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Original Article

Propofol sedation versus no sedation in detection of pharyngeal and upper gastrointestinal superficial squamous cell carcinoma using endoscopic narrow band imaging: a multicenter prospective trial

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Abstract: Intravenous propofol can provide a superior quality of sedation compared to standard sedation for upper gastrointestinal endoscopy. However, the utility of propofol sedation for the endoscopic early detection of superficial pharyngeal and esophageal squamous cell carcinoma has not been investigated. In a multicenter, prospective trial, 255 patients with esophageal squamous cell carcinomas (ESCCs) were assigned to receive propofol sedation or no sedation according to their own willingness. The primary aim was to compare the detection rates of superficial cancer in the pharyngeal region and the esophagus between two groups. The secondary aim was to evaluate factors associated with technical adequacy. The detection rate was higher in the propofol sedation vs. no sedation group for H&N region (6.06% vs. 2.40%), but not significantly (P=0.22). However, the small lesion (less than 10 mm in diameter) detection rate was higher in sedation vs. no sedation group for H&N region (88.89% vs. 33.33%; P=0.048). The median time for pharyngeal observation in the sedation group was faster than in the no sedation group (20.6 s vs. 44.3 s; P<0.001). Ninety-five percent of H&N region evaluations were totally complete in sedation compared with sixty percent in the no sedation group (P<0.001). The overall p value indicated that only smoking habit was associated with incomplete pharyngeal observation (P<0.05), and it was more difficult to accomplish a complete pharyngeal observation in patients who smoked more than 10 packs per day. Intravenous propofol sedation compared to no intravenous sedation during conventional upper gastrointestinal endoscopy can facilitate a more complete pharyngeal examination and increase the detection rate of superficial H&N squamous cell carcinoma in high risk patients.

Keywords: Esophageal squamous cell carcinoma, head and neck cancer, superficial cancer, high-risk patients, propofol sedation

Introduction

Squamous cell carcinoma is the most common histologic type of primary malignancy affecting the esophagus and the head and neck (HN). It is usually diagnosed at an advanced stage and consequently has a poor 5-year survival rate [1, 2]. Narrow band imaging (NBI) is an innovative optical image-enhancing technology available on some video endoscopes. Using NBI, mucosal microvascular irregularities may delineate areas of early neoplasia in the head and neck and gastrointestinal tract [3]. Many reports have confirmed that NBI was easy to use and could improve the detection rate of superficial esophageal squamous cell carcinoma (ESCC) as well as head and neck squamous cell carcinoma (HNSCC) [4-6]. Nevertheless, endoscopists' unfamiliarity with the NBI features, as well as concerns about increased patient dis-

