ORIGINAL RESEARCH

Validation of Ni's Grading and European Laryngological Society Grading for Laryngeal Lesions: A Prospective Cross-sectional Study

Vivek Soman[1], Jayakumar R Menon[2], Manju E Issac[3], Basil Varghese[4]

Received on: 11 December 2023; *Accepted on:* 31 December 2023; *Published on:* xxxx

Abstract

Aims and background: Laryngeal carcinomas comprise one-third of all head and neck carcinomas. Early detection of these lesions is pertinent for curative and functional preservation. Narrow band imaging (NBI) is a novel biological endoscopic tool enabling *in vivo* differentiation of nonmalignant from malignant laryngeal lesions.

Ni et al. proposed a classification of laryngeal lesions based on intraepithelial papillary capillary loops (IPCL) patterns from type I to V. The European Laryngological Society (ELS) introduced a simpler classification in 2015, categorizing vascular changes as either longitudinal or perpendicular. The present study is aimed at identifying the angiogenetic pattern of different laryngeal lesions and validating the two different grading systems.

Materials and methods: Preoperative flexible laryngoscopy coupled NBI evaluation was done for 30 consecutive patients with laryngeal lesions posted for excision biopsy and graded according to both Ni's and ELS grading. The biopsy results of the lesions were correlated with preoperative NBI gradings.

Results: Of the 30 patients, 23 (76.7%) were males, and seven (23.3%) were females. The maximum number of patients, 13 (43.3%) belonged to Ni's grade V, whereas 15 patients (50%) each showed longitudinal and perpendicular pattern blood vessels, respectively in ELS grading. A total of 14 patients (46.7%), five patients (16.7%), and 11 patients (36.7%) were revealed to be benign, dysplastic, and malignant, respectively on biopsy. Both Ni's and ELS grading had a statistically significant association with the benign or malignant nature of the lesion. The sensitivity and specificity of Ni's grading were 84.2 and 90.9%, and of ELS grading were 78.9 and 100%, respectively. Both these gradings had similar measures of agreement with histopathological examination (HPE) (measured by Cohen's κ).

Conclusion: The NBI is a useful diagnostic tool in evaluating laryngeal pathologies.

Clinical significance: The ELS grading system which is convenient and easy to use than Ni's grading can be reliably used for classifying laryngeal lesions.

Keywords: Histopathological examination, Hoarseness, Laryngeal cancer, Laryngoscopy, Narrow band imaging.

International Journal of Phonosurgery & Laryngology (2024): 10.5005/jp-journals-10023-1251

Introduction

Laryngeal carcinoma comprises one-third of all head and neck cancers. Its early stages are curable with radiation or surgery, whereas late stages require multimodal management and have a worse outcome. Early detection is crucial in maintaining vocal function and increasing the chances of successful treatment outcomes.[1] Early detection is often challenging, and computed tomography (CT) and magnetic resonance imaging (MRI) can detect only larger lesions in this area and fail to detect superficial mucosal abnormalities.[2] The standard method for evaluating precancerous and cancerous lesions in the larynx is through the use of white light laryngoscopy with biopsy. One demerit associated with white light (WL) endoscopy alone is that it fails to identify minute epithelial changes and is less sensitive in differentiating benign from malignant lesions *in vivo*.[1]

Narrow band imaging (NBI) has emerged as a great tool in the early identification of laryngeal cancer. Although initially developed for identifying lesions of the upper gastrointestinal system, its use gradually extended to laryngology.

