

Etiologic Features in Patients with Unilateral Vocal Fold Paralysis in Taiwan

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Background: To develop an updated screening, treatment and follow-up strategy for acquired unilateral vocal fold paralysis (UVFP), this Taiwan study investigated concurrent etiologies in patients treated in a tertiary medical center.

Methods: This retrospective study was conducted at the voice centers of Chang Gung Memorial Hospital, Keelung, and Chang Gung Memorial Hospital, Linkuo Medical Center, Taiwan. Outpatient and inpatient medical records of patients with UVFP treated between January, 2002 and March, 2006 were retrospectively reviewed. Patients with laryngeal/hypopharyngeal malignancies, those with incomplete examination and follow-up data and those with congenital UVFP were excluded from the study.

Results: One hundred sixty-one patients, including 104 females and 57 males, with ages ranging from 15 to 85 years, met the inclusion criteria. One hundred ten patients (68%) had left side UVFP. The causes were iatrogenic in 48%, subclinical tumor in 12%, neck trauma in 7%, radiation effect in 6% and other causes in 5%. Thyroidectomy was the most common surgical cause of UVFP ($n = 51$). The most common origins of subclinical tumors were the thyroid ($n = 8$) and lung ($n = 6$). In patients younger than 30 years, neck trauma was a major cause of UVFP.

Conclusions: A tailored management strategy for UVFP is needed because vocal fold immobilization is an important sign of various underlying diseases. Extended follow-up is crucial in idiopathic UVFP due to the risk of undiagnosed subclinical tumor.

(Chang Gung Med J 2009;32:290-6)

Key words: unilateral vocal fold paralysis, etiology, iatrogenic, neoplasm, neck trauma

General physicians usually refer patients with phonation difficulty to otolaryngologists for further evaluation after conservative management. Unilateral vocal fold paralysis (UVFP), a major cause of dysphonia, can be detected by laryngoscopic inspection. Unilateral vocal fold paralysis is secondary to many known causes including trauma,

malignancy and surgery. Although UVFP can be idiopathic, it may also be a presenting feature of many serious underlying disease processes. Accordingly, UVFP should be considered a physical sign rather than a diagnosis, and its exact cause should be actively investigated in all patients because its etiology determines its prognosis and

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Received: Apr. 2, 2008; Accepted: Jun. 26, 2008

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management.

One cause of UVFP is damage to any part of the vagus nerve as it travels from its origin in the high medulla to its most important branch, the recurrent laryngeal nerve. Studies in other countries have demonstrated that the most common etiologies of UVFP vary in both time and/or geographic location. In 1981, Kearsley *et al.* reported that malignancy, mainly lung carcinoma, was the leading cause of vocal fold paralysis in a study in Australia.⁽¹⁾ Eighteen years later, Havas *et al.* demonstrated that iatrogenic causes such as surgery had replaced malignancy as the most common etiology in the same country⁽²⁾ Moreover, Rosenthal *et al.*, in the largest retrospective etiologic investigation of vocal fold immobility to date, observed a shift in the major etiology of UVFP from extralaryngeal malignancies to nonthyroid surgical procedures.⁽³⁾ The aim of this study was to evaluate the etiology of acquired UVFP and analyze differences from previous studies this disorder in Taiwan populations.

METHODS

Patients and evaluations

This retrospective study enrolled 187 consecutive patients with UVFP who visited and registered at the voice centers of Chang Gung Memorial Hospital, Keelung, and Chang Gung Memorial Hospital, Linkuo Medical Center in northern Taiwan from January, 2002 to March, 2006. In all patients, UVFP was confirmed using a flexible or rigid laryngoscope with a stroboscope. Exclusion criteria included UVFP due to laryngeal/hypopharyngeal malignancies, incomplete examinations and follow-ups and UVFP due to congenital origin in young patients. Patient data, including age, gender, and clinical features such as duration of symptoms and side of vocal fold paralysis, medical and surgical history and imaging studies were reviewed in each patient.

All patients who presented with UVFP during the study period underwent plain chest radiographs, thyroid sonography, and esophagoscopy. Thyroid echo-guided aspiration cytology were performed when mass lesions were noted. If the diagnosis remained obscure, a detailed neurological examination and computed tomography scan of the brain, neck and/or chest were performed depending on the

suspected lesion site. These patients were followed-up regularly with appropriate clinical and imaging studies for 6 months or until a definite diagnosis could be made. If further examinations failed to reveal the exact cause after 12 months follow-up, the UVFP etiology was classified as idiopathic.

