CANCER DIAGNOSIS & PROGNOSIS
1: 427-434 (2021) doi: 10.21873/cdp.10057

Transoral Endoscopic Examination of the Oropharynx With Tongue Protrusion, Phonation, and Open Mouth

RYOTA TOMIOKA, HIROKI SATO, ISAKU OKAMOTO, AKIRA SHIMIZU and KIYOAKI TSUKAHARA

Department of Otorhinolaryngology, Head and Neck Surgery, Tokyo Medical University, Tokyo, Japan

Abstract. *Background/Aim: We examined the diagnostic performance of the tongue protrusion with phonation and open mouth (TOPPOM) method for visualizing structures of the oropharynx. Patients and Methods: Transoral endoscopy was performed on 20 healthy participants to evaluate 12 oropharynx subsites under three conditions: open mouth (OM), phonation with open mouth (POM), and TOPPOM. Each subsite was scored from 0 to 2 depending on subsite visualization, and the scores were summed. Images of subsite-adjacent mucosa were similarly scored. Results: The total scores were significantly higher for TOPPOM than for POM and for POM than for OM. Such scores were observed for both the palatine arches, both palatine tonsils, the left lingual tonsillar sulcus, and the vallecula. Conclusion: TOPPOM enables visualization of the oropharynx through transoral endoscopic examination, and TOPPOM with conventional transnasal endoscopy may enable early detection of oropharyngeal carcinomas and lesions and improve the performance of pre- and post-treatment evaluations.*

The incidence of oropharyngeal squamous cell carcinoma (OPSCC) is increasing, especially in developed countries, among individuals aged ≤60 years (1). Human papillomavirus is a risk factor for OPSCC; the increase in the prevalence of human papillomavirus infection over the last few decades has attributed to the significant increase in OPSCC incidence (2-4). Advances in transoral surgery and the emergence of transoral robotic surgery (TORS) have resulted in a paradigm shift in treatment strategies for OPSCC (5, 6). Transoral surgery is a minimally invasive treatment option for OPSCC; however, accurate and early preoperative endoscopic diagnosis is crucial for enabling radical resection of the lesions through this approach. Traditionally, transoral examination of the oropharynx is performed macroscopically using a head mirror, headlight, and tongue depressor; this method remains widely used at present. Recent advances in optical instruments have enabled detailed observation of the structure of the pharynx and mucosal surfaces using electronic endoscopes, enabling early-stage head-and-neck cancer detection, including that of the oropharynx (7). There have been very few reports on the endoscopic examination of the oropharynx; a gastrointestinal endoscope has been used in all previous studies (8, 9). Moreover, there have been no endoscopic studies in the field of otorhinolaryngology. We anticipate that accurate endoscopic diagnosis in the field of otorhinolaryngology will contribute to the detection of early-stage OPSCC.

Patients and Methods

We performed transoral endoscopy of the oropharynx in healthy participants using a flexible endoscope, which is appropriate for otorhinolaryngology, tongue protrusion, and phonation procedures, without a tongue depressor, to examine the diagnostic performance of the tongue protrusion with phonation and open mouth (TOPPOM) method for visualizing structures of the oropharynx.

Study design. Twenty healthy participants between the ages of 20 and 75 years were enrolled for the present study. The exclusion criteria were as follows: head-and-neck diseases, including those of the oral cavity and oropharynx, underlying systemic diseases, pregnancy, and breastfeeding. All clinical investigations were conducted according to the principles of the Declaration of Helsinki. The study and all its protocols were approved by the Tokyo Medical University Ethics Committee (Registration number: SH3690). All participants understood the purpose of the study and provided written informed consent before any of the procedures were carried out.

This article is freely accessible online.

Correspondence to: Hiroki Sato, Department of Otorhinolaryngology, Head and Neck Surgery Tokyo Medical University, 6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo 160-0023, Japan. Tel: +81 333426111, Fax: +81 333469275, e-mail: satohiro@tokyo-med.ac.jp

Key Words: Oropharynx, endoscopy, tongue protrusion, oropharyngeal carcinoma, head-and-neck carcinoma, transoral surgery.

Endoscopy procedure. An Olympus ENF-VH videoscope (Olympus Medical Systems, Tokyo, Japan) was used for otorhinolaryngology, and the images were recorded on an Olympus VISERA ELITE video system (Olympus Medical Systems). Endoscopy was performed with the participants seated with their head placed in a fixed position (Figure 1). The examiner inserted the endoscope transorally without using a tongue depressor. The oropharynx was then observed in the following three conditions: 1) with the participant opening the mouth only (open mouth; OM), 2) with phonation and open mouth (POM), and 3) with TOPPOM. Participants were instructed to open their mouth as wide as possible; subsequently, some were instructed to phonate a long 'e' (as in egg) and some were instructed to protrude their tongue. During the individual procedures, 12 oropharyngeal subsites (Figure 2A-L) and the proximity of the mucosa to each of the 12 subsites (Figure 3A-H) were observed. The subsites were as follows: the soft palate, left and right anterior palatine arches, left and right palatine tonsils, left and right posterior palatine arches, posterior oropharyngeal wall, left and right lingual tonsillar sulcus, tongue base, and vallecula.

