



Is there any association between esophagogastric endoscopic findings and laryngeal cancer?☆

Najmeh Doustmohammadian^a, Masoud Naderpour^{b,*}, Manochehr Khoshbaten^{c,d},
 A'azam Doustmohammadian^e

^aDepartment of Otorhinolaryngology, Semnan University of Medical Sciences, Semnan, Iran

^bDepartment of Otorhinolaryngology, Tabriz University of Medical Sciences, Tabriz, Iran

^cDepartment of Gastroenterology and Hepatology, Tabriz University of Medical Sciences, Tabriz, Iran

^dLiver and Gastrointestinal Disease Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

^eFaculty of Nutrition Sciences and Food Technology, Nutrition Research Department, National Nutrition and Food Technology Research Institute, Shahid Beheshti University, M.C.

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Abstract

Purpose: The aim of the study was to survey the association between prevalence of acid-related inflammation in the upper digestive tract and laryngeal cancer.

Materials and methods: A case-control study was done in an otolaryngology ward at an academic university. Totally, 65 patients with laryngeal cancer and 65 cancer-free matched controls underwent esophagogastroduodenoscopy, and endoscopic findings were collected.

Results: In the case group, positive endoscopic findings were significantly higher than the control group (87.7% vs 58.5%; $P < .001$). Laryngeal cancer patients had erosive esophagitis, and gastritis ± other findings more than the control group (48 vs 29 cases) and the difference was statistically significant.

Conclusion: The difference between endoscopic findings in cases and controls was statistically significant. Severe inflammation and erosion existed in patients with laryngeal cancer that could be due to increased acid secretion. Our study supported the hypothesis that gastric acid and pepsin play a role in laryngeal cancer.

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1. Introduction

Laryngeal cancer is one of the more common cancers in human beings. Factors that correlate with it include tobacco use, alcohol abuse, or a sibling with head and neck cancer. In addition, there is an association between laryngeal cancer and the presence of human papilloma virus, previous

radiotherapy, previous head and neck cancer, and chemical carcinogens [1]. Some studies have investigated role of *Helicobacter pylori* in laryngeal cancer [2,3]. Although the relationship is not proven, acid pepsin diseases is regarded as a risk factor for laryngeal carcinoma.

Some studies have investigated role of acid reflux in laryngeal carcinoma and other studies have suggested other reflux components—bile (alkaline) and chlorhydro-peptic components in particular—as possible risk factors of laryngeal cancer [4–10].

None of the published studies have compared gastrointestinal (GI) endoscopic findings between patients with laryngeal carcinoma and cancer-free controls.

Our study evaluated GI endoscopic findings related to acid pepsin diseases such as inflammation, erosion, and ulcer between the 2 groups.

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* Corresponding author. Department of Otorhinolaryngology, Tabriz University of Medical Sciences, Tabriz, Iran. Tel.: +98 09141164977.

E-mail address: naderpoom@yahoo.com (M. Naderpour).

2. Materials and methods

Totally, 65 patients who had undergone laryngoscopy and biopsy with the definite diagnosis of squamous cell carcinoma (SCC) as well as those who had undergone total or partial laryngectomy between May 2006 and February 2008 at academic hospitals affiliated to Tabriz University of Medical Sciences (Iran) were investigated. These patients underwent esophagogastroduodenoscopy (EGD), and endoscopic findings were collected.

The control group (65 patients) consisted of hospitalized patients with anemia or other illnesses not associated with HP. They did not have signs of laryngeal cancer in medical history and laryngoscopy. These controls, similar to the case group, underwent EGD, and endoscopic findings were collected. A complete medical history including demographic data such as age and sex, cigarette smoking, and alcohol was obtained from each patient.

Clinical characteristics and laboratory variables were compared by independent-sample *t* test, χ^2 test, and Fisher exact test. A *P* value of less than .05 was considered statistically significant. All analyses were performed using the Statistical Package for the Social Science software (SPSS, SPSS Inc, Chicago, IL).

3. Results

Our case group included 63 males and 2 females with a mean age of 61.75 ± 7.70 years. The control group consisted of 63 males and 2 females with a mean age of 61.66 ± 7.62 years.

