedures (WLI, NBI, AFI, and LCE) were conducted for all 16 SESCCs. LCE was performed using a spray catheter

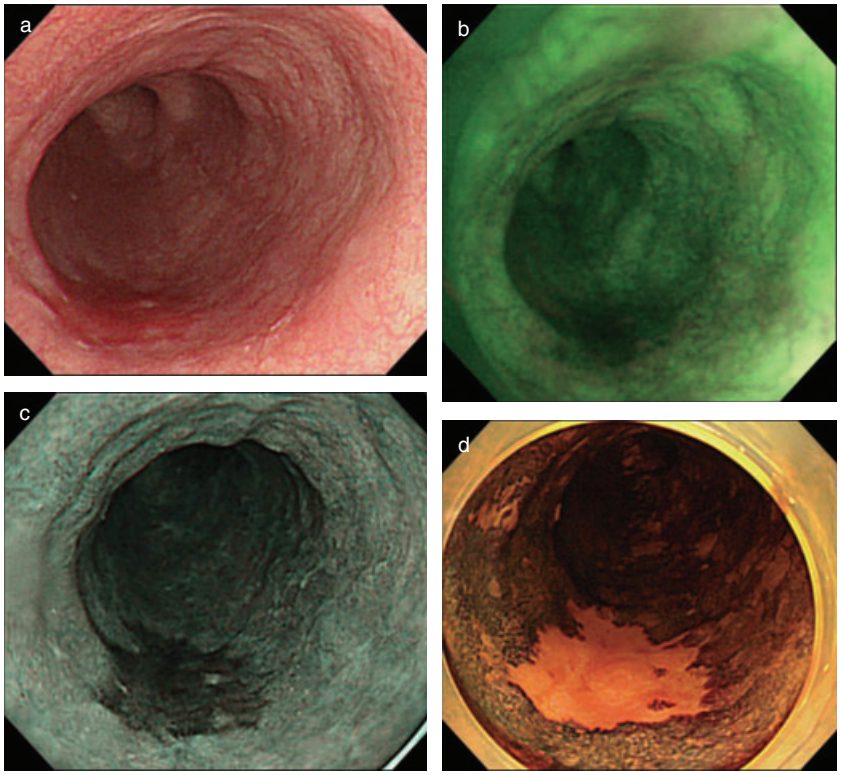

Fig. 1 Images of superficial esophageal squamous cell carcinoma: depressed-type mucosal cancer, <20 mm in diameter. (a) The reddish and slightly depressed lesion is seen at the 6 o'clock position on the ordinary white-light image. (b) On the autofluorescence image, the lesion shows as dark green. (c) The lesion is revealed as a well-demarcated brownish area on the narrow-band image. (d) Lugol chromoendoscopy depicts the lesion as an unstained area corresponding to the reddish and brownish areas of the white-light image and narrow-band image, respectively.

and 10–20 mL of a 2% Lugol solution. Images of all the SESCCs from each method were saved digitally.

Review and setup of endoscopic images

The endoscopic images were all reviewed retrospectively by two endoscopists (Y.Y., K.G.) and all endoscopic findings for each lesion were mutually agreed upon. Then, the two endoscopists produced 20 image sets selected from endoscopic images of the 16 SESCCs, each set containing still images of WLI, NBI, AFI, and LCE of the same lesion taken from same angle.

Questionnaire survey

A questionnaire survey was administered to 25 endoscopists, not including the two in charge of the retrospective review (Y.Y., K.G.), on the same day and while they were all gathered in one room. Prior to the questionnaire, the two endoscopists (Y.Y., K.G.) demonstrated representative endoscopic findings of non-tumorous mucosa and SESCCs on AFI and NBI images as follows: non-tumorous mucosa of esophageal lumen was displayed as light green on AFI images and as gray on NBI images. Esophageal blood vessels were displayed as dark green on AFI images and as brown or cyan on NBI images. The SESCCs were depicted as dark green or magenta areas on AFI images, and as brownish areas on NBI images (Figs 1,2).