RESULTS

During the study period, 26 UVFP patients were excluded due to a final diagnosis of laryngeal/hypopharyngeal cancer ($n = 21$), incomplete examinations and follow-ups ($n = 3$) or congenital anomaly with UVFP ($n = 2$). Therefore, 161 patients, including 104 females and fifty-seven males, with ages ranging from 15 to 85 years, were selected for further analysis. Of these patients, 110 (68%) had left side UVFP. The duration from vocal dysfunction to the first visit at our clinic varied from 20 days to 10 years. Fig. 1 demonstrates that etiologies were identified in 78% of the subjects. Iatrogenic UVFP was the most common etiology; the remaining causes included subclinical tumor, external neck trauma, radiation effect and others.

In this study, the leading cause of UVFP in Taiwan was iatrogenic problems. Table 1 summarizes the various surgical procedures resulting in postoperative UVFP. Most of the seventy-eight patients with iatrogenic UVFP (70%) had undergone

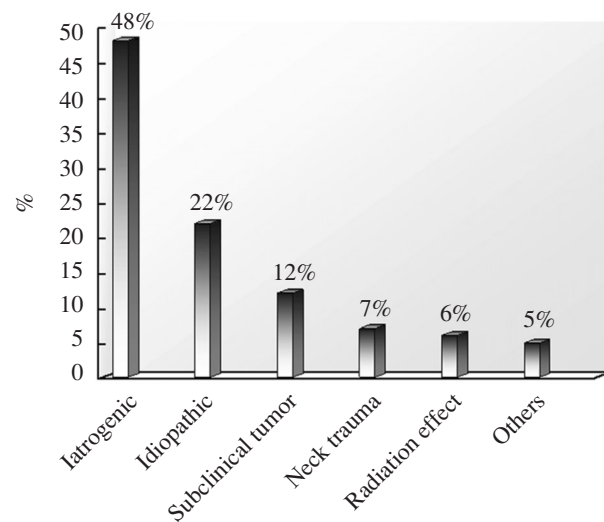


Fig. 1 Etiologic distribution of patients with unilateral vocal fold paralysis in Taiwan ($n = 161$).

Table 1. Surgical Procedures in 78 Patients with Iatrogenic Unilateral Vocal Fold Paralysis

Surgical site	Procedures	n (%)
Neck		55 (70)
	Thyroidectomy	51 (65)
	Cervical spine decompression	3 (4)
	Carotid endarterectomy	1 (1)
Chest		13 (17)
	Pneumonectomy	5 (6)
	Thoraco/mediastinoscopy	5 (6)
Brain		10 (13)
	Craniotomy	7 (9)
	Others	3 (4)

surgical procedures involving the neck. Chest surgery (17%) and brain surgery (13%) may have also induced UVFP. Thyroidectomy (65%) was the most common surgical procedure before the onset of UVFP.

Twenty-one (13%) patients had subclinical tumors associated with UVFP in the study population. Nineteen of these patients had malignant neoplasms confirmed by histopathology after presentation with UVFP. The other two cases were diagnosed as benign cerebello-pontinal angle meningioma. The tumor area distribution ($n = 21$), in descending order of frequency, was lung cancer (57%) followed by cancer of the esophagus (19%), thyroid (14%) and cerebello-pontinal angle meningioma (10%).

Correlations with malignancy were identified in forty-seven (29%) subjects. These neoplasms originated from the thyroid (46%), lung (30%), nasopharynx (11%), breast (9%) and esophagus (4%). Although these malignant tumors seldom infiltrate or compromise the laryngeal nerve, UVFP may still occur after surgery and radiotherapy.

The right vocal fold was affected in about one third of the subjects, and iatrogenic causes were more common in right side (64%) than left side UVFP (38%) (two tailed Fisher exact test, $p < 0.001$). The etiologic distribution in the patients with right side UVFP ($n = 51$) was iatrogenic (64%), idiopathic (13%), subclinical tumor (7%), neck trauma

(7%), and other causes (9%). Of all surgical procedures, thyroidectomy was the leading cause of both right and left side vocal fold palsy.