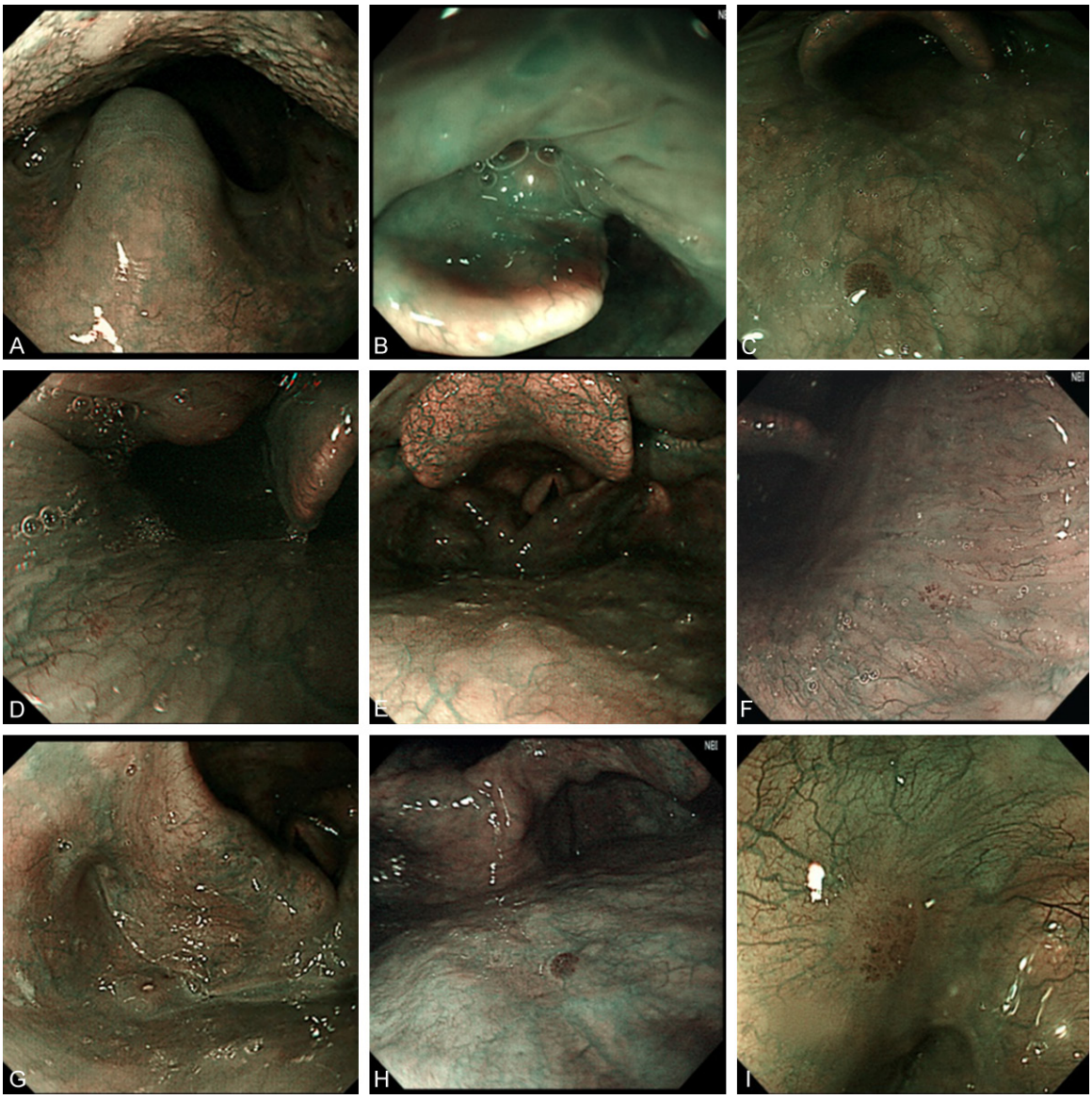

Figure 1. The process of pharyngeal observation using NBI. A. Soft palate and uvula. B. Upper epiglottic cartilage. C. Posterior oropharyngeal wall. D. Left lateral oropharyngeal wall. E. Posterior hypopharyngeal wall. F. Right lateral oropharyngeal wall. G. Right lateral hypopharyngeal wall and right pyriform sinus. H. Epiglottis. I. Left lateral hypopharyngeal wall and left pyriform sinus.

comfort and prolonged examination times have discouraged the adoption of using NBI for routine pharyngeal and esophageal examinations.

Intravenous opiate with or without a benzodiazepine (standard sedation), or only topical pharyngeal anesthesia commonly are used for endoscopic examinations to reduce patients' procedural discomfort and recovery time, and to increase their compliance with the recommendation for endoscopic examination [7, 8]. However, others have reported a more than 20% incomplete pharyngeal examination rate using either of these anesthesia methods, potentially leading to a decrease in superficial squamous cell carcinoma detection rates, which prevalence was ranging from 2.2% to 11.0% and 2.9% to 9.9% in pharyngeal and esophageal region, respectively [5, 6, 9-11]. Intravenous propofol can provide a superior quality of sedation compared to standard sedation, and has been used worldwide for endoscopic examinations [12]. However, the utility of propofol sedation for the endoscopic early

