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의학 석사 학위논문

Prognostic Value of the Posterior Cricoarytenoid Muscle Atrophy in Computerized Tomography scans for Unilateral Vocal Fold Paralysis Recovery

일측성대마비 예후 예측에서 컴퓨터 단층촬영상 후윤상피열근 위축의 역할

2018년 02월

서울대학교 대학원
임상의과학과 전공

심 예 지

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ABSTRACT

Prognostic Value of the Posterior Cricoarytenoid Muscle Atrophy in Computerized Tomography scans for Unilateral Vocal Fold Paralysis Recovery

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Objectives: To evaluate a prognostic value of the posterior cricoarytenoid (PCA) muscle atrophy observed on neck computed tomography (CT) in patients with unilateral vocal fold paralysis.

Study design: Retrospective cohort study

Methods: CT images of 87 with unilateral vocal fold paralysis (UVFP) were evaluated to identify the PCA muscle atrophy and to measure the severity of the PCA muscle atrophy in semi-quantitative manner. The grading of the PCA muscle atrophy was compared with the recruitment pattern of laryngeal electromyography (LEMG) and restoration of vocal fold movement.

Results: The PCA muscle was identifiable on CT in 73 subjects. Using the PCA muscle atrophy as an indicator of UVFP, we correctly predicted the paralysis in 69 (94.5%). Grade of the PCA muscle atrophy is significantly correlated with recruitment pattern of LEMG. If the positive result is defined as the PCA muscle showed moderate to severe degree of atrophy, we could predict the persistent UVFP in 88% of patients.

Conclusion: Our study demonstrated that the PCA muscle atrophy is possible prognostic factor of UVFP with high positive predictive value.

Keywords: vocal fold paralysis, computed tomography, electromyography, posterior cricoarytenoid muscle.

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LIST OF ABBREVIATIONS

UVFP: Unilateral vocal fold paralysis

LEMG: Laryngeal electromyography

ASA: Abnormal spontaneous activity

CT: Computed tomography

PCA: Posterior cricoarytenoid

TA: Thyroarytenoid

EMRs: Electronic medical records

VF: Vocal fold

PPV: Positive predictive value

NPV: Negative predictive value

VFP: vocal fold paralysis

INTRODUCTION

Laryngeal framework surgery is considered as the best treatment option for permanent unilateral vocal fold paralysis (UVFP) in terms of managing voice problem and dysphagia effectively.1 It is necessary to confirm the patient' s vocal fold paralysis will persist permanently without recovery, regarding that framework surgery is irreversible.

Since Weddel and Pattle presented laryngeal electromyography (LEMG),2 it has been used to evaluate nerve damage and predict the prognosis in UVFP.3 Many researchers have found LEMG findings indicating poor prognosis, such as abnormal spontaneous activity (ASA), fibrillations, positive sharp waves and absence or reduced number of normal motor unit potentials.2,4-7 Studies have shown predictive value of LEMG for persistent UVFP ranged from 75% to 90%.2,4,7-12

Computed tomography (CT) of the neck and chest is performed essentially in UVFP patients to exclude organic etiology that might cause dysfunction of the vagus nerve or recurrent laryngeal nerve.13 Additionally, there are many CT findings associated with a recurrent laryngeal nerve paralysis such as ipsilesional enlargement of laryngeal ventricle, ipsilesional wide pyriform sinus, medially positioned and thick aryepiglottic fold

and posterior cricoarytenoid (PCA) muscle atrophy.14-16

Considering that PCA muscle is innervated by recurrent laryngeal nerve, same as thyroarytenoid (TA) muscle, denervation atrophy of PCA muscle could be a prognostic factor for UVFP.

The purpose of this study is to determine a prognostic value of PCA muscle atrophy observed in CT scan which is taken for initial evaluation of UVFP patients.

MATERIALS AND METHODS

Study design

This was a single-center retrospective cohort study. The study was approved by the local ethics committee at Seoul National University Hospital. EMRs of 100 subjects diagnosed with UVFP from June 2011 to May 2015 were reviewed. Data on sex, age, side of paralysis, etiology and results of LEMG and videostroboscopic exam were collected from electronic medical records (EMRs). CT scans were reviewed by two of the authors who were blind to the clinical information of the subjects. Subjects without neck CT were excluded (n=9). To avoid any bias caused by acute denervation, subjects who underwent CT within 3 months of symptom onset were excluded (n=4). Among 87 subjects, 14 subjects whose muscle contour was rated as vague by either of the reviewers were excluded. Total 73 subjects were included in the analysis predicting presence of vocal fold paralysis using CT findings. To investigate the relationship between PCA muscle atrophy and LEMG findings, 53 subjects whose CT and LEMG had interval less than one month were included. To evaluate the prognostic value of PCA muscle in UVFP, 46 subjects who had VF movement restoration or had follow up duration more than 18 months were included.