Evaluation. Scores were assigned as follows at all 12 subsites of the oropharynx under each of the three conditions: 2 points when the entire subsite was clearly observed, 1 point when only partial observation was possible, and 0 points when the subsite was not observed at all. The proximity images of the mucosa for each subsite were also recorded and scored in the same way, *i.e.*, 2 points were awarded if the dendritic vasculature in the background of the mucosa could be clearly observed, 1 point if it could not be clearly observed, and 0 points if it could not be observed at all. The numbers of these regions were the same as the number of subsites. The primary endpoint was the total score (out of 48), representing the view of all subsites and proximity images of the mucosa. The rate of the endpoint was compared between the three conditions through superiority comparison. The secondary endpoint was the total score (out of 4) relating to the complete view of individual oropharynx subsites and proximity images. The rate of the secondary endpoint was compared among the three conditions. One otorhinolaryngologist acted as the examiner and three other otorhinolaryngologists evaluated the endoscopic images.

Statistical analysis. Continuous data are presented as the mean±standard deviation. The scores were compared between the OM, POM, and TOPPOM conditions using the Kruskal–Wallis and Dann-Bonferroni tests. A *p*-value <0.05 was considered a statistically significant difference. All statistical analyses were performed using SPSS version 24.0 (IBM Corp., Armonk, NY, USA).

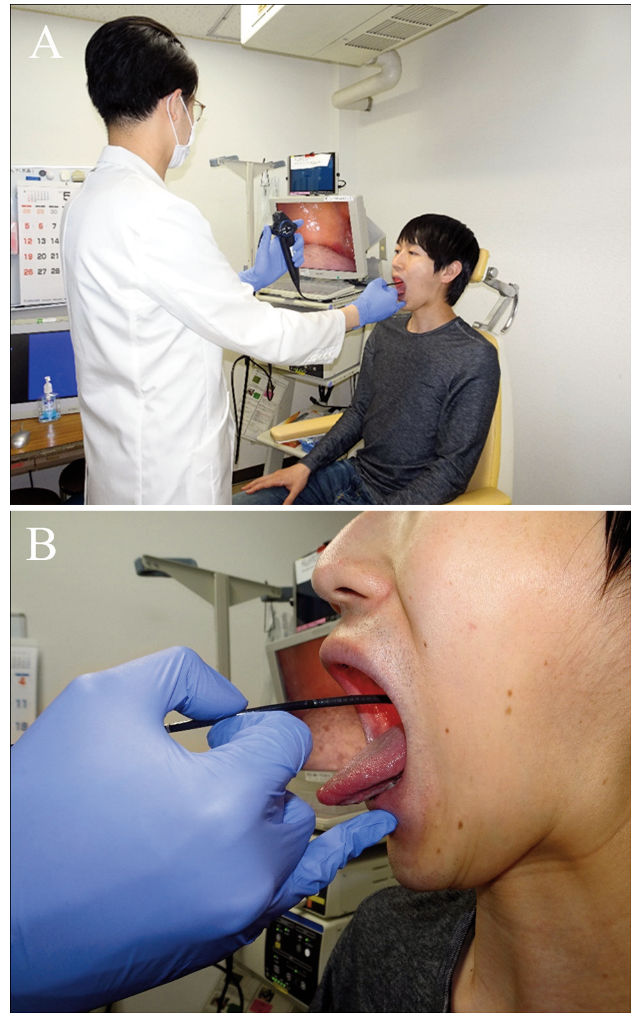

Figure 1. *Photographs demonstrating the subject's posture (A) and mouth position (B) during oropharyngeal examination with tongue protrusion and phonation with open mouth (TOPPOM condition).*

Results

The mean total score for all oropharynx subsites during OM, POM, and TOPPOM were 15±4.86, 27±4.86, and 34±4.19 points, respectively. The differences in the mean scores between OM and POM, OM and TOPPOM, and POM and TOPPOM were statistically significant ($p<0.001$ for all) (Figure 4, Table I). Evaluation of the scores of individual subsites revealed that in six of the subsites – the left and right anterior palatine arches, left and right palatine tonsils, left lingual tonsillar sulcus, and vallecula – the scores were significantly higher for TOPPOM than for POM and significantly higher for POM than for OM. However, the scores for the soft palate, left and right posterior palatine arches, right lingual tonsillar sulcus, posterior wall, and tongue base were significantly higher during POM and TOPPOM than during OM, and there was no significant difference between the scores for POM and TOPPOM (Figure 5, Table I).