Narrow band imaging (NBI) has been in use in laryngology for >10 years now. According to the NBI operational principle, the depth of light penetration is dependent on the wavelength.[3] NBI uses two narrow bands of blue (415 nm) and green light (540 nm), which display superficial capillary and subepithelial vessels, respectively, furnishing a high-contrast image of the tissue surface. NBI can identify minor and superficial mucosal lesions that may be missed on conventional

[1–3]Department of Laryngology, Dr Jayakumar's Institute of Laryngology, Thiruvananthapuram, Kerala, India

[4]Department of Laryngology, Tata Trust Government Hospital, Kasaragod, Kerala, India

Corresponding Author: Vivek S, Department of Laryngology, Dr Jayakumar's Institute of Laryngology, Thiruvananthapuram, Kerala, India, Phone: +919447776906, e-mail: viveksoman3@gmail.com

How to cite this article: Soman V, Menon JR, Issac ME, *et al.* Validation of Ni's Grading and European Laryngological Society Grading for Laryngeal Lesions: A Prospective Cross-sectional Study. Int J Phonosurg Laryngol 2024;https://doi.org/10.5005/jp-journals-10023-1251.

Source of support: Nil

Conflict of interest: Dr Jayakumar R Menon is associated as the National Advisory Board member of this journal and this manuscript was subjected to this journal's standard review procedures, with this peer review handled independently of this editorial board member and her research group.

WL endoscopy.[2] It can also demarcate mucosal abnormalities without the use of dyes. In rigid or flexible scopes incorporated with NBI, it can be easily enabled by pressing a button.[4]

Ni et al. 2011 published the first description of vascular patterns in laryngeal lesions based on intrapapillary capillary loops (IPCL) in five types (types I–V). Type V is further subdivided into Va, Vb, and Vc.[1] The European Laryngological Society (ELS) suggested a simpler way to classify glottic vascular changes using NBI. They propose dividing these changes into two categories—longitudinal (which is not suspicious) and perpendicular (which is suspicious). Longitudinal patterns are typically seen in benign lesions, while perpendicular patterns may indicate papillomatosis, squamous intraepithelial neoplasia (SIN), or invasive carcinoma.[5]

The purpose of this study is to examine various laryngeal abnormalities based on the angiogenetic pattern and to validate the above two different classification (Ni's vs ELS) systems in laryngeal lesions.

Materials and Methods

The study was performed by enrolling 30 patients who presented to the laryngology outpatient department (OPD) diagnosed with laryngeal lesions, who were posted for excision of the lesion and subsequent histopathological study. The study period was from May 2021 to 2022. The study was approved by the Institutional Ethics Committee (IEC), and we obtained informed consent from each patient before including them in the study. Exclusion criteria include allergy to lignocaine, intractable dyspnea, history of unstable angina, and patients who did not consent to the study. Before surgery, all patients had a preoperative endoscopic evaluation using a transnasal flexible fiberscope VISERA ELITIZ OTV-5200 (Olympus Medical Systems, Tokyo, Japan), which can provide images both in NBI and white light modes. Prior to the endoscopic examination, the surfaces of the patient's nasal cavities were numbed and lubricated with a gel containing 2% lidocaine hydrochloride. The flexible endoscope was used to examine the nasal passages, nasopharynx, oropharynx, hypopharynx, and larynx. First, the entire larynx was observed using standard white light, and then the narrow-band imaging mode was used for further visualization. The lesions on NBI were classified according to both available classification systems—Ni's (Table 1 and Fig. 1) and ELS (Table 2). The consensus evaluation of the two endoscopists was taken for the grading. Representative images were recorded and kept for analysis. All these lesions were subsequently removed by phonomicrosurgical approach or excision biopsy. The histopathologic assessment after surgery was done by a pathologist who did not know about the mucosal and vascular patterns seen during the endoscopy. The histopathological reports were classified as benign, dysplastic, or malignant. Histopathological diagnosis was taken as the gold standard. The statistical analysis software Statistical Package for the Social Sciences (SPSS) 20.0 (IBM Corp., Armonk, New York) was used for this study. The accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the diagnosis of laryngeal lesions in both Ni's and ELS classifications were calculated. Fischer's exact test was used to test the association of grading with the nature of the lesion, and $p < 0.05$ was considered statistically significant. Cohen's κ statistics were utilized to measure the agreement between the NBI endoscopic diagnoses and the pathological ones.

