DOI: 10.4274/MMJ.galenos.2023.42383
Medeni Med J 2023;38:111-119

Original Article

Comparison of 3 Grading Systems (House-Brackmann, Sunnybrook, Sydney) for the Assessment of Facial Nerve Paralysis and Prediction of Neural Recovery

Fasiyal Sinir Felci Değerlendirmesi ve Nöral İyileşme Öngörüsü için 3 Derecelendirme Sisteminin (House-Brackmann, Sunnybrook, Sydney) Karşılaştırılması

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ABSTRACT

Objective: Currently, multiple classification systems exist for the assessment of facial nerve paralysis. This study was designed to choose the most practical system for use in a clinical setting depending on the clinician need. We compared the responsiveness of the 3 facial nerve grading systems, i.e., House-Brackmann, Sydney, and Sunnybrook, as the subjective method and compared the outcomes with the objective method, i.e., the nerve conduction study. The correlation between the subjective and objective assessments was determined.

Methods: A total of 22 consented participants with facial palsy was assessed with photos and videography recordings where they performed 10 standard facial expressions. The severity of facial paralysis was evaluated with the House-Brackmann, Sydney, and Sunnybrook grading scales subjectively and with the facial nerve conduction study objectively. The assessments were repeated after 3 months.

Results: A Wilcoxon signed-rank test showed that there were statistically significant change in all three gradings after 3-month of assessment. The responsiveness of the nerve conduction study was significant for the nasalis and orbicularis oris muscles. It was not significant for the orbicularis oculi muscle. The nasalis and orbicularis oculi showed statistically significant correlation with the three classification systems except for the orbicularis oculi muscle.

Conclusions: All three grading systems, House-Brackmann, Sydney, and Sunnybrook, showed statistically significant responsiveness after 3 months of evaluation. The nasalis and orbicularis oculi muscle can be used to predict facial palsy recovery because they showed strong positive and negative correlations with the extent of facial nerve degeneration from the nerve conduction study.

Keywords: Facial nerve palsy, House-Brackmann classification system, Sydney classification system, Sunnybrook classification system, nerve conduction study

ÖZ

Amaç: Günümüzde, fasiyal sinir felcinin değerlendirilmesi için birden fazla sınıflandırma sistemi mevcuttur. Bu çalışma, klinisyen ihtiyacına bağlı olarak klinik ortamda kullanım için en pratik sistemi seçmek amacıyla yapılmıştır. Subjektif yöntem olarak 3 fasiyal sinir derecelendirme sisteminin, yani House-Brackmann, Sydney ve Sunnybrook'un duyarlılığı karşılaştırıldı ve sonuçlar objektif yöntemle, yani sinir iletim çalışmasıyla karşılaştırıldı. Subjektif ve objektif değerlendirmeler arasındaki korelasyon belirlendi.

Yöntemler: Fasiyal felci olan toplam 22 gönüllü katılımcı, 10 standart yüz ifadesi uyguladıkları fotoğraf ve video kayıtlarıyla değerlendirildi. Fasiyal felcin şiddeti subjektif olarak House-Brackmann, Sydney ve Sunnybrook derecelendirme skalaları ile objektif olarak fasiyal sinir iletim çalışması ile değerlendirildi. Değerlendirmeler 3 ay sonra tekrarlandı.

Bulgular: Wilcoxon signed-rank testi, 3 aylık değerlendirmenin ardından üç derecelendirmenin hepsinde istatistiksel olarak anlamlı bir değişiklik olduğunu gösterdi. Sinir iletim çalışmasının duyarlılığı, nasalis ve orbicularis oris kasları için anlamlıydı. Orbicularis oculi kası için anlamlı değildi. Nasalis ve orbicularis oculi, orbicularis oculi kası haricinde, üç sınıflandırma sistemi ile istatistiksel olarak anlamlı korelasyon gösterdi.

Sonuçlar: Üç derecelendirme sisteminin tümü, House-Brackmann, Sydney ve Sunnybrook, 3 aylık değerlendirmenin ardından istatistiksel olarak anlamlı duyarlılık gösterdi. Nasalis ve orbicularis oculi kası, sinir iletim çalışmasından elde edilen fasiyal sinir dejenerasyonunun derecesi ile güçlü pozitif ve negatif korelasyonlar gösterdikleri için fasiyal felç iyileşmesini tahmin etmek için kullanılabilir.