Discussion

Our study demonstrates that TOPPOM allows significantly better endoscopic observation than POM or OM alone. Furthermore, observation of the anterior palatine arches, palatine tonsils, lingual tonsillar sulcus, and vallecula was significantly improved during TOPPOM compared to that

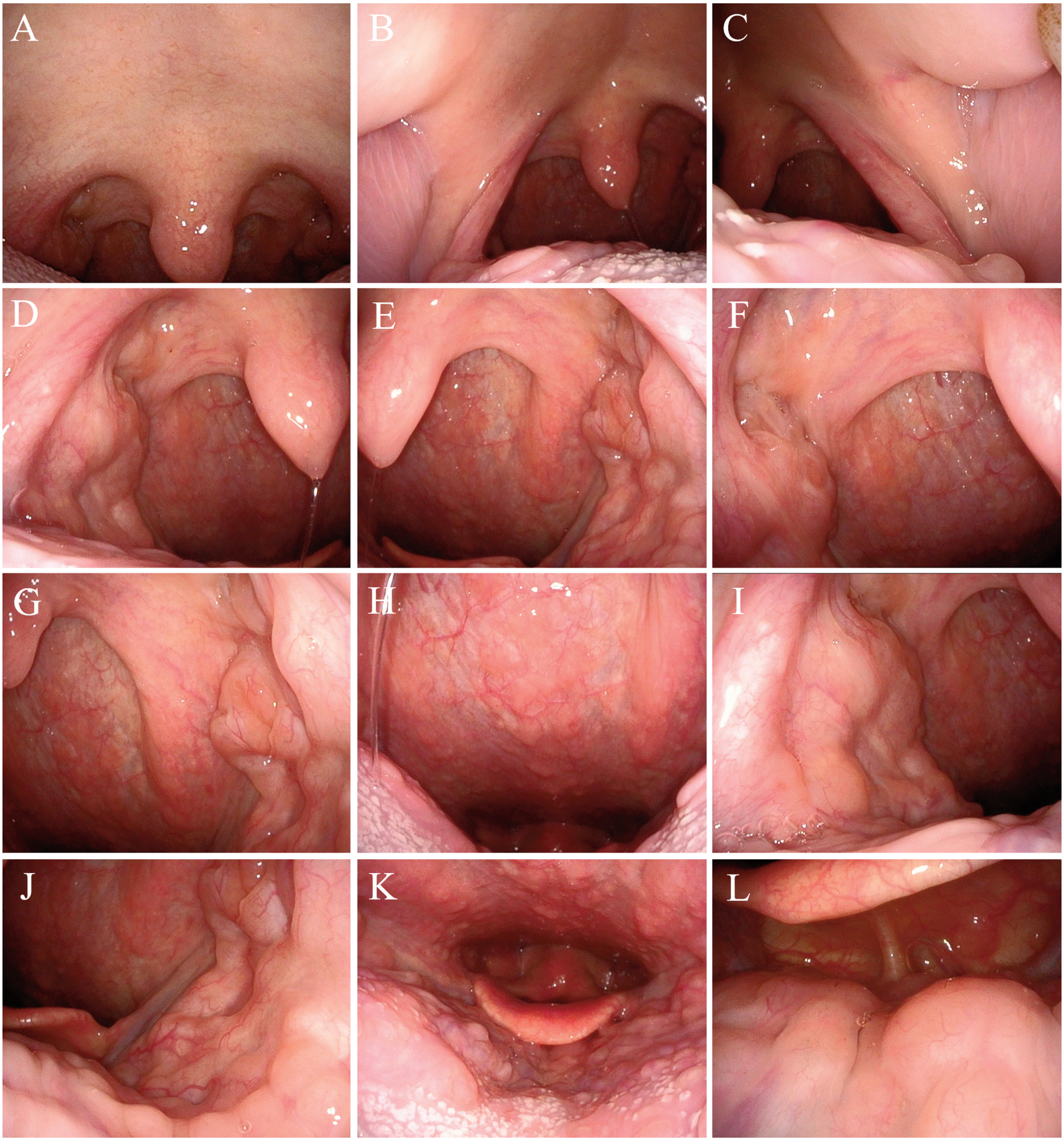

Figure 2. *Endoscopic images of the oropharyngeal subsites observed with tongue protrusion and phonation with open mouth (TOPPOM condition). Photographs show the (A) soft palate, (B, C) left and right anterior palatine arches, (D, E) left and right palatine tonsils, (F, G) left and right posterior palatine arches, (H) posterior oropharyngeal wall, (I, J) left and right lingual tonsillar sulcus, (K) tongue base, and (L) vallecula.*

during POM or OM only, whereas all subsites of the oropharynx were more easily observed during POM than during OM only. This could be attributed to the phonation of a long 'e' that raises the soft palate and widens the pharyngeal cavity. In addition, tongue protrusion causes the lower edges of the anterior palatine arches to be pulled anteriorly by the tongue. This extends the pharyngeal cavity forward, allowing the lower edges of the anterior palatine arches and palatine

