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Correlation Between Accompanying Symptoms of Facial Nerve Palsy, Clinical Assessment Scales and Surface Electromyography

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ABSTRACT

Background: This retrospective study aimed to determine whether there were correlations between the number and type of accompanying symptoms of peripheral facial nerve palsy, and surface electromyography (SEMG) and clinical assessment scales to help diagnosis.
Methods: There were 30, cases of peripheral facial nerve palsy at Visit 1 to the Korean Medicine Hospital, Dong-eui University, 22 cases at Visit 2 and 10 cases at Visit 3. The study period was from July 19, 2021 to November 31, 2021. Symptoms were evaluated three times (with two-week intervals which began 7 days from onset) using SEMG, clinical assessment scales and accompanying symptoms. In this study, the House-Brackmann grading system (HBGS), and the Yanagihara's unweighted grading system (Y-score) clinical assessment scales were used. The Pearson or Spearman correlation was used for statistical analysis.
Results: On Visit 1, the number of accompanying symptoms of peripheral facial nerve palsy had no significant correlation with other measures. On Visits 1-3, the HBGS score had a significant negative correlation with the Y-score. On Visit 2, most of the mean values measured had significant correlations with each other although not between SEMG-Z and SEMG-O that Z means a zygomaticus muscle and O means a orbicularis oris muscle. On Visit 3, the number of accompanying symptoms significantly correlated with the clinical assessment scales. The HBGS score, Y-score, and SEMG measurements (except SEMG-Z) had significant correlations with each other. A significant positive correlation between SEMG-Z and SEMG-T was noted.
Conclusion: We predict accompanying symptoms can be used to diagnose the peripheral facial nerve palsy including both clinical assessment scales and SEMG measurements at 2-5 weeks after onset.

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Introduction

Facial nerve palsy is the most common cranial nerve disorder and has a sudden onset. Paralysis of unilateral facial muscles occurs and the eyes and mouth deviate to one side, and this is accompanied by other symptoms. It is also called "Guanwasa" in Korea [1,2]. The following are the two types of facial nerve palsy: central and the peripheral. Central facial nerve palsy can be caused by a cerebrovascular condition/disease or brain tumor, and peripheral facial nerve palsy can be idiopathic, or due to the herpes zoster virus, or trauma.

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Bell's palsy accounts for approximately 70% of peripheral facial nerve palsy cases and has a prevalence of 20 per 100,000 individuals worldwide. There is no difference in the incidence of Bell's palsy according to sex or race [3], no clear causes have been reported, it has a sudden onset, and approximately 7% of patients experience recurrence during a 10-year interval [4]. Symptoms of Bell's palsy generally peak on the 7th day of onset and are gradually relieved within 3 weeks to 3 months [5]. Approximately 70% of patients with Bell's palsy recover spontaneously within 6 months without treatment [5].

Ramsay-Hunt syndrome is the 2nd most common type of peripheral facial paralysis and is caused by the herpes zoster virus. Fifty-four percent of these patients show unsatisfactory recovery, and the overall prognosis is believed to be worse than Bell's palsy [6].

Korean medicine uses various treatments for facial palsy, including acupuncture, pharmacopuncture, herbal medicine, physical therapy, Chuna therapy [7], electroacupuncture [8], and embedding therapy [9]. Along with the main symptom of facial nerve palsy there are several other symptoms including ear pain, taste disorder, hyperacusis, tinnitus, and lacrimation. These symptoms may appear 3-7 days before or after the facial palsy and are one of the main reasons why patients experience discomfort.

Measurement of facial palsy symptoms is performed using clinical assessment scales and surface electromyography (SEMG), however, there is a lack of research on the relationship between these tests and the accompanying symptoms. Therefore, we retrospectively analyzed data from patients with facial palsy to determine whether there was an association between these tests and the accompanying symptoms.

Materials and Methods

Study patients

This study was a retrospective study conducted using data from inpatient and outpatient records of patients with peripheral facial palsy at the Department of Acupuncture and Moxibustion Medicine, Facial Nerve Palsy Center of Korean Medicine Hospital, Dong-eui University. Data from July 19, 2021 to November 31, 2021 was collated. Patients gave informed consent to the use of their medical records. Of the total cases (39, 1st examinations at Visit 1), 30 cases met the inclusion criteria.

