

Imaging Modalities in the Etiologic Evaluation of Unilateral Vocal Fold Paralysis

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Summary: Objective. This study aimed to investigate the roles of computed tomography (CT) and neck ultrasonography (US) in evaluating unilateral vocal fold paralysis (UVFP) of unknown etiology and to compare our results with those of other studies to assess the differences in etiology of UVFP.

Methods. We investigated the medical records of 202 eligible patients with UVFP. In total, 168 underwent chest CT, 118 underwent neck CT, and 108 underwent head CT. One hundred and three patients were also evaluated with high-resolution neck US. The etiologic causes of UVFP were also determined.

Results. Of the 202 eligible patients, the occult cause of the UVFP was determined in 96 patients (47.5%). Idiopathic causes were the most common etiologies ($n = 106$). In occult causes group, chest lesions were the most common diseases causing paralysis (52 cases) and included lung cancer ($n = 28$) and mediastinal malignancy ($n = 8$). More than half of the neck lesions were of thyroid origin. Of the 18 thyroid lesions, 12 were thyroid malignancies. Chest CT had an intermediate yield of 30.9% (52 of 168). Neck US had a diagnostic yield close to that of neck CT (26.2%).

Conclusion. UVFP may result mainly from idiopathic, lung cancer, mediastinal, and thyroid malignancies. The initial use of neck US as an alternative to CT may be advocated for the determination of diseases resulting in UVFP.

Key Words: Computed tomography—Etiology—Recurrent laryngeal nerve—Ultrasonography—Vocal fold paralysis.

INTRODUCTION

Vocal fold paralysis (VFP) refers to vocal fold immobility that results from neurogenic causes.¹ VFP is caused by a number of different pathologies that variably involve the anatomic course of the vagus and recurrent laryngeal nerves.^{2,3} These nerves, which are responsible for vocal fold movement, travel an extended course, originating at the base of the skull and passing through the carotid sheath and upward around the subclavian artery or aortic arch to the trachea-esophageal groove and the larynx.⁴ The most common causes of VFP include the malignancy, iatrogenic injury, and inflammatory process, while other causes are rare.⁵ In adult patients, most VFP presents unilaterally, and VFP is not uncommon in clinical practice.² Unilateral vocal fold paralysis (UVFP) may be asymptomatic and may be identified as coincidental, but it can also lead to dysphonia and dysphagia.

The primary task of an otorhinolaryngologist confronted with a patient who presents with UVFP and no clear etiology is to evaluate the patient for possible causes. The first step is to conduct a full ear, nose, and throat examination, particularly with endoscopic inspection of the larynx. A chest x-ray (CXR), computed tomography (CT), magnetic resonance imaging (MRI), and neck ultrasonography (US) can then be used to investigate the possible causes.^{6–10} Diagnostic CT can be used to evaluate the neck and upper thorax for possible sites of nerve injury; US has high sensitivity in the thyroid and neck regions; and MRI may be superior to CT for assessing the skull base.¹¹ Fluorodeoxyglucose uptake positron emission tomography-

computed tomography has also contributed to identification of causes in patients with UVFP.¹² Thus, systemic workup is warranted for patients with UVFP, but no consensus has been reached regarding the proper assessment of causes of UVFP, and the best approach remains a matter of debate. Prompt identification of etiologic diseases is important because many of them will be locoregionally advanced and involve major vital structures.

We investigated the role of CT and neck US in evaluating UVFP of unknown etiology. In addition, we compared our results with those of previous studies to assess the differences in the etiology of UVFP.