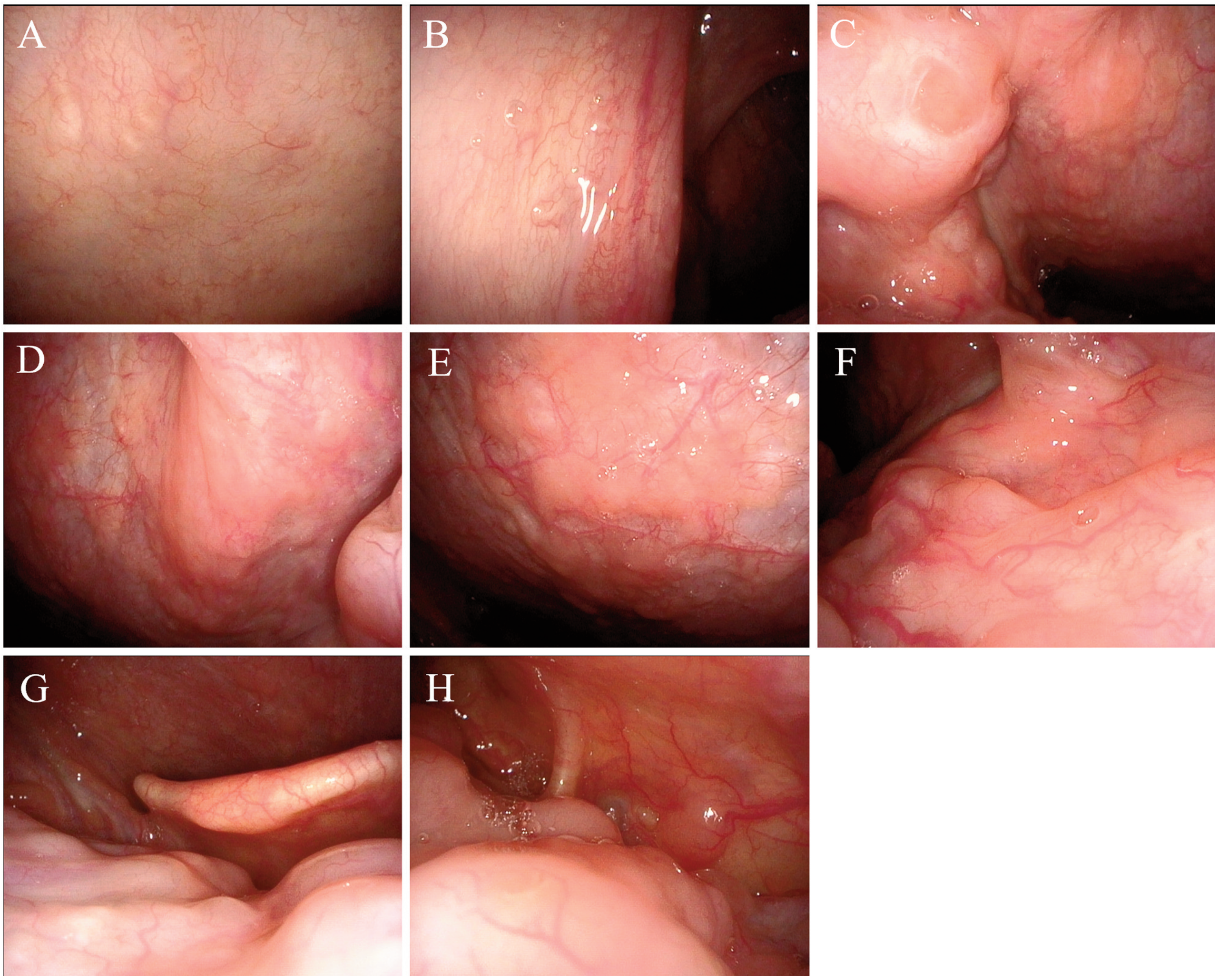

Figure 3. *Proximity endoscopic images of the mucosa for the oropharyngeal subsites observed with tongue protrusion and phonation with open mouth (TOPPOM condition). Photographs show the (A) soft palate, (B) right anterior palatine arche, (C) right palatine tonsil, (D) left posterior palatine arche, (E) posterior oropharyngeal wall, (F) left lingual tonsillar sulcus, (G) tongue base, and (H) vallecula.*