Laryngeal CT

Contrast-enhanced CT scans were obtained from the skull base (upper orbit rim) to bronchial bifurcation with section thickness 2-3.5mm, parallel to vocal folds and laryngeal ventricles, using Somaton Sensation 16 scanner (Siemens, Erlangen, Germany) and iodinated contrast media (Optiray; Mallinckrodt, St. Louis, MO, USA). PCA muscle is identifiable on axial section of CT scan as a triangular muscle bundle along the posterior margin of the cricoid cartilage (Fig. 1). Atrophy of PCA muscle was defined as decreased bulk in the axial plane of CT which was seen as shortening of the anterior to posterior dimension with or without increased fatty tissue immediately posterior to the cricoid cartilage or anterior to the muscle, relative to the normal side.17 The side of atrophy of PCA muscle was assessed independently by two reviewers. If PCA muscle contour was hard to identify, it was rated as "vague". If the muscle contour was clearly identifiable, PCA atrophy was given a grade of 0 to 3 compared with the normal side, where 0 = normal (visible both PCA muscle bodies or less than 25% reduction in PCA muscle mass), 1 = mild atrophy (25-50% reduction), 2 = intermediate atrophy (50-75% reduction), and 3 = severe atrophy (no visible PCA muscle or decreased more than 75%) (Fig. 2). Any case for which there was a disagreement on grading was reviewed by the two reviewers together and a

consensus was made. In addition, laryngeal ventricular enlargement on the CT scans, which is known as one of the reliable radiologic features of UVFP, was also evaluated.

Laryngeal electromyography

For each patient, LEMG was performed and interpreted by well-experienced electromyographer in office-based settings. Patient was positioned supine with neck extension. 26-gauge monopolar electrode connected with ground electrode placed on the clavicle was inserted through the cricothyroid membrane into the thyroarytenoid muscle and the cricothyroid muscle. The position of the needle was confirmed by making the patient pronounce /i:/ sound and perform the Valsalva maneuver.18 Synergy on Nicolet DEX system (Natus Medical Inc., San Carlos, CA) was used to record motor unit recruitment tracings. If the position of electrode is unclear, the target muscle was confirmed by ultrasonography (Medison 128 BW prime, Samsung Medison Co, Ltd, Korea).19 LEMG recruitment was classified into 5-grade subjective scales; 0 = normal/dense, 1 = mildly reduced, 2 = moderately reduced or discrete, 3 = single fiber pattern and 4 = no activity.18

Statistical analysis

Statistical analyses were performed using the SPSS version 22.0 for Windows (IBM SPSS Statistics, Chicago, IL, USA). For

bivariate analyses, $\chi 2$-test or Fisher's exact test were used for categorical data. Correlation analysis was performed using non-parametric methods (Spearman's rs and Kendall's tau Tb). The positive predictive value (PPV) and the negative predictive value (NPV) were calculated using the grade of PCA atrophy. The PPV gives the percentage of patients with a positive test result (poor prognosis) who actually have VFP. The NPV gives the probability that the patient restored from VFP indeed, when the test is negative (good prognosis).

RESULTS

The subjects included in this study consisted of 45 (61.6%) males and 28 (38.4%) females. Their age ranged from 15 to 85 years with an average 57.5 years. 52 subjects had left VFP (71.2%) while remaining 21 had right VFP (28.8%). The most frequent cause of UVFP was idiopathic (52, 71.2%), followed by iatrogenic (11, 15.1%), cancer invasion (5, 6.9%), trauma (2, 2.7%), post-intubation (2, 2.7%) and central (1, 1.4%).

The results of predicting the side of VFP using PCA muscle atrophy seen on CT by the two reviewers were entirely consistent. We predicted the presence of UVFP correctly in 69(94.5%) of 73 subjects. When using ventricular enlargement, a commonly used finding of suspicion of UVFP on CT, we could correctly predict UVFP only in 38 (52.1%) ($p<0.001$).