MATERIALS AND METHODS

A retrospective chart review was conducted of all adult patients diagnosed with UVFP at the otorhinolaryngology outpatient clinic from 2008 to 2017. Approval was obtained from the Local Ethics Committee of Istanbul Training and Research Hospital Institutional Review Board before the study. We investigated the medical records of 956 patients with VFP at first encounter. Exclusion criteria were patients with primary laryngeal or pharyngeal tumors; those with previously known cancers of the head and neck, thyroid, lung or esophagus; other metastatic cancers of the neck; surgery that resulted in the UVFP; exposure to laryngeal trauma; a history of prolonged intubation; or known neurologic diseases. Because prior radiation to the head and neck region is considered a potential cause of recurrent laryngeal palsy, patients with this history were also excluded from the study. In total, 754 patients who had the above criteria were excluded from the study. The remaining 202 eligible patients were evaluated by contrast-enhanced direct coronal CT imaging with a slice thickness of 3–5 mm; 168 were examined by chest CT, 118 by neck CT, and 108 patients by head CT. Of the 118 patients with neck CT, 103 were also evaluated by high-resolution US of neck. In addition,

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among the patients with UVFP, 32 underwent MRI for further evaluation. All patients consented to full evaluation of their UVFP and underwent procedures during late follow-up. For 70 cases where a lesion suspicious of a tumor was detected, the patients underwent fine needle aspiration, or excisional or endoscopic biopsy, and the diagnosis was finalized. In total, 26 cases were diagnosed on the basis of clinical and other laboratory tests. A total of 39 patients with lung cancer, mediastinal malignancy, and esophageal tumors were evaluated for distant metastasis and metastatic lymph nodes by positron emission tomography-computed tomography.

We evaluated our results on the etiology of paralysis with those of previous reports, comparing the roles of CT and neck US.

Statistical analysis

The descriptive statistics included the mean, standard deviation, median, minimum and maximum frequencies, and ratio values of the data. The distribution of the variables was measured by the Kolmogorov-Smirnov test. The Mann-Whitney *U* test was used to analyze the quantitative data. The chi-square test was used for analysis of qualitative data. A value of $P < 0.05$ was accepted as significant. Statistical analysis was conducted using the *SPSS 22.0 for Windows* (SPSS Inc., IBM Corp., Armonk, NY) software package.

RESULTS

This study included 202 patients who, at first presentation, were determined to have UVFP of unknown etiology. The 142 male and 60 female patients had a mean age of 57.1 years, ranging from 16–90 years. Paralysis mostly involved the left side ($n = 139$, 68.8%). Of the 202 included patients, the occult cause of the UVFP was determined in 96 patients (47.5%), whereas the remaining 106 patients had no specific cause of the

paralysis established (idiopathic). In one of the patients, both a meningioma and a benign thyroid tumor were detected.

The characteristics of the 96 patients with known causes and the etiology of the UVFP are summarized in [Tables 1–2](#). Lesions in the chest region were the most common diseases causing UVFP (52 cases) and included lung cancer ($n = 28$), mediastinal malignancy ($n = 8$), and esophageal cancer ($n = 2$). These tumors accounted for the vast majority of UVFP causes. More than half of the neck lesions were of thyroid origin. Of the 18 thyroid lesions, 12 were thyroid malignancies, 10 were papillary thyroid carcinoma, and 2 were medullary thyroid carcinoma. Malignancies caused UVFP in 55 patients (57.3%) and benign lesions caused it in 41 patients (42.7%).

The mean age of the patients was significantly higher in the occult cause group than in the idiopathic group ($P = 0.003$). The number of male patients was also significantly higher in the occult cause group than in the idiopathic group ($P = 0.020$). No significant difference was noted between the idiopathic and occult cause groups regarding the paralysis laterality ($P = 0.133$) ([Table 3](#)), or between the malignant and benign groups regarding the age, sex distribution, and paralysis laterality of the patients ($P = 0.807$, $P = 0.607$, $P = 0.118$, respectively). All lesions in the brain in the present study were benign, whereas the number of malignant lesions of the chest region significantly exceeded the number of benign lesions ($P = 0.000$, $P = 0.000$, respectively). In contrast, the percentages of benign and malignant lesions were similar in the group with neck diseases ($P = 0.782$) ([Table 4](#)). Evaluation of the ability of a CT to achieve a diagnosis revealed that chest CT had an intermediate yield of 30.9% (52 of 168) and neck CT and brain CT had lower yields, at 24.5% (29 of 118) and 14.8% (16 of 108), respectively. Besides 2 patients (cricoid chondrosarcoma and cervical vertebra bony spur), 27 other patients were diagnosed by neck US. Neck US had a diagnostic yield close to that obtained with neck CT (26.2%) ([Table 5](#)).

