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Live Teaching of Image Enhanced Endoscopy using High Resolution Digital Video Transport System and Internet2 - The IEE International Teaching Project

Session IV:
Image Enhanced Endoscopy in the Colon

The July 10th (July 9th at Stanford) event is one of a series of sessions to test the concept of teaching and sharing gastrointestinal endoscopic knowledge between major hospitals over long distances. The teaching session between Kyoto University,Japan; Stanford University, USA; Kyushu University, Japan; and Hanyang University Medical Center, South Korea builds on experience from similar events that have been run between surgeons in Kyushu and surgeons at many other sites in Japan, Korea and other Asian countries.

The focus at this event will be on its efficacy in teaching diagnostic principles in the endoscopic detection and diagnosis of early gastrointestinal cancer in the colon. You will participate in a collaborative presentation and discussion, and you will evaluate the efficacy of this as a learning event.

Pre-Test Questions

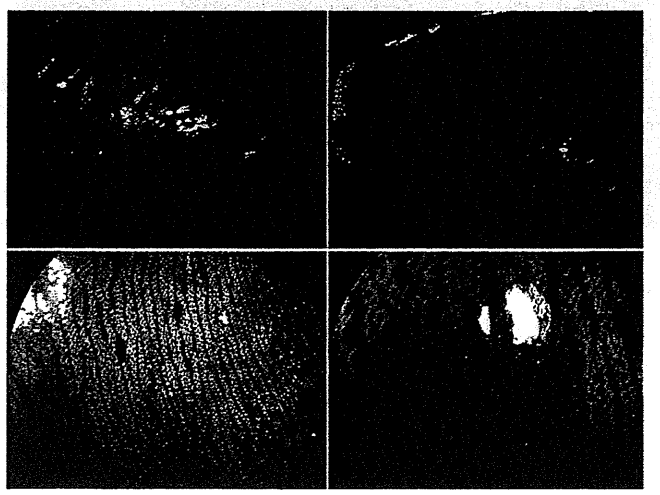
Please answer the five questions below BEFORE the lecture session.

講義の前に以下の５つの質問に答えてください。

Participant Number: _____ Name of Institution: _____

1. What colonic lesion morphology is most likely to harbor high grade dysplasia/ carcionoma in situ, at the time of detection, irrespective of the lesion size?
   A. Pedunculated
   B. Sessile
   C. Superficially elevated
   D. Completely flat
   E. Depressed

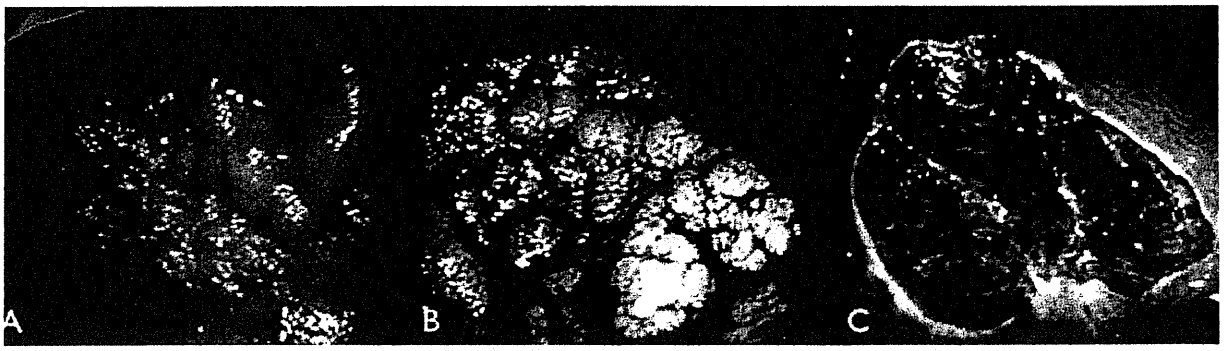
2. Identify any suspicious abnormality in this image. Please outline (using a pen) entire area that appears abnormal. If the image below appears normal and no abnormality is suspected, then please do not mark, and leave the image blank.



3. What is the suspected histopathology of the lesion identified in the image below?

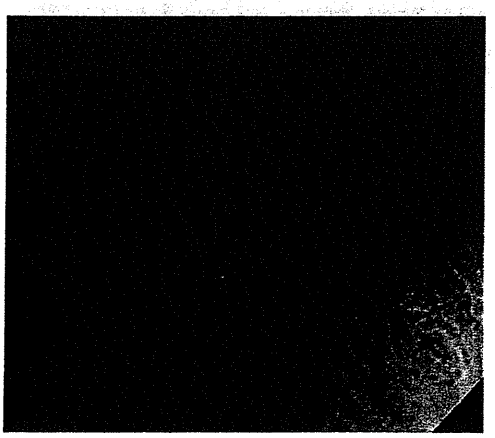
A. Normal.
B. Hyperplastic.
C. Adenoma.
D. High grade dysplasia/carcinoma in situ.
E. Invasive Adenocarcinoma.

4. A nonpolypoid colorectal lesion is seen in white light (A) and indigo carmine (B). Based on the immediate post mucosectomy site (C), what would be your next step?