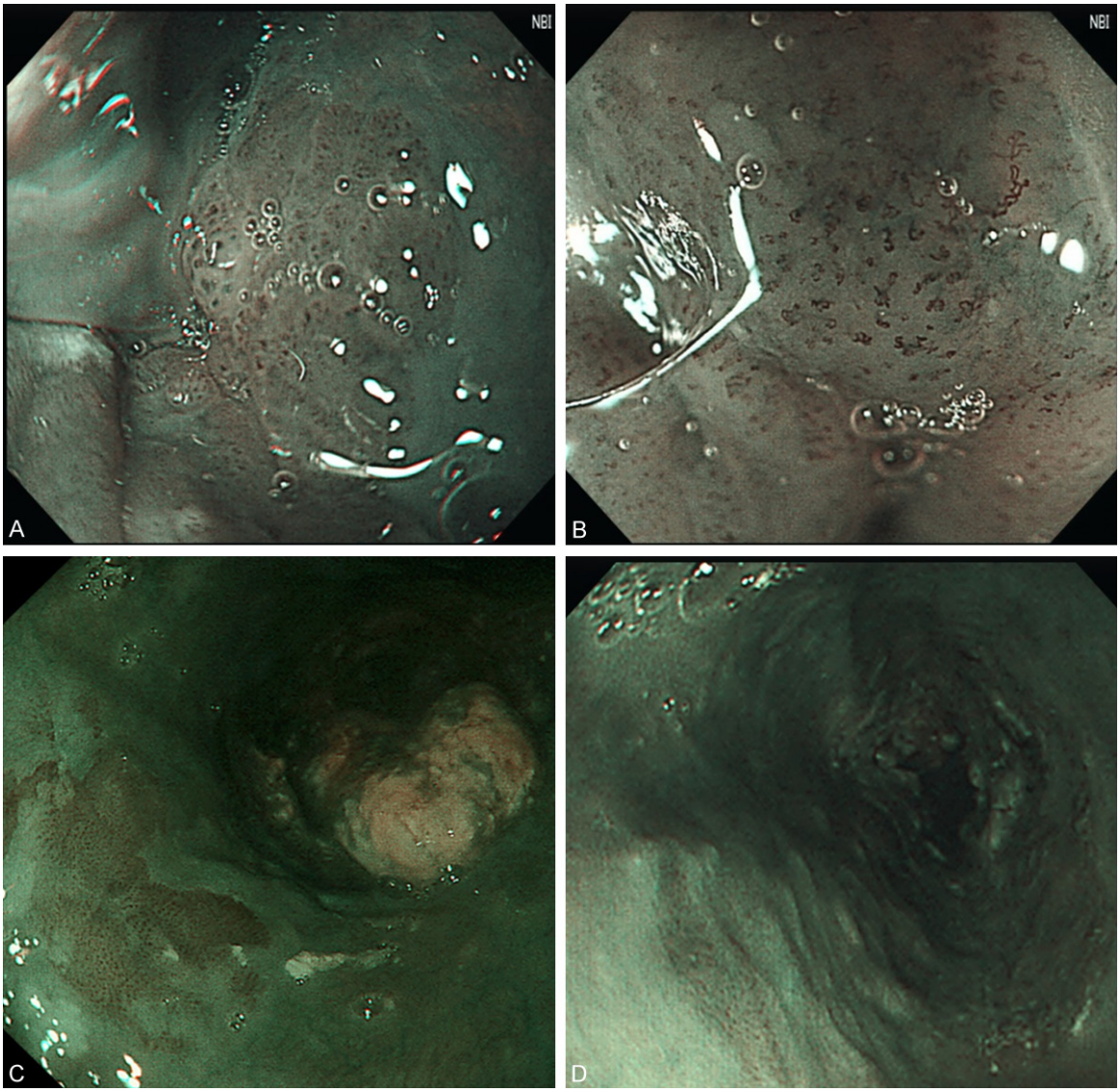

Figure 2. Superficial cancer in the head and neck region and esophagus. A. Non-magnifying NBI shows a well-demarcated brownish area in head and neck region of a patient with ESCC. B. Magnifying NBI shows many tiny dots in the brownish area. C. Scattered brown dots and absent of vessel branch were observed in a well-demarcated brownish area on NBI. D. Non-magnifying NBI shows two well-demarcated brownish area in the esophagus of a patient with ESCC.

detection of superficial ESCC and HNSCC has not been investigated. Therefore we conducted a prospective trial comparing propofol sedation to no sedation for the endoscopic detection of superficial ESCC and HNSCC in patients at high risk for these malignancies.

