Vascular Evaluation in Laryngeal Diseases

Comparison Between Contact Endoscopy and Laser Doppler Flowmetry

Michihiko Sone, MD; Eisuke Sato, MD; Hideo Hayashi, MD; Yasushi Fujimoto, MD; Tsutomu Nakashima, MD

Objective: To determine the efficacies of 2 methods for evaluating vascular changes in laryngeal diseases.

Design: Prospective comparative study.

Setting: University hospital.

Patients: Twenty-four adults planning to undergo laryngomicrosurgery for unilateral lesions in their vocal cords.

Intervention: Vascular evaluation was performed using contact endoscopy and laser Doppler flowmetry during laryngomicrosurgery.

Main Outcome Measures: Morphological and physiological variables of the vascular changes.

Results: Contact endoscopy examinations revealed changes in the fine vascular network patterns in the vocal cords. Hypervascularity was present in patients with polyps but not in those with nodules, and the degree of vascularity was variable in patients with malignant neoplasms. Patients with papillomas and patients in the postradiation therapy group showed hypovascularity with losses in the capillary network. Laser Doppler flowmetry revealed high mean blood flows in patients with polyps, dysplasia, and malignant neoplasms, whereas patients with papillomas and those in the postradiation therapy group had low blood flows. The variables measured by laser Doppler flowmetry and endoscopy were strongly correlated.

Conclusion: Evaluations of morphological and physiological changes of vascularity in laryngeal diseases are important for understanding their pathophysiology, and combining contact endoscopy and laser Doppler flowmetry is useful in such evaluations.

Arch Otolaryngol Head Neck Surg. 2006;132:1371-1374

Morphological and physiological methods can be used to evaluate laryngeal diseases. Investigations of vascular changes in laryngeal diseases include assessing the morphological structure of vessels and measuring the volume and velocity of blood flow. Such vascular evaluations are important for understanding the pathophysiology of laryngeal diseases and for determining effective treatments. For example, angiogenesis is a critical determinant of tumor growth, and measurement of angiogenesis in laryngeal cancer is reportedly useful in predicting lymph node metastasis. Microvascular evaluations of pathology specimens have been reported in laryngeal cancer and in other organ diseases. These pathological measurements of abnormalities of vessels have been used as the gold standard method but might include congested vessels, and the findings may not reflect the actual blood flow. Moreover, such evaluations of vascular conditions in the human larynx are limited. In the present study, we aimed to assess the vascular conditions in laryngeal diseases morphologically and physiologically by observation of vessels by contact endoscopy and blood flow measurement by laser Doppler (LD) flowmetry, both of which were performed during laryngomicrosurgery.

We herein report the results of vascular evaluations in laryngeal diseases using the 2 methods. We also discuss their correlation and usefulness.

Methods

Twenty-four adults planning to undergo laryngomicrosurgery for unilateral lesions in their vocal cords were included in the present study. The diagnoses were polyp (3 patients), papilloma (3 patients), squamous cell carcinoma (SCC) (3 patients), carcinoma in situ (CIS) (3 patients), granulation (3 patients), nodule (2 patients), cyst (2 patients), hyperplasia (1 patient), and dysplasia (1 patient). Three other patients (having diagnoses of polyp, hy-
perplasia, and granulation) had medical histories of radiotherapy for laryngeal cancer and were evaluated together as the postradiation therapy group. Experienced pathologists made these pathological diagnoses using biopsy specimens obtained at surgery.

All patients provided their informed consent to participate before the beginning of the study. Two procedures were conducted with the patient under general anesthesia: vascular assessment by contact endoscopy, followed by measurement of the blood flow by LD flowmetry.

**VASCULAR OBSERVATION BY CONTACT ENDOSCOPY**

A contact endoscope for the larynx (8715AA; Karl Storz, Tuttingen, Germany) was used for this evaluation. After overviews of the larynx were obtained at the typical ×1 power setting, the endoscope was placed on lesions in the vocal cords, and the vessels were observed at a power of ×60. Networks of vessels could be clearly identified without staining the vocal cord with methylene blue, which is the standard method. Video images were obtained using a telecam-high resolution, single-chip video system with autoexposure for endoscopic procedures (Storz Endovision Telecam System; Karl Storz) and a xenon light source (type 20133120; Karl Storz). The condition of vessels in the lesions was compared with that in contralateral areas (without lesions) of the vocal cords. The status of the vessels was classified into 3 categories according to their numbers and sizes: (1) hypervascularity, (2) moderate vascularity, and (3) hypovascularity (Figure 1). Moreover, video images of the most vascularized area identified in each patient were transferred to an image analysis system (Win-ROOF; Mitani, Osaka, Japan). The total vessel area in a field (in pixels) was determined using a tracing device, and the percentage ratio of the vessel area to the total area in the field was determined. This procedure was repeated twice, with the mean ratios evaluated in each patient.