tonsils, which are hidden by the tongue during POM, to be clearly observed. The mean scores of the lingual tonsillar sulcus, tongue base, and vallecula were good and were the highest in TOPPOM, followed by POM, and the lowest in OM. There was a significant difference between the scores in TOPPOM and POM for the left lingual tonsillar sulcus and vallecula only. The lingual tonsillar sulcus, tongue base, and vallecula are deep within the oropharynx; therefore, they were difficult to observe in some cases because of the gag reflex, which may have affected the results. Observation of the soft palate, anterior palatine arches, palatine tonsils, posterior palatine arches, and posterior wall by transnasal endoscopy, which is commonly used by otorhinolaryngologists, is likely to be insufficient because these subsites are generally tangential to a nasal endoscope and are difficult to observe. Images of the posterior wall are particularly difficult to obtain because this region is tangential to the transnasal endoscope. Transoral endoscopy provides an effective alternative because the soft palate, anterior and posterior palatine arches, palatine tonsils, and posterior wall are perpendicular to the endoscope, enabling easy observation.

The traditional macroscopic method of surgery involves a head mirror, headlight, and tongue depressor and enables observation in one direction only since the equipment remains outside of the oral cavity. The angle of insertion of the endoscope can be optimized to observe the mucosal surfaces from various angles, enabling detection of superficial cancers and lesions in the palatine tonsil crypts. In addition, because the endoscope can reach deep inside the oral cavity, a tongue depressor is not necessary to achieve a good field of view.

Table I. *Observation scores of the oropharynx and comparison between the three procedure conditions.*

	Mean TS	SP	RAPA	LAPA	RPT	LPT	RPPA	LPPA	PW	RLTS	LLTS	TB	Vallecula
OM	15	3.5	2.0	2.0	1.4	1.6	1.7	1.7	1.9	0.2	0.1	0.27	0.1
POM	27	3.9	3.1	2.9	2.6	2.7	2.7	2.7	3.0	1.3	1.2	1.1	0.7
TOPPOM	34	4.0	3.9	3.8	3.7	3.5	3.4	3.3	3.4	2.3	2.3	1.8	1.5
p-Value													
OM *vs*. POM	**<0.001**	**0.003**	**<0.001**	**0.007**	**<0.001**	**0.002**	**0.002**	**0.007**	**0.001**	**0.004**	**0.005**	**0.011**	**0.042**
OM *vs*. TOPPOM	**<0.001**	**0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**
POM *vs*. TOPPOM	**<0.001**	1.000	**0.013**	**0.020**	**0.018**	**0.014**	0.115	0.128	0.36	0.081	**0.011**	0.079	**0.026**

OM: Open mouth; POM: phonation with open mouth; TOPPOM: tongue protrusion with phonation and open mouth; TS: total score; SP: soft palate; RAPA: right anterior palatine arch; LAPA: left anterior palatine arch; LPPA: left posterior palatine arch; RPT: right palatine tonsil; LPT: left palatine tonsil; RPPA: right posterior palatine arch; LPPA: left posterior palatine arch; PW: posterior wall; RLTS: right lingual tonsillar sulcus, LLTS: left lingual tonsillar sulcus; TB: tongue base. Bold font indicates statistical significance. Statistical analyses included the Kruskal–Wallis test and Dann-Bonferroni correction.

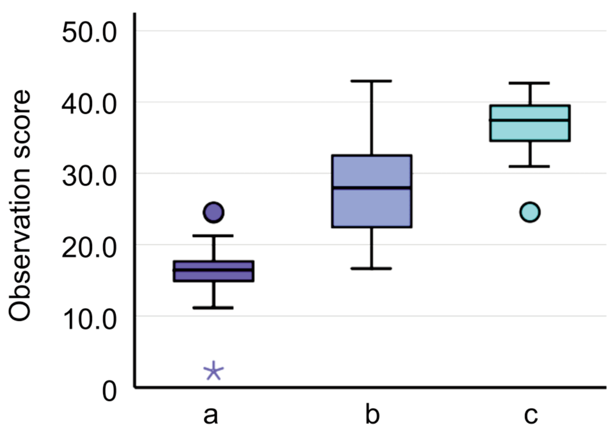

Figure 4. *Box plot showing the total scores for the (a) open mouth, (b) phonation with opening mouth, and (c) tongue protrusion and phonation with open mouth conditions. The differences in the mean scores between OM and POM, OM and TOPPOM, and POM and TOPPOM were statistically significant (p<0.001 for all). Whiskers indicate the range of numbers from maximum to minimum, circles indicate outliers, and asterisks indicate extreme outliers.*

However, the observation of deep subsites of the oropharynx such as the lingual tonsillar sulcus, tongue base, and vallecula is considered to be poor, as indicated by the low mean score even during TOPPOM. Since these parts are well observed using conventional transnasal endoscopy, the transnasal endoscopy and the TOPPOM method should be used together in routine medical practice.