Grouping of the patients with UVFP by age (Fig. 2) yielded some interesting information. In the younger age group (15 to 30 years old), neck trauma (50%) was the most frequent reason for UVFP. All of these patients were motorcyclists and had external neck trauma with UVFP due to traffic accidents. Subsequently, iatrogenic causes were most common in patients in the 4th decade of life.

DISCUSSION

In the present study, the authors diagnosed approximately sixty UVFP patients annually in a voice clinic. As patients with UVFP usually have intermittent or persistent difficulty speaking, breathing and swallowing, each patient was carefully evaluated because correctly identifying the etiology of UVFP was important for selecting the appropriate therapeutic strategy and devising an effective follow-up program. Although UVFP may be secondary to surgery or idiopathic, there was a risk of subclinical tumors such as lung, thyroid, or brain cancers in our survey. A “side-specific” evaluation of suspicious malignancies as a cause of vocal fold paralysis, advocated by Furukawa *et al.*⁽⁴⁾ in 1994, includes neck ultrasound and chest radiographs; if these initial tests are inconclusive, a chest CT scan should be performed for left-side UVFP only. However, Merati *et al.*, in a national survey by the American-Broncho-Esophagological Association (ABEA), reported that

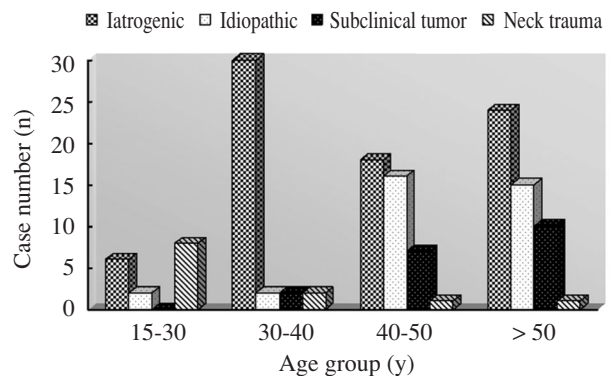


Fig. 2 Age distribution of the four most frequent causes of unilateral vocal fold paralysis ($n = 144$).

chest radiographs and CT scans with contrast along the course of the recurrent laryngeal nerve were more commonly performed and recognized examinations than serum testing and magnetic resonance imaging by current practitioners.⁽⁵⁾ In the experience of the authors, serial chest radiographs and thyroid sonography and echo-guided aspiration cytology for mass lesions are the preferred first-line imaging studies if the patient has no history of surgery or trauma.

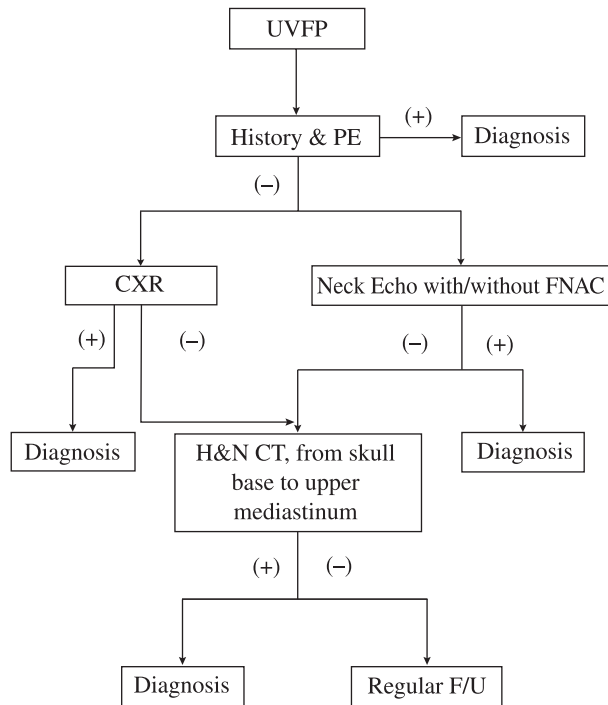
Surgery was a cause in nearly half (48%) of these cases. Although surgical procedures are similarly likely to damage the right or left recurrent laryngeal nerve (46% versus 54%), iatrogenic causes were more prevalent in the right side UVFP group (right: left = 64%: 38%; $p < 0.001$). The left recurrent laryngeal nerve traverses the aortal arch, which is a longer route to the larynx than that of the right recurrent laryngeal nerve. Damage from surrounding mediastinal neoplasms is more frequent and could explain the relatively lower proportion of non-iatrogenic causes on the right side. Thirty-two percent of the studied subjects had undergone thyroidectomy. Thyroidectomy has become a common surgical procedure and is now the most common cause of UVFP in the United States⁽³⁾ and in Taiwan. Although the incidence of UVFP after thyroidectomy is not high, a more precise operative technique and use of an intraoperative nerve detector would further decrease the rate of this complication.