Of these 30 patients from the 1st examination (Visit 1), eight were excluded from the 2nd examination (Visit 2) for not visiting the hospital within the examination period (due to complete recovery of facial nerve palsy, long distance, and personal reasons). Of the 22 patients from the 2nd examination (Visit 2), 12 were excluded for the same reasons. There were 10 patients included in the 3rd examination (Visit 3). All patients included in the examination were subsequently analyzed.

This retrospective study was conducted with the approval of the Institutional Review Board (no.: DH-2021-06) of the Korean Medical Hospital, Dong-eui University.

Inclusion criteria

Patients were between 19 and 80 years old, with facial nerve palsy symptoms present (above House-Brackmann Grade 2), within 7 days from onset, and who had given informed consent.

Exclusion criteria

Patients were excluded from the study if they reported facial nerve palsy due to other causes such as central facial nerve palsy, trauma, or tumor, and individuals with a disease that could affect facial electromyography for reasons other than facial nerve palsy. In addition, individuals who were judged inappropriate for this study were excluded.

Methods

In this study, patients judged to be suitable were evaluated three times at about two-week intervals (Visit 1 to Visit 3). Using the clinical assessment scales [House-Brackmann grading system (HBGS) and Yanagihara's unweighted grading system(Y-score)] and SEMG, the degree of facial nerve palsy was measured, and accompanying symptoms were investigated on Visit 1 (which was within 7 days from onset), and Visit 2 and 3, which were 2 and 4 weeks after Visit 1, respectively. All patients were evaluated in the same manner.

Accompanying symptoms of facial nerve palsy

The accompanying symptoms were divided into six groups: (1) the cephalic and facial regions; (2) eyes; (3) ears, mouths; (4) the cervical region; and (5) the whole body. The sum of the number of accompanying symptoms was obtained by asking the patient (Table 1).

Clinical assessment scale

There were two types of clinical assessment scales used in this study. The House-Brackmann grading system (HBGS) which is a system published by House JW and Brackmann DE in 1985. It is classified from 1 to 6 according to the overall level of facial palsy. The higher the grade, the more severe the paralysis symptoms. The HBGS is the most commonly used method to evaluate facial nerve palsy [10]. The other clinical assessment scale used was the Yanagihara's unweighted grading system (Y-score). It is used to objectify patients' symptoms of facial nerve palsy. It classifies the facial function into 10 domains, and each domain scores from 0 to 4 points (0 total paresis; 1 severe paresis; 2 moderate paresis ; 3 slight paresis; and 4 normal), the sum of all the scores was performed without weighting. The maximum score is 40 points [11].

SEMG

SEMG is studied in Korean medicine to understand facial paralysis. Lee et al [12] investigated volunteers i.e., without facial paralysis, to understand the severity of symptoms and treatment effects for facial conditions/diseases. Moreover, Kim et al [13] studied the correlation between the clinical assessment scales and SEMG test results of facial nerve palsy, and determined that the ratio of measured SEMG values had a statistically significant negative correlation with the HBGS, and a positive correlation with the Y-score.

A Korean medicine doctor who was familiar with facial muscles and sufficiently knew how to use the SEMG measuring device (QEMG-4 XL; Laxtha, Daejeon, Korea) and the surface

Table 1. Accompanying Symptoms of Facial Palsy.

Types of accompanying symptoms of facial palsy		Yes	No
Cephalic and facial region	Facial discomfort, paresthesia, or pain		
	Facial spasm		
	Synkinesis		
	Headache		
Eyes	Decreased or increased secretion of tears		
	Crocodile tears syndrome		
	Xerophthalmia		
Ears	Post auricular pain		
	Pain inside the ear (external auditory canal and internal)		
	Pruritus around the ear		
	Blisters around auricle, ear canal, periphery of the ear		
	Hypoacusis and hyperacusis		
	Tinnitus		
Mouth	Hypogeusia and ageusia		
	Hypergeusia and dysgeusia		
	Hypoptyalism		
	Discomfort when eating		
	Pronunciation inaccuracies		
Cervical region	Pain in the neck and shoulder area		
Whole body	Dizziness		
	General fatigue and weakness		