Among the 53 subjects whose CT and LEMG had interval less than one month, grade of the PCA muscle atrophy was as follows: 4 (7.6%) with grade 0, 23 (43.4%) with grade 1, 19 (35.8%) with grade 2, and 7 (13.2%) with grade 3. LEMG recruitment grading was as follows: 14 (26.4%) with grade 0, 16 (30.2%) with grade1, 15 (28.3%) with grade 2, 2 (3.8%) with grade 3, and 6 (11.3%) with grade 4. The relationship of LEMG findings and the PCA muscle atrophy was shown in Table 1.

There was a significant correlation between the grade of LEMG and PCA muscle atrophy (p value of Spearman and Kendall's correlation studies were 0.047 and 0.041, respectively).

Of the 46 subjects who had VF movement restoration or had follow up duration more than 18 months, 7 (15.2%) had restoration of vocal fold movement and 39 (84.8%) had persistent vocal fold immobility at the last follow up. Results of PCA atrophy grading were dichotomized and predictive values were calculated (Table 2). When grade 0-1 was defined as negative result and grade 2-3 as positive result, PPV was 88% and NPV was 19%. When grade 3 was considered as positive result and grade 0-2 as negative result, PPV was 100% and NPV was 17.1%. PPV and NPV using dichotomized LEMG grade (grade 0-1 as negative result and grade 2-4 as positive result) were 96.5% and 33.3%, respectively.

DISCUSSION

In current study we focused on the relationship between atrophy of the PCA muscle and UVFP. The TA muscle also could be found in CT, but the degree of atrophy is often difficult to notice because it shows various features depending on the position of paralyzed vocal fold and the plane of CT cuts.17 Enlarged laryngeal ventricle could be used substitutingly, since atrophy of the TA muscle makes the laryngeal ventricle to be passively enlarged. Contrary to TA muscle, PCA muscle is easily identifiable on axial CT scan as a triangular muscle shadow along the posterior aspect of the cricoid cartilage.17 Because the PCA muscle is surrounded by fat pad, the muscle shadow is well delineated from the posterior cricoid pharyngeal mucosa. In our study, presence of UVFP was correctly predicted in 94.5% using the PCA muscle atrophy, while only 52.1% was correctly predicted using the enlarged laryngeal ventricle which reflects TA muscle atrophy. In the 4 cases where the side of VFP was not correctly recognized, no significant difference was found between the PCA muscles of both sides.

From this study, we demonstrated that the PCA muscle atrophy can be measured semi-quantitatively on CT in most patients with UVFP and that there was a significant correlation between muscle recruitment pattern on LEMG and the degree of the PCA

muscle atrophy. Unfortunately, because the PCA muscle is not a routine target for LEMG due to its invasiveness, we couldn't compare the degree of the PCA muscle atrophy with the PCA muscle EMG. However, given that recurrent laryngeal nerve innervates both TA and PCA muscles, it is reasonable to think these two muscles are denervated at the same degree when there is a high vagal injury or a complete neurotmesis of recurrent laryngeal or vagus nerve. In current study, as well, there was a significant correlation between grading of LEMG recruitment and PCA muscle atrophy.

In the treatment process of patients with UVFP, predicting restoration of vocal fold movement is one of the crucial issues in relation to the timing of framework surgery. Waiting for from 6 months to 12 months before considering framework surgery is generally accepted given the axonal regeneration of laryngeal nerve.1 If we can predict the recovery from the UVFP, the patients won't have to suffer from dysphonia or aspiration while waiting for framework surgery, and temporary treatment such as injection laryngoplasty is not needed. Injection laryngoplasty provides excellent voice restoration in acute or subacute vocal fold paralysis. However, for those who receiving framework surgery, there is a shortcoming that the residual injected material in the vocal folds may affect the final outcome of the surgery. We hypothesized that the atrophy of the PCA muscle might have prognostic information of UVFP because PCA muscle

bulk reflects neural regeneration of recurrent laryngeal nerve. In current study, we found that the PCA muscle atrophy could predict persisting UVFP with high positive predictive value which was comparable to that of LEMG. There have been studies tried to predict prognosis of UVFP by LEMG. LEMG generally has a good predictive value for a positive test result, and in particular, it was up to 100% with synkinesis information and quantitative EMG data.4,9,10,20,21 Although LEMG could well predict the poor prognosis of the UVFP, to obtain more stable surgical outcome, surgeons should wait until the denervation atrophy process is over before performing the framework surgery, as denervated laryngeal muscles go through a denervation atrophy process, which takes various period of time after denervation.22-2422-24 Predicting prognosis using PCA muscle atrophy might contribute to decision making in UVFP patients, in respect of that PCA muscle atrophy connotes both nerve degeneration and degeneration atrophy of vocal fold. In addition, it has the advantage of using CT for initial work up, different from LEMG with its invasiveness.