Then, the aforementioned 20 image sets were shown to the endoscopists who simultaneously watched all four still images (WLI, NBI, AFI, and LCE) in each image set on one screen at a time. The image sets were projected sequentially, with each set being displayed for 1 min. The endoscopists were asked to complete a questionnaire regarding the ease-of-detection of the SESCCs, scoring the WLI, NBI, and AFI images on a scale of 0 to 10 relative to a perfect score of 10 for LCE images as follows: equal or comparable to LCE image, 10 or 9; easy to detect but inferior to LCE image, 8 or 7; somewhat easy to detect, 6 or 5; somewhat difficult to detect, 4 or 3; difficult to detect, 2 or 1; impossible to detect, 0. The mean scores for WLI, NBI, and AFI images, including stratified analysis by endoscopist or lesion characteristics, were then compared.

Statistical analysis

All quantitative data were summarized as mean ± standard deviation. For the questionnaire survey, mean scores for WLI, NBI, and AFI images

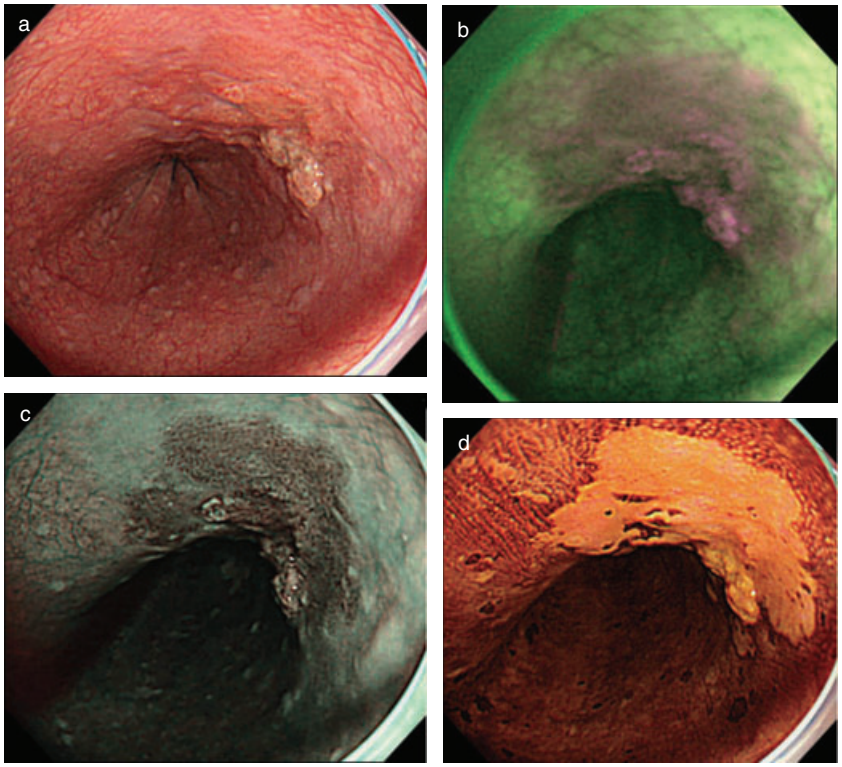

Fig. 2 Images of superficial esophageal squamous cell carcinoma: flat/elevated-type submucosal cancer, ≥20 mm in diameter. (a) The reddish flat lesion with white elevated components is seen at the 1 o'clock position on the ordinary white-light image. (b) On the autofluorescence image, elevated components of the lesion are displayed as magenta and the surrounding flat part as magenta or dark green. (c) The lesion is revealed as a well-demarcated brownish area on the narrow-band image. (d) Lugol chromoendoscopy depicts the lesion as an unstained area corresponding to the reddish and brownish areas of the white-light image and the narrow-band image, respectively.

evaluated by all 25 endoscopists were compared, and then the mean scores were compared versus stratified endoscopist characteristics: age (<35 and ≥35 years), endoscopy experience (<10 and ≥10 years), board certification of the Japan Gastroenterological Endoscopy Society (with and without), number of SESCC cases previously encountered (<15 and ≥15 cases), experience of AFI endoscopy (with and without), and experience of NBI endoscopy (with and without). Mean scores for the three kinds of endoscopy images were also compared versus stratified lesion characteristics: diameter of tumor (small, <20 mm; large, ≥20 mm) and macroscopic tumor type (depressed and flat/elevated).

Statistical comparisons of the scores were carried out using the Wilcoxon signed rank test. All probability values were assumed to be statistically significant at <0.05. All statistical analyses were performed using statistical software (STATA 8.0; STATA Co, College Station, Texas, USA).