electrode (Noraxon Dual Electrodes Product #272S; 2.0 cm; Noraxon, Arizona, USA) performed the SEMG measurement. The following three facial areas were respectively measured using a method previously published [14]. Firstly, after attaching the surface electrodes to the Yangbaek (GB14) on both sides which corresponds to the frontalis muscle, the patients were asked to raise both eyebrows as much as possible to create wrinkles on the forehead, hold for 3 seconds, relax for 5 seconds, and repeat 3 times (SEMG-F). Secondly, after attaching the surface electrodes to the center of Jichang (ST4) and Gwallyeo (SI18), which corresponds to the zygomaticus muscle, the patients were asked to raise their cheeks following the instructions in the first step (SEMG-Z). Thirdly, after attaching the surface electrodes to the point 1 cun lateral from the Seungjang (CV24) which corresponds to the orbicularis oris muscle, the patients were asked to make the motion of "Oh" on both lips following the instructions in the 1st step, called (SEMG-O).

Statistical analysis

Statistical processing was performed using SPSS Version 22.0 for Windows program (SPSS Co. USA). To analyze the correlation between clinical assessment scales, SEMG, and the accompanying symptoms of facial palsy, the Spearman correlation analysis was used for Visit 1 and 2, and the Pearson correlation analysis was performed on data for Visit 3 after the Shapiro-Wilk normality test was used. The correlation coefficient was indicated in the results, and the level of statistical significance was $p < 0.05$.

Results

General characteristics of the study patients

This study included 30, 22, and 10 cases on Visit 1, 2, and 3, respectively. On Visit 1, of the 30 patients, 10 (33%) were male and 20 (67%) were female patients, with a total mean age of 59.87 ± 10.04 years. Palsy was noted on the right side in 14 (47%) cases and on the left side in 16 (53%) cases. Additionally, Bell's palsy was noted in 29 (97%) cases and Ramsay-Hunt was noted in 1 (3%) case. On Visit 2, of the 22 patients, 8 (36%) were male and 14 (64%) were female patients, with a total mean age of 60.41 ± 10.39 years. Palsy was noted on the right side in 12 (55%) cases and on the left side in 10 (45%) cases. Furthermore, Bell's palsy was noted in 21 (95%) cases and Ramsay-Hunt was noted in 1 (5%) case. On Visit 3, of the 10 patients, 4 (40%) were male and 6 (60%) were female patients, with a total mean age of 55.50 ± 11.70 years. Palsy was noted on the right side in 3 (30%) cases and on the left side in 7 (70%) cases. Moreover, Bell's palsy was noted in 10 (100%) cases (Table 2).

Average measurements

The mean number of accompanying symptoms were 6.53 ± 2.81, 4.86 ± 3.63, and 4.50 ± 3.66 on Visit 1, 2, and 3, respectively.

Table 2. General Characteristics of the Patients.

		Visit 1 (N = 30)	Visit 2 (N = 22)	Visit 3 (N = 10)
Age (y)		59.87 ± 10.04	60.41 ± 10.39	55.50 ± 11.70
Sex	Male	10 (33)	8 (36)	4 (40)
	Female	20 (67)	14 (64)	6 (60)
Site of facial palsy	Right	14 (47)	12 (55)	3 (30)
	Left	16 (53)	10 (45)	7 (70)
Cause of facial palsy	Bell's Palsy	29 (97)	21 (95)	10 (100)
	Ramsay-Hunt syndrome	1 (3)	1 (5)	0 (0)

Data are presented as mean ± SD or *n* (%).

Table 3. Average of Measurements.

Mean values	Visit 1 (N = 30)	Visit 2 (N = 22)	Visit 3 (N = 10)
Number of accompanying symptoms	6.53 ± 2.81	4.86 ± 3.63	4.50 ± 3.66
HBGS	3.60 ± 0.56	2.91 ± 0.81	2.60 ± 0.84
Y-score	15.47 ± 6.00	25.05 ± 10.04	28.00 ± 10.51
SEMG-F	22.19 ± 18.52	38.96 ± 27.48	48.70 ± 24.17
SEMG-Z	41.42 ± 24.71	64.56 ± 41.39	65.36 ± 29.66
SEMG-O	44.13 ± 21.69	56.00 ± 30.83	58.51 ± 28.98
SEMG-T	35.71 ± 13.32	54.88 ± 27.21	57.50 ± 23.16

Data are presented as mean ± SD.
HBGS, House-Brackmann grading system; Y-score, Yanagihara's unweighted grading system; SEMG, surface electromyography.