Table 1: Ni's classification (2011)

Type I	Thin, oblique, and arborescent vessels are interconnected and IPCLs are almost invisible
Type II	Diameter of oblique and arborescent vessels is enlarged, and IPCLs are almost invisible
Type III	IPCLs are obscured by white mucosa
Type IV	IPCLs are recognized as small dots
Type V	Va—IPCL appears as solid or hollow, with a brownish, speckled pattern and various shapes Vb—IPCLs appear as irregular, tortuous, line-like shapes Vc—IPCLs appear as brownish speckles or tortuous, line-like shapes with an irregular distribution, scattered on the tumor surface

Table 2: European Laryngological Society classification (2016)

Longitudinal vascular pattern	Benign lesions
Perpendicular vascular pattern	Papillomatosis, SIN, and malignant lesions

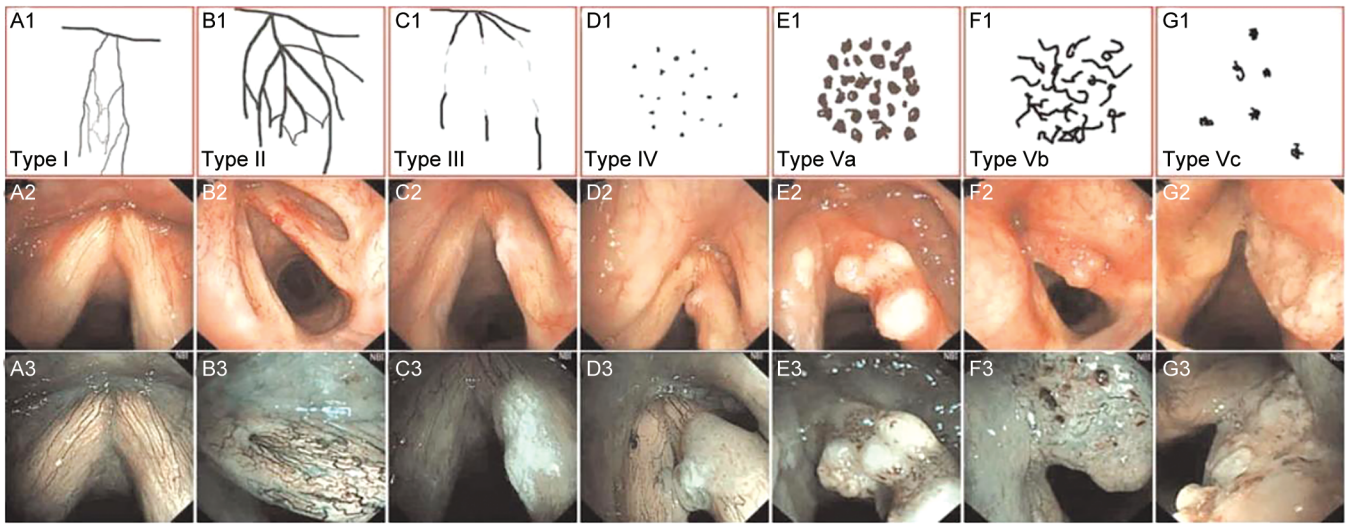

Fig. 1: Diagram of microvascular and endoscopic view of vocal cords in white light and NBI (adapted from Ni's 2011 classification)

Results

Among the total 30 patients studied, 23 were males (76.7%) and seven were females (23.3%). The youngest patient in the study group was 22 years old and the eldest was 76 years old with mean age of 55 years. The number of patients falling into different grades of NBI classification using Ni's grading and ELS grading are represented in Figures 2 and 3, respectively.