A. Magnification.
B. Biopsy.
C. Closure of mucosal defect.
D. Repeat EMR.
E. Continue withdrawal examination.

5. What is the suspected histopathology of the colonic lesion shown using NBI in the image below?



A. Normal.
B. Hyperplastic.
C. Adenoma.
D. High grade dysplasia/carcinoma in situ
E. Invasive Adenocarcinoma.

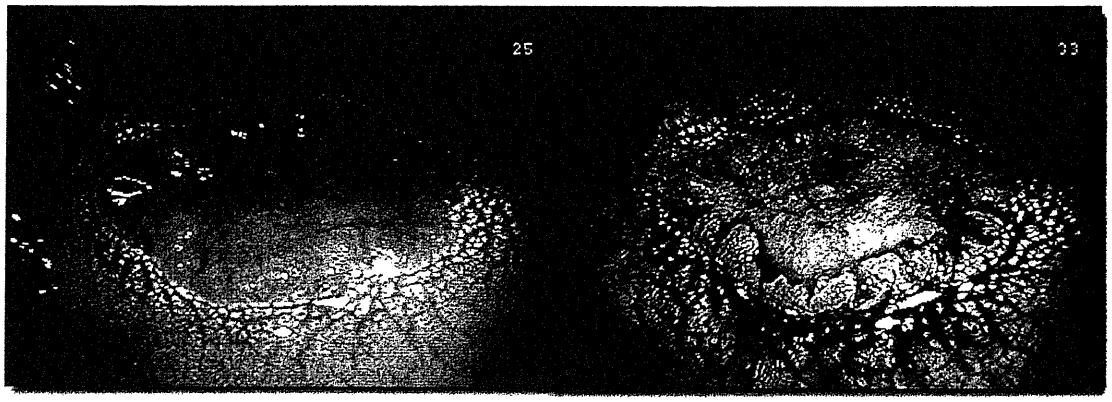
POST-Test Questions

Please answer the five questions below only AFTER the lecture session.

講義の後に以下の５つの質問に答えてください。

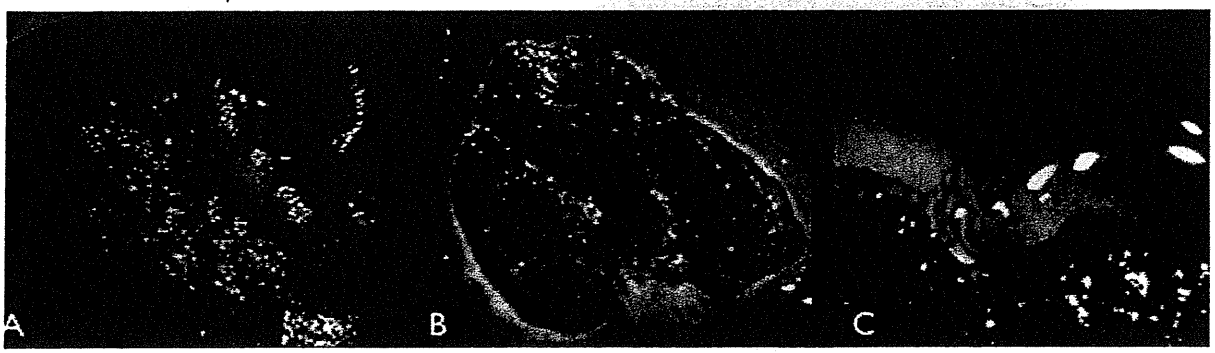
Participant Number: _____ Name of Institution: _____

1. What is the suspected histopathology of the lesion identified in the image below?



A. Normal.
B. Hyperplastic.
C. Adenoma.
D. High grade dysplasia/carcinoma in situ.
E. Invasive Adenocarcinoma.

2. A nonpolypoid colorectal lesion is seen (A). Based on the immediate post mucosectomy site (B) with magnification (C), what would be your next step?

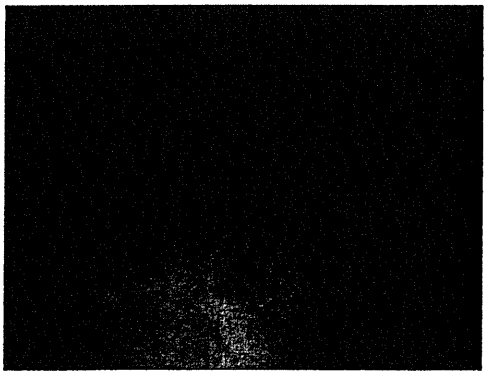


A. Increase magnification.
B. Image enhanced endoscopy technique.
C. Removal of residual lesion.
D. Closure of mucosal defect.
E. Continue withdrawal examination.

3. What colonic lesion morphology is most likely to harbor invasive cancer, at the time of detection, irrespective of the lesion size?

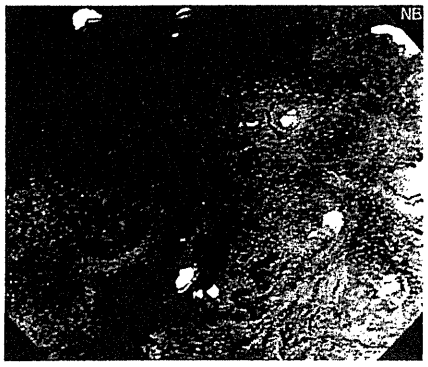
A. Pedunculated
B. Sessile
C. Superficially elevated
D. Completely flat
E. Depressed

4. What would be your next step during a post mucosectomy surveillance colonoscopy, in the image below?



A. Continue to withdrawal.
B. Image enhanced endoscopy.
C. Biopsy.
D. Mucosectomy.

5. What is the suspected histopathology of the colonic lesion shown using NBI in the image below?



A. Normal.
B. Hyperplastic.
C. Adenoma.
D. High grade dysplasia/carcinoma in situ.
E. Invasive Adenocarcinoma.

Exit Questionnaire

Instructions:
Please answer the following questions by marking the circle that best describes your answer, or filling in the blanks.
Thank you,
The Research Team at Stanford University, SUMMIT and VA Palo Alto Heath Care System, GI Section.