One limitation is that if there was a poor demonstration of the fat between PCA muscle and pharyngeal wall, there was a poor distinction of PCA muscle. 13 patients (16.1%) had vague contour of PCA muscle and excluded from current study, although most of the study population showed good distinction.

Future prospective studies with larger population may identify more solid results and confirm the utility of the PCA muscle atrophy for prognosis estimation.

CONCLUSION

The PCA muscle atrophy could be the predictive factor in unilateral vocal fold paralysis patients with high PPV. Planning the framework surgery before long might be carefully considered, if severe PCA muscle atrophy is shown on CT scan which is taken three months after the onset of symptoms.

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Table 1. Relationship between LEMG recruitment and the PCA atrophy grading (n=53)

		PCA Atrophy Grading				Total
		0	1	2	3	
Recruitment Grading	0	3	5	6	0	14
	1	0	10	5	1	16
	2	0	6	6	3	15
	3	0	0	1	1	2
	4	1	2	1	2	6
Total		4	23	19	7	53

Table 2. Predictive values of PCA atrophy in UVFP (n=46)

	VFP (−)	VFP (+)	NPV / PPV (%)
PCA atrophy (−) (grade 0−1)	4	17	19 / 88
PCA atrophy (+) (grade 2−3)	3	22	
PCA atrophy (−) (grade 0−2)	7	34	17.1 / 100
PCA atrophy (+) (grade 3)	0	5	

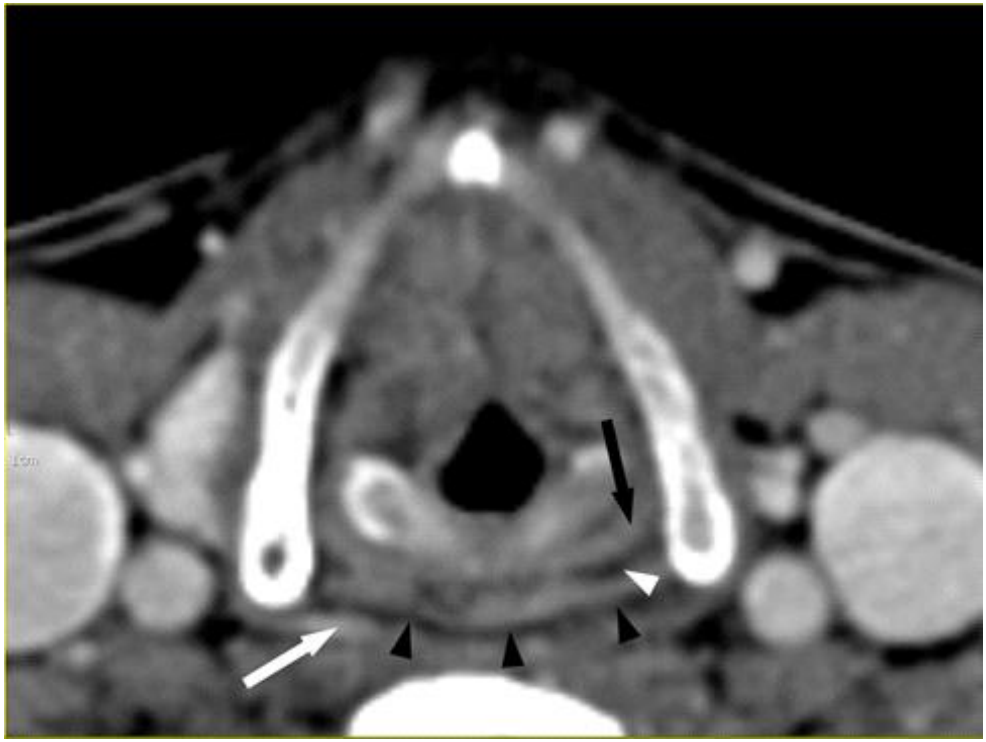

Figure 1. Axial CT image of normal larynx

Long black arrow indicates left PCA muscle; black arrow head, pharyngeal mucosal space; white long arrow, inferior constrictor muscle; white arrow head, fat pad covering PCA muscle.