Both abduction and adduction of the vocal cords are controlled by branches of the vagus nerve, which in turn originates from the brainstem and travels along the carotid sheath. Invasion or compression of the vagus or its branch, the recurrent laryngeal nerve, can result from skull base tumors, thyroid cancer, lung cancer, esophageal cancer and metastases to the mediastinum. Therefore, a delicate, systemic examination is imperative for this consideration. In this study, subclinical tumors, mostly lung and mediastinal neoplasms, had induced UVFP in a significant portion (9%). Seven of the eight patients with subclinical thyroid cancer who were diagnosed by screening thyroid sonography with aspiration cytology underwent further surgical pathology during the 12-month follow-up period. However, thyroid cancer was confirmed in one of the initial idiopathic cases two years later. This might have resulted from a very small, slowly growing thyroid lesion which could not be accurately detected by thyroid sonography.

Accordingly, the follow-up period for suspected thyroid masses should be even longer than for other causes and should include aspiration cytology in addition to thyroid sonography. Previous studies reported one to eight cases of UVFP induced by lung cancer annually^(1,6) whereas this study documented two cases annually. Although the prevalence of lung cancer is different in each country, the incidence of UVFP in these patients is apparently similar. Most patients with lung cancer presenting with UVFP in the current study were identified on the first visit, but in one case, the lung mass was detected by serial chest radiography after 3 months of follow up. We suggest serial chest plain radiography in UVFP patients and chest CT in high risk patient groups. Therefore, a subclinical tumor must be excluded by a longer follow-up period before UVFP is considered idiopathic.^(7,8) A flowchart for evaluation of UVFP is shown in Fig. 3.

UVFP may be caused not only by direct invasion of malignant tumors, but also by complications of cancer therapy. Extensive excisions in thyroid, lung and esophageal cancer may all cause vocal fold paralysis from mechanical damage or excision of the vagus nerve or its recurrent laryngeal branch. Likewise, radiotherapy for nasopharyngeal and breast cancer can produce similar effects. Radiation-induced UVFP has been reported in other studies.^(8,9) This is related to the high remission rate for nasopharyngeal carcinoma induced by modern treatments. This, combined with multiple neuropathy, most frequently 10th and 12th cranial nerve palsy, is characteristic in these patients and can differentiate it from viral vagal neuropathy. Moreover, all patients with breast cancer-related UVFP should be treated on an individual basis, and the possibility of recurrence should be ruled out by imaging studies before classifying these cancers as radiation-induced UVFP.

In this study, 21.7% of UVFP cases were attributed to idiopathic causes. In a previous study,⁽⁷⁾ the rate at which patients regained vocal cord function after idiopathic UVFP was only 40% and this usually occurred within 3 months. However, the prognosis of idiopathic UVFP was not satisfactory. An effective treatment for unilateral vocal fold paralysis is still unknown. Accordingly, a thorough study, preferably community-based, is needed clarify the resolution rate and the most effective treatment protocol for idiopathic UVFP.



Abbreviations: UVFP: unilateral vocal fold paralysis; FNAC: fine needle aspiration cytology; CXR: chest x-ray; PE: physical examination; H&N CT: head and neck computerized tomography; F/U: follow up; (+): Positive finding; (-): Negative finding.

Fig. 3 Flowchart for evaluation of unilateral vocal fold paralysis.