Part A: Background Information

1. Year of birth: 19____ Subject Number_____

2. Mark the circle that best describes your current level of gastrointestinal training:

Intern (PGY 1)	○	Gastroenterology Fellow	○
PGY2-3	○	Attending	○
PGY4-5	○	Faculty	○
PGY6+	○	Other:	○

3. How many gastroendoscopy procedures did you perform in the last year in which you:

	Less than 5	5-9	10-14	15-19	20 or more
Served as the lead endoscopist	○	○	○	○	○
Assisted the lead endoscopist	○	○	○	○	○
Observed and/or held endoscope	○	○	○	○	○

4. Please list the 4 procedures in which you participated most frequently in the last year:

1)_____

2)_____

3)_____

4)_____

Part B: Please rate the quality of the technical components of the session:

Technical Components	Not Usable (1)	Difficult to use (2)	Degraded but still usable (3)	Some interference but usable (4)	No interference (5)
1. Quality of Endoscopy Images	O	O	O	O	O
2. Quality of Audio	O	O	O	O	O
3. Quality of Conferencing Video	O	O	O	O	O

Part C: Please rate the usefulness of the information components of the session:

Information Components	Low (1)	(2)	Medium (3)	(4)	High (5)
1. Endoscopy Images and Video	O	O	O	O	O
2. Commentary from remote faculty	O	O	O	O	O
3. Commentary from local faculty	O	O	O	O	O
4. Interaction with remote audience	O	O	O	O	O
5. Discussion within local audience	O	O	O	O	O

Part D: Please give us your opinion of the overall value of this type of live surgery events.

Overall Rating	Definitely Would Not (1)	Not Likely (2)	Not Sure (3)	Very Likely (4)	Definitely Would (5)
6. If a 45-60 minute session of this type (a remote presentation with collaborative discussion) were readily available to you at your hospital/medical school, (e.g. once a month) on a topic in your surgical area of interest, how likely would you be to watch it?	O	O	O	O	O

Part E: Addition comments.

Please write any additional comments you have:

Answer Key
Televideo Teaching Session, Image Enhanced Endoscopy – Colon:

Pre-Test Questions:

1. E. Depressed
2. None – Normal Colonic Mucosa with Innominate Grooves and Pits
3. C. Adenoma
4. A. Magnification
5. E. Invasive Adenocarcinoma

Post-Test Questions:

1. E. Invasive Adenocarcinoma
2. C. Removal of Residual Lesion
3. E. Depressed
4. B. Image Enhanced Endoscopy
5. E. Invasive Adenocarcinoma

Short Communication

Health Risk Appraisal Models for Mass Screening for Esophageal and Pharyngeal Cancer: An Endoscopic Follow-up Study of Cancer-Free Japanese Men

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Abstract

Purpose: **To assess the performance of our health risk appraisal (HRA) models for screening individuals at high risk of esophageal/pharyngeal squamous cell carcinoma (EPSCC).**

Methods: **Based on the results of our previous case-control study, we invented HRA models that enable screening for EPSCC cases in Japanese men with high sensitivity and specificity based on either their aldehyde dehydrogenase-2 genotype (HRA-G model) or alcohol flushing (HRA-F model) and drinking, smoking, and dietary habits. Follow-up endoscopy combined with esophageal iodine staining (median follow-up period: 5.0 years) was done on 404 Japanese men (50-78 years) who were registered as cancer-free controls in the previous study.**

Results: **The follow-up endoscopy resulted in a diagnosis of 6 esophageal SCC (T_{is} in 5 and T_1 in 1), 1 hypopharyngeal SCC (T_2), and 1 oropharyngeal SCC (T_2). Seven and 6 of the 8 EPSCC cases were in the top 10% risk group at baseline according to the HRA-G and HRA-F models, respectively. The EPSCC detection rates per 100 person-years in the top 10% risk groups by the HRA-G and HRA-F models were 4.38 (95% confidence interval, 1.76-9.01) and 3.48 (95% confidence interval, 1.28-7.58), respectively. Their age-adjusted relative risk was 95.1- and 26.3-fold, respectively ($P < 0.0001$), higher than in the bottom 90% risk groups.**

Conclusions: **The high detection rates for EPSCC in the top 10% risk group of this preliminary follow-up study were in good agreement with those predicted by the HRA models and thus encouraged the screening based on our HRA models in larger populations of Japanese men.** (Cancer Epidemiol Biomarkers Prev 2009;18(2):651–5)

Introduction

Recent technical improvements in endoscopes and growing understanding of the endoscopic findings of early squamous cell carcinoma (SCC) in the esophagus (1, 2) and pharynx (3) have made it possible to detect esophageal/pharyngeal SCC (EPSCC) early. Treatment of early esophageal SCC by endoscopic mucosectomy has become a widespread practice in Japan and has succeeded in improving the prognosis of this high-mortality cancer (2, 4, 5), and early pharyngeal SCC can also be treated by endoscope-guided mucosectomy (6). Therefore, it is important to identify individuals at increased risk of EPSCC and offer them the opportunity to undergo detailed examination by upper aerodigestive tract endoscopy combined with esophageal iodine staining. Without using the esophageal iodine staining, more than half of intraepithelial or mucosal esophageal SCC would be missed (1, 7).