Materials and methods

Patients

We drew from patients with diagnoses of esophageal squamous cell carcinoma or high-grade intraepithelial neoplasia (HGIN), because this patient population has a high risk of synchronous and metachronous ESCC and HNCC [4, 13, 14]. The inclusion criteria were: (i) Patients with advanced ESCC or previously treated for ESCC by endoscopic resection with an age of 20 years or older; (ii) Patients were able to consent; (iii) Patients without significant cardiorespiratory or medical comorbidities; and (iv) Patients without allergy to lidocaine anesthetic spray. The exclusion criteria were: (i) Previous surgical resection for ESCC or HNSCC;

Table 1. Characteristics of Patients

	Sedation (n=132)		No Sedation (n=123)		
	N0.	%	N0.	%	P
Age years					
Median	60		64		0.423
Range	29-80		37-85		
Male sex	105	79.55	100	81.3	0.724
Alcohol habit					
Yes	64	48.48	67	54.47	0.339
No	68	51.52	56	45.53	
Smoking habit					
No. of smokers	72	54.55	67	54.47	0.991
Depth of invasion					
Tis-T1a	41	31.06	34	27.64	0.549
T1b	13	9.85	16	13.01	0.427
T2	29	21.97	32	26.02	0.449
T3	45	34.09	38	30.89	0.586
T4	4	3.03	3	2.44	0.773

(ii) Prior chemotherapy, radiotherapy, or chemoradiotherapy for ESCC or HNSCC; (iii) Esophageal and pharyngeal stricture; (iv) Presence of emergency procedures or serious complications.

Study design

This study was a multi-center prospective trial. The consent form was approved by the Institutional Review Board of each center, and patients who were enrolled in the trial signed the consent form. Patients themselves chose to either receive intravenous propofol sedation or no sedation. Both groups of patients received topical oro-pharyngeal lidocaine spray to minimized pharyngeal sensitivity [15]. Those in the sedation group received 40 to 80 milligrams of intravenous propofol. Narrow band imaging was used to endoscopically inspect the uvula, posterior oropharyngeal wall, epiglottis, posterior hypopharyngeal wall, pyriform sinuses, and esophagus (**Figure 1**). An assistant physician recorded the results on the case record form, and we only included patients according to the inclusion criteria.

Sample size

The sample size was calculated to detect the smallest difference (α=0.05; β=0.10) between the sedation and no sedation groups. We used 20% as the smallest clinically relevant difference. Previous reports suggested that a major factor affecting superficial lesion detection rates was sedation status [7, 15]. Therefore, we used patient tolerance and self-reported comfort to calculate sample size. We estimated a sample size of 200 patients (100 per group) would allow us to detect a difference as small as 20% with a type I error of 0.05 and a power of 80%. We recruited an additional 40 patients or more in anticipation of instances of ineligibility or withdrawal during the examination because of discomfort.

Study protocol

In this study, we considered lesions with slightly elevated lower than 5 mm, flat or a shallow depression. The primary outcome was the rate of superficial ESCC and HNSCC lesion detection. Secondary outcomes included doctor's satisfaction, patient's satisfaction and time taken for pharyngeal observation. Doctor's satisfaction was defined as the completeness of the examination (technical adequacy) evaluated by the endoscopist after each examination. A complete pharyngeal examination was defined as photo-documentation of all 9 pharyngeal areas (**Figure 1**), a partial-complete evaluation was defined as photo documentation of more than 5 but less than 9 pharyngeal areas, and an incomplete evaluation was less than 5 pharyngeal areas documented. Only complete evaluations of pharyngeal area were considered a satisfied evaluation. Patient's satisfaction was assessed using a questionnaire to rate as follows: (1) acceptable with no pain; (2) partly acceptable with a little pain; (3) unacceptable or painful.

Endoscopic examination

Before the study started, all the participating endoscopists received training by reviewing NBI images of superficial ESCC and HNSCC lesions, and agreed upon a standardized method of examining the pharynx and esophagus. Briefly, 9 pharyngeal areas were required according to Saito et al [11] with slight modifications, and all esophageal areas from the cervical esophagus to the esophagogastric junction were evaluated according to Nagami et al [14] and Muto et al [4]. A lesion with a well-demarcated brownish area, scattered brown dots and absent of vessel branch (**Figure 2**) were consid-

Table 2. Superficial Cancer in the Head and Neck Region and the Esophagus

	Sedation (132)		No Sedation (123)		
	No.	%	No.	%	*P*
Head and neck					
No. of patients	8	6.06%	3	2.40%	0.22
No. of lesions per patient					
1	7	5.30%	3	2.40%	>0.999
≥2	1	0.76%	0	0%	
Total No. of super patient Head and	9		3		
Size threshold, mm					
<10 mm	8		1		0.048
11-20 mm	1		2		
>20 mm	0		1		
Histologic diagnosis					
HGIN or carcinoma in situ	8		3		>0.999
Microinvasive cancer	1		0		
Esophagus					
No. of patients	25	18.94%	26	21.14%	0.661
No. of lesions per patient					
1	23	17.42%	22	17.89%	0.668
≥2	2	1.52%	4	3.25%	
Total No. of super patient Head and	27		30		
Size threshold, mm					
<10 mm	16		14		0.502
11-20 mm	4		8		
>20 mm	7		8		
Histologic diagnosis					
HGIN or carcinoma in situ	21		21		0.506
Microinvasive cancer	6		9		