The maximum number of patients belonged to Ni's type V; that is, 14 patients (46.6%) and the least number of patients belonged to Ni's type IV are two patients (6.7%). There were 15 patients each with longitudinal (Fig. 4) and perpendicular (Fig. 5) vascular changes respectively when assessed by using ELS grading. On histopathological examination (HPE) the lesions were found to be benign in 14 (46.7%), dysplastic in five (16.7%), and malignant in 11 (36.7%) patients. The histological diagnosis of the subjects are as follows—laryngeal polyps in eight (26.7%) patients, laryngeal cyst in two (6.7%) patients, vocal nodule in one (3.3%), papillomatosis in three (10%), moderate dysplasia in two (6.7%) patients, severe dysplasia in one (3.3%) patient, cervical intraepithelial neoplasia in two (6.7%) patients and invasive cancer in 11 (36.6%) patients. Both the grading systems employed in the present study showed a statistically significant association with the benign or malignant nature of the lesion with *p*-value < 0.001 (Tables 3 and 4). The sensitivity, specificity, PPV, and NPV of both these grading systems were calculated and represented in Table 5.

The measure of agreement between the two classification systems with HPE was calculated using Cohen's κ. Cohen's κ was

Table 3: Association of Ni's classification with the histological nature of the lesion

	HPE type		
Ni's grade	*Benign*	*Malignant*	*p-value#*
Benign	16 (94.1%)	1 (5.9%)	<0.001*
Malignant	3 (23.1%)	10 (76.9%)	
Total	19	11	

#, Fischer exact test; *, statistically significant

Table 4: Association of ELS classification with the histological nature of the lesion

	HPE type		
ELS grade	*Benign*	*Malignant*	*p-value#*
Benign	15 (100%)	0	<0.001*
Malignant	4 (26.7%)	11 (73.3%)	
Total	19	11	

