

The role of contact endoscopy in screening for premalignant laryngeal lesions: A study of 141 patients

Marisa Klančnik, MD; Ivo Glunčić, MD, PhD; Draško Cikojević, MD, PhD

Abstract

At their earliest stage, pathologic lesions of the laryngeal epithelium are macroscopically invisible. Ideally, these lesions should be detected before their clinical manifestations appear so that prompt management can be initiated. However, most diagnostic modalities are unable to detect early premalignant lesions. We conducted a retrospective study of the use of contact endoscopy in analyzing the vocal fold mucosal epithelium in adults who had been operated on at our hospital under general anesthesia for various nonlaryngeal diseases. After we identified 71 such patients who were smokers, we chose an almost equal number of nonsmokers (n = 70) for comparison purposes. In all, our study population was made up of 141 patients—51 men and 90 women, aged 21 to 78 years (mean: 52). All patients had normal findings on preoperative laryngeal endoscopy. Our goal was to determine if the routine use of this diagnostic modality is justified in selected cases. Contact endoscopy identified dysplastic vocal fold lesions in 4 patients and chronic laryngitis in 3; all 7 of these patients were smokers. Since early laryngeal lesions are not macroscopically evident, early detection of these changes by other means is associated with a better prognosis and easier management. Our study demonstrates that the use of contact endoscopy during general anesthesia as a standard diagnostic method in long-time cigarette smokers is fully justified.

Introduction

Even the mildest abnormality of the vocal folds can lead to hoarseness. Ideally, changes in the vocal fold

mucosa will be detected early on, before they manifest clinically. One diagnostic modality that is useful in this regard is contact endoscopy. This noninvasive method provides an insight into the microscopic picture of laryngeal mucosa epithelium. With this simple and noninvasive method, cells are analyzed in vivo, thus avoiding the possibility of cell damage and distortion.

Contact endoscopy was first described by Hamou et al in 1984 in a gynecologic diagnosis.¹ In the 1990s, Andrea et al reported the use of contact endoscopy in examining the vocal folds² and the nasal mucosa.³ Arens et al⁴ confirmed the efficacy of contact endoscopy in examining the larynx, and Cikojević et al⁵ demonstrated that it was superior to frozen-section histopathology in diagnosing laryngeal pathology. These and other studies⁶⁻⁹ have shown that contact endoscopy is a reliable method in the diagnosis of malignant and premalignant diseases.

In this article, we describe our study of contact endoscopy in examining the epithelium of the vocal fold mucosa in smokers and nonsmokers who were free of clinical symptoms of laryngeal disease.

Patients and methods

For this retrospective study, we studied the use of contact endoscopy to analyze the mucosal epithelium of the vocal folds of 71 smokers who were operated on at our hospital under general anesthesia for the treatment of various nonlaryngeal diseases. For comparison purposes, we chose an almost equal number of nonsmokers (n = 70) who had undergone the same type of procedures. In all, our study population was made up of 141 patients—51 men and 90 women, aged 21 to 78 years (mean: 52). Indications for surgery included thyroid disease, nasal septal deviation, nasal polyposis, cervical cysts, and other conditions. All patients had normal findings on preoperative laryngeal endoscopy.

From the University Department of ENT-Head and Neck Surgery, Split University Hospital Center, Split, Croatia.

Corresponding author: Draško Cikojević, MD, PhD, University Department of ENT-Head and Neck Surgery, Split University Hospital Center, Spinčićeva 1, HR-21000 Split, Croatia. Email: drasko.cikojevic@st.t-com.hr

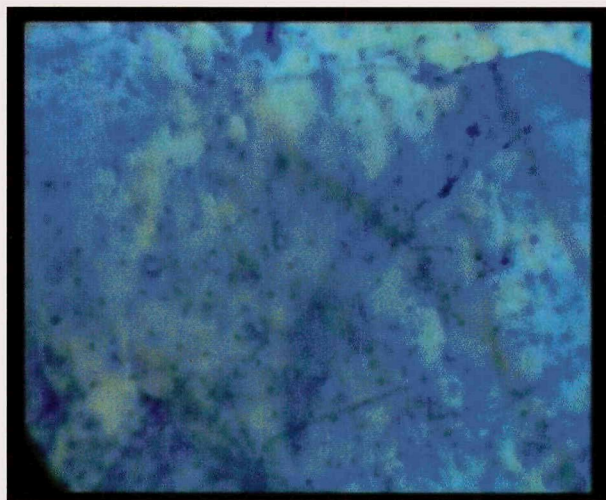


Figure 1. Contact endoscopy shows normal vocal fold epithelium (original magnification $\times 60$).

