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A STUDY ON THE DIAGNOSTIC USEFULNESS OF ELECTRONEUROGRAPHY(ENOG) AS PREDICTIONG FACTORS FOR BELL'S PALSY PROGNOSIS USING ROC CURVE ANALYSIS

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ABSTRACT
Bell's palsy is a type of idiopathic facial paralysis that is caused by various virulence factors and results in a poor prognosis. This spontaneous facial paralysis that has various causes should be accurately diagnosed in clinical settings at an early stage, and one of the methods used at this stage is electroneuronography (ENoG). The ENoG test analyzes and quantitatively evaluates the degeneration of the facial muscles. The progression and improvement of the disease are measured using the results of the ENoG. This study was conducted among 185 Bell's palsy patients who were enrolled at D hospital in Korea, and the diagnostic utility of their ENoG results were analyzed using regression and ROC curve analysis methods.

KEYWORDS: Bell' palsy, Facial nerve palsy, Electroneuronography(ENoG), ROC curve.

1. INTRODUCTION
Since the facial nerve passes through a narrow space within the skull compared to other cranial nerves, it is prone to damage caused by surgery, injury or infection.[1] Another cause of damage is facial paralysis caused by an increased pressure from a tumor that surrounds the facial nerve.[2] Facial paralysis is divided into central paralysis and peripheral paralysis, and Bell's palsy and Ramsay-Hunt syndrome are the two major types of peripheral paralysis.[2,3]

Bell's palsy, as a type of idiopathic facial paralysis, is a disease caused by the unknown weakening of the function of the facial nerve and its paralysis, and it is the most common type of facial paralysis diseases.[2,4] Injuries, various types of stress, herpes zoster virus, epstein-barr virus, etc. are recognized as the main causes of acute Bell's palsy.[5]

One of the symptoms of Bell's palsy is Bell's phenomenon in which the eyeball of the paralyzed side moves outward when closing the eyes, which means that the extraocular muscle is not paralyzed, a symptom used to diagnose myasthenia gravis.[6] The symptoms of Bell's palsy differ depending on the level of damage to the facial nerve, and when all the facial nerves are blocked, all the facial muscles of expression are also paralyzed.[6-7] Bell's palsy is diagnosed through a typical examination of clinical symptoms, an electrophysiological test. etc.[8]

In the case of Bell's palsy, the progress of natural treatment over time is examined, and if it does not recover naturally, medicines are administered as an auxiliary treatment such as steroid treatment to reduce inflammatory responses, and medicines to kill viruses.[9]

The exact causes of Bell's palsy have not been proven, and thus it is critical to examine the level of damage to the facial nerve and determine its cause in an early diagnosis for better prognosis.[10] To do so, in a clinical setting, nerve conduction studies are performed on patients with facial paralysis, and one of them is electroneurography (ENoG), a non-invasive method, in which compound muscle evoked potentials are measured by applying electro-stimulation under the skin.[11] Unlike other nerve conduction studies, in ENoG, amplitude is a key factor in interpretation, and the following concept of the response rate is used. The response rate = the side with a functional disorder (mV) / the healthy side (mV). Normally, when the level of damage to the nerve is lower than 10%, it is diagnosed as normal.[11, 12] The results of the test are mostly interpreted using the House-Brackmann scale (HBSG) into 6 grades from Level I (normal) to Level V (total paralysis).[12]

Studies on the predictive factors of Bell's palsy have been actively conducted around the world, and recently a few studies on Bell's palsy using ENoG have been also conducted in Korea.[13-15] However, there is almost no

study on the usability of ENoG as a diagnostic marker for patients with Bell's palsy in Korea. In this regard, in this study, the ROC curve was measured to analyze the diagnostic usability of ENoG for patients with Bell's palsy.

2. MATERIALS AND METHODS

2.1. Subjects

This study was conducted among 185 patients who came in Busan St. Mary's Hospital for treatment from 2002 to 2010 and were diagnosed with peripheral facial nerve paralysis. They were selected based on the following criteria, and this study was conducted using their medical records in a retrospective manner.

2.1.1 Criteria for selection

Subjects were selected among those who were diagnosed with peripheral facial nerve paralysis and came in for treatment within 5 days from the day of the occurrence of the disease, and to whom ENoG was performed.

2.1.2. Criteria for exemption

Those with peripheral nerve disorders as a complication of diabetes, those with facial paralysis which seemed to occur due to the infection of viruses, and those with facial skin diseases were excluded from the subjects.

2.2. METHODS

2.2.1 Variables for statistical analysis

The following 29 variables were analyzed: age, gender, the duration of the first examination, recurrence, pain, hearing loss, tinnitus, dizziness, high blood pressure, cardiovascular disorders, thyroid diseases, kidney diseases, Hb, Hct, glucose, AST, ALT, BUN, Cr, MST, HBGS grades, treatment duration, facial contracture, facial spasm, synkinesis, side effects, etc.