A mutant allele encoding an inactive subunit of aldehyde dehydrogenase-2 (*ALDH2**2) is prevalent in East Asian populations (e.g., prevalence of the *ALDH2**2 allele is 24% in a Japanese population; ref. 8) and drinking a small amount of alcohol results in severe acetaldehydemia and unpleasant alcohol flushing responses in individuals with inactive ALDH2 (9). Acetaldehyde is an established carcinogen in experimental animals (10) and is suspected to play a critical role in cancer development in humans (11). Case-control studies among Japanese (12-16) and Taiwanese (13, 17, 18)

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Risk factors		Score (select one each for A-E)	
ALDH2 genotype and alcohol drinking			
*ALDH2*1/*1*			
Never/rare	(<1 unit/w)	-12.94	A
Light	(1-8.9 units/w)	0.00	
Moderate	(9-17.9 units/w)	1.72	
Heavy	(18+ units/w)	2.34	
Ex-drinker		2.18	
*ALDH2*1/*2*			
Never/rare	(<1 unit/w)	-0.29	
Light	(1-8.9 units/w)	1.76	
Moderate	(9-17.9 units/w)	4.02	
Heavy	(18+ units/w)	4.49	
Ex-drinker		3.92	
*ALDH2*2/*2*			
Never/rare	(<1 unit/w)	0.37	
Light	(1-8.9 units/w)	0.00	
Drinks strong alcoholic beverages frequently			
	Yes	1.52	B
	No	0.00	
Smoked 30 pack-years or more			
	Yes	0.86	C
	No	0.00	
Eats green-yellow vegetable almost every day			
	Yes	0.00	D
	No	0.49	
Eats fruit almost every day			
	Yes	0.00	E
	No	0.54	

Total score = A + B + C + D + E

Predicted risk	Total score
Bottom 25%	≤1.02
25-49%	1.03-2.33
50-74%	2.34-3.60
75-89%	3.61-4.56
Top 10%	4.57+

Figure 1. HRA model for esophageal cancer that includes ALDH2 genotype. 1 unit = 22 g ethanol.

and prospective studies among Japanese alcoholics (19, 20) have consistently shown a markedly increased risk of EPSCC in drinkers possessing *ALDH2*1/*2*. Our previous case-control studies confirmed that alcohol drinking especially in individuals with inactive ALDH2, tobacco smoking, a preference for drinking concentrated alcoholic beverages straight, and less intake of green and yellow vegetables increased the risk of EPSCC in Japanese men (12, 16, 21). Based on the data we obtained in that study, simple health risk appraisal (HRA) models were developed to be able to quantitatively assess individual risk of developing EPSCC in the form of a risk score (22). A cross-validation study, which used a simulation-based approach to assess the performance of a statistical model, predicted that ~60% of the EPSCC in the entire population could be detected by examining only people with the top 10% risk scores of the HRA models (sensitivity ≈ 60% and specificity ≈ 90%; ref. 22). Furthermore, the detection rate of esophageal SCC in people with the top 10% risk score (positive predictive value) was expected to be >2%. If it is possible to achieve these performances levels in an actual mass screening, a very efficient approach to early detection of EPSCC in Japanese men will have been achieved.

The present study was a 7-year follow-up study of cancer-free men who were the controls in our previous case-control study and was conducted to confirm that the good performance of HRA models predicted by the cross-validation study was also achieved in an actual follow-up study, where the subjects were examined repeatedly by using a combination of upper aerodigestive tract endoscopy and esophageal iodine staining.

Materials and Methods

Study Population. We previously conducted a case-control study of 234 male cases with esophageal SCC and 634 male cancer-free controls and reported the results (12). The cancer-free controls were men who came to two Tokyo clinics for annual health checkups between September 2000 and December 2001, and most of them were ordinary residents or workers living in Tokyo or surrounding areas. The cancer-free controls who had been recruited in one of the two clinics and diagnosed as cancer-free by upper gastrointestinal endoscopy when they registered to participate in the previous study were sent annual letters of invitation to be screened by endoscopy. As of April 2007, 404 (81.3%) of the 497 eligible men ages 50 to 78 years had undergone a combination of follow-up endoscopic screening and esophageal iodine staining at least once, and they were enrolled in the present study. The Ethics Committee of the Kurihama Alcoholism Center reviewed and approved the proposal for this study, and each of the participants gave his informed consent.

Endoscopic Screening. Endoscopy was done with an Olympus Q240 or Q240Z panendoscope (Olympus Optical) by one of the authors (Y.K.), who is an expert in the field of upper gastrointestinal endoscopy. The endoscope was inserted into the pharynx, and it was carefully examined while removing secretions by

suction. After advancing the endoscope beyond the upper esophageal sphincter, the esophageal mucosa was flushed with 40 mL water through the biopsy port. Conventional endoscopic inspection was done from the esophagus down to the duodenum, and the esophagus was stained with then 10 mL of 1.5% iodine solution and inspected again. Mucosal biopsy specimens were collected from lesions that remain distinctly unstained by iodine, if their greatest diameter was ≥5 mm. At the end of the screening procedure, the esophageal mucosa was rinsed with 20 mL of 2.5% sodium thiosulfate solution, and the gastric contents were removed by suction.

Measurement of Risk Factors. At the time of baseline registration for the previous study, each participant was asked to fill out a simple questionnaire that asked the questions concerning alcohol flushing responses, drinking habits, smoking habits, and diet (12). Alcohol flushing is a surrogate marker of inactive ALDH2 and the sensitivity and specificity of the flushing questionnaire for identifying inactive ALDH2 in a Japanese male population were 90% and 88%, respectively (21). The PCR-RFLP method has been done on lymphocyte DNA samples to determine their ALDH2 genotype (refSNP ID: rs671) of all participants in the previous case-control study (12).