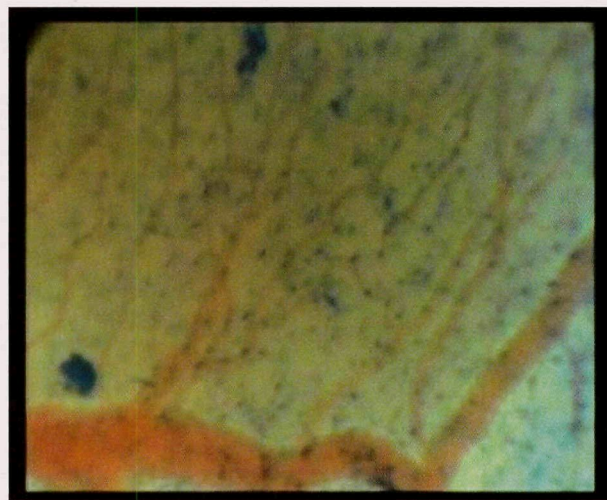


Figure 2. This view shows chronic laryngitis with regular microvasculature of the vocal fold (original magnification $\times 60$).

Upon induction of endotracheal anesthesia, the vocal fold mucosa was stained with 1% methylene blue. After 1 minute, a contact endoscope was placed against the vocal fold and moved along it from the anterior commissure toward the posterior aspect. The examination was captured on video. This was done on both vocal folds. A pathologist later analyzed the video images. A biopsy for histopathology was not routinely performed during the procedure; however, a biopsy was subsequently recommended for those patients who were found to have a pathologic lesion.

Findings on contact endoscopy were classified into four categories: *normal mucosa*, *chronic laryngitis*, *dysplasia*, and *squamous cell carcinoma*:

Normal mucosa. The stratified squamous epithelial cells are homogeneously distributed. The nuclei are small, pyknotic, and dark blue, and the cytoplasm is large and light blue (figure 1).

Chronic laryngitis. Cells are homogeneously distributed. The nuclei are slightly enlarged, and they have rounded edges. There might be slight hyperchromatism, but chromatin is uniformly and finely granulated and free of major chromatin abnormalities (figure 2).

Dysplasia. The cell population is heterogeneous. The nuclei are enlarged, variedly shaped, and hyperchromatic. The nucleus-to-cytoplasm ratio is weighted in favor of the nucleus. There is an increase in the number of mitoses, and dyskaryosis, anisokaryosis, and dyschromatism are present (figure 3).

Squamous cell carcinoma. There is a pronounced heterogeneity of the cell population. Nuclear hyperchromatism and an irregular chromatin distribution

are seen, and there is an increase in the size and number of irregularly shaped nuclei. The nucleus-to-cytoplasm ratio is tilted in favor of the nucleus.

Our study was approved by our hospital's Ethics Committee, and written informed consent was obtained from all patients.

Results

Contact endoscopy detected abnormal findings in 7 of the 71 smokers (9.9%) and in none of the nonsmokers. Four smokers had a dysplastic vocal fold lesion (1 grade I lesion and 3 grade II lesions) and 3 had chronic laryngitis.

A higher incidence of premalignant pathology was associated with a greater number of cigarettes per day. No pathologic lesions were observed in 21 patients who smoked 10 or fewer cigarettes per day (table 1).

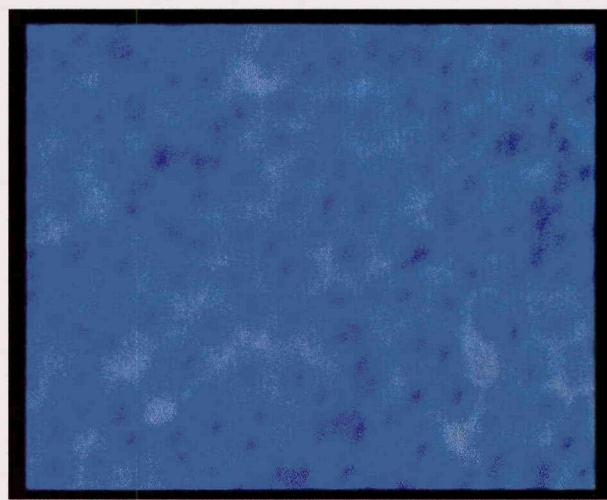


Figure 3. This view shows dysplasia (original magnification $\times 150$).