The mean values of the HBGS were 3.60 ± 0.56, 2.91 ± 0.81, and 2.60 ± 0.84 on Visit 1, 2, and 3, respectively. The mean values of the Y-score were 15.47 ± 6.00, 25.05 ± 10.04, and 28.00 ± 10.51 on Visit 1, 2, and 3, respectively. The mean values of the SEMG assessment ratio of the frontalis muscle were 22.19 ± 18.52, 38.96 ± 27.48, and 48.70 ± 24.17 on Visit 1, 2, and 3, respectively. The mean values of the SEMG assessment ratio of the zygomaticus muscle were 41.42 ± 24.71, 64.56 ± 41.39, and 65.36 ± 29.66 on Visit 1, 2, and 3, respectively. The mean values of the SEMG assessment ratio of the orbicularis oris muscle were 44.13 ± 21.69, 56.00 ± 30.83, and 58.51 ± 28.98 on Visit 1, 2, and 3, respectively. The mean values of the average of three parts of SEMG were 35.71 ± 13.32, 54.88 ± 27.21, and 57.50 ± 23.16 on Visit 1, 2, and 3, respectively (Table 3).

Correlations between number of accompanying symptoms, clinical assessment scales and SEMG from the onset to 1 week

From the onset of symptoms to 1 week later, at Visit 1, the number of accompanying symptoms had no significant correlation with other measures. The HBGS had a significant negative correlation with the Y-score. SEMG-F had significant positive correlations with SEMG-O and SEMG-T. Significant positive correlations between SEMG-Z and SEMG-T, and between SEMG-O and SEMG-T were noted. Among them, the positive correlation between SEMG-O and SEMG-T was the most significant (Table 4).

Correlations between accompanying symptoms, clinical assessment scales and SEMG approximately 2-3 weeks after onset

Approximately 2-3 weeks after onset of symptoms, at Visit 2, the number of accompanying symptoms had a significant positive correlation with the HBGS, and significant negative correlations with the Y-score, SEMG-F, SEMG-Z, SEMG-O and SEMG-T. The HBGS had significant negative correlations with the Y-score, SEMG-F, SEMG-Z, SEMG-O, and SEMG-T. The Y-score had significant positive correlations with SEMG-F, SEMG-Z, SEMG-O, and SEMG-T. SEMG-F had significant positive correlations with SEMG-Z, SEMG-O, and SEMG-T. Significant positive correlations between SEMG-Z and SEMG-T, and between SEMG-O and SEMG-T were noted. Among them, the positive correlation between the Y-score and SEMG-T was the most significant (Table 5).

Correlations between accompanying symptoms, clinical assessment scales and SEMG approximately 4-5 weeks after onset

Approximately 4-5 weeks after onset of symptoms, at Visit 3, the number of accompanying symptoms had a significant positive correlation with the HBGS and a significant negative correlation with the Y-score. The HBGS had significant negative correlations with the Y-score, SEMG-F, SEMG-O, and SEMG-T. The Y-score had significant positive correlations with SEMG-F, SEMG-O,

Table 4. Correlations between Accompanying Symptoms, Clinical Assessment Scales and SEMG from Onset to 1 week.

N = 30		HBGS	Y-score	SEMG-F	SEMG-Z	SEMG-O	SEMG-T
Symptoms	r (*p*)	0.119 (0.530)	−0.175 (0.335)	−0.352 (0.057)	0.042 (0.824)	0.013 (0.946)	−0.135 (0.476)
HBGS	r (*p*)		−0.423* (0.020)	−0.141 (0.456)	0.253 (0.177)	−0.254 (0.175)	−0.019 (0.921)
Y-score	r (*p*)			0.339 (0.067)	0.121 (0.523)	−0.045 (0.813)	0.086 (0.651)
SEMG-F	r (*p*)				−0.020 (0.918)	0.403* (0.027)	0.548* (0.002)
SEMG-Z	r (*p*)					−0.005 (0.981)	0.534* (0.002)
SEMG-O	r (*p*)						0.737* (< 0.001)

HBGS, House-Brackmann grading system; Y-score, Yanagihara's unweighted grading system; SEMG, surface electromyography.
* $p < 0.05$.

Table 5. Correlations Between the Accompanying Symptoms, Clinical Assessment Scales and SEMG Approximately 2-3 Weeks After Onset.