We calculated the HRA score to assess the risk of esophageal SCC in each subject at the time of registration based on alcohol drinking, either ALDH2 genotype (HRA-G model) or alcohol flushing (HRA-F model), smoking, and intake of vegetables and fruit according to the previously reported method (22). The subjects were classified into five risk categories according to their HRA scores: bottom 25%, 25% to 49%, 50% to 74%, 75% to 89%, and top 10%. The procedures used to make these calculations are summarized in Fig. 1 (HRA-G) and Fig. 2 (HRA-F). The HRA score was calculated as the sum of the scores (A-E), which were logarithms of the multivariate odds ratio of each factor estimated in the previous case-control study (12, 21). We further simplified the HRA-F model by converting the scores to small integers ("integer score" in Fig. 2), so that the categorization of the risk group was approximately the same as the categorization based on the original scores (22).

Statistical Analyses. The cancer detection rates during the follow-up period were calculated by the person-year method, with "person-year" defined as time from the baseline examination to either cancer detection or the most recent follow-up examination, whichever came first. The 95% confidence interval (95% CI) of the detection rate was estimated based on a Poisson distribution. The relationships between the HRA score at baseline and results of subsequent endoscopic screening are expressed as relative risk of cancer detection rate adjusted for decade of age by the Mantel-Haenszel method. All statistical analyses were done with the SAS statistical package (version 9.1; SAS Institute).

Results

The mean follow-up period was 4.4 years [median (25th and 75th percentiles), 5.0 (3.3, 5.6) years; range, 0.1- 6.7 years]. There were no significant differences between the distribution of the HRA scores of the subjects who underwent the follow-up screening and those who did not ($P > 0.4$, Fisher's exact test; data not shown). Follow-up endoscopy resulted in a diagnosis of primary esophageal SCC in 6 subjects, SCC in 5 (T_{is}), and SCC

Risk factors		Original score	*(Integer score)*	
Alcohol flushing and drinking				
Any flushing				
Never/rare	(<1 unit/w)	0.00	*(0)*	
Never flushing				
Light	(1-8.9 units/w)	0.24	*(1)*	
Moderate	(9-17.9 units/w)	2.31	*(5)*	
Heavy	(18+ units/w)	2.75	*(6)*	
Ex-drinker		3.31	*(7)*	
Current/former flushing				
Light	(1-8.9 units/w)	1.90	*(4)*	
Moderate	(9-17.9 units/w)	3.75	*(9)*	
Heavy	(18+ units/w)	4.29	*(10)*	A
Ex-drinker		3.61	*(8)*	
Drinks strong alcoholic beverages frequently				
	Yes	1.28	*(3)*	B
	No	0.00	*(0)*	
Smoked 30 pack-years or more				
	Yes	0.96	*(2)*	C
	No	0.00	*(0)*	
Eats green-yellow vegetable almost every day				
	Yes	0.00	*(0)*	D
	No	0.50	*(1)*	
Eats fruit almost every day				
	Yes	0.00	*(0)*	E
	No	0.45	*(1)*	

Total score = A + B + C + D + E

Predicted risk	Total score	
	Original	*Integer*
Bottom 25%	≤1.18	*0-2*
25-49%	1.19-2.78	*3-5*
50-74%	2.79-3.80	*6-8*
75-89%	3.81-4.70	*9-10*
Top 10%	4.71+	*11+*

Figure 2. HRA model for esophageal cancer that includes alcohol flushing.

Table 1. Detection rate and relative risk of cancer during the follow-up period according to risk category based on the HRA models

	No. cohort members	Person-years of follow-up	SCC of esophagus			SCC of esophagus/pharynx		
			n	Per 100 person-years (95% CI)	RR* (95% CI)	*n*	Per 100 person-years (95% CI)	RR* (95% CI)
HRA models								
HRA-G (n = 404)								
Risk category								
Lower 25%	104	483.8	0			0		
25-49%	96	430.3	0			0		
50-74%	118	519.5	0	0.06 (0.00-0.34)	1.0 (reference)	0	0.06 (0.00-0.34)	1.0 (reference)
75-89%	44	189.0	1			1		
Top 10%	42	160.0	5	3.13 (1.01-7.29)	67.8 (6.44-714)	7	4.38 (1.76-9.01)	95.1 (10.4-1,048)
HRA-F, original score (n = 393)								
Risk category								
Lower 25%	101	463.5	0			0		
25-49%	98	446.7	0			0		
50-74%	88	394.8	2	0.13 (0.02-0.46)	1.0 (reference)	2	0.13 (0.02-0.46)	1.0 (reference)
75-89%	61	253.9	0			0		
Top 10%	45	172.3	4	2.32 (0.63-5.94)	17.5 (3.12-98.3)	6	3.48 (1.28-7.58)	26.3 (5.15-134)

NOTE: HRA-G: ALDH2 activity was assessed by genotyping; HRA-F: ALDH2 activity was assessed based on the results of a questionnaire regarding alcohol-related flushing (see also Figs. 1 and 2).
*Relative risk of person-year detection rate adjusted for age by the Mantel-Haenszel method. All $P < 0.0001$ for comparisons between the top 10% and the bottom 90% categories.

plus basaloid carcinoma in 1 (T_1) and primary SCC of the hypopharynx (T_2) and oropharynx (T_2) in 1 subject each. At baseline, all 8 subjects who were diagnosed with EPSCC at follow-up were moderate/heavy drinkers (>200 g ethanol/wk) and heterozygotes for inactive ALDH2, and 7 of them reported current/former alcohol flushing. Seven of the subjects with EPSCC had smoked ≥30 pack-years, 5 did not eat green-yellow vegetables almost every day, and 7 did not eat fruit almost every day.