Table 1. Correlation between pathologic findings on contact endoscopy and the number of cigarettes per day

	Cigarettes per day (n)					Total
	1 to 10	11 to 20	21 to 30	31 to 40	≥41	
No. smokers	21	15	17	13	5	71
Pathologic finding on contact endoscopy	None	1 laryngitis	2 dysplasia	1 dysplasia, 1 laryngitis	1 dysplasia, 1 laryngitis	7

The severity of the pathologic vocal fold findings was directly proportional to the length of time the patient had been a smoker. All 15 patients who had smoked for 10 years or less were free of pathologic lesions. The incidence of lesions was substantially higher in patients who had smoked for 20 years or more (table 2).

Discussion

Approximately 98% of all patients with laryngeal carcinoma are long-time smokers.¹⁰⁻¹² Therefore, we would expect to find a higher prevalence of early premalignant laryngeal lesions in this population. In our study, contact endoscopy demonstrated early pathologic findings in 7 of the 71 smokers (9.9%) and in none of the 70 nonsmokers.

Contact endoscopy is the only diagnostic method that enables precise *in vivo* microlocalization of early vocal fold lesions. As a result, macroscopically invisible changes can be identified, and sampling of the target site can be performed. It is true that exfoliative cytology can also identify macroscopically occult lesions, but this method requires sampling of the entire vocal fold surface, and therefore the precise location of the pathologically altered cells is difficult to determine.¹³

Healthy and pathologically unaltered mucosa can be visualized on autofluorescence endoscopy. Healthy mucosa appears as a greenish area, while altered mucosa is reddish or purple.⁴ However, this method does not provide a microscopic image of the lesion, and inflammation frequently yields false-positive results.

Contact endoscopy, on the other hand, provides insight into the mucosal microvascularization; enhanced and regular microvascularization indicates an inflammatory process (figure 2), and pathologic microvascularization points to a malignancy. The growth of a tumor is accompanied by development of its own microvascularization, which is irregular and easily discernible on contact endoscopy.

The findings of our study were in concordance with others in that the development of a laryngeal lesion was more common in smokers than nonsmokers and that it was directly correlated with the number of cigarettes per day and the number of years a patient had been smoking.¹⁰⁻¹² Others have shown that the prevalence of both precancerous lesions and benign lesions (e.g., polyps, cysts, etc.) is also greater in cigarette smokers.¹⁰ Early detection of macroscopically invisible laryngeal lesions is associated with a better prognosis and easier management. It is noteworthy that some laryngeal lesions disappear when the irritating factor (e.g., smoking) is eliminated.^{14,15}

Our study demonstrates that the use of contact endoscopy as a standard diagnostic method in long-time cigarette smokers during procedures performed with general anesthesia is fully justified. This noninvasive method should also be performed in smokers with voice alterations because it provides a microscopic insight into the nature of pathologic lesions of the vocal fold mucosa epithelium.

Table 2. Correlation between pathologic findings on contact endoscopy and the number of years of smoking

	Years of smoking (n)					Total
	1 to 10	11 to 20	21 to 30	31 to 40	≥41	
No. smokers	15	19	16	10	11	71
Pathologic finding on contact endoscopy	None	1 laryngitis	1 dysplasia, 1 laryngitis	1 dysplasia	2 dysplasia, 1 laryngitis	7