N = 22		HBGS	Y-score	SEMG-F	SEMG-Z	SEMG-O	SEMG-T
Symptoms	r (*p*)	0.512* (0.015)	−0.504* (0.017)	−0.551* (0.008)	−0.576* (0.005)	−0.462* (0.030)	−0.653* (0.001)
HBGS	r (*p*)		−0.842* (< 0.001)	−0.531* (0.011)	−0.541* (0.009)	−0.563* (0.006)	−0.731* (< 0.001)
Y-score	r (*p*)			0.630* (0.002)	0.687* (< 0.001)	0.661* (0.001)	0.895* (< 0.001)
SEMG-F	r (*p*)				0.607* (0.003)	0.642* (0.001)	0.758* (< 0.001)
SEMG-Z	r (*p*)					0.414 (0.055)	0.798* (< 0.001)
SEMG-O	r (*p*)						0.778* (< 0.001)

HBGS, House-Brackmann grading system; Y-score, Yanagihara's unweighted grading system; SEMG, surface electromyography.
* $p < 0.05$.

Table 6. Correlations Between the Accompanying Symptoms, Clinical Assessment Scales and SEMG Approximately 4-5 Weeks after Onset.

N = 10		HBGS	Y-score	SEMG-F	SEMG-Z	SEMG-O	SEMG-T
Symptoms	r (*p*)	0.684* (0.029)	−0.670* (0.034)	−0.339 (0.338)	−0.564 (0.089)	−0.539 (0.108)	−0.583 (0.077)
HBGS	r (*p*)		−0.903* (< 0.001)	−0.848* (0.002)	−0.453 (0.189)	−0.667* (0.035)	−0.766* (0.010)
Y-score	r (*p*)			0.817* (0.004)	0.584 (0.076)	0.785* (0.007)	0.861* (0.001)
SEMG-F	r (*p*)				0.439 (0.205)	0.656* (0.040)	0.808* (0.005)
SEMG-Z	r (*p*)					0.569 (0.086)	0.817* (0.004)
SEMG-O	r (*p*)						0.888* (0.001)

HBGS, House-Brackmann grading system; Y-score, Yanagihara's unweighted grading system; SEMG, surface electromyography.
* $p < 0.05$.

and SEMG-T. SEMG-F had significant positive correlations with SEMG-O and SEMG-T. Significant positive correlations between SEMG-Z and SEMG-T, and between SEMG-O and SEMG-T were noted. Among them, the negative correlation between the HBGS and Y-score was the most significant (Table 6).

Discussion

Facial nerve palsy is a condition/disease where there is central and peripheral nerve paralysis in which temporary weakness or a lack of movement affects one side of the face and the eyes and mouth deviate. Peripheral facial nerve palsy is a disorder involving a facial nerve, specifically, the seventh cranial nerve. It is a disorder in which paralysis and dysfunction appear in the damaged area of the facial nerve. Patients may show multiple accompanying symptoms including facial discomfort, paresthesia, pain, hypoacusis or hyperacusis, tinnitus, ageusia, xerophthalmia, hypoptyalism, and dizziness [15]. Peripheral facial palsy is associated with ipsilateral pain around the mastoid or migraine following 2-3 days of facial muscle paralysis. In total paralysis, the patients cannot close their eyes, they may drool, and have dysarthria. If the lesion is above the cuneiform ganglion, the amount of tears decreases, and if the stapedial nerve is paralyzed, hyperacusis occurs. When the chorda tympani is paralyzed, the frontal two-thirds of the tongue loses the sense of taste, and the amount of saliva decreases [16].

There are clinical assessment scales and electrophysiological tests to evaluate facial nerve palsy. The clinical evaluation methods include the HBGS, Y-score, and Sunnybrook Facial Grading System. The electrophysiological tests include the nerve conduction study, electromyography (EMG), and the nerve excitability test [17].

The HBGS was first introduced by House in 1983, and was used internationally as a method to evaluate facial nerve palsy; it was modified and published by House and Brackman in 1985 [10]. It has the advantage of simplicity during examinations and ease of understanding the patient's condition by using a grade. However, it lacks objectivity owing to its subjective evaluation method, and it is difficult to quantify the various degrees of paralysis because of its simplicity. Therefore, it cannot reflect minute changes in the facial function [10,18].

The Y-score, which was introduced by Yanagihara in 1976, is a method used to evaluate facial nerve palsy and is widely used in Japan [11]. It classifies facial function into 10 domains, evaluates them separately, and makes it possible to evaluate various states of paralysis. However, it does not consider secondary deficits, it is highly subdivided, and this makes evaluations inconvenient and calculations complicated [11,18].