Anahtar kelimeler: Fasiyal sinir felci, House-Brackmann sınıflandırma sistemi, Sydney sınıflandırma sistemi, Sunnybrook sınıflandırma sistemi, sinir iletim çalışması

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Received: 19 January 2023
Accepted: 21 April 2023
Online First: 22 May 2023

Cite as: Mat Lazim N, Ismail H, Abdul Halim S, Nik Othman NA, Haron A. Comparison of 3 Grading Systems (House-Brackmann, Sunnybrook, Sydney) for the Assessment of Facial Nerve Paralysis and Prediction of Neural Recovery. Medeni Med J 2023;38:111-119

INTRODUCTION

An intact facial nerve is highly critical for individual communication, emotional expression, and social integration. The facial nerve arises from the pons and contains motor, sensory, and parasympathetic (secretomotor) fibers that provide innervation to many areas of the head and neck. Essentially, it will control all muscles of facial movement and expression; thus, any facial palsy will cause significant psychological and social problems due to facial disfigurement[1]. The disfigurement can range from oral incontinence, which makes it difficult to eat or drink, to speech deficiencies including misreading nonverbal facial cues and an inability to blink, which causes dry eyes and consequent corneal damage[2]. The most distressing condition in people with facial palsy is their inability to smile and convey emotion[3].

A study by the Sydney facial nerve clinic reported that iatrogenic trauma was the most frequent cause of facial nerve palsy, followed by Bell's palsy, congenital herpes zoster oticus, and trauma[4]. Iatrogenic trauma is mostly caused by surgical procedures near the facial nerve, mainly parotid gland surgery. The facial nerve runs between the superficial and deep lobes of the parotid glands. A superficial or total parotidectomy carries a higher risk of iatrogenic injury to the facial nerve, both to its main trunk and branches. Despite advances in surgical technique, many patients who undergo parotid surgery continue to develop postoperative facial palsy, with occurrence rates of up to 57% for temporary paresis and approximately 7% for permanent facial palsy described in published data[5-7]. In practice, the most common branch that is frequently affected is the marginal mandibular branch because of its small caliber, which makes it difficult to identify. Additionally, even minimal traction on the nerve during dissection can cause temporary paresis. The severity of facial palsy can be evaluated using two main methods, either subjective or objective. The subjective method is by using the facial nerve classification systems, i.e., the House-Brackmann (HB), Sydney, and Sunnybrook systems. The objective assessment includes electrodiagnostic testing, either nerve conduction study (NCS), electromyography, or electroneurography. A universally accepted classification system that is highly reliable is necessary, and this is crucial for accurately determining the degree of palsy in the patient so that an optimum treatment can be performed[8,9].

The (HB) system was approved by the American Academy of Otolaryngology-Head & Neck Surgery facial nerve dysfunction committee as the reference standard for grading facial palsy. It was introduced by the Los Angeles otolaryngologists, Dr. John W. House and Dr. Derald E. Brackmann in 1985. The system uses a six-point scale, where grade I corresponds to normal and grade VI to complete flaccid paralysis. Although it is simple to use in a clinical setting, it has not been widely adopted because it is not sensitive enough to record changes that are clinically significant[10,11].

Due to the above limitations of the HB grading system, there are a few new grading systems that have been proposed, such as Burres and Fisch, Nottingham, Yanagihara, Sydney, and Sunnybrook (Toronto) facial grading systems. Among them, the Sunnybrook (Toronto) facial grading system has advantages ahead. The Sunnybrook facial grading system comprises a regional scale involving facial symmetry at rest, voluntary movements, and synkinesis. The composite score ranges from 0 to 100, where 100 corresponds to normal facial function and 0 corresponds to complete paralysis. Researchers are using this method more and more frequently because it has been demonstrated to be repeatable, to have minimal interobserver and intraobserver variability, and to be responsive to changes over time and as a consequence to treatments[12]. It is also widely accepted and validated in North America and other countries[11-14]. Besides, it is also a reliable system even with naive raters, and the reliability is excellent when performed in the usual intuitive way[15].