References

1. Hamou J, Salat-Baroux J, Coupez F, De Brux J. Microhysteroscopy: A new approach to the diagnosis of cervical intraepithelial neoplasia. *Obstet Gynecol* 1984;63(4):567-74.
2. Andrea M, Dias O, Santos A. Contact endoscopy of the vocal cord: Normal and pathological patterns. *Acta Otolaryngol* 1995;115(2):314-16.
3. Andrea M, Dias O, Macor C, et al. Contact endoscopy of the nasal mucosa. *Acta Otolaryngol* 1997;117(2):307-11.
4. Arens C, Glanz H, Dreyer T, Malzahn K. Compact endoscopy of the larynx. *Ann Otol Rhinol Laryngol* 2003;112(2):113-19.
5. Cikojević D, Glunčić I, Pesutić-Pisac V. Comparison of contact endoscopy and frozen section histopathology in the intraoperative diagnosis of laryngeal pathology. *J Laryngol Otol* 2008;122(8):836-9.
6. Wardrop PJ, Sim S, McLaren K. Contact endoscopy of the larynx: A quantitative study. *J Laryngol Otol* 2000;114(6):437-40.
7. Xiaoming H, Haiqiang M, Manquan D, et al. Examination of nasopharyngeal epithelium with contact endoscopy. *Acta Otolaryngol* 2001;121(1):98-102.
8. Pak MW, To KF, Leung SF, van Hasselt CA. In vivo diagnosis of persistent and recurrent nasopharyngeal carcinoma by contact endoscopy. *Laryngoscope* 2002;112(8 Pt 1):1459-66.
9. Warnecke A, Averbek T, Leinung M, et al. Contact endoscopy for the evaluation of the pharyngeal and laryngeal mucosa. *Laryngoscope* 2010;120(2):253-8.
10. Cikojević D, Glunčić I, Klančnik M. Cigarette smoking and progression of laryngeal lesions. *Coll Antropol* 2010;34(Suppl 1):45-8.
11. Sugár J, Vereczkey I, Tóth J. Some etio-pathogenetic factors in laryngeal carcinogenesis. *J Environ Pathol Toxicol Oncol* 1996;15(2-4):195-9.
12. Ahrens W, Jöckel KH, Patzak W, Elsner G. Alcohol, smoking, and occupational factors in cancer of the larynx: A case-control study. *Am J Ind Med* 1991;20(4):477-93.
13. Cikojević D, Glunčić I, Pesutić-Pisac V. Role of exfoliative cytology in diagnosis of laryngeal tumors. *Acta Cytol* 2007;51(5):762-72.
14. Maier H, Gewelke U, Dietz A, Heller WD. Risk factors of cancer of the larynx: Results of the Heidelberg case-control study. *Otolaryngol Head Neck Surg* 1992;107(4):577-82.
15. Sezer O, Jakob C, Niemöller K. Angiogenesis in cancer. *J Clin Oncol* 2001;19(13):3299-3301.

Continued from page 176

were analyzed separately, the improvements were seen in general benefit (+60), physical benefit (+59), and social benefit (+50).

The strengths of our study protocol include the relatively large number of participants (N = 39) and the use of a validated tool. The lack of a nonsurgical comparison group might be considered a limitation of our study, but it is one that is difficult to overcome in a disease process that does not have an acceptable nonsurgical alternative. Also, many patients in our study underwent more than one surgical technique, which makes precise comparisons of the results of each technique difficult to ascertain.

In conclusion, this study suggests that nasal valve surgery plays an important role in symptom control of patients with nasal blockage and that it significantly improves patients' general, physical, and social quality of life.

Acknowledgments

We thank the staff of the Department of Statistics at the University of Sheffield for their assistance.

References

1. Raghavan U, Jones NJ. The nasal valve and its management. In: Gleeson MJ, ed. *Scott-Brown's Otorhinolaryngology Head and Neck Surgery*. 7th ed. London: Oxford University Press; 2008:3005-14.
2. Mink PJ. Le nez comme voie respiratoire. *Presse Otolaryngol (Belge)* 1903:481-96.
3. Wittkopf M, Wittkopf J, Ries WR. The diagnosis and treatment of nasal valve collapse. *Curr Opin Otolaryngol Head Neck Surg* 2008;16(1):10-13.
4. Wustrow TP, Kastenbauer E. Surgery of the internal nasal valve. *Facial Plast Surg* 1995;11(3):213-27.
5. Bridger GP. Physiology of the nasal valve. *Arch Otolaryngol* 1970;92(6):543-53.
6. Robinson K, Gatehouse S, Browning GG. Measuring patient benefit from otorhinolaryngological surgery and therapy. *Ann Otol Rhinol Laryngol* 1996;105(6):415-22.
7. Paniello RC. Nasal valve suspension. An effective treatment for nasal valve collapse. *Arch Otolaryngol Head Neck Surg* 1996;122(12):1342-6.
8. Lee DS, Glasgold AI. Correction of nasal valve stenosis with lateral suture suspension. *Arch Facial Plast Surg* 2001;3(4):237-40.
9. Guyuron B, Michelow BJ, Englebardt C. Upper lateral splay graft. *Plast Reconstr Surg* 1998;102(6):2169-77.
10. Park SS. The flaring suture to augment the repair of the dysfunctional nasal valve. *Plast Reconstr Surg* 1998;101(4):1120-2.
11. Khosh MM, Jen A, Honrado C, Pearlman SJ. Nasal valve reconstruction: Experience in 53 consecutive patients. *Arch Facial Plast Surg* 2004;6(3):167-71.
12. Rhee JS, Poetker DM, Smith TL, et al. Nasal valve surgery improves disease-specific quality of life. *Laryngoscope* 2005;115(3):437-40.

Copyright of ENT: Ear, Nose & Throat Journal is the property of Vendome Group LLC and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.