In the clinical assessment scales, a highly significant correlation between the HBGS and Y-score was reported by Kim and Xu et al [19] who determined that the Y-score reflected paralysis more precisely in incomplete recovery and in the after-effect stages.

SEMG is a noninvasive method whereby the motor function of the muscle group of that site can be evaluated by attaching electrodes to the surface of the skin to measure electrical activity of the muscle. Currently, along with the nerve conduction study, and EMG (intramuscular motor function detection), which are widely used in facial palsy, SEMG has been studied for its objectivity as a measured value and is use in examinations of individuals with facial nerve palsy [20,21]. However, there are insufficient studies on the correlation between the number of accompanying symptoms related facial nerve palsy and the HBGS, Y-score, and SEMG. Therefore, we retrospectively analyzed and reported the observed correlations

The accompanying symptoms did not have a significant correlation with other measures on Visit 1; however, on Visit 2, they had a significant positive correlation with the HBGS, and significant negative correlations with the Y-score and all SEMG measurements. On Visit 3, they also had a significant positive correlation with the HBGS, and a significant negative correlation with the Y-score.

The HBGS on Visit 1 had a significant negative correlation with the Y-score. On Visit 2, HBGS had significant negative correlations with the Y-score and all SEMG measurements. On Visit 3, HBGS had significant negative correlations except for the accompanying symptoms and SEMG-Z.

The Y-score on Visit 2 had significant positive correlations with all SEMG measurements. On Visit 3, it had significant positive correlations with all SEMG measurements except for SEMG-Z.

On Visit 1, except for a few significant correlations between SEMG measurements, most showed no significant correlations. Furthermore, SMEG measurements in the zygomaticus muscle area showed negative and positive errors in relation to other measures on Visit 1. They had no significant correlations with SEMG-O on Visit 2 and other values except SEMG-T on Visit 3.

However, significant correlations were observed in most of the results between the clinical assessment scales and SEMG measurements on Visit 2 and 3, although, not on Visit 1. This finding was consistent with the results report by Kim et al who determined that SEMG can be used as an objective evaluation tool for facial nerve palsy and as a prognostic factor for facial palsy similar with other electrophysiological tests [20].

Therefore, because the accompanying symptoms showed significant correlations with the HBGS, Y-score, and all SEMG measurements on Visit 2 and the HBGS and Y-score on Visit 3, when diagnosing peripheral facial nerve palsy, the accompanying symptoms, including both clinical assessment scales and SEMG measurements, should be considered at 2-5 weeks after onset that the accompanying symptoms have a significant positive correlation with the HBGS, and nagative correlations with the Y-score and all SMEG measurements.

There are three possible reasons that SEMG measurements had errors in relation to other measures. The first is believed to be due to the very early measurement date of Visit 1, which was from onset to 1 week. The nerve conduction velocity tracks and observes the changes in nerve conduction that resulted from denatured nerves and abnormal response of its dominant muscles. It is typically tested more than 7 days after the onset of facial paralysis [22]. To identify nerve damage sites, the appropriate test time for fine needle EMG is usually 14 days after the onset [23]. Seong et al [24] reported that electroneurography measured on 6-8 days after onset showed a more significant correlation than that measured 3-5 days after onset using EMG measured 14 days after onset of symptoms. In the studies by Kim [20] and Ryu et al [21], SEMG was measured between 1 and 2 weeks from onset. The second possible reason is that in the zygomaticus region, there are several muscles, such as the

zygomaticus major and minor muscles, and during the examination it is difficult to accurately attach the surface electrode to the relevant muscle due to the facial curve. Moreover, the movement performed by the patient is a complex movement of several muscles. Therefore, it is presumed that the test accuracy decreased due to several factors that may affect the results. A third reason is believed to be attributable to the relatively small number of patients studied. Therefore, in the future larger sample sizes are needed to power the study.

Author Contributions

Writing original draft: GHK. Study Settings: YMC, HMY and GHK. Data collection: GHK, JHP, TKK and EJL. Data analysis: GHK and SEJ. Writing – review and editing: GHK, JCS, CHK and HMY.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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Ethical Statement

This research did not involve any human or animal experiments.

Data Availability

All relevant data are included in this manuscript.

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