In contrast to the Sunnybrook grading system, which uses a regional scale, the Sydney facial grading system assesses facial actions based on the individual anatomic branch of the facial nerve that produces each movement. It possesses strong intersystem association and good intrasystem reliability for evaluating voluntary movement. Berner et al.[16], 2019 reported that the Sunnybrook classification system is ideal to assess facial synkinesis compared to the HB systems[17]. This is supported by a study of facial motion using 3-D dynamic analysis and correlated with the subjective grading systems by Zhao et al.[18] who reported the same[17]. Additionally, Berg et al.[19] reported that the Sunnybrook grading system is comparable to HB and is easy and quick to be used[18].

Importantly, synkinesis, or aberrant facial muscle movement that happens with voluntary movement of a different face muscle group, is intensively studied. Both systems demonstrated a low degree of dependability for determining synkinesis but were highly varied19. Even though various classifications had been developed, facial grading systems cannot be compared easily as one has its advantages and disadvantages such as high interobserver variability. If a uniform facial grading system is to be created, more information on the practice outcomes

and efficacy of the current grading systems should be gathered8. It is desirable that individuals with facial palsy receive an appropriate assessment and prompt treatment so that their quality of life can be significantly improved.

Thus, this study was conducted to compare the responsiveness of 3 facial nerve grading systems, HB, Sydney, and Sunnybrook, in order to select an optimum standard system to be employed in the clinical situation. The NCS was used as an objective test to determine the correlation between the subjective and objective assessment of facial nerve palsy.

MATERIALS and METHODS

This study was conducted at the Otorhinolaryngology-Head and Neck Surgery (ORL-HNS) clinic, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan and Hospital Raja Perempuan Zainab II, Malaysia from May 2021 to May 2022. Written informed consent was obtained from each participant, and the study protocol was accepted by the National Medical Research Register of Malaysia (NMRR-21-522-58619) and the Human Research Ethics Committee of USM School of Medical Sciences (JEPeM) (protocol code: USM/JEPeM/21020199, date: 16th May 2021). A quasi-experimental and post-test study was conducted for 24 participants with peripheral facial nerve palsy (lower motor neuron palsy). However, 2 patients were excluded from the study because of unconsent for post-test study, and the patients passed away due to underlying chronic illnesses before the post-study was conducted. Thus, 22 participants were recruited for this study.

The sampling size was determined using r, Pearson's correlation coefficient test. The value for the correlation coefficient (r) was taken from the study by Kim et al.[20]. Considering type I of error 5% (α) and type II (of β) error 20%, the corrected sample size (n_c) with 10% anticipated dropout is 24. The participants were selected using a convenience sampling method based on inclusion and exclusion criteria. The inclusion criteria were patients diagnosed with any peripheral facial nerve palsy (lower motor neuron palsy) and patients aged between 18 and 70 years. The exclusion criteria were those patients with facial skin disease or who had previously undergone facial plastic surgery and reconstruction.

Consented participants were seated comfortably in a private room in the ORL-HNS clinic of the HUSM and HRPZ II clinics and a clinical proforma, which consisted of demographic data, past medical and surgical history, the etiology of the palsy, site of injury, and duration of the palsy were documented. The patient's facial palsy was assessed with a series of photo documentation and videography of 10 standard facial expressions (Figure 1). This was recorded using a smartphone with a Samsung Exynos 9825 processor and 10MP, rear camera 12MP + 16MP + 12MP. Then, the facial palsy was graded using three different classification systems: the HB, Sydney, and Sunnybrook systems. The median time between the onset of paralysis and first evaluation was 14 days.

The assessment was performed by a single researcher (a trainee in ORL-HNS) only, and she was blinded to patients premorbid and aetiology.

1. House Brackman Grade

The system is a gross classification that involves a six-point scale with grade I being normal and grade VI being flaccid paralysis. Any reduction in score indicates the improvement of facial palsy.

2. Sydney Classification

It is based on the anatomical segment of the facial nerve responsible for supplying each action. The total maximum score of 15 indicates normal facial function, while 0 is the minimum score. Any increments in the score indicate improvement in facial palsy.