RESULTS

Table 1 summarizes the clinicopathologic and endoscopic findings of the 16 enrolled patients with 16 SESCCs. There were 14 men and two women, with a mean age of 65 ± 9 years (range 52–79 years). The mean diameter of the 16 lesions was 22 ± 16 mm

Table 1 Patient characteristics

Age (years; mean ± SD, range)	65 (9 (52–79)	
Gender (*n* = male, %)	14 (88%)	
Diameter of tumor (mm; mean ± SD, range)	22 (16 (6–70)	
Differentiated type of tumor (*n*, %)	Well to moderately 15 (94%)	Poorly 1 (6%)
Tumor depth (*n*, %)	Mucosa 14 (88%)	Submucosa 2 (12%)
Macroscopic tumor type (*n*, %)	Depressed 10 (63%)	Flat/elevated 6 (37%)
Color tone of tumor (*n*)		
WLI (Reddish/Whitish/Same†)	8/0/2	3/1/2
AFI (Dark green/Magenta/Same†)	8/2/0	2/3/1
NBI (Brownish/Same†)	9/1	5/1
LCE (Unstained/Same†)	10/0	6/0

†Same color as surrounding non-tumorous mucosa. AFI, autofluorescence imaging; LCE, lugol chromoendoscopy; NBI, narrow-band imaging, SD, standard deviation; WLI, white-light imaging.

(range 6–70 mm). All 16 lesions were endoscopically or surgically resected and confirmed histologically as SCC with no adenocarcinoma or special-type carcinoma. Of the 16 lesions, 15 demonstrated well to moderately differentiated SCC and one was poorly differentiated. The 16 SESCCs histologically consisted of 14 mucosal and two submucosal carcinomas; macroscopically, 10 (62%) lesions were of the depressed type, and six (38%) of the flat/elevated type.

On WLI images, 11 (69%) of the 16 lesions were reddish in appearance, one (6%) was whitish and four (25%) were the same color as the surrounding non-tumorous mucosa. On AFI images, the non-tumorous mucosa background was displayed as light green: 10 (63%) of the lesions showed as a dark-green area, five (31%) as magenta, and one (6%) appeared as the same color as the surrounding non-tumorous mucosa. On NBI images, the background of the non-tumorous mucosa was displayed as a grayish tone: 14 (88%) of the 16 lesions were displayed as a brownish area and two (12%) as the same color as the surrounding non-tumorous mucosa. LCE depicted all 16 lesions (100%) as an unstained area. Image sets representative of those used in the questionnaire survey are shown in Figures 1 and 2.

The mean scores for ease-of-detection for SESCCs, evaluated by all 25 endoscopists, are shown in Table 2. The mean score for NBI was significantly higher than that for WLI and AFI. No significant differences between the WLI and AFI scores were found.

Table 3 shows the mean scores for ease-of-detection for SESCCs stratified by endoscopist characteristics. In all the analyses, regardless of experience of NBI endoscopy, the mean scores for NBI were significantly higher than those for WLI and AFI. The mean scores for AFI were significantly higher than those for WLI among young endoscopists, those who had less than 10 years of endoscopy experience, those who had no board certification, and those who had previously encountered fewer than 15 cases of SESCC. No significant differences in the mean scores between WLI and AFI were seen with respect to other endoscopist characteristics including experience of AFI endoscopy.

Table 4 presents the mean scores for ease-of-detection for SESCCs stratified by lesion characteristics. The mean scores for NBI were significantly

Table 2 Overall assessment of mean scores for ease-of-detection of superficial esophageal squamous cell carcinomas

		Ease-of-detection (Mean score ± SD)	*P*-value*	
All endoscopists ($n = 25$)	WLI	6.6 ± 2.2	$P < 0.0001$	NS
	NBI	7.9 ± 2.1	$P < 0.0001$	
	AFI	6.7 ± 2.3		

*Wilcoxon signed rank test. AFI, autofluorescence imaging; NBI, narrow-band imaging; WLI, white-light imaging.