Abbreviations: HGIN, high-grade intraepithelial neoplasia.

ered as suspected "superficial cancer". Biopsy specimen or ER specimen were used for histologic diagnosis for suspected "superficial cancer". The location and size of superficial cancer confirmed by histology was recorded. All procedures were performed using a video-endoscopy system (EVIS LUCERA system, Olympus), with a high-resolution upper gastrointestinal endoscope (GIF-H260 or GIF-H260Z, Olympus).

Before endoscopy, all patients received oral Simethicone Emulsion (Berlin-Chemie AG, Germany) to wash the pharyngeal and esophageal surface mucosa, and 10 milliliters of lidocaine for pharyngeal anesthesia. During the procedure, we measured the time to examine and photo-document the required 9 pharyngeal areas (a complete examination). The time was not measured in patients who had an incomplete examination, who had H&N lesions requiring biopsy, or who had late stage ESCC with esophageal stricture. When appropriate, biopsies were taken after completing a full esophagogastroduodenoscopy (EGD).

Pathologic evaluation

Two experienced pathologists classified the biopsy specimens into superficial cancers (high-grade intraepithelial neoplasia and micro-invasive squamous cell carcinoma) and non-cancers (chronic esophagitis) according to Vienna Classification [16].

Statistical analysis

The continuous variables are expressed as medians and ranges. Continuous data were compared using the MannWhitney U test. Pearson's Chi-square test or Fisher's exact test was used for categorical variables. Odds ratios of significant factors associated with unsatisfied evaluation were analyzed with logistic regression. Characteristics with $P<0.2$ were included in the univariate and multivariate regression models. It has statistical significance with the discrepancy of $P<0.05$. Data were analyzed using statistical software (SPSS version 17.0; SPSS Inc, Chicago, IL).

Results

Patient background

Between October 2013 and August 2014, 255 patients (males/females =205/50; median age, 62 years; 69 lesions in total) meeting the inclusion criteria were enrolled, including 78 patients with a history of advanced ESCC. The

Table 3. Pharyngeal examination and technical adequacy

	Sedation n=132		No Sedation n=123		
	NO.	%	NO.	%	P
Patient's satisfaction					
Acceptable	124	93.94	84	68.29	P<0.001
Partial acceptable	7	5.30	24	19.51	
Unacceptable	1	0.76	15	12.20	
Pharyngeal observation					
Complete	126	95.45	74	60.16	P<0.001
Partial Complete	6	4.55	29	23.58	
Incomplete	0	0.00	20	16.26	
Examination time					
Median	20.6		44.3		P<0.001

Table 4. Factors affecting incomplete pharyngeal observation (unsatisfied evaluation)

	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
Sex				
Male	0.87 (0.35, 2.16)	0.76		
Female	1			
Age years				
<60	1		1	0.115
>60-70	3.30 (1.20, 9.10)	0.02	2.10 (1.04, 4.22)	0.038
>70	1.57 (0.60, 4.09)	0.359	1.18 (0.59, 2.35)	0.642
Alcohol				
No	1			
Yes	0.68 (0.33, 1.38)	0.285		
Smoking				
No	1		1	0.025
<10	0.69 (0.25, 1.89)	0.475	0.81 (0.33, 2.02)	0.652
>10	3.20 (0.14, 7.37)	0.007	3.99 (0.21, 7.78)	0.007

clinical characteristics of the two groups did not differ significantly in age, sex, alcohol consumption, smoking habits and depth of tumor invasion (**Table 1**). In both groups, most of the patients were newly diagnosed ESCC.

Distribution of histologically confirmed superficial cancers

The diagnostic yields for superficial cancer in the esophagus and H&N region between the two groups are summarized in **Table 2**. The detection rate was higher in the propofol sedation vs. no sedation group for H&N region (6.06% vs. 2.40%), but not significantly (P=0.22). However, the small lesion (less than 10 mm in diameter) detection rate was higher in sedation vs. no sedation group for H&N region (88.89% vs. 33.33%; P=0.048). In the esophagus, 25 patients with 27 lesions of superficial cancers were detected in sedation group (18.94%; 25 of 132), 26 patients with 30 lesions of superficial cancers were detected in no sedation group (21.14%; 26 of 123).