According to the concept of field cancerization, head-and-neck squamous cell carcinoma and esophageal squamous cell carcinoma frequently exist synchronously or metachronously (10), and a strong connection between excessive drinking and smoking and multicentric carcinogenesis has been demonstrated (11). Such cases require comprehensive examination of the head-and-neck region including the oropharynx and esophagus.

Diagnosis of superficial head-and-neck carcinoma, including of the oropharynx, can be achieved using digestive endoscopes (7, 12). In otorhinolaryngology, however, macroscopic observation is routinely conducted using a head mirror and headlight (13, 14). Furthermore, the endoscopes used in otorhinolaryngology are small, meaning that only charge-coupled devices (CCDs) with small diameters can be attached, resulting in inferior images compared to those obtained with large-diameter digestive endoscopes attached to high-resolution CCDs; moreover, image enhancement was not introduced until recently. Collectively, these factors hindered the detection of superficial carcinoma. In recent years, the potential image quality of otorhinolaryngology endoscopes has improved with the advent of narrow band imaging, in which vascular information is emphasized and expressed. Therefore, it has become possible to diagnose minute lesions that are difficult to recognize by white light observation by visualizing characteristic vascular abnormalities in tumor tissue (15), permitting the detection of superficial carcinomas during screening of high-risk patients--such as those with esophageal carcinomas--for head-and-neck carcinoma (16). Early detection means that minimally invasive treatment including transoral resection is possible, which helps to maintain organ function and quality of life (17). We consider that the use of the TOPPOM method can further increase the rate of early detection of oropharyngeal carcinoma by enabling comprehensive examination of the oropharynx.

New techniques have been developed for examining the hypopharynx, such as the modified Killian method (18), and clear observation of this region as far as the esophageal orifice is now possible. We think that detailed examination of the head-and-neck region using the modified Killian method in conjunction with transnasal endoscopy should be