2.2.2 Formulation of hypothesis

The prevalence rate of facial paralysis (Bell's paralysis) is affected by different factors. To evaluate the explanatory power of factors, regression analysis was conducted, and the ROC curve of each grade was analyzed to assess the diagnostic value of ENoG, which has not been researched in Korea.

2.2.3 Control of variables

Among 508 patients with facial paralysis initially selected for this study, the following variables were controlled.

Those with Ramsay-Hunt syndrome, those with virus-induced paralysis, those who quit receiving treatment, and variables of which frequency was very low (tinnitus, dizziness) were excluded, and those who came in the hospital for treatment 5 days or later after the occurrence of the disease, and those whose facial nerves seemed to be paralyzed due to other diseases were also excluded. A total of 185 patients were selected for analysis.

2.3. Processing of statistics

2.3.1 Logistic regression analysis

In an initial diagnosis of facial paralysis, the HBGS method (5 grades) was used, and variables associated with diseases were used in this study. The linearity of independent and dependent variables was tested using the frequency distribution of SPSS. Error terms, independence and multicollinearity were tested through residual analysis. and examined using the Durbin-Watson test of SPSS model summary, variance inflation factor (VIF) analysis and condition index. The predictive factors and risk grades of Bell's palsy 3 months after the initial diagnosis were analyzed through regression analysis using SPSS 18.0.

2.3.2 ROC curve analysis

Based on the 5 grades of the HBGS, the accuracy and precision of each grade were measured, and their explanatory power was analyzed. The ENoG test was performed based on the response rate from 0% to 100%, and the best accuracy and precision values of each result were analyzed using SPSS 18.0.

3. RESULTS

3.1. General characteristics

Table 1 shows the general characteristics of a total of 185 subjects, 89 males (48.1%) and 96 females (51.9%). The results of the initial diagnosis showed that those of Grade 4 or higher accounted for 62.7%, and that the prognosis 3 months after treatment was 33.5%. The share of those who felt pain during the initial diagnosis was 33.5%, and that of those who experienced hearing loss were 71.9%. That of those who showed over 50% of decrease in the ENoG was significantly high (69.8%).

Table 1: Summary of the clinical information and results of clinical tests.

Variables		Patient (n [%])
Sex	Female	89 [48.1]
	Male	96 [51.9]
Age	< 55 years old	132 [71.3]
	≥ 55 years old	53 [28.4]
Initial grading of HBSG score	≤ Grade IV	116 [62.7]
	≥ Grade V or VI	69 [37.3]
HBSG score at 3 month after onset	≤ Grade II	123 [66.5]
	≥ Grade IV	62 [33.5]
Recurrence	absent	169 [91.3]
	present	16 [8.7]
Pain	absent	62 [33.5]
	present	123 [69.5]
Hearing loss	absent	133 [71.9]
	present	52 [28.1]
Dizziness	absent	165 [89.2]
	present	20 [10.8]
Hypertension	absent	123 [66.5]
	present	62 [33.5]
Disease	Bell's palsy	185 [100.0]
	Ramsay-hunt SD.	0 [0.0]
ENoG	< 50%	56 [30.2]
	≥ 50%	129 [69.8]

Abbreviation: HBSG; House Brackmann scale, ENoG;

electroneuronography.

3.2 Predictive factors and risk grades of Bell's palsy

The results of logistic regression analysis showed that a total of 4 disease-related variables were screened, and expressed as the following regression equation: $y\{In(P/(1-P)\}= 0.51X^1+1.31X^2-1.39X^3$ (X^1:age, X^2: initial grade, X^3: ENoG). The fitness of the model was verified using the Wald test. Those aged 55 years or older showed approximately 1.69 times worse prognosis than those younger than 55 years, and those who had a higher initial grade showed 4.41 times worse prognosis. Those who had a low ENoG level showed poor prognosis (Table 2).

Table 2: Logistic Regression Prediciting the Probability of Poor Prognosis for Facial Paralysis from the Condition 3 Month after Onset of Paralysis.

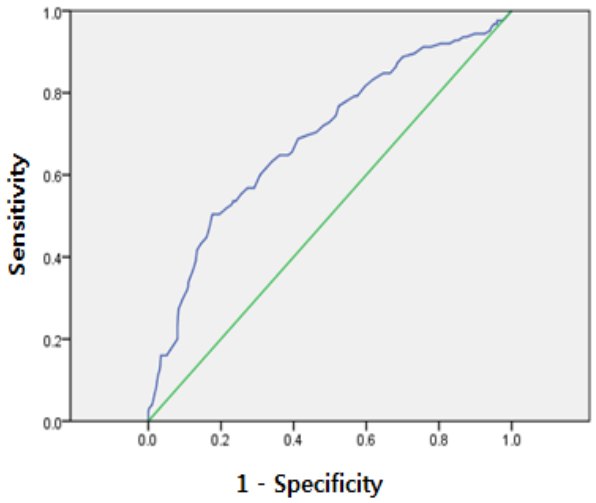
Independent Variable	B	SE	Wals	*P*	Odd ratio
Age	.51	.24	5.41	.018	1.69
Initial grading of paralysis	1.31	.31	22.15	.000	4.41
ENoG	-1.39	.23	37.36	.000	.206