3. Sunnybrook Classification

The final (composite) score is derived by total voluntary movement minus the total resting symmetry score and total synkinesis (Figure 2). It varies from 0 to 100, where 0 stands for total paralysis and 100 stands for normal facial function. Any increments in the score indicate improvement in facial palsy.

Subsequently, the participants were sent for a NCS at the Neurophysiology Laboratory, Department of Neurosciences of HUSM. The NCS used several electrode patches that were taped or pasted to the skin, particularly around the eye (orbicularis oculi muscle), nose (nasalis muscle), and angle of the mouth (orbicularis oris muscle), which were supplied by the facial nerve. Several brief electrical pulses were sent to the nerve. Compound muscle action potential or electrical activity arising from the activation of muscle fibers was recorded. The units for the nerve conduction studies are amplitude (milivolt) and latency (miliseconds). However, in the study, amplitude was used as it was more significant than latency when comparing the affected and normal sides of facial asymmetry. The formula used for calculation was;

Facial nerve degeneration (FND) = [1 – n] x 100%

n= affected facial nerve amplitude (divided by)

normal facial nerve amplitude

(If it was ≥75% FND, it indicates a poor prognosis).

All participants were referred to physiotherapy in HUSM only to ensure that the standardized method was performed. Later, they were evaluated again at 3 months for improving facial nerve paresis. All participants were interviewed, examined, and clinically assessed by the researchers. The nerve conduction test was performed by a trained paramedic staff at the neurophysiology lab. This test lasted for about twenty to thirty minutes for each participant.

Statistical Analysis

All categorical data were presented in frequency and percentage, while the numerical data were presented in the median and interquartile range due to non-normal distribution. We applied the Wilcoxon signed-rank test and Spearman's rho test accordingly in the analysis. The p level of less than 0.05 was considered statistically significant. Statistical analysis was performed using version 26 of the SPSS software (SPSS Inc, Chicago, IL).

RESULTS

The demographic characteristics of our study are reported in Table 1. Out of the 24 participants, there were 10 (41.7%) males and 14 (58.3%) females. The median age was 42.00 (IQR: 26.0) years. Among them, 41.7% had