**MEASUREMENT OF THE BLOOD FLOW BY LD FLOWMETRY**

Evaluations by LD flowmetry were performed soon after the observations using the contact endoscope. We prepared the 3.0-mm noncontact probe of an LD flowmeter (Omegawave, Tokyo, Japan), which was designed specifically for measuring blood flow in the larynx. This LD flowmeter measured the blood flow even when the probe was kept up to 5 mm from the mucosa at a selected point, to avoid the possible effect of depressing the vessels. The probe was fixed to a stabilized desk, and the blood flow in lesions (where the contact endoscope was applied) and in contralateral areas (without lesions) of the vocal cords was measured. After the blood flow had stabilized, 5-second mean values were obtained. The percentage ratio of the mean blood flow in the lesion to that in the contralateral area was calculated and evaluated. Measurement of the ratios of LD output between bilateral sides was reported as a reliable method in a preliminary study using healthy vocal cords, in which the recorded blood flow differed between bilateral vocal cords by less than 10%.

**STATISTICAL ANALYSIS**

Endoscopy observation data in each of the 3 categories and LD flowmetry values in each patient were analyzed using Kruskal-Wallis test. The results from assessments by LD flowmetry and endoscopic video images were analyzed using Pearson product moment correlation coefficient test.

**RESULTS**

Contact endoscopic examinations revealed changes of fine vascular network patterns on the mucosa and submucosa of the vocal cords. Capillary rupture and dilation of vessels were evident in patients with polyps. The degree of vascularity was variable in patients with SCC and CIS, with 2 patients showing hypervascularity and 4 patients showing hypovascularity. All 3 patients with pap-

---

**Figure 1.** Example images of hypervascularity, moderate vascularity, and hypovascularity.
illomas and the patients in the postradiation therapy group showed hypovascularity with losses in the capillary network. The image analysis was performed in all patients, and it was easy to classify the status of the vessels into the 3 categories of hypervascularity, moderate vascularity, and hypovascularity.

In each patient, blood flow was measured successfully using the LD flowmeter. The highest mean blood flow ratio (349%) occurred in the patient with dysplasia. Patients with SCC and CIS also had high mean blood flow ratios of 155% and 158%, respectively. The mean ratios in patients with polyps and nodules were 218% and 72%, respectively. The ratios in patients with papillomas and in patients in the postradiation therapy group were 65%. The correlation of the 3 categories by endoscopy observation and the values in each patient by LD flowmetry is shown in Figure 2. The mean outputs of LD flowmetry in the groups with hypovascularity, moderate vascularity, and hypervascularity were 86.6%, 188.9%, and 242.5%, respectively, which were significantly different.

The percentage ratios of the vessel area could be determined from endoscopic video images in 16 of 24 patients. In some patients, especially those with polyps and those in the postradiation therapy group, it was difficult to clearly identify vessels because of hyperkeratotic thickening of the mucosa. The results from the assessments by endoscopy and LD flowmetry were strongly correlated, as shown in Figure 3.

**COMMENT**

The present study shows that combining the 2 methods is useful in evaluations of vascular changes in laryngeal diseases. Contact endoscopy for the larynx was originally developed to allow in situ investigations of the superficial layer of the vocal cord epithelium.3 After staining the vocal cord with methylene blue, this endoscopic technique enables the cells, nuclei, and cytoplasm of the vocal mucosa to be observed. This technique identifies the vascular abnormalities in different disorders and assists in diagnoses of conditions of the larynx.

Our study demonstrates the usefulness of this endoscopic technique in evaluating the vascularity of the vocal cord without requiring any staining procedure.