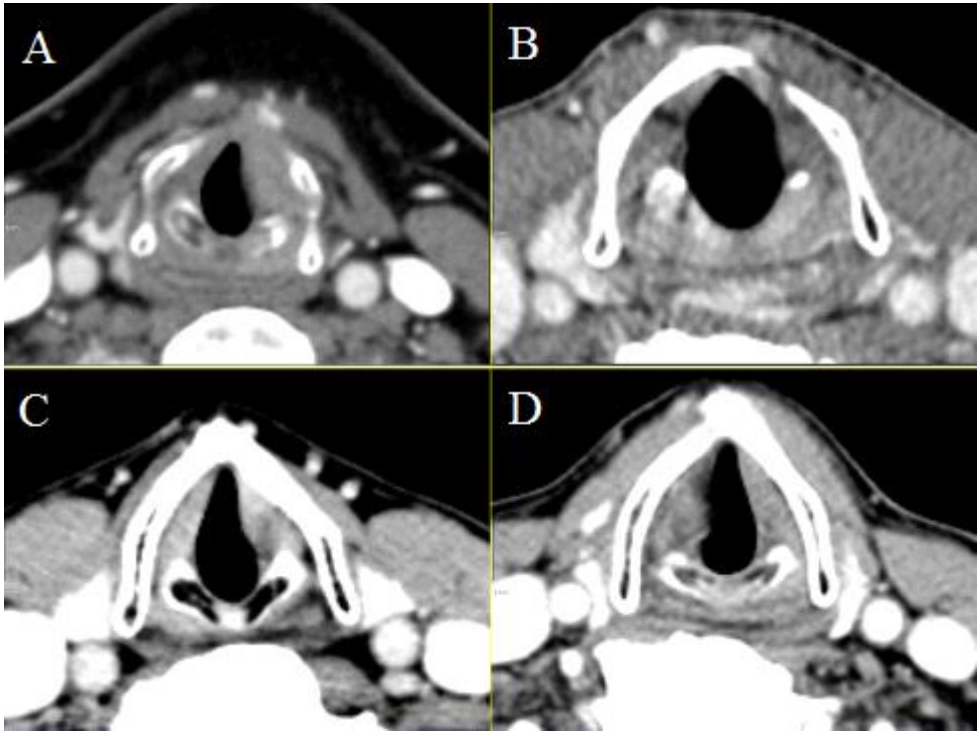

Figure 2. Grading system for the PCA muscle atrophy

A. Grade 0. Both PCA muscles are showing symmetric volume.

B. Grade 1. Right PCA muscle shows mild asymmetry.

C. Grade 2. Left PCA muscle shows marked atrophy leaving shallow muscle shadow.

D. Grade 3. No traceable PCA muscle shadow on the right side.

국문초록

목적: 일측성대마비 환자의 예후 예측에서 경부 컴퓨터단층촬영 영상에서 관찰 되는 후윤상피열근 위축의 역할을 알아보고자 함.

연구대상 및 방법: 본 연구는 후향적 코호트 연구로서, 일측성대마비환자 87명의 컴퓨터단층촬영 영상에서 후윤상피열근 위축 여부와 방향을 확인하였고, 반정량적으로 후윤상피열근 위축의 정도를 측정 하였으며, 후두근전도 결과 및 성대마비의 회복 여부와 후윤상피열근 위축 정도 간의 관계를 확인하였다.

결과: 87명 중 73명의 컴퓨터단층촬영 영상에서 후윤상피열근을 확인할 수 있었다. 후윤상피열근 위축을 성대마비의 지표로 삼았을 때, 73명 중 69명 (94.5%)에서 성대마비가 있는 측을 정확히 예측하였다. 후윤상피열근 위축의 정도와 후두근전도 결과는 유의한 상관관계를 보였다. 컴퓨터단층촬영상 성대마비 양성 소견을 후윤상피열근이 중등도에서 중증 정도의 위축을 보인 것으로 정의한 경우, 컴퓨터단층촬영 영상에서 양성 소견을 보인 환자의 88 %에서 일측성대마비 지속여부를 올바르게 예측할 수 있었다.

결론: 본 연구에서는 컴퓨터단층촬영 영상에서 보이는 후윤상피열근 위축이 양성 예측도가 높은 일측성대마비의 예후 인자임을 확인하였다.

주요어: 성대마비, 컴퓨터단층촬영, 근전도, 후윤상피열근

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