TABLE 1.
The Characteristics and Etiology of Adult Unilateral Vocal Fold Paralysis in 202 Patients

| | Min–Max | Median | Mean \pm SD/ n – % | |
|----------------------|--------------|--------|-------------------------|-------|
| Age | 16–90 | 59 | 57.1 \pm 15.1 | |
| Sex | | | | |
| | Female | | 60 | 29.7% |
| | Male | | 142 | 70.3% |
| Paralysis laterality | | | | |
| | Right | | 63 | 31.2% |
| | Left | | 139 | 68.8% |
| Etiology | | | | |
| | Idiopathic | | 106 | 52.5% |
| | Occult cause | | 96 | 47.5% |
| Occult cause | | | | |
| | Benign | | 41 | 42.7% |
| | Malignant | | 55 | 57.3% |
| Head disease | | | 16 | 16.7% |
| Chest disease | | | 52 | 54.2% |
| Neck disease | | | 29 | 30.2% |

Abbreviation: SD, standard deviation.

TABLE 2.
Etiologic Causes of Unilateral Vocal Fold Paralysis (N = 202 Patients)

| Cause | Number (N) |
|--|------------|
| Neck disease | |
| Thyroid cancer | 12 |
| Thyroid benign lesion | 6 |
| Laryngosel | 3 |
| Cervical vertebrae bony spur | 2 |
| Vagal schwannoma | 2 |
| Nasopharyngeal cancer metastasis | 2 |
| Parotid gland malignant tumor | 1 |
| Cricoid chondrosarcoma | 1 |
| Total | 29 |
| Chest disease | |
| Lung cancer | 28 |
| Mediastinal malignancy | 8 |
| Tuberculosis complications | 4 |
| Pulmonary proliferative disease | 4 |
| Esophageal cancer | 2 |
| Remnant thymus | 2 |
| Thorachal vertebrae tumor | 1 |
| Aortic aneurysm | 3 |
| Total | 52 |
| Head disease | |
| Benign tumors (meningioma) | 5 |
| Cerebrovascular disease | 5 |
| Other cerebral lesions | 6 |
| Total | 16 |
| Idiopathic | 106 |
| Total number of eligible patients | 202 |

DISCUSSION

Occult diseases were detected in 96 of 202 patients (47.5%) with UVFP in the present study, while the remaining patients (52.5%) were idiopathic. In a similar study, Kang et al reported the identification of subclinical diseases in 36 of 153 patients (23%) with unexplained UVFP.¹³ When the apparent causes and surgical cases were included in the study, the incidences of occult and idiopathic causes differed.¹⁴ Indeed, in the present

study, UVFP of occult etiology had a higher incidence than that reported in previous studies.^{13–15} Because of different incidences of cancers and other diseases in different countries, the most common causes and lesion detection rates of UVFP vary by country. Despite that, the occurrence of subclinical neoplasm resulting in UVFP has decreased in the recent decades with early diagnosis of cancers using imaging modalities.