Contact endoscopy allowed observation of healthy vocal cords, changes of the network in lesions, and capillary ruptures in patients with polyps. We classified the vessels according to their numbers and sizes into 3 categories. The mean outputs of LD flowmetry differed significantly between the 3 groups, but this evaluation was limited by its subjective nature. Hyperkeratotic thickening of the mucosa in some patients with SCC or CIS resulted in their vessels being classified as hypovascular; hence, this condition might manifest different results from those of LD flowmetry evaluations. Therefore, we aimed for a more objective assessment of video images using an image analysis system.

The methods available for measuring blood flow in the larynx include tissue oxygen pressure measurement,5 microsphere surface technique6 and LD flowmetry. The microsphere technique cannot be applied to patients with laryngeal diseases. Although LD flowmetry has been applied to the ear, including the human inner ear,9 its application in the larynx is limited.9 The LD flowmeter in the present study measures the blood flow of vessels located up to 1 mm below the surface of the mucosa, and this depth is similar to the thickness of the mucosa in the healthy vocal cord. The noncontact probe of this flowmeter measures the blood flow, while avoiding the possible effect of depressing the vessels.

A study11 using LD flowmetry found that the flow values were lower in patients with laryngeal SCC compared with healthy patients. Blood flows among healthy patients and patients with SCC were compared in that study. In a preliminary study, LD flowmetry values varied among individuals with healthy vocal cords, so we evaluated the percentage ratio of the value of blood flow in the lesion to that in the contralateral area in each patient. Patients with SCC and CIS and the patient with dysplasia had high ratios on LD flowmetry that were attributed to the presence of angiogenesis in these diseases. This high ratio in patients with malignant neoplasms...
might be useful as a predictor of the effectiveness of chemoradiotherapy. In fact, chemoradiotherapy was effective in patients with advanced malignant neoplasms with high blood flow ratios. Patients with polyps had a high ratio, which supports the finding of no causative association between ischemic changes and the formation of vocal cord polyps. All patients with papillomas and those in the postradiation therapy group had low ratios that were consistent with the evaluations by contact endoscopy. However, we could not draw accurate conclusions on the vascularity in each type of laryngeal disease because of the few patients examined. Detailed examinations of blood flow in each type of laryngeal disease should be performed in the future.

We tried to make pathological measurements of abnormalities of vessels, which have been used as the gold standard method for measuring angiogenesis in several diseases. We used the microvascular volume as the evaluation tool, as determined by a video image analysis system. Biopsy specimens to assess the lesions were limited; there seemed to be no significant correlation between values obtained by LD flowmetry and those obtained pathologically (data not shown). This finding suggests that factors other than microvascular volume affect blood flow in laryngeal diseases; we are planning to investigate this further.

The present 2 methods for vascular evaluations of abnormalities of laryngeal diseases have advantages and disadvantages. Evaluations by contact endoscopy and LD flowmetry are possible during laryngomicrosurgery without further invasion. Angiogenesis in laryngeal cancer may be of value in predicting lymph node metastasis, so data obtained by applying these methods during surgery could be useful for determining the most effective treatments. Although evaluations by contact endoscopy are subjective and LD flowmetry is objective, contact endoscopy is preferred for checking the overall condition of lesions.

A strong correlation was observed between the ratios obtained using the 2 methods. This finding suggests that contact endoscopy and LD flowmetry are useful for evaluations of vascular changes in laryngeal diseases.

In conclusion, evaluations of vascular changes in laryngeal diseases are important for understanding their pathophysiology or pathogenesis. Combining contact endoscopy and LD flowmetry is useful in such evaluations.

Submitted for Publication: April 7, 2006; final revision received July 19, 2006; accepted August 22, 2006.

Correspondence: Michihiko Sone, MD, Department of Otorhinolaryngology, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku Nagoya 466-8550, Japan (michsone@med.nagoya-u.ac.jp).

Author Contributions: Drs Sone, Sato, Hayashi, Fujimoto, and Nakashima had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Sone, Fujimoto, and Nakashima. Acquisition of data: Sone, Sato, Hayashi, and Fujimoto. Analysis and interpretation of data: Sone. Drafting of the manuscript: Sone, Sato, Hayashi, and Fujimoto. Critical revision of the manuscript for important intellectual content: Sone and Nakashima.

Financial Disclosure: None reported.

REFERENCES