Table 1 shows the detection rate of cancer during the follow-up period according to risk category based on the HRA-G and HRA-F models. Five of the 6 esophageal SCC patients and 7 of the 8 EPSCC patients had been classified in the top 10% risk category based on the HRA-G model, and 4 of the esophageal SCC patients and 6 of the EPSCC patients had been classified in the top 10% risk category based on the HRA-F model. The detection rate of esophageal SCC per 100 person-years (95% CI) was 3.13 (1.01-7.29) and 2.32 (0.63-5.94) in the top 10% risk group based on HRA-G and HRA-F models, respectively, and that for EPSCC was 4.38 (1.76-9.01) and 3.48 (1.28-7.58), respectively. The age-adjusted relative risk in the top 10% risk group was much larger than in the bottom 90% risk group and the difference was highly significant ($P < 0.0001$) in both models. The results based on the HRA-F model obtained with integer scores were very similar to the results obtained with the original scores (data not shown).

Discussion

We invented HRA models that allow prediction of ~60% of patients with EPSCC while referring only the top 10% of risk category of Japanese high-risk men for endoscopic screening (22). The present study investigated whether the HRA models would perform well in terms of actual endoscopic screening for cancer during a 7-year follow-up of Japanese men. The results showed that 7 (88%) of the 8 EPSCCs developed in individuals ranked in the top 10% risk category according to the HRA-G model and 6 (75%) developed in individuals ranked in the top 10% risk category according to the HRA-F model, showing better performance in comparison with the proportions (= sensitivity) predicted by the cross-validation method (65.4% and 57.9%, respectively; ref. 22). It was noteworthy that the esophageal cancers detected were in the very early stage (T_{is} cancer in 5 and T_1 cancer in 1). An esophageal cancer detection rate by endoscopy in men ages ≥40 years was reported to be 0.39% in the Research Center for Cancer Prevention and Screening of the National Cancer Center (23), where esophageal iodine staining was applied when the mucosal surface did not appear normal. We estimated the esophageal cancer detection rates in the top 10% category according to the HRA-G model and HRA-F model to be 2.40% and 2.12%, respectively, based on the overall detection rate (0.39%) in the Research Center for Cancer Prevention and Screening (22), and those rates were in good agreement with the results of the present study (3.13 and 2.32, respectively, per 100 person-years). The high skill level of the endoscopists and the use of esophageal iodine staining probably contributed to the high rates of esophageal cancer detection in the Research Center for Cancer Prevention and Screening and the present study, because more than half of the cases of intraepithelial or mucosal SCC in the esophagus would have been missed without esophageal iodine staining (1, 7). The precise incidence of esophageal T_{is} SCC in the Japanese general population and its natural course are unknown, and they will be topics of future research.

Our follow-up study had several potential limitations. The intervals between the follow-up screening and the baseline screening that confirmed freedom from cancer

were short, and the very small number of cancer cases may have limited the assessment of the relationship between the HRA scores and actual rate of cancer development. Although the follow-up was incomplete (81.3%), there were no significant differential follow-up biases. The performance of HRA models could depend on the difference in distributions of risk factors between the background population of the present study and the target population to which the HRA models are applied (22). Further investigation of the relationship in a large, long-term prospective study in different populations with a high follow-up rate is clearly warranted.

Our HRA-F model enables many people to identify their own risk of EPSCC very easily, and public awareness campaigns using the HRA-F model will help persuade high-risk persons to undergo endoscopic screening and enable detection of EPSCC early or enable them to change their lifestyle to prevent ESCC. Although the number of cancers detected was small, the very good performance of the HRA models in this preliminary follow-up study provided evidence supporting the validity of the HRA risk scores for selecting individuals at high-risk of EPSCC and encouraged the use of these new models for screening in larger populations of Japanese men. Further study is needed to confirm the effectiveness of this approach in large Japanese populations.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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ORIGINAL ARTICLE

PROSPECTIVE STUDY OF EARLY DETECTION OF PHARYNGEAL SUPERFICIAL CARCINOMA WITH THE NARROWBAND IMAGING LARYNGOSCOPE

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Abstract: *Background.* The newly developed narrowband imaging (NBI) gastrointestinal endoscope makes possible the detection of superficial carcinoma in the oropharynx and hypopharynx, which is difficult with the conventional laryngoscope. Here, we investigated whether the combined use of laryngoscope with NBI allows the detection of superficial carcinoma in this region.

Methods. A total of 51 superficial, histologically confirmed lesions in 29 patients were studied. The quality of visualization of superficial carcinoma in the oropharynx and hypopharynx using the NBI-equipped laryngoscope was evaluated in comparison with the results by conventional laryngoscopy.

Results. The NBI laryngoscope provided better detection of the irregular microvascular pattern of carcinoma than the conventional laryngoscope ($p < .05$) and better visualization of the demarcation line ($p < .05$), and thus significantly better visualization of the lesions.

Conclusion. The NBI laryngoscope may play an important role in the diagnosis and treatment of superficial carcinoma in the oropharynx and hypopharynx. ©2008 Wiley Periodicals, Inc. *Head Neck* **31:** 189–194, 2009

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Keywords: head and neck cancer; laryngoscopy; pharynx; narrowband imaging; squamous cell carcinoma in situ

The detection of early-stage pharyngeal cancer remains a difficult clinical challenge, particularly cases occurring in the oropharynx and hypopharynx. This difficulty contrasts with the situation in the esophagus, where Lugol chromoendoscopy greatly facilitates early detection.[1] Lugol staining cannot be used in the head and neck region, however, owing to the severe mucosal irritation it causes, which produces pain and discomfort and can result in aspiration into the airway.

The recent introduction of noninvasive narrowband imaging (NBI) gastrointestinal (GI) endoscopy for the head and neck region has allowed the detection of squamous cell carcinoma (SCC) in situ in the oropharynx and hypopharynx.[2] In present practice, the otolaryngologist observes the oropharynx and hypopharynx with a transnasal laryngoscope, but a GI endoscope cannot be used for

Table 1. Instrument specifications.