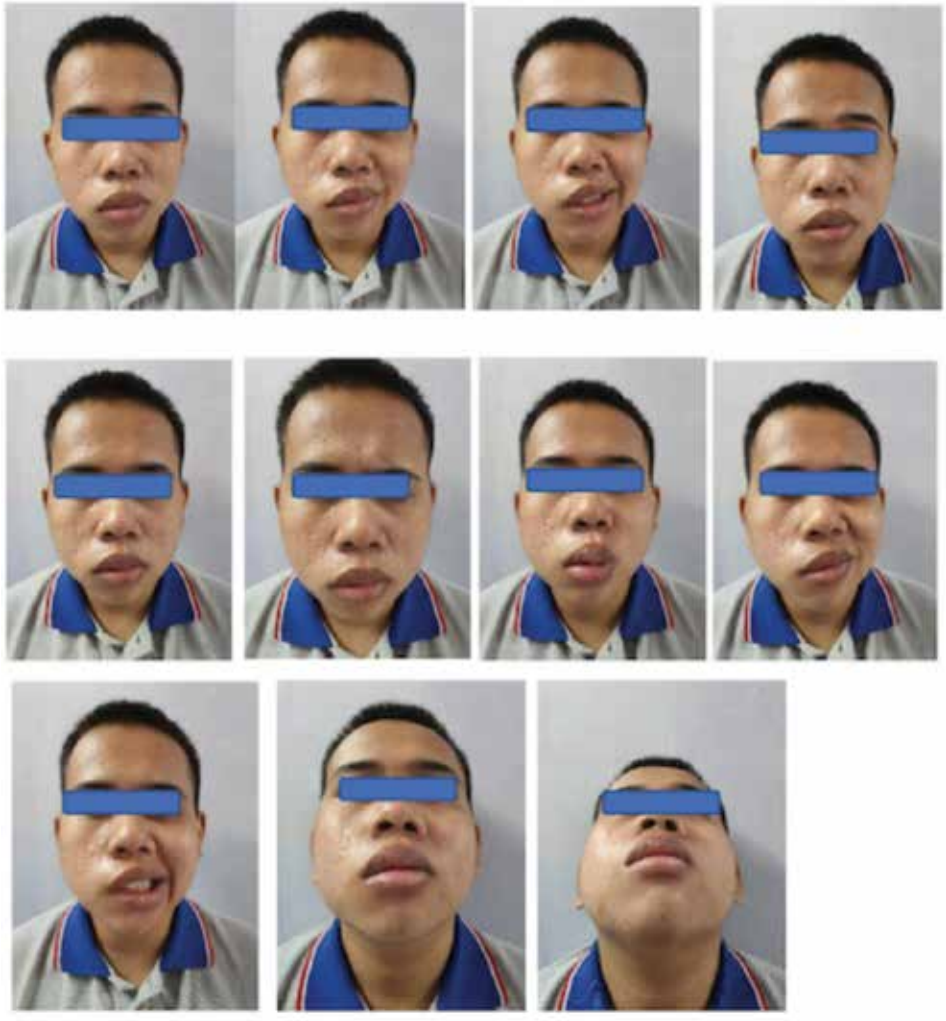

Figure 1. A ten standard facial expression. Top row from the right were at rest or repose, small closed-mouth smile, large smile showing teeth and elevation of eyebrows. Middle row from the right were closure of eyes gently, closure of eyes tightly, puckering of lips and showing bottom teeth. Below row from the right were snarling or wrinkling of the nose and nasal.