#, Fischer exact test; *, statistically significant

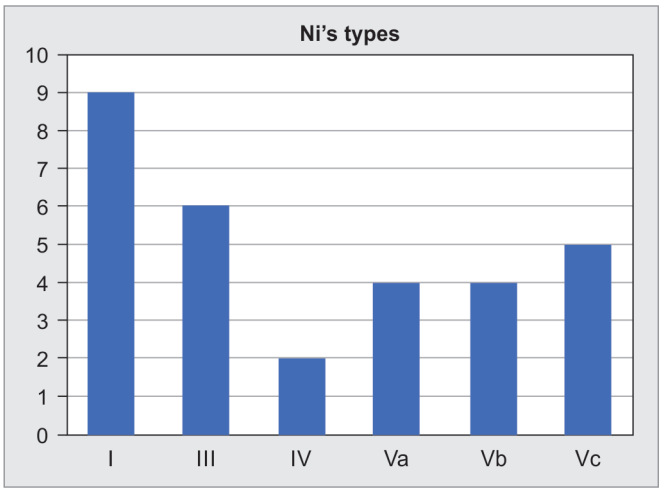

Fig. 2: Frequency distribution using Ni's grading

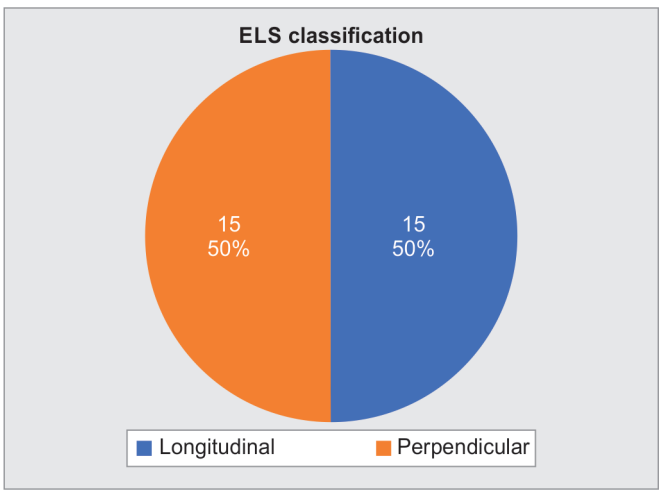

Fig. 3: Frequency distribution according to ELS grading

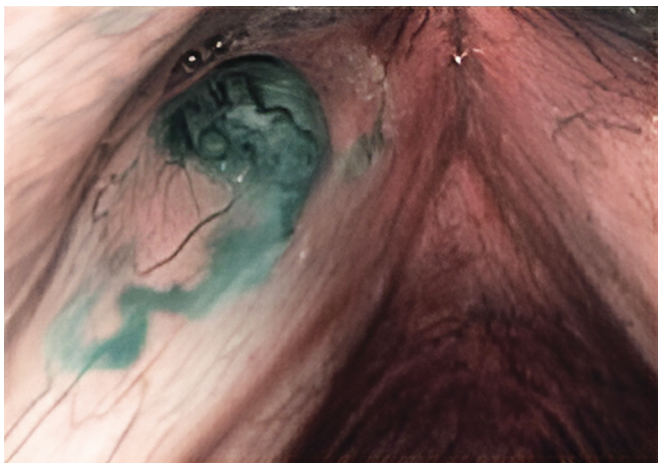

Fig. 4: Longitudinal vessel pattern in ELS grading

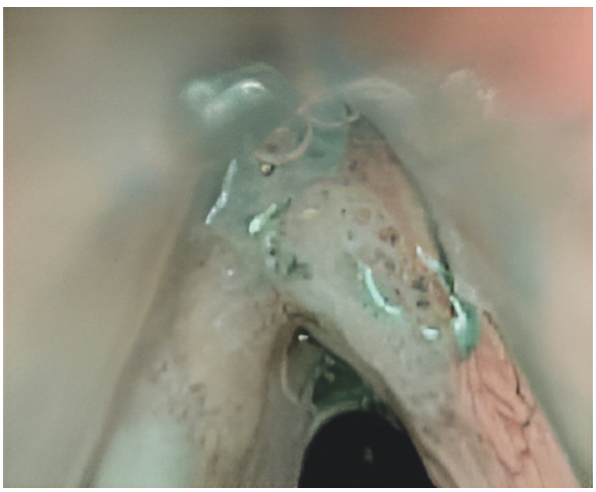

Fig. 5: Perpendicular vessel pattern in ELS grading

Table 5: Diagnostic effectiveness of Ni's classification vs ELS classification

	Ni's classification	*ELS classification*
Sensitivity	84.2%	78.9%
Specificity	90.9%	100%
PPV	94.1%	100%
NPV	76.9%	73.3%

found to be 0.724 for Ni's grading and 0.733 for ELS grading. Both of these grading systems show substantial agreement with biopsy results using κ statistics (κ 0.61–0.80).

Discussion

Over the years, the examination techniques for the larynx have undergone several changes. It began with the use of laryngeal mirrors and then advanced to rigid telescopes and flexible laryngoscopes. Now, we have endoscopes equipped with chip-on-tip cameras, which offer high-quality images.[6] Considerable advancements in diagnostic accuracy have been observed as a result of the enhanced optics of the scope.[7] The evolution of innovative biologic endoscopic techniques like NBI allows highlighting even minute epithelial and vascular changes aiding in vivo diagnosis of neoplasms.[8] The principle of NBI in laryngeal imaging is that short-wavelength light falls within the absorption spectrum of hemoglobin in the blood vessels, facilitating clearer visualization of these vascular structures and giving a contrast image between the microvasculature and the surrounding mucosa.[9] NBI facilitates visualization of IPCL, which are essential determinant of diagnosing epithelial lesions.[1] The transition from premalignant to malignant growth leads to significant changes in the structure and organization of vessels.[10] Early diagnosis of these lesions is desirable because it permits higher treatment success and thus a higher survival rate.