In our study, both age and number of male patients were significantly higher in the occult group than in the idiopathic group. This can be explained by the high risk of developing malignancy because of the excessive smoking behavior, especially in older male populations. Another cause may be the fact that cardiac and cerebrovascular diseases might have a close relationship to the aging of society in recent years—an idea also expressed by Takano et al.¹

The differential diagnosis of UVFP can be quite broad, but malignant neoplasm has been reported as the most common cause of extralaryngeal VFP.¹⁶ In the present study, occult diseases were detected primarily in the chest (54.2%) and neck (30.2%), in agreement with the findings of Kang et al.¹³ Several studies also showed higher incidence of subclinical chest than neck lesions as main reason for UVFP.^{9,10}

In our study, lung cancers and thyroid gland malignancies were the most common causes of UVFP. A similar observation was reported by Bando et al.⁸ Mediastinum involvement, and especially by metastatic lymph nodes, was the other common site in our study. These malignancies can be easily located with screening modalities. For this purpose, CXR can be used as a detection method for the diagnosis of thorax malignancies.^{7,8} Kang et al. reported that CXR identified 58.9% of chest lesions when used as a diagnostic tool; however, chest CT scans revealed 100% of both the extent of the disease and the nature of the tumors.¹³ Regardless of whether patients with negative or positive CXR require further evaluation, a diagnostic chest CT scan must absolutely be used for disease confirmation. In our study, chest CT provided the best diagnostic yield, in accordance with the literature. Therefore, in our opinion, the use of chest CT may be the correct choice for detecting the cause of unexplained UVFP.

The benign and malignant causes of neck diseases had close rates; 18 of the 29 cases were of thyroid origin in the neck and

TABLE 3.
Comparison of Idiopathic and Occult Cause Groups

| | | Idiopathic | | Occult Cause | | <i>P</i> * |
|----------------------|--------|---------------------|--------|---------------------|--------|---------------|
| | | Mean ± SD/ n – % | Median | Mean ± SD/ n – % | Median | |
| Age | | 54.0 ± 16.1 | 56.0 | 60.5 ± 13.2 | 60.5 | 0.003† |
| Sex | Female | 39 | 36.8% | 21 | 21.9% | 0.020‡ |
| | Male | 67 | 63.2% | 75 | 78.1% | |
| Paralysis laterality | Right | 38 | 35.8% | 25 | 26.0% | 0.133‡ |
| | Left | 68 | 64.2% | 71 | 74.0% | |

* *P* < 0.05 in bold denote statistical significance.

† Mann-Whitney *U* test.

‡ Chi-square test.

Abbreviation: SD, standard deviation.

TABLE 4.
Comparison of Benign and Malignant Etiologic Causes in Unilateral Vocal Fold Paralysis

| | | Benign | | Median | Malignant | | <i>P</i> * | |
|----------------------|--------|---------------------|-------|--------|---------------------|--------|------------|---------------|
| | | Mean ± SD/ n – % | | | Mean ± SD/ n – % | Median | | |
| Age | | 59.5 | 15.2 | 61.0 | 61.3 | 11.6 | 60.0 | 0.807† |
| Sex | Female | 10 | 24.4% | | 11 | 20.0% | | 0.607‡ |
| | Male | 31 | 75.6% | | 44 | 80.0% | | |
| Paralysis laterality | Right | 14 | 34.1% | | 11 | 20.0% | | 0.118‡ |
| | Left | 27 | 65.9% | | 44 | 80.0% | | |
| Brain | | 16 | 39.0% | | 0 | 0.0% | | 0.000‡ |
| Chest | | 13 | 31.7% | | 39 | 70.9% | | 0.000‡ |
| Neck | | 13 | 31.7% | | 16 | 29.1% | | 0.782‡ |

* *P* < 0.05 in bold denote statistical significance.

† Mann-Whitney *U* test.

‡ Chi-square test.

Abbreviation: SD, standard deviation.

12 of those were thyroid carcinomas. Neck CT and neck US have been frequently used to reveal the possible causes of UVFP in the neck, and both methods have their own advantages and disadvantages. The use of neck US and neck CT scan has been investigated separately and well demonstrated in prior assessments of UVFP.^{10,13} Our retrospective study is one of the few studies comparing these two imaging modalities.