3.3 ROC analysis of ENoG of each grade

The area under the curve (AUC) of each grade means the accuracy of the screening tool, and it is calculated by adding the values of sensitivity and specificity and dividing the sum by 2. The AUC of each grade is as shown in Table 3, and the AUC of patients of Grades 1-3 was 0.7 or smaller, and that of patients of Grades 4 and 5, 0.7 or larger. The graph of the results of ROC analysis of Grade 4 is as shown in Figure 1. The cutoff values of the two grades were selected as follows: the highest score in the sensitivity test, and the lowest score in the specificity test (Table 4).

Table 3: ROC curve analysis for HBSG and ENoG test.

HBSG	Are Under Curve(AUC)	ENoG cutoff value (%)
1 statge	0.525	66.5
2 statge	0.543	71.6
3 statge	0.615	60.5
4 statge	0.694	59.5
5 statge	0.653	51.6



[Figure 1] ROC curve graph for ENoG of HBSG 4 stage.

For result of ROC analysis, AUC for ENoG of HBSG 4 stage was 0.694.

Table 4: Determination of cutoff value for ENoG of HBSG 4 stage.

ENoG (%)	Sensitivity	1 - Specificity
9.50	0.976	0.961
26.50	0.960	0.929
57.50	0.741	0.405
58.50	0.748	0.389
59.50	0.759	0.355
60.50	0.721	0.341
61.50	0.724	0.321
85.50	0.232	0.082
95.50	0.072	0.018

4. DISCUSSION

Facial paralysis is one of the commonly diagnosed cranial nerve diseases of which symptom is the drooping eye and mouth due to the paralysis of the facial muscles.[3] In particular, Bell's palsy accounts for over 90% of facial paralysis symptoms, and the exact causes of Bell's palsy have not been proven yet.[2,5] Facial paralysis can be diagnosed with clinical symptoms in a qualitative manner. One of diagnostic methods used to diagnose is ENoG, a quantitative analysis method, in which compound action potentials are measured by applying electro-stimulation to the facial nerves of the both sides of the face, and it is frequently used to evaluate the degeneration of the nerves and the prognosis of the symptom.[4] If the results of ENoG are lower by over 10% than those of the normal condition, surgical treatment should be provided, and it is also known that the results of ENoG measured within one week after the occurrence of the symptom are significant.[6, 13]

Studies on each symptom based on the results of ENoG have been actively conducted overseas, but the results of the earlier studies do not coincide well with the conditions of patients in Korea. This study aimed to evaluate the diagnostic utility of ENoG, one of the required tests for the diagnosis of facial paralysis, and some of the desired results were obtained.

Variables to be controlled were chosen, and, among 503 patients initially selected for this study, a total of 185 patients were selected for analysis. The reason is that by excluding the facial paralysis diseases of which causes were obvious, and the influence of the diseases that were known to be highly related to facial paralysis. The improvement rate of facial paralysis 3 months after natural treatment and medicinal treatment was 28.2%, and this study was conducted among patients who were diagnosed within one week after the occurrence of the symptom.

Firstly, to evaluate the diagnostic values of factors to predict prognosis, logistic regression analysis was conducted on the selected variables 3 months after the occurrence of the symptom. The results of analysis showed that 3 variables affected the prevalence rate, and ENoG was the only variable but for pathological data. In particular, the odd ratio of ENoG was 0.206, indicating that the prevalence rate differs significantly depending on the value.

One thing notable in this study is that the cutoff value was set for each grade of the HBSG. There is no officially recognized cutoff value for each grade, and it is even more difficult to find data on this in Korea. As shown in Table 3, the AUC of Grades 1, 2 and 3 is lower than 70%, and thus it was difficult to find any significant diagnostic value. The AUC of Grades 4 and 5 was also lower than 70%, but Grade 4 (69.4%) seemed to have a diagnostic value. In addition, the curve shown in Figure 1 is similar to the ROC curve that is commonly recognized to be 'fair.'

To determine the cutoff value of Grade 4 of the HBSG that showed significant results, the results of the sensitivity and 1-specificity tests were listed in Table 4. Considering high scores in the sensitivity test and low scores in the 1-specificity test, it was found that 59.5% would be suitable as the cutoff value.

Recently, various methods such as CT, evoked potentials, PET-CT, etc. have been used to diagnose facial paralysis, and studies on them have been also actively conducted. Still the most widely used electrophysiological test is ENoG, and thus it is also necessary to conduct studies on ENoG. There is a study conducted overseas that found that the accuracy and specificity of ENoG were lower than those of the MST test[15], but the results of this study indicated that ENoG may not be a useful marker to diagnose patients with minor facial paralysis at an early stage, but that it can be utilized as a competitive diagnostic marker for patients with severe facial paralysis of Grade 4 or higher.

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