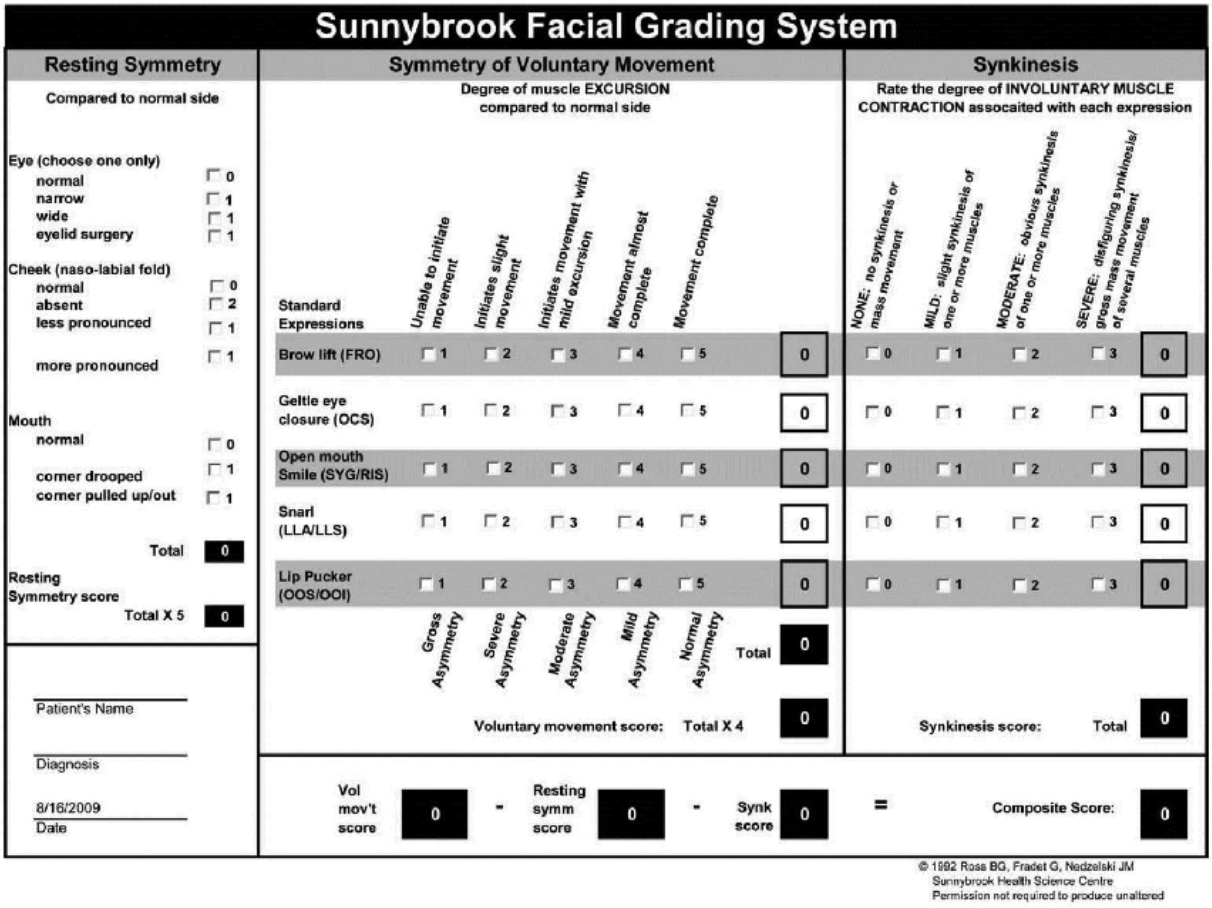

Figure 2. Sunnybrook facial grading system

Table 1. Patient characteristics (n=24).					
Variables		**n**	**(%)**	**Median**	**(IQR)**
Age				42.00	26.0
Gender	Male	10	41.7		
	Female	14	58.3		
Occupation	Unemployed	12	50.0		
	Employed	12	50.0		
Comorbidities	No	14	58.3		
	Yes	10	41.7		
Aetiology	Bell Palsy	13	54.2		
	Temporal bone fracture	4	16.7		
	Diabetic neuropathy	4	16.7		
	Otitis externa	2	8.3		
	Cholesteatoma	1	4.2		
Site of palsy	Right	15	62.5		
	Left	9	37.5		
Elapsed time				14.00	49
IQR: Interquartile range					

comorbidities. The most common causes of facial palsy were Bell's palsy 13 (54.2%), followed by temporal bone fracture 4 (16.7%), diabetic neuropathy 4 (16.7%), otitis externa 2 (8.3%) and cholesteatoma 1 (4.2%). Most of them had the right facial nerve affected (62.5%), while the rest had left facial nerve affected (37.5%). Table 2 represents the comparison of responsiveness for the three grading systems, HB, Sydney and Sunnybrook. A Wilcoxon signed-rank test showed that using HB, there were statistically significant changes in nerve-grading assessment (p<0.001). Indeed, the median HB score pre- and post-3 months was significantly reduced. In addition, using the Sydney classification system, there were also statistically significant change in nerve grading assessment (p<0.001). Indeed, the median Sydney score pre- and post - 3 months increased significantly.

The responsiveness of the NCS is shown in Table 3. A Wilcoxon signed-rank test showed that there was a significant change in the Nasalis muscle after 3 months (p=0.010). The median score pre- and post-3 months was significantly reduced. Also, there was a significant change in Orbicularis Oris muscle after 3 months (p=0.042). The median score pre- and post-3 months was significantly reduced. However, the Orbicularis oculi muscle was not significantly different. At the initial visit, 9.09% (n=22) of participants had more than 75% FND from the orbicularis oris muscle, while none was recorded for the nasalis muscle, and after 3 months, all of them had improvement.

A Spearman rank-order correlation was run to determine the correlation between subjective and objective assessments of facial nerve palsy, as shown in Table 4. The NCS was the objective assessment, while the other three classification systems was the subjective assessment. For the nasalis muscle, there was a strong positive correlation and statistically significant HB score (r=0.554, p=0.008). In contrast, there was a strong negative correlation and statistically significant difference between Sydney and Sunnybrook scores with (r=-0.548, p=0.008) and (r=-0.565, p=0.006) respectively. For the orbicularis oris muscle, there was also a strong positive correlation and statistically significant HB score (r=0.515, p=0.014). On the contrary, there was a strong negative correlation and statistically significant between Sydney and Sunnybrook scores with (r=-0.592, p=0.004) and (r=-0.660, p=0.001) respectively. For the orbicularis oculi muscle, however, there were no significant correlations among the 3 classification systems.

Table 2. Responsiveness of 3 facial nerve grading systems; (n=22), based on the obtained scores.

	Pre		Post		
Score	**Median**	**(IQR)**	**Median**	**(IQR)**	**p-value***
House-Brackmann	3.00	1.00	2.00	1.00	<0.001
Sydney	7.50	5.00	13.00	4.00	<0.001
Sunnybrook	57.50	34.0	93.50	19.0	<0.001

IQR: Interquartile range, *Wilcoxon signed-rank test

Table 3. Responsiveness of nerve conduction study (n=22), based on the muscle action potential.