The prevalence of smoking and alcohol consumption was 78.5% and 29.2% in the laryngeal cancer group and 73.8% and 26.2% in the control group, respectively. The characteristics of the case and the control group are presented in Table 1. The cases and the controls were matched in terms of age, sex, amount, and duration of tobacco and alcohol consumption and did not have any significant differences.

Endoscopic GI findings in the 2 groups are shown in Figs. 1 and 2. The common finding is EGD in both groups was erosive gastritis. Fifty-seven laryngeal cancer patients and 38 controls had positive endoscopic findings related to acid pepsin diseases such as mucosal erythema and erosion and ulcer (without GI symptoms in medical history). Positive endo-

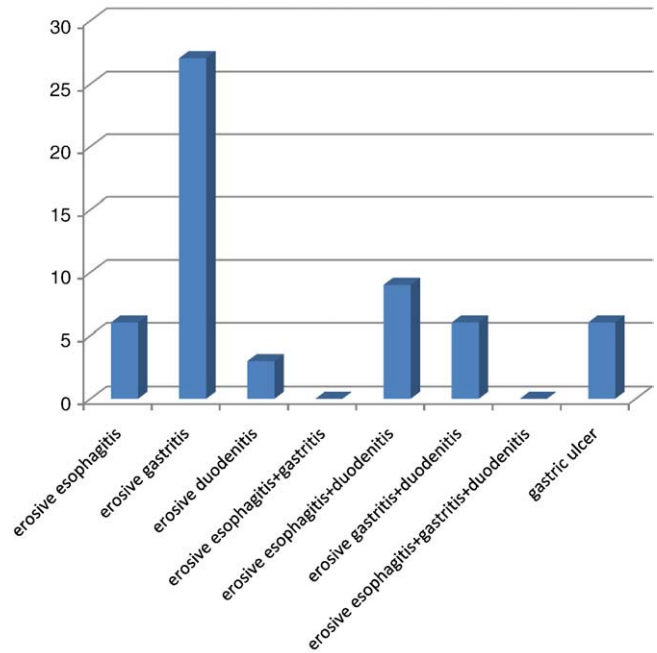


Fig. 1. Endoscopic findings in the case group.

scopic findings were higher in laryngeal cancer patients, and the difference was statistically significant ($P < .001$, χ^2 test).

Erosive esophagitis and erosive gastritis ± other findings was higher in cases than controls and the difference was statistically significant ($P = .001$).

In patients with laryngeal cancer, gastric ulcer was seen in 6 cases, but it was not found in any of the controls. The difference was statistically significant ($P = .012$).

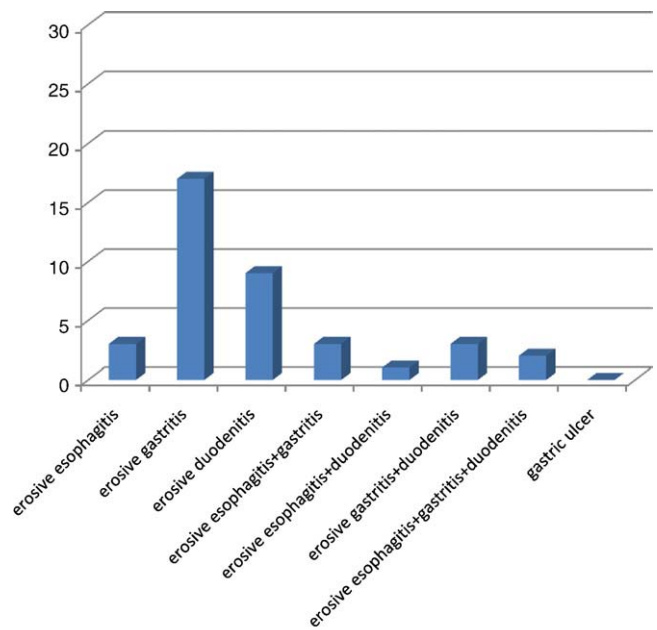


Fig. 2. Endoscopic findings in the control group.