Table 3 Comparison of the mean scores for ease-of-detection of superficial esophageal squamous cell carcinomas, stratified by endoscopist characteristics

		Mean Score ± SD	*P*-value*		Endoscopy experience		Mean score ± SD	*P*-value*		Board certification		Mean score ± SD	*P*-value*	
Age														
<35 years ($n = 13$)	WLI	6.5 ± 2.3	$P < 0.0001$	$P = 0.0035$	<10 years ($n = 14$)	WLI	6.5 ± 2.3	$P < 0.0001$	$P = 0.014$	With ($n = 13$)	WLI	6.7 ± 2.1	$P < 0.0001$	NS
	NBI	7.8 ± 2.2	$P < 0.0001$			NBI	7.8 ± 2.2	$P < 0.0001$			NBI	8.1 ± 2.0	$P < 0.0001$	
	AFI	7.0 ± 2.1				AFI	6.8 ± 2.2				AFI	6.6 ± 2.4		
≥35 years ($n = 12$)	WLI	6.8 ± 2.1	$P < 0.0001$	NS	≥10 years ($n = 11$)	WLI	6.9 ± 2.1	$P < 0.0001$	NS	Without ($n = 12$)	WLI	6.5 ± 2.1	$P < 0.0001$	$P = 0.007$
	NBI	8.2 ± 2.0	$P < 0.0001$			NBI	8.2 ± 2.0	$P < 0.0001$			NBI	7.8 ± 2.2	$P < 0.0001$	
	AFI	6.6 ± 2.5				AFI	6.8 ± 2.4				AFI	7.0 ± 2.2		
Number of SESCC case previously encountered		Mean score ± SD	*P*-value*		Experience of AFI		Mean score ± SD	*P*-value*		Experience of NBI		Mean score ± SD	*P*-value*	
<15 cases ($n = 8$)	WLI	6.3 ± 2.3	$P < 0.0001$	$P = 0.009$	With ($n = 10$)	WLI	7.0 ± 2.0	$P < 0.0001$	NS	With ($n = 11$)	WLI	7.0 ± 2.0	$P < 0.0001$	NS
	NBI	7.7 ± 2.2	$P < 0.0001$			NBI	8.2 ± 2.0	$P < 0.0001$			NBI	8.2 ± 1.9	$P < 0.0001$	
	AFI	6.8 ± 2.2				AFI	7.0 ± 2.3				AFI	7.0 ± 2.2		
≥15 cases ($n = 17$)	WLI	7.0 ± 2.1	$P < 0.0001$	NS	Without ($n = 15$)	WLI	6.4 ± 2.3	$P < 0.0001$	NS	Without ($n = 14$)	WLI	6.4 ± 2.4	$P < 0.0001$	NS
	NBI	8.2 ± 2.0	$P < 0.0001$			NBI	7.8 ± 2.2	$P < 0.0001$			NBI	7.8 ± 2.2	$P < 0.0001$	
	AFI	6.9 ± 2.4				AFI	6.7 ± 2.3				AFI	6.6 ± 2.4		

*Wilcoxon signed rank test. AFI, autofluorescence imaging; NBI, narrow-band imaging; SD, standard deviation; SESCC, superficial squamous cell carcinoma; WLI, white-light imaging.

Table 4 Comparison of the mean scores for ease-of-detection of superficial esophageal squamous cell carcinomas, stratified by lesion characteristics

Diameter of tumor		Mean score ± SD	*P*-value*		Macroscopic tumor type		Mean score ± SD	*P*-value*	
Small, <20 mm ($n = 9$)	WLI	6.4 ± 2.5	$P < 0.0001$	$P = 0.003$	Depressed ($n = 10$)	WLI	7.3 ± 2.0	$P < 0.0001$	$P = 0.0006$
	NBI	7.9 ± 2.2	$P < 0.0001$			NBI	9.0 ± 1.5	$P < 0.0001$	
	AFI	6.1 ± 2.5				AFI	6.9 ± 2.0		
Large, ≥20 mm ($n = 7$)	WLI	6.9 ± 1.9	$P < 0.0001$	$P < 0.0001$	Flat/elevated ($n = 6$)	WLI	5.7 ± 2.1	$P < 0.0001$	$P = 0.0001$
	NBI	8.0 ± 2.0	$P = 0.0014$			NBI	6.4 ± 2.0	NS	
	AFI	7.5 ± 1.8				AFI	6.6 ± 2.6		

*Wilcoxon signed rank test. AFI, autofluorescence imaging; NBI, narrow-band imaging; SD, standard deviation; WLI, white-light imaging.

higher than those for WLI and AFI in all groups except for flat/elevated lesions, in which group the mean score for NBI was lower than that for AFI but the difference was not significant. The mean scores for AFI were significantly higher than those for WLI in large (diameter ≥20 mm) and flat/elevated lesions but significantly lower than those for WLI in small (diameter <20 mm) and depressed lesions.