		Pre		Post		
CMAP		**Median**	**(IQR)**	**Median**	**(IQR)**	**p-value***
Oculi	FND	40.84	50.67	50.00	26.55	0.391
Nasalis	FND	47.92	34.05	22.18	43.36	0.010
Oris	FND	36.84	28.98	26.97	34.04	0.042

FND: Facial nerve degeneration, IQR: Interquartile range, *Wilcoxon signed-rank test

Table 4. Correlation between subjective and objective assessment of facial nerve palsy (n=22).

Nerve conduction study (FND)	House-Brackmann		Sydney		Sunnybrook	
	r	**p-value***	**r**	**p-value***	**r**	**p-value***
Orbicularis oculi	0.404	0.062	-0.325	0.140	-0.324	0.142
Nasalis	0.554	0.008	-0.548	0.008	-0.565	0.006
Orbicularis oris	0.515	0.014	-0.592	0.004	-0.660	0.001

FND: Facial nerve degeneration, *Spearman's rho test

DISCUSSION

There are various causes of facial palsy reported in the literature. In our study, we found that the dominant pathology was Bell's palsy 13 (54.2%), followed by temporal bone fracture 4 (16.7%), diabetic neuropathy 4 (16.7%), otitis externa 2 (8.3%) and cholesteatoma 1 (4.2%). In a larger series, these studies also reported that Bell's palsy is the most common cause of facial palsy[20-22]. However, in the Sydney facial nerve clinic, their retrospective study reported that iatrogenic trauma was the most frequent etiology for the facial nerve palsy, followed by Bell's palsy, congenital, herpes zoster oticus, and trauma[4]. Bell's palsy is peripheral facial nerve palsy accounting for up to 80% of all cases of facial palsy[23]. Although there is no known cause for idiopathic facial nerve palsy, it is crucial to rule out other possibilities before establishing a final diagnosis[24,25]. Most people are predicted to recover with satisfactory restoration of function despite the widespread damage occurring at the nerve level[26].

Facial nerve palsy can be graded using different classification systems. The existing grading systems recently reviewed by House divide the grading system into three categories: gross, regional, and specific[27]. The gross category is simple and clear but does not give specific details on facial function. The regional category considers the unique area of the facial nerve that needs to be added to the final score. The specific category was more focused on specific items of various functions using closed-ended questions[27,28]. New scales have been introduced because of the HB system's innate subjectivity and have some limitations[29]. There is no definitive standard for comparison when comparing grading systems. However, because the HB is well known, simple, easy to understand, and highly applicable in practice, all new grading systems are compared to it.

This study compared the subjective classification systems, i.e., HB, Sydney, and Sunnybrook with the objective assessment, i.e., the facial NCS. All 3 classification systems showed a statistically significant effect on the responsiveness of the facial palsy changes 3 months after the first evaluation. Therefore, despite variations in their evaluation description, all systems are equivalent and acceptably reliable. This is because the variability of the scores in each system, the distribution of the scores, and the statistical significance of the differences between the systems have a significant influence on these results. Kanerva et al.[30] reported that the large overlap between the composite scores for HB and Sunnybrook demonstrated the approximation character of both subjective grading systems. The conversion are as follows: HB I equal to 100, HB II equal to 70-99, HB III equal to 43-69, HB IV equals to 26-42, HB V equals to 13-25 and HB VI equals to 0-12[30]. Even though they were approximate, the Sunnybrook facial grading scale was shown to be more sensitive to changes after therapeutic intervention[31]. These findings were similar to our study as we documented an increment of score in Sunnybrook grading after therapy, whereas the HB scale score decreased significantly. Another study found a moderate overall agreement in correlation between the HB and Sunnybrook scale[32].

To date, there is no much data available to compare Sydney and Sunnybrook systems. A study by Coulson et al.[33] investigated the reliability of the 3 classification systems and reported that both Sydney and Sunnybrook have good reliability for clinical grading of voluntary movement. The assessment of synkinesis was shown to have high reliability with HB grading system[33]. Even though both systems measured synkinesis, they were highly variable and had poor reliability[34,35]. This finding is similar in our study, where the median difference between Sydney and Sunnybrook scores at the initial visit and 3 months was small. This might be because the raters in the study were untrained with both grading systems and an individual variation in their scoring of synkinesis.