Table 1 Characteristics of the patients with and without laryngeal cancer

Patient characteristic	With laryngeal cancer	Without laryngeal cancer	<i>P</i>
Mean age ± SD (y)	61.75 ± 7.70	61.66 ± 7.62	.945
Men	63	63	1
Tobacco use	51 (78.5%)	48 (73.8%)	.537
Alcohol use	19 (29.2%)	17 (26.2%)	.695
Other risk factors	-	-	-

4. Discussion

Gastroesophageal reflux (GER) disease, one of the most prevalent health disorders in the Western world, is strongly associated with adenocarcinoma of the esophagus [11-14].

The diagnosis of erosive esophagitis represents true GER with very high specificity as it is an effect of peptic injury to the esophagus mucosa, but it is very rarely caused by anything other than reflux. In our study, acid pepsin-related diseases in the upper digestive tract (esophagitis, gastritis, duodenitis, and gastric ulcer) were more in patients with laryngeal cancer than controls.

Survey of the endoscopic findings in laryngeal cancer patients has not been done so far. In 1976, it was first suggested that inflammatory diseases could cause laryngeal cancer [15], and in 1980, it was further proposed that GER could play a causal role in laryngeal and pharyngeal carcinogenesis [16,17].

In our study, the difference in endoscopic findings between the 2 groups was statistically significant, and patients with laryngeal cancer had more severe inflammation and erosion that could be due to the increased gastric acid that plays a critical role in mucosal lesion.

In a study by Mercante et al [4], 274 patients with malignant neoplasm of the oral cavity, pharynx, and larynx were investigated by EGD and biopsy, and the results were compared with a control group of cancer-free individuals from the same hospital. Statistical analysis revealed a significant difference between the 2 groups ($P = .0001$). In this study, on the basis of endoscopic data, they found that a high percentage of nonsmoking patients were affected by GER and SCC of the upper parts of the airway and the GI system.

In a study by EI-Serag et al [5], 8228 hospitalized patients with laryngeal cancers were compared to 32 912 hospitalized controls. Among hospitalized persons, the prevalence of GER disease was higher in patients with laryngeal cancer (8.9% vs 4%; $P < .0001$).

In other study, the study population consisted of 36 consecutive individuals with confirmed SCC of the larynx, and 125 lifetime nonsmoking and nondrinking cancer-free subjects were selected to form the control group. Patients with laryngeal cancer had a higher prevalence of GER disease than the control subjects ($P < .0001$) [6].

Nilsson et al [18] investigated the association between GER and cancers of the larynx and pharynx. During the follow-up period, 30 cases of laryngeal were detected in the cohort study. Slightly increased risks of laryngeal cancer were observed in the total reflux cohort. After stratification to exclude cohort members with a diagnosis of alcoholism, no significant increase in the risk of laryngeal cancer was found compared with the general population. A potential weakness of the study was that data on smoking, a well-established risk factor for laryngeal cancer, were not available for adjustment.

Other studies have investigated the role of other reflux components such as bile and pepsin as possible risk factors of laryngeal cancer [9,10].

Galli et al [9] investigated the role of acid and alkaline reflux in laryngeal SCC. In group A, pH measurement showed pathologic reflux in 80.9% (17/21) of the patients with no typical symptoms in 63.7% of them. The difference was significant with respect to the control group. Group B included 40 consecutive gastrectomized patients with biliary or alkaline reflux. In group B, 6 of 40 (15%) had preneoplastic lesions or a history of laryngeal tumor. The difference was significant with respect to the control group.

Cammarota et al [10] investigated the association between gastric surgery and cancer of the larynx. The study included 828 consecutive patients with laryngeal cancer (cases) and 825 controls with acute myocardial infarction. Previous gastrectomy was reported by 8.1% of the cases and 1.8% of the controls ($P < .0001$). The study concluded that previous gastric surgery was associated with an increased risk of laryngeal cancer. A periodic laryngeal examination should be considered in long-term follow-up of the patients with gastric resection.

In our study, as other studies, most of the patients with laryngeal cancer had no GI symptoms [19]. Patients with laryngeal cancer had more severe inflammation and erosion without GI symptoms. Furthermore, EGD may be useful for evaluation GI disorders in patients with laryngeal cancer, and acid suppression postlaryngeal cancer therapies may have protective effects on laryngeal cancer recurrence rate. In our study, acid pepsin-related diseases in the upper digestive tract were more in patients with laryngeal cancer than controls. In reality, this study only evaluated association not causation between gastric acid and pepsin and laryngeal cancer.

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