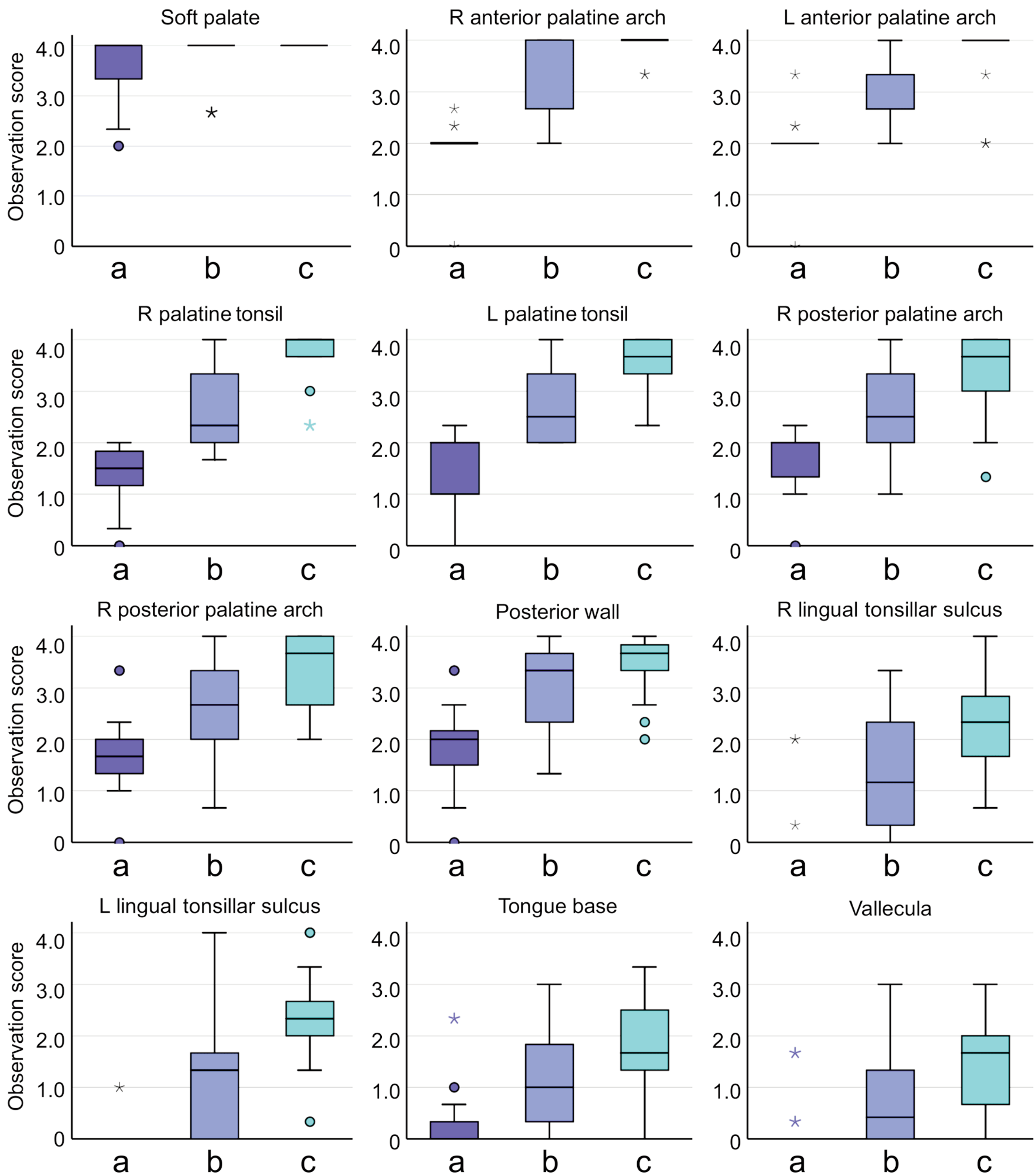

Figure 5. *Box plot showing total scores for each oropharyngeal subsite in the (a) open mouth, (b) phonation with open mouth, and (c) tongue protrusion and phonation with open mouth conditions. Whiskers indicate the range of numbers from maximum to minimum, circles indicate outliers, and asterisks indicate extreme outliers. R: Right; L: left.*

combined with the TOPPOM method to include observation of the oral cavity. This will not only improve the results when screening this region but will also contribute to improving medical care for malignancies through facilitating pre-treatment diagnosis, preoperative determination of resection scope and evaluation of treatment outcomes for oropharyngeal lesions as well as other inflammatory and benign diseases. Recently, good outcomes have been reported in oropharyngeal carcinoma following TORS (19), and we believe that accurate diagnosis of the extent of cancerous lesions by endoscopy using the TOPPOM method will greatly contribute to complete resection with TORS and other transoral resective procedures.

This study has some limitations that should be acknowledged. First, we included only healthy participants; thus, no lesions of the oropharynx were examined. Evaluation of lesions in routine clinical practice using our suggested method should be conducted. Second, we did not compare our results with macroscopic observations. However, the comparison would be difficult since the evaluation of macroscopic observations is subjective, and the evaluation of endoscopic images is objective (as in the present study).

The TOPPOM method can improve the results of transoral endoscopy of the oropharynx and enable comprehensive examination with conventional transnasal endoscopy of the head-and-neck region. The literature on transoral endoscopic examination of the oropharynx is scarce, and the TOPPOM method may contribute to the discovery of the cause of early oropharyngeal cancer and cancer of unknown primary origin in addition to reducing oversight. Moreover, early detection enables prompt treatment and allows for the selection of a less invasive treatment. Future studies should investigate whether the ability to diagnose early oropharyngeal cancer could be improved by using this method.

Conflicts of Interest

The Authors declare that they have no competing interests in relation to this study.

Authors' Contributions

RT was responsible for data collection and analysis, drafting and editing the manuscript. HS was responsible for idea development, study design, data analysis, drafting and editing the manuscript. IO and AS were responsible for data analysis. KT was responsible for idea development and study design. All Authors read and approved the final manuscript.

References

1 Chaturvedi AK, Anderson WF, Lortet-Tieulent J, Curado MP, Ferlay J, Franceschi S, Rosenberg PS, Bray F and Gillison ML: Worldwide trends in incidence rates for oral cavity and oropharyngeal cancers. J Clin Oncol *31(36):* 4550-4559, 2013. PMID: 24248688. DOI: 10.1200/JCO.2013.50.3870

2 Chaturvedi AK, Engels EA, Pfeiffer RM, Hernandez BY, Xiao W, Kim E, Jiang B, Goodman MT, Sibug-Saber M, Cozen W, Liu L, Lynch CF, Wentzensen N, Jordan RC, Altekruse S, Anderson WF, Rosenberg PS and Gillison ML: Human papillomavirus and rising oropharyngeal cancer incidence in the United States. J Clin Oncol *29(32)*: 4294-4301, 2011. PMID: 21969503. DOI: 10.1200/JCO.2011.36.4596

3 Mehanna H, Beech T, Nicholson T, El-Hariry I, McConkey C, Paleri V and Roberts S: Prevalence of human papillomavirus in oropharyngeal and nonoropharyngeal head and neck cancer – systematic review and meta-analysis of trends by time and region. Head Neck *35(5)*: 747-755, 2013. PMID: 22267298. DOI: 10.1002/hed.22015

4 Windon MJ, D'Souza G, Rettig EM, Westra WH, van Zante A, Wang SJ, Ryan WR, Mydlarz WK, Ha PK, Miles BA, Koch W, Gourin C, Eisele DW and Fakhry C: Increasing prevalence of human papillomavirus-positive oropharyngeal cancers among older adults. Cancer *124(14)*: 2993-2999, 2018. PMID: 29710393. DOI: 10.1002/cncr.31385