DISCUSSION

Based on the results of this study, we suggest that the novel-enhanced imaging techniques, NBI and AFI, could not replace LCE but could be a potential technology in detecting SESCC because their highest mean score, given to NBI in nonstratified analysis, was around eight points, which means 'easy to detect but inferior to LCE.'

NBI images were more similar to those of LCE than those of WLI or AFI: the visualizing power of NBI seems most similar to that of LCE, and NBI might be more useful than AFI or WLI in detecting SESCC.

Approximately 88% of the 16 SESCCs were displayed as a well-demarcated brownish area on NBI. We suggest that SESCCs often appear as reddish lesions either because they are hemoglobin-rich or because microvascular proliferation and/or dilatation are involved.[10] Therefore, NBI appears to facilitate clear recognition of SESCCs without Lugol staining.

Recent clinical reports have indicated the utility of NBI in diagnosing superficial pharyngeal or esophageal SCC. NBI endoscopy was considered helpful in the early detection of SCC in oropharyngeal and hypopharyngeal sites that were unsuitable for LCE due to the risk of aspiration.[15] In a multicenter study, NBI endoscopy was suggested to be better than WLI endoscopy in the detection and diagnostic accuracy of pharyngeal and esophageal SCC,[16] and Yoshida *et al.* reported that NBI improved the diagnostic accuracy of magnifying endoscopy for assessing the invasion depth of SESCC.[10] Therefore, NBI is a promising technique not only for detection but also in determining therapeutic strategy in superficial esophageal SCC.

The mean scores from our questionnaire indicated that AFI was significantly inferior to NBI, yet it was evaluated as significantly superior to WLI by younger or less experienced endoscopists. Many years may be required for less experienced endoscopists to gain sufficient experience in endoscopic diagnosis of SESCC, as esophageal SCC is relatively rare.[8] Thus, we suggest that AFI endoscopy might help reduce the risk of SESCC being overlooked by younger or less experienced endoscopists.

AFI was also evaluated as significantly superior to WLI for large or flat/elevated lesions; furthermore, AFI surpassed NBI in the mean scores for elevated lesions, although the difference was not significant. This result might be new evidence supporting the view of Uedo *et al.* who, even though they used a slightly different AFI system, revealed an advantage for AFI over WLI in diagnosing the extent of five SESCCs: all five of their lesions were flat/elevated and four were large, ≥20 mm in diameter.[9]

We suggest that the evaluation of AFI images depends on the color tones of the lesions. In AFI, fluorescence intensity is influenced by the thickness of the mucosal surface. The non-tumorous background mucosa was displayed as light green on AFI, while half of the flat/elevated lesions were displayed as magenta, and most of the depressed lesions as dark green. Consequently, the stark differences in color tones between flat/elevated lesions and background appeared to provide a higher recognition capability than the less obvious differences between depressed lesions and background. Moreover, these results support the conclusion of previous reports that AFI video endoscopy may improve the detection of early neoplasia in Barrett's esophagus[12,14] because early neoplasia is more often flat/elevated than SESCC is.[3,18]

In contrast, AFI was assessed as significantly inferior to WLI and NBI for small or depressed lesions. We are concerned that this result might seriously decrease the clinical utility of AFI in the early detection of SESCC because mucosal lesions indicated for EMR are often smaller than 20 mm or depressed.[3,19,20]

A number of clear limitations to the study must be described. First, this comparative study was based on the results of a questionnaire survey using endoscopic still images. Consequently, the on-site and real-time diagnostic powers of WLI, AFI, and NBI endoscopy and LCE remain obscure. Second, the endoscopists who participated in the survey all belonged to our department. Furthermore, all of the endoscopic still images used in the questionnaire were selected by particular endoscopists. Thus, a selection bias of respondents and endoscopic images cannot be excluded.

In conclusion, while NBI and AFI endoscopy might not replace LCE, they are free from the stimulus of Lugol solution and a risk of allergic reaction. NBI might be more useful than AFI or WLI in detecting SESCC. AFI seems to have both superior and inferior visualizing power to WLI depending on characteristics of endoscopists or SESCC lesions. Therefore, AFI will be useful in combination with WLI.

In the future, randomized crossover prospective studies, conducted in particular in a nonexpert setting, are required to assess the real diagnostic performance of the novel endoscopy techniques NBI and AFI for detecting SESCC.