The necessity for a shared language to categorize and convey the NBI findings among clinicians and researchers led to the evolution of different classification systems. The classification proposed by Ni et al. in 2011 got widespread recognition among the head and neck community. They divided the different IPCL changes into five types (I–V), judging them based on this as benign (from types I–IV) and malignant (type V). Although the description of blood vessel patterns was comprehensive, many found it cumbersome to apply in the clinical setting because of the intrinsic complexity and to lack of a clear and distinct threshold that can differentiate between benign and malignant lesions.[5] Arens et al. put forward a simpler approach to classify these lesions into benign (longitudinal vessels) and premalignant or malignant (perpendicular) lesions.[11]

Particular attention should be paid to the perpendicular vascular changes and neoplastic neoangiogenesis in diagnosing laryngeal carcinoma since tumors depend on a continuously growing vascular network. In the study by Bertino et al., NBI allowed for a diagnostic improvement of 11% in defining the margins of the lesions and identifying lesions that cannot be seen with white light. Additionally, there was an 18% improvement in diagnosing potential malignancies.[12]

The data analysis of our study shows that the participants ranged from 22 to 76 years with a mean age of 55 years. The study by Davaris et al.[4] also had a similar age distribution of subjects, with a mean age of 56 years and a range of 21–86. The mean age was higher in the study by Missale et al.,[5] which is 61.8 years. In the study by Ni et al.,[1] the maximum number of patients 44 (42.3%), belonged to the NBI type V. Our study also has maximum subjects in Ni's type V. Out of the 11 cases of invasive carcinoma, 10 belonged to Type V, and one case belonged to type III on Ni's classification which is also similar to the study by Ni et al., where 37 out of 42 cases of invasive carcinoma fell in Type V. According to the study, NBI has a sensitivity of 91.3% and a specificity of 91.6% in predicting the diagnosis of laryngeal carcinoma.[1] Our study (classified using Ni's classification) has slightly less sensitivity and specificity, was 84.2 and 90.9%, respectively. Using ELS classification, Šifrer et al.[13] studied 80 vocal cord lesions in which the presence of a perpendicular vascular pattern was diagnostic for carcinoma *in situ* squamous cell carcinoma with a sensitivity of 100%, specificity of 95%, PPV of 88%, and NPV of 100%. Further analysis evaluating a larger cohort of 288 vocal cords gave similar results (sensitivity 98%, specificity 95%, PPV 88%, and NPV 99%).[14] In our study, classifying using ELS classification had a sensitivity of 78.9%, a specificity of 100%, a PPV of 100%, and an NPV of 73.3%. The agreement of the histopathological diagnosis with classification systems was done using κ statistics. Cohen's κ was 0.724 and 0.733 for Ni's types and ELS classification, respectively. Furthermore, the ELS classification has demonstrated excellent interobserver reliability with a κ value greater than 0.81 in all tested scenarios. This reliability has been confirmed in two independent centers, which further supports the reproducibility of the findings when using this classification.

Advantages of NBI as a Tool

In endoscopes incorporated with NBI, it can be done easily by pushing the thumb control switch in the apparatus. It requires no prior drug application or use of any staining techniques. It can be used as an "optical biopsy" technique, which means the nature of the lesion can be deciphered before removal.

Limitations of the Study

The diagnostic effectiveness in the dysplastic group could not be fully ascertained because of the limited number of subjects in the dysplastic group. Interpreting IPCL changes can sometimes be challenging and requires a learning curve.

Future Research

In the future, the focus of research should be on creating practical software that can provide real-time analysis for the head and neck region, utilizing artificial intelligence algorithms that have been proven effective in previous studies.[15,16] Thus increasing the objectivity and detection rate, as enacted in gastrointestinal tract tumors.[17,18]

Conclusion

The NBI is a promising tool in the *in vivo* diagnosis of malignant from nonmalignant lesions. Both the Ni's and ELS classifications employed for the evaluation of laryngeal lesions have high sensitivity and specificity and are associated with the biological behavior of the lesion. The authors recommend the usage of intrinsically simpler and practical ELS classification which may allow a better diagnostic capability in the clinical setting for distinguishing benign ones from papillomatosis, SIN, and invasive carcinomas.

Orcid

Vivek Soman https://orcid.org/0000-0002-5379-7039
Manju E Issac https://orcid.org/0009-0002-6990-8589
Basil Varghese https://orcid.org/0000-0003-4578-3718

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