5 Tamaki A, Rocco JW and Ozer E: The future of robotic surgery in otolaryngology – head and neck surgery. Oral Oncol *101*: 104510, 2020. PMID: 31841882. DOI: 10.1016/j.oraloncology.2019.104510

6 Tateya I, Shiotani A, Satou Y, Tomifuji M, Morita S, Muto M and Ito J: Transoral surgery for laryngo-pharyngeal cancer - The paradigm shift of the head and cancer treatment. Auris Nasus Larynx *43(1)*: 21-32, 2016. PMID: 26298233. DOI: 10.1016/j.anl.2015.06.013

7 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 *28(9)*: 1566-1572, 2010. PMID: 20177025. DOI: 10.1200/JCO.2009.25.4680

8 Hamada K, Ishihara R, Yamasaki Y, Akasaka T, Arao M, Iwatsubo T, Shichijo S, Matsuura N, Nakahira H, Kanesaka T, Yamamoto S, Takeuchi Y, Higashino K, Uedo N, Kawahara Y and Okada H: Transoral endoscopic examination of head and neck region. Dig Endosc *30(4)*: 516-521, 2018. PMID: 29637617. DOI: 10.1111/den.13071

9 Kawada K, Okada T, Sugimoto T, Kishimoto S and Kawano T: Intraoropharyngeal U-turn method using transnasal esophagogastroduodenoscopy. Endoscopy *46(Suppl 1 UCTN)*: E137-E138, 2014. PMID: 24756261. DOI: 10.1055/s-0033-1359192

10 Slaughter DP, Southwick HW and Smejkal W: Field cancerization in oral stratified squamous epithelium; clinical implications of multicentric origin. Cancer *6(5)*: 963-968, 1953. PMID: 13094644. DOI: 10.1002/1097-0142(195309)6:5 <963::aid-cncr2820060515>3.0.co;2-q

11 Morita M, Kuwano H, Ohno S, Sugimachi K, Seo Y, Tomoda H, Furusawa M and Nakashima T: Multiple occurrence of carcinoma in the upper aerodigestive tract associated with esophageal cancer: reference to smoking, drinking and family history. Int J Cancer *58(2)*: 207-210, 1994. PMID: 8026883. DOI: 10.1002/ijc.2910580211

12 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 *101(6)*: 1375-1381, 2004. PMID: 15368325. DOI: 10.1002/cncr.20482

13 Lin CH, Hsu HT, Chen PY, Huon LK, Lin YZ and Hung SH: Head mirror versus headlight: illumination, visual identification and visual acuity for otolaryngological examination. J Laryngol Otol *127(8)*: 744-748, 2013. PMID: 23834741. DOI: 10.1017/S0022215113001424

14 Rowlands J, Mal RK and Thornton MR: Headlight or head mirror? Eur Arch Otorhinolaryngol *263(6)*: 601-602, 2006. PMID: 16525821. DOI: 10.1007/s00405-006-0020-3

15 Zhou H, Zhang J, Guo L, Nie J, Zhu C and Ma X: The value of narrow band imaging in diagnosis of head and neck cancer: a meta-analysis. Sci Rep *8(1)*: 515, 2018. PMID: 29323235. DOI: 10.1038/s41598-017-19069-0

16 Watanabe A, Tsujie H, Taniguchi M, Hosokawa M, Fujita M and Sasaki S: Laryngoscopic detection of pharyngeal carcinoma in situ with narrowband imaging. Laryngoscope *116(4)*: 650-654, 2006. PMID: 16585874. DOI: 10.1097/01.mlg.0000204304.38797.34

17 Achim V, Bolognone RK, Palmer AD, Graville DJ, Light TJ, Li R, Gross N, Andersen PE and Clayburgh D: Long-term functional and quality-of-life outcomes after transoral robotic surgery in patients with oropharyngeal cancer. JAMA Otolaryngol Head Neck Surg *144(1)*: 18-27, 2018. PMID: 29075740. DOI: 10.1001/jamaoto.2017.1790

18 Sakai A, Okami K, Sugimoto R, Ebisumoto K, Yamamoto H, Maki D, Saito K and Iida M: A new technique to expose the hypopharyngeal space: The modified Killian's method. Auris Nasus Larynx *41(2)*: 207-210, 2014. PMID: 24183396. DOI: 10.1016/j.anl.2013.10.012

19 Smith RV, Schiff BA, Garg M and Haigentz M: The impact of transoral robotic surgery on the overall treatment of oropharyngeal cancer patients. Laryngoscope *125(Suppl 10)*: S1-S15, 2015. PMID: 26436491. DOI: 10.1002/lary.25534

Received September 14, 2021
Revised October 1, 2021
Accepted October 4, 2021