Device	Laryngoscope	Gastrointestinal endoscope
Device name	VISERA ENF-V2 (Olympus Medical Systems, Tokyo, Japan)	EVIS LUSERA GIF TYPE H260Z (Olympus Medical Systems, Tokyo, Japan)
NBI imaging procedure	Synchronous	Sequential
Zoom function	–	+
Max magnification	35	80
Distal end outer diameter (mm)	3.2	10.8
Flexible tube outer diameter (mm)	3.4	10.5
Working length (mm)	300	1030
Angulation range	Up, 130 degrees; down, 130 degrees	Up, 210 degrees; down, 90 degrees Right, 100 degrees; left, 100 degrees

transnasal observation owing to its large size. In addition, the laryngoscope uses a conventional white light sourced from a xenon lamp.

We speculated that the combined use of a laryngoscope with the NBI system may assist otolaryngologists in the early detection of cancer. To our knowledge, however, the visibility of superficial carcinomas in the oropharynx and hypopharynx on conventional and NBI laryngoscopy has not been compared.

Here, we investigated whether the NBI-equipped laryngoscope provides better detection of superficial carcinoma in the oropharynx and hypopharynx than the conventional laryngoscope.

PATIENTS AND METHODS

Equipment. The NBI system used here is based on a modification of the spectral features of the NBI GI endoscope in which an optical color separation filter was used to narrow the bandwidth of spectral transmittance. The filter, placed in the optical system of the light source, eliminates all wavelengths except 2 narrow bands with central wavelengths of 415 and 540 nm, respectively. The image is reproduced in the processor using the information provided by these 2 bands. Using a set containing 415- and 540-nm filters, the microvasculature pattern is seen in brown, and the contrast between normal mucosa and malignant lesions is more clearly enhanced. These narrow-bandwidth filters make it possible to visualize malignant lesions, in particular those lesions with a developed microvasculature.

The system is equipped with an ENF-V2 laryngoscope (Olympus Medical Systems, Tokyo, Japan), light source (CLV-160B, Olympus Medical Systems, Tokyo, Japan), and video system center (CV-160B, Olympus Medical Systems, Tokyo, Japan). Specifications of the laryngoscope and GI endoscope are compared in Table 1.

Patients Characteristics and Evaluation Methods. Patients with superficial carcinoma in the oropharynx and hypopharynx originally detected with a GI endoscope were examined using a laryngoscope in conjunction with the NBI system. The definition of superficial carcinoma is provided in Table 2.

A total of 51 superficial lesions in 29 patients were observed between May 2006 and July 2007. All lesions were histologically confirmed SCC. Laryngoscopic evaluation was performed in the seated position. The patient drank a half-cup of water immediately prior to examination to remove saliva on the mucosa of the oro- and hypopharynx. The insertion tube was introduced through a nasal passage, with the examiner observing the live images on the color video monitor. Superficial lesions initially underwent laryngoscope observation using a conventional light source, followed by NBI examination of the same area.

Table 2. *Definition of superficial carcinoma.*

Characteristic	Description
Macroscopic appearance	Elevated (less than 5 mm) Flat Depressed (not ulcerous)
Histology	Squamous cell carcinoma High-grade intraepithelial dysplasia

Table 3. Patient and lesion characteristics.

Characteristic	Value
No. of patients	29
Age (range), y	62 (48–74)
Sex, men/women	27/2
Smoking habit	
Yes	28
No	1
Drinking habit	
Yes	28
No	1
Esophageal cancer	
Yes	24
No	5
mLVL	
Yes	27
No	2
No. of lesions	51
Primary site	
Hypopharynx	
Pyriform sinus	29
Posterior pharyngeal wall	5
Postcricoid area	3
Oropharynx	
Posterior pharyngeal wall	4
Soft palate	4
Base of tongue	2
Tonsil	1
Larynx	
Arytenoid	2
Aryepiglottic fold	1

Abbreviation: mLVL, multiple Lugol-voiding lesion.

Superficial SCCs show several typical endoscopic findings, specifically an irregular microvascular pattern and well-demarcated line between the normal epithelium and cancerous lesion.[3,4] Here, we found that the ability to visualize the lesion using the laryngoscope depended on these 2 features for both the conventional light source and NBI system, and all lesions studied were identified by an irregular microvascular pattern and demarcation line by GI endoscope.

All images were digitally recorded and evaluated for effectiveness in visualizing lesions by 2 experienced otolaryngologists (T.U. and T.H.), who assigned a scored grade to each image according to the quality of visualization of 1, poor; 2, good; and 3, excellent.[5] Scores were then statistically analyzed using the Mann–Whitney U test. Procedure times were measured according to the time indicated on the monitor screen of the videoendoscope. All statistical analyses were performed with the SPSS statistical software package (version 10.0; SPSS, Chicago, IL).

All patients gave written informed consent, and the study protocol was reviewed and approved by the ethics committee of our hospital.

RESULTS

Patient and lesion characteristics are shown in Table 3. Median age was 62 years (range, 48–74), with a men to women ratio of 27:2. A total of 51 superficial lesions were evaluated in 29 patients. The pyriform sinus was the most frequent primary site (37 of 51 lesions; 73%). Endoscopic images were obtained using both the conventional and NBI systems in all cases without difficulty. The color features of images obtained by the NBI system differed from those of the conventional video endoscope system, with the NBI system images appearing brownish. The results of evaluation based on quality of visualization with both the conventional and NBI systems are shown in Table 4. The irregular microvascular pattern was better visualized by NBI than the conventional laryngoscope ($p < .05$) (Figures 1 and 2). Further, the demarcation line of the mucosa was not shown clearly with the conventional laryngoscope, but was well visualized with the NBI laryngoscope ($p < .05$) (Figures 2 and 3). The NBI laryngoscope thus provided significantly better visualization of the lesions than the conventional laryngoscope.