Head diseases were uncommon causes of UVFP in our study (16.7%). Similar results (10.6%) were reported by Takano et al.¹ All the brain lesions were benign; five were meningioma. A previous report by Kang et al found four tumors located at the base of the skull, including brainstem meningioma that resulted in similar UVFP.¹³ MRI offers improved resolution, especially for the skull base and brainstem, and requires no exposure to ionizing radiation. Therefore, it may be superior to CT for assessing these regions.¹¹

Because of the high radiation risks and the lack of cost-effectiveness of the recommended imaging modalities, evidence-based recommendations are essential for guiding the tests of routine imaging in UVFP. For this purpose, some authors have advocated for new offerings in recent years. However, no specific clinical algorithm can reveal the etiology of UVFP. Our preference was helical CT that included the skull base (108 patients), neck (118 patients), and thorax (168 patients) to determine the etiology of unknown UVFP. Additionally, 103 patients were evaluated by high-resolution US of neck.

TABLE 5.
Comparison of Yields of CT and Neck US in This Study

| | Patients (n) | Pathology (n) | Diagnostic Yield (%) |
|----------|-----------------|------------------|-------------------------|
| Head CT | 108 | 16 | 14.8 |
| Neck CT | 118 | 29 | 24.5 |
| Chest CT | 168 | 52 | 30.9 |
| Neck US | 103 | 27 | 26.2 |

Abbreviations: CT, computed tomography; US, ultrasonography.

Contrast-enhanced CT is a very useful imaging tool that can appropriately detect most of the occult diseases that cause UVFP.¹³ However, the diagnostic yield varies depending on the region. The chest CT provided the best diagnostic yield (30.9%); this yield was 24.5% for neck CT in 96 patients with UVFP in our retrospective study. In a retrospective series of 36 UVFP, Terris et al found a 35% diagnostic yield for neck CT.¹⁷ Ramadan et al also reported a diagnostic yield of 55% in their series.¹⁸ Part of this difference may reflect that the surgical causes included in previous published studies were comparatively high. The yield of head CT was the lowest (14.8%) in our study.

Ultrasonography has a high sensitivity for neck lesions, especially thyroid pathologies, as well as for lesions of the supraclavicular region, metastatic involvements of the jugular chain and tracheoesophageal groove, and any lesions involving the cervical vagus nerve, except for specific regions such as the skull base and infraclavicular region.¹⁰ It is also an easily accessible and inexpensive screening tool that is radiation free, using a nonmagnetic field generally. Another important advantage is that fine needle aspiration under US guidance can also be done at the same time and in office conditions. Neck US can be utilized to detect the most occult neck diseases that cause UVFP, as reported previously.^{19,20} Because neck US has almost the same diagnostic yield as neck CT (26.2% and 24.5%, respectively) and other advantages, US can give as much information as CT for evaluating the subclinical neck diseases that result in UVFP. However, cost-effectiveness is an important issue today and must be considered in clinical practice and management.²¹ Although the costs of the various imaging modalities vary in different countries, CT and US are widely used in many countries of the world as cost-effective modalities.

Neck CT and neck US are effective methods in determining lesions in the etiology of UVFP. However, in cases where the presence of incidental lesions in the neck makes it difficult to establish the relationship between lesion and paralysis, in addition to these imaging techniques, more advanced and electrophysiological tests may be needed.

Our opinion is that chest CT and neck US are very useful imaging techniques to determine the causes of UVFP. The neck CT is of questionable utility in the differential diagnosis of thyroid tumors and causes radiation exposure of the patients. Future prospective multicenter studies with a larger number of patients would reveal more information and confirm the diagnostic sensitivity of neck CT versus neck US. Novel diagnostic algorithms are still needed for the use of US as the primary method, particularly in special populations like children, pregnant women, and patients from regions with frequent thyroid malignancies.

CONCLUSION

We found the most common etiologies of UVFP to be idiopathic, lung cancer, mediastinal, and thyroid malignancies. Our results suggest that CT and US workup have similar diagnostic yield for neck pathology in the evaluation of patients with UVFP.

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