Table 2 summarizes the four main causes of UVFP consistently reported in the studies of Ramadan *et al.*,⁽¹⁰⁾ Yumoto *et al.*,⁽¹¹⁾ and Rosenthal *et al.*,⁽³⁾ and the present study. The most common causes of UVFP in the current report were similar to those in the Rosenthal *et al.* study because of similar timing of the data collection. The patients in the study by Rosenthal *et al.*⁽³⁾ were treated in 1995-2005 whereas the patients in the current study were treated from 2002-2006. The prevalence of neck trauma was high in the current review because motorcycles are still a very common transportation mode in Taiwan. Blunt neck trauma from the helmet safety strap is common. The proper use and size of the safety helmet should be studied to prevent this trauma.

Although some patients with thyroidectomy-induced cases of UVFP have permanent paralysis, a

Table 2. Literature Review of Four Main Causes of Unilateral Vocal Fold Paralysis

	Ramaden et al ⁽¹⁰⁾ (1991-1994)	Yumoto et al ⁽¹¹⁾ (1987-1997)	Rosenthal et al ⁽³⁾ (1996-2005)	Ko et al (2002-2006)
Surgery	29.6%	42.7%	46.3%	48.4%
Malignancy	31.6%	22.4%	13.5%	11.8%
Idiopathic	16.3%	17.4%	17.6%	21.7%
Neck trauma	7.1%	2.1%	2.2%	7.4%

few regain vocal function because of the changed position of the paralyzed vocal fold. When paralyzed vocal folds return to medial position, patients can feel their voices return. Otherwise, surgical treatment modalities have been developed for patients with poor compensation for UVFP, including various techniques of laryngeal framework surgery or injection laryngoplasty. The most common substances for injection are biologic implants such as autogenous fat, or alloplastics such as Teflon and Gortex. Laryngeal framework surgery was developed for vocal cord medialization, including thyroplasty or strap muscle transposition. These methods can achieve good short- to intermediate-term effects.^(10,12,13)

In conclusion, the causes of UVFP in Taiwan differ slightly from those reported in Western studies. Because thyroidectomy is one of the most common surgeries in Taiwan, related iatrogenic UVFP is also common. Prolonged follow-up is necessary in cases of idiopathic UVFP. Routine thyroid sonography with aspiration cytology is mandatory for as long as two years after diagnosis of UVFP. The etiology of UVFP differs according to age. Neck trauma-induced UVFP is more common in young patients. Accordingly, understanding geographic variations in UVFP etiology is vital, not only for treatment but also to identify the cause.

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台灣單側聲帶麻痺患者之病因特徵

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背景： 探討目前台灣醫學中心後天性單側聲帶麻痺患者的致病因，進而發展早期篩檢、治療及追蹤的方式。

方法： 針對長庚紀念醫院基隆院區及林口醫學中心附設嗓音中心的病患來做回溯性研究。收集 2002 年 2 月到 2006 年 3 月於院內住院或是門診診斷單側聲帶麻痺的病患，依照病歷追溯方式來探討致病因，其中因喉癌或下咽癌所致的單側聲帶麻痺，先天性單側聲帶麻痺等病例均被排除，未能有完整追蹤病史的病患也予以排除。

結果： 收集 161 位患者，57 位男性，104 位女性，年齡自 15 歲至 85 歲。左側聲帶麻痺有 110 位，佔 68%；右側聲帶麻痺有 51 位，佔 32%。致病因為：醫源性 (iatrogenic) 佔 48%，無臨床症狀的腫瘤 (subclinical tumor) 佔 12%，頸部外傷 (neck trauma) 佔 7%，放射治療影響 (radiation effect) 佔 6%，及其他原因 (other causes) 佔 5%。甲狀腺切除手術 (thyroidectomy) 是最常見造成單側聲帶麻痺的手術 (病例數為 51)。因腫瘤侵犯造成聲帶麻痺的腫瘤，常見的是源自甲狀腺 (病例數為 8) 及肺 (病例數為 6)。在低於 30 歲以下年輕病患則是以頸部外傷為主要的致病因。

結論： 因為單側聲帶麻痺對許多疾病是一個重要的徵兆，因此適時修正的處置是必要的。即便是病患經診察後並未發現明顯的致病因，但仍有些腫瘤在早期並不易診斷，因此針對原因不明的自發性單側聲帶麻痺宜延長追蹤時間。
(長庚醫誌 2009;32:290-6)

關鍵詞： 單側聲帶麻痺，致病因，醫源性，腫瘤，頸部外傷

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受文日期：民國97年4月2日；接受刊載：民國97年6月26日

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