Acknowledgments

The authors thank Mr Shunji Takei, Nobuyuki Doguchi, and Sakae Takehana (Olympus Medical Systems Corp.) for instructing us about the mechanism and principle of AFI. The prototype endoscopy equipment was provided by Olympus Medical Systems Corp.

References

1 Enzinger P C, Mayer R J. Esophageal cancer. N Engl J Med 2003; 349: 2241–52.
2 Siewert J R, Ott K. Are squamous and adenocarcinomas of the esophagus the same disease? Semin Radiat Oncol 2006; 17: 38–44.
3 Kodama M, Kakegawa T. Treatment of superficial cancer of the esophagus: a summary of responses to a questionnaire on superficial cancer of the esophagus in Japan. Surgery 1998; 123: 432–9.
4 Pech O, May A, Rabenstein T *et al.* Endoscopic resection of early oesophageal cancer. Gut 2007; 56: 1625–34.
5 Mori M, Adachi Y, Matsushima T *et al.* Lugol staining pattern and histology of esophageal lesions. Am J Gastroenterol 1993; 88: 701–5.
6 Inoue H, Ray J F, Lightdale C. Lugol chromoendoscopy for esophageal squamous cell cancer. Endoscopy 2001; 33: 75–9.
7 Dubuc J, Legoux J L, Winnock M *et al.* Endoscopic screening for esophageal squamous cell carcinoma in high-risk patients: a prospective study conducted in 62 French endoscopy centers. Endoscopy 2006; 57: 690–5.
8 Marugame T, Kamo K I, Katanoda K *et al.* Cancer incidence and incidence rates in Japan in 2000: estimates based on data from 11 population-based cancer registries. Jpn J Clin Oncol 2006; 36: 668–75.
9 Uedo N, Iishi H, Tatsuta M *et al.* A novel videoendoscopy system by using autofluorescence and reflectance imaging for diagnosis of esophagogastric cancers. Gastrointest Endosc 2005; 62: 521–8.
10 Yoshida T, Inoue H, Usui S *et al.* Narrow-band imaging system with magnifying endoscopy for superficial esophageal lesions. Gastrointest Endosc 2004; 59: 288–95.
11 Kara M A, Smits M E, Rosmolen W D *et al.* A randomized cross-over study comparing light-induced fluorescence endoscopy with standard videoendoscopy for the detection of early neoplasia in Barrett's esophagus. Gastrointest Endosc 2005; 61: 671–8.
12 Kara M A, Peters F P, ten Kate F J W *et al.* Endoscopic video autofluorescence imaging may improve the detection of early neoplasia in patients with Barrett's esophagus. Gastrointest Endosc 2005; 61: 679–85.
13 Kara M A, Peter F P, Fockens P *et al.* Endoscopic video-autofluorescence imaging followed by narrow band imaging for detecting early neoplasia in Barrett's esophagus. Gastrointest Endosc 2006; 64: 176–85.
14 Curvers W L, Singh R, Song L M *et al.* Endoscopic tri-modal imaging for detection of early neoplasia in Barrett's oesophagus: a multi-centre feasibility study using high-resolution endoscopy, autofluorescence imaging and narrow band imaging incorporated in one endoscopy system. Gut 2008; 57: 167–72.
15 Muto M, Nakane M, Katada C *et al.* Squamous cell carcinoma in situ at oropharyngeal and hypopharyngeal mucosal sites. Cancer 2004; 101: 1375–81.
16 Muto M, Saito Y, Ohmori T *et al.* Multicenter prospective randomized controlled study on the detection and diagnosis of superficial squamous cell carcinoma by back-to-back endoscopic examination of narrowband imaging and white light observation. Gastrointest Endosc 2007; 65: AB 110.
17 Japanese Society for Esophageal Disease. Guideline for the Clinical and Pathologic Studies on Carcinoma of the

Esophagus, 1st English edn. Tokyo: Kanehara & Co Ltd., 2001.
18 May A, Günter E, Roth F *et al.* Accuracy of staging in early oesophageal cancer using high resolution endoscopy and high resolusion endosonography: a comparative, prospective, and blinded trial. Gut 2004; 53: 634–40.
19 Katada C, Muto M, Manabe T *et al.* Local recurrence of squamous cell carcinoma of the esophagus after EMR. Gastrointest Endosc 2005; 61: 219–25.
20 Takeshita K, Tani M, Inoue H *et al.* Endoscopic treatment of early oesophageal or gastric cancer. Gut 1997; 40: 123–7.