NCS is a tool used to objectively measure FND. The degree of Wallerian degeneration can be determined by comparing the damaged nerve compound motor action potential (CMAP) to the contralateral side[36,37]. In comparison to the normal side, our study showed that the damaged side CMAP amplitudes of the examined muscles were much lower. Previous studies have also found that electrodiagnosis significantly confirms facial nerve palsy[38-41]. In this study, we tested the orbicularis oculi, nasalis, and orbicularis oris muscles for their responsiveness and found that the orbicularis oculi was the only muscle that was not significant among the three muscles. This agrees with a study by Verma and Jain[42] who evaluated the CMAP amplitude between the affected and unaffected sides separately and revealed that the order of amplitudes from low to high was: orbicularis oculi, nasalis and orbicularis oris.

The nasalis and orbicularis oris muscles also had a significant correlations with the three-classification system except for the orbicularis oculi muscle. This is similar to other studies where they reported that the nasal alae and orbicularis oris was the most reliable muscles for the electrodiagnostic test[43]. The reason for the absence of the orbicularis oculi muscle was not significant probably due to the responses obtained were usually from activation of the masseter or temporalis muscle and not from the

orbicularis oculi alone. The different amplitude across the three muscles might reflect either the anomaly of the muscle or the nerve branch itself. Among our patients, the predominant axonal type of injury is seen, which corresponds with the other study[43].

NCS was valuable in determining the prognosis of facial nerve palsy in the subacute phase. A significant risk factor for delayed or incomplete recovery is total facial paralysis. In our study (n=22), none of the patients presented with total facial palsy. However, 12 (54.54%) of them had incomplete recovery and 10 (45.45%) showed complete recovery after 3 months. Among patients with complete recovery, all had less than 75% FND from the orbicularis oris muscle. Thus, the degree of FND could be attributable to predict recovery[43].

There are few limitations encountered during the study, and the major one was the small number of participants. This was due to government-imposed travel restrictions and the fact that this study was conducted during the coronavirus disease-2019 era, and a relatively small number of patients sought medical attention. This study might be more reliable and produce more accurate results with a larger sample size and a longer study period. Another obstacle faced during this study was related to the short follow-up duration, with a 3-month gap only due to limited study duration.

CONCLUSION

All three grading systems, HB, Sydney, and Sunnybrook, showed responsiveness for assessing facial nerve paresis. However, in this study, there were no differences found between the three grading systems in detecting facial nerve recovery. The study also discovered that they displayed robust positive and negative relationships with the degree of FND, which was determined by the NCS. The nasalis and orbicularis oris muscles were the most reliable to be used in predicting nerve recovery. The study showed that clinicians can use any of the three grading systems and supplemented with nerve conduction studies to accurately measure the nerve degeneration of facial nerve paresis, so that optimum treatment can be performed.

Acknowledgment: We would like to acknowledge the Malaysia Society of Otorhinolaryngology-Head and Neck Surgeon (MSOHNS) for providing the grant to complete this study with project code (MSO-08-2021; 304/PPSP/6150215/M173).

Ethics

Ethics Committee Approval: The study protocol was accepted by the National Medical Research Register of Malaysia (NMRR-21-522-58619) and the Human Research Ethics Committee of USM School of Medical Sciences (JEPeM) (protocol code: USM/JEPeM/21020199, date: 16th May 2021).

Informed Consent: Written informed consent was obtained from each participant.

Peer-review: Externally peer-reviewed.

Author Contributions

Concept: N.M.L., Design: N.M.L., Data Collection and/or Processing: N.M.L., S.A.H., N.A.N.O., A.H., Analysis and/or Interpretation: H.I., S.A.H., N.A.N.O., A.H., Literature Search: N.M.L., H.I., A.H., Writing: N.M.L., H.I., S.A.H., N.A.N.O.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: This research has received financial support from Malaysia Society of Otorhinolaryngology-Head and Neck Surgeon MSOHNS, MSO-08-2021.

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