Pharyngeal examination and technical adequacy

In **Table 3**, the mean time for the pharyngeal observation was 20.6 seconds (range 10-39) and 44.3 seconds (range 19-60) in the sedation and no sedation groups respectively. Ninety-five percent of H&N region evaluations were totally complete (technical adequacy; 9 high resolution images of pharyngeal areas were taken) versus 60% among the no sedation group, while the examination was not technically adequate in 29 and 20 (23.58% and 16.26%; partial complete and incomplete) patients among the no sedation group because of excessive gag reflex. The difference was statistically significant for technical adequacy of pharyngeal observation between two groups (P<0.001).

The patient satisfaction questionnaire results showed that in the sedation group 93.94% of the patients scored 1 (acceptable with no pain or a little pain), 5.30% scored 2 (partly acceptable with some pain), and 0.67% scored 3 (unacceptable or painful). In the no sedation group, 68.29% scored 1, 19.51% scored 2, and 12.20% scored 3. The proportion of patient satisfaction was greater in the sedation than no sedation group (P<0.001).

Factors associated with technical adequacy of H&N region observation

In **Table 4**, the univariate logistic regression model indicated that patient age (>60) and smoking habit were associated with incomplete pharyngeal observation (P<0.05). Mu-

ltivariate logistic regression indicated that patient age (>60) (OR: 2.10, 95% CI: 1.04-4.22, P=0.038) and smoking habit (>10) (OR: 3.99, 95% CI: 0.21, 7.78, P=0.007) were associated with incomplete pharyngeal observation. However, the overall *P* value indicated that only smoking habit were associated with incomplete pharyngeal observation (P<0.05), and patients with more than 10 packs-per-day were more difficult to accomplish a complete evaluation.

Discussion

Squamous cell carcinoma is the most common histologic type of head and neck and esophageal cancer [1, 2]. Unfortunately most patients with HNSCC and ESCC who present with the typical symptoms of dysphagia and weight loss have advanced disease. But most of superficial esophageal and H&N (pharyngeal) cancers are asymptomatic. Smoking, ethanol and acetaldehyde in alcoholic beverages are known risk factors for SCC [17]. Because of field cancerization, patients with ESCC or HNSCC are at high risk for the development of multiple SCCs [18]. Previous studies demonstrated that NBI was an effective method for detecting and diagnosing superficial SCC [4, 14].

Abraham et al. reported an almost 76% technical adequacy and 79% patient satisfaction rate in patients administered titrated intravenous doses of meperidine and/or midazolam *versus* 46% and 47% respectively in patients who received normal saline placebo [7]. Saito et al [11] reported an almost 80% complete pharyngeal evaluation rate with only topical pharyngeal anesthesia (viscous lidocaine or lidocaine spray) in patients who had a prior previous experience with upper gastrointestinal endoscopy. Conversely, patients who receive either standard intravenous sedation or topical pharyngeal anesthesia may have an incomplete pharyngeal evaluation rate of more than 20%, possibly missing a lesion. Our results demonstrated an almost 96% successful procedure and 94% satisfaction in patients administered intravenous doses of propofol.

It was reported that most endoscopists in the western country use midazolam and meperidine for endoscopy, while propofol, either alone or in combination with other drugs, is used in a small proportion of patients [19]. However, most of the endoscopists in China use propofol with high satisfaction, citing its quicker sedation and recovery times, as well as an improved experience for both the patient and the endoscopist [20].

A number of studies revealed that sedation with propofol was safer and more effective than with midazolam and meperidine. The morbidity in using propofol without the assistance of aesthesiologist was 0.19%, no cases of mortality with a total of 82, 620 procedures [20]. Some prospective studies indicated that propofol offers adequate level of sedation during endoscopy [21]. However, there has not a study to verify the diagnostic yield of propofol sedation for early ESCC or HNSCC detection, which led us to carry out this prospective investigation.