Representative NBI pictures of SCC in situ at the pyriform sinus are shown in Figure 4. A close-up view shows scattered brownish dots, and the demarcation line of the mucosa is clearly depicted. Median observation time by conventional white light and NBI was 75 and 121 seconds, respectively, showing no statistically significant difference.

Endoscopic mucosal resection was performed for 49 lesions. No patient had severe complications related to the endoscopic mucosal resection procedure. Of the remaining 2 patients, 1 underwent peroral excision and the second total pharyngolaryngectomy and reconstruction with a jejunal free flap because the lesion was too large for removal by endoscopic mucosal resection. Finally, 41 lesions were diagnosed as carcinoma

Table 4. Visualization quality of conventional laryngoscopy and NBI laryngoscopy.

	Conventional	NBI
Irregular microvasculature pattern		
Poor	31	2
Good	6	0
Excellent	14	49
Demarcation line		
Poor	39	11
Good	7	8
Excellent	5	32

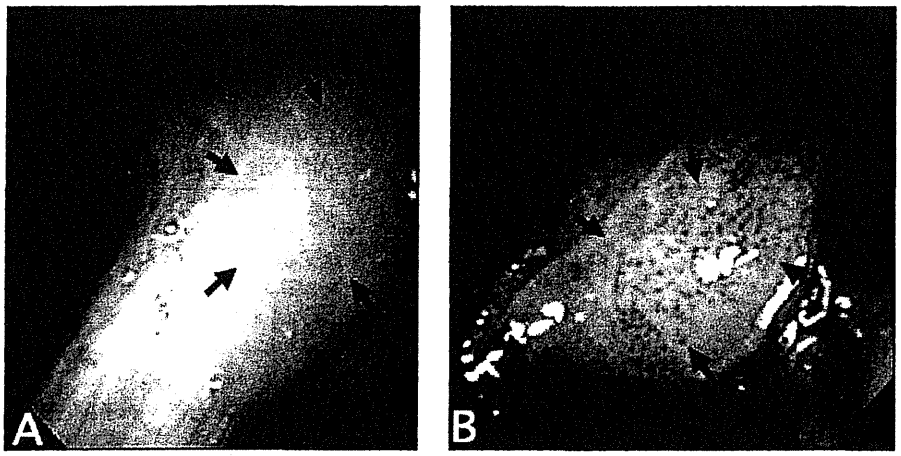

FIGURE 1. Comparison of endoscopic images of a pyriform sinus mucosal lesion. (**A**) On conventional laryngoscopy, the irregular microvascular pattern is unclear. (**B**) The irregular mucosal microvascular pattern is well visualized by narrowband imaging (NBI) laryngoscopy.

in situ and the remaining 10 as microinvasive cancer.

DISCUSSION

Here, we show that the NBI laryngoscope provides better detection of SCC in situ in the oropharynx and hypopharynx than the conventional laryngoscope. These results indicate an important role for the NBI laryngoscope in the diagnosis and treatment of superficial cancer in this region.

The development of synchronous and metachronous SCC at head and neck mucosal sites in patients with cancer of the head and neck is well recognized as the field cancerization phenomenon,[6] and multiple development of cancer in this region is closely associated with decreased patient survival.[7] Although these patients should therefore undergo intensive screening and surveillance, no effective screening or follow-up modalities have to date been developed. Muto et al[1] reported that multiple occurrence of Lugol-voiding lesions was closely associated with the field cancerization phenomenon. In this study, 27 patients (93%) had multiple Lugol-voiding lesions in the background esophageal mucosa. In addition, multifocal superficial lesions at oropharyngeal and hypopharyngeal mucosal sites were iden-

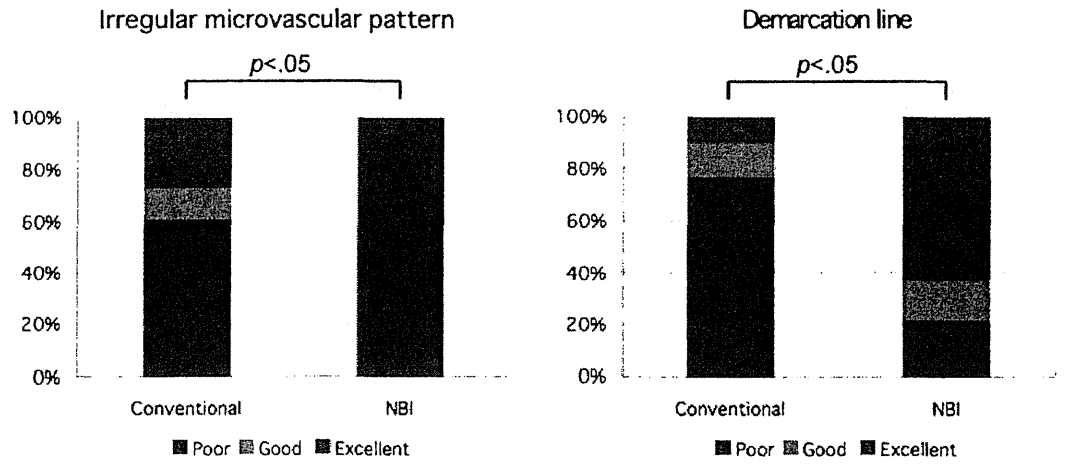

FIGURE 2. Comparison of visualization scores by conventional and NBI laryngoscopy. Both the irregular microvascular pattern and demarcation line are better visualized by NBI than conventional laryngoscopy.