In this study, the endoscopist must change to NBI mode to inspect uvula, posterior oropharyngeal wall, epiglottis, posterior hypopharyngeal wall, pyriform sinus and esophagus on endoscopic examination. Patients were assigned to receive sedation or no sedation according to their own willingness. In both groups, most of the patients were newly diagnosed ESCC and have not had previous experience of EGD, which can partially explained a lower totally complete pharyngeal region evaluation rate (60.16%).

Once an altered epithelium exhibiting irregularly distributed brown dots within a well demarcated brownish area was detected in the pharynx or esophagus, it was examined in greater detail to aid the intrapapillary capillary loop (IPCL) classification. If IPCL type IV or V was observed, it is highly indicated a dysplasia or cancer, and treatment such as biopsy, EMR or ESD was considered according to lesion size. After the procedure was completed, an assistant physician should record the results on the case record form, and we only included patients with advanced ESCC or previously treated for ESCC by ER with an age of 20 years or older for further statistics.

In our study, most of the small lesions (less than 10 mm in diameter) in pharyngeal region could be found with propofol sedation and the difference were statistically significant compared with no sedation group (P=0.048). A longer mean time for the pharyngeal region observation and lower rate of complete pharyngeal

observation with patients acceptable were observed in no sedation group. Univariate and multivariate analyses revealed that smoking habit was an independent risk factor for incomplete pharyngeal observation. Smoking is also definite risk factors for SCC [17]. Taken together, it is better to persuade a patient with heavy smoking habit to accept EGD under propofol sedation. We also compared the relationship between pharyngeal lesion detection and incomplete pharyngeal observation, and no significant difference was found. The reasons might be a relatively small pharyngeal lesions detected in no sedation group. In addition, most patients in our study had no previous experience of EGDE, and the complete observation rate was 60.16%, which can lower the detection rate of pharyngeal lesions.

To our knowledge this is the first study to assess the effectiveness of propofol sedation for the endoscopic detection of early ESCC or HNSCC. Our data suggests intravenous propofol sedation compared to no intravenous sedation during conventional upper gastrointestinal endoscopy can facilitate a more complete pharyngeal examination and increase the detection rate of superficial H&N squamous cell carcinoma in high risk patients. Propofol sedation for pharyngeal observation during conventional upper GI endoscopy is highly recommended for high-risk patients.

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Disclosure of conflict of interest

None.

Abbreviations

ESCCs, esophageal squamous cell carcinomas; NBI, narrow band imaging; HNSCC, head and neck squamous cell carcinoma; HGIN, high-grade intraepithelial neoplasia.

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References

[1] Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T and Thun MJ. Cancer statistics, 2008. CA Cancer J Clin 2008; 58: 71-96.

[2] Enzinger PC and Mayer RJ. Esophageal cancer. N Engl J Med 2003; 349: 2241-2252.

[3] Muto M, Nakane M, Katada C, Sano Y, Ohtsu A, Esumi H, Ebihara S and Yoshida S. Squamous cell carcinoma in situ at oropharyngeal and hypopharyngeal mucosal sites. Cancer 2004; 101: 1375-1381.

[4] Muto M, Minashi K, Yano T, Saito Y, Oda I, Nonaka S, Omori T, Sugiura H, Goda K, Kaise M, Inoue H, Ishikawa H, Ochiai A, Shimoda T, Watanabe H, Tajiri H and Saito D. Early detection of superficial squamous cell carcinoma in the head and neck region and esophagus by narrow band imaging: a multicenter randomized controlled trial. J Clin Oncol 2010; 28: 1566-1572.

[5] Lee CT, Chang CY, Lee YC, Tai CM, Wang WL, Tseng PH, Hwang JC, Hwang TZ, Wang CC and Lin JT. Narrow-band imaging with magnifying endoscopy for the screening of esophageal cancer in patients with primary head and neck cancers. Endoscopy 2010; 42: 613-619.

[6] Watanabe A, Taniguchi M, Tsujie H, Hosokawa M, Fujita M and Sasaki S. The value of narrow band imaging endoscope for early head and neck cancers. Otolaryngol Head Neck Surg 2008; 138: 446-451.

[7] Abraham NS, Fallone CA, Mayrand S, Huang J, Wieczorek P and Barkun AN. Sedation versus no sedation in the performance of diagnostic upper gastrointestinal endoscopy: a Canadian randomized controlled cost-outcome study. Am J Gastroenterol 2004; 99: 1692-1699.

[8] Triantafillidis JK, Merikas E, Nikolakis D and Papalois AE. Sedation in gastrointestinal endoscopy: current issues. World J Gastroenterol 2013; 19: 463-481.

[9] Dubuc J, Legoux J, Winnock M, Seyrig J, Barbier J, Barrioz T, Laugier R, Boulay G, Grasset D, Sautereau D, Grigoresco D, Butel J, Scoazec J, Ponchon T and Societe Francaise d'Endoscopie D. Endoscopic screening for esophageal squamous-cell carcinoma in high-risk patients: a prospective study conducted in 62 French endoscopy centers. Endoscopy 2006; 38: 690-695.

[10] Nonaka S, Saito Y, Oda I, Kozu T and Saito D. Narrow-band imaging endoscopy with magnifi-

cation is useful for detecting metachronous superficial pharyngeal cancer in patients with esophageal squamous cell carcinoma. J Gastroenterol Hepatol 2010; 25: 264-269.
[11] Saito M, Yamashita K, Tanuma T, Kaneto H, Murakami K, Onodera K, Shimizu H, Sakamoto H, Hosokawa-Motoya M, Arimura Y and Shinomura Y. Pharyngeal cancer surveillance using narrow band imaging during conventional upper gastrointestinal endoscopy. Digestion 2013; 88: 229-234.
[12] Al-Awabdy B and Wilcox CM. Use of anesthesia on the rise in gastrointestinal endoscopy. World J Gastrointest Endosc 2013; 5: 1-5.
[13] Shimizu Y, Tukagoshi H, Fujita M, Hosokawa M, Kato M and Asaka M. Metachronous squamous cell carcinoma of the esophagus arising after endoscopic mucosal resection. Gastrointest Endosc 2001; 54: 190-194.
[14] Nagami Y, Tominaga K, Machida H, Nakatani M, Kameda N, Sugimori S, Okazaki H, Tanigawa T, Yamagami H, Kubo N, Shiba M, Watanabe K, Watanabe T, Iguchi H, Fujiwara Y, Ohira M, Hirakawa K and Arakawa T. Usefulness of nonmagnifying narrow-band imaging in screening of early esophageal squamous cell carcinoma: a prospective comparative study using propensity score matching. Am J Gastroenterol 2014; 109: 845-854.
[15] Abraham N, Barkun A, Larocque M, Fallone C, Mayrand S, Baffis V, Cohen A, Daly D, Daoud H and Joseph L. Predicting which patients can undergo upper endoscopy comfortably without conscious sedation. Gastrointest Endosc 2002; 56: 180-189.
[16] Schlemper RJ, Riddell RH, Kato Y, Borchard F, Cooper HS, Dawsey SM, Dixon MF, Fenoglio-Preiser CM, Flejou JF, Geboes K, Hattori T, Hirota T, Itabashi M, Iwafuchi M, Iwashita A, Kim YI, Kirchner T, Klimpfinger M, Koike M, Lauwers GY, Lewin KJ, Oberhuber G, Offner F, Price AB, Rubio CA, Shimizu M, Shimoda T, Sipponen P, Solcia E, Stolte M, Watanabe H and Yamabe H. The Vienna classification of gastrointestinal epithelial neoplasia. Gut 2000; 47: 251-255.
[17] Secretan B, Straif K, Baan R, Grosse Y, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Cogliano V and WHO International Agency for Research on Cancer Monograph Working Group. A review of human carcinogens-Part E: tobacco, areca nut, alcohol, coal smoke, and salted fish. Lancet Oncol 2009; 10: 1033-1034.
[18] Slaughter DP, Southwick HW and Smejkal W. Field cancerization in oral stratified squamous epithelium; clinical implications of multicentric origin. Cancer 1953; 6: 963-968.
[19] Porostocky P, Chiba N, Colacino P, Sadowski D and Singh H. A survey of sedation practices for colonoscopy in Canada. Can J Gastroenterol 2011; 25: 255-260.
[20] Heuss LT, Froehlich F and Beglinger C. Changing patterns of sedation and monitoring practice during endoscopy: results of a nationwide survey in Switzerland. Endoscopy 2005; 37: 161-166.
[21] Gasparovic S, Rustemovic N, Opacic M, Premuzic M, Korusic A, Bozikov J and Bates T. Clinical analysis of propofol deep sedation for 1,104 patients undergoing gastrointestinal endoscopic procedures: a three year prospective study. World J Gastroenterol 2006; 12: 327-330.