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Predicting value for incomplete recovery in Bell's palsy of facial nerve ultrasound versus nerve conduction study

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HIGHLIGHTS

- Our study compares the clinical usefulness of nerve ultrasound and nerve conduction study in patients with Bell's palsy.
- Nerve Ultrasound may show abnormally increased facial nerve diameter in the acute phase of Bell's palsy.
- The predictive value of facial nerve ultrasound for incomplete recovery is lower than that of the nerve conduction study.

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ABSTRACT

Objective: This longitudinal study aims at assessing the predictive value of facial nerve high-resolution ultrasound (HRUS) for incomplete clinical recovery in patients with Bell's palsy, the most common facial nerve disease.
Methods: We prospectively enrolled 34 consecutive patients with Bell's palsy. All patients underwent neurophysiological testing (including facial nerve conduction study) and HRUS evaluations 10–15 days (T1), one month (T2), and three months (T3) after the onset of Bell's palsy. Patients who did not experience complete recovery within three months were also evaluated after six months (T4). We have then compared the accuracy of HRUS with that of the facial nerve conduction study in predicting incomplete clinical recovery at three and six months.
Results: At T1, the facial nerve diameter, as assessed with HRUS, was larger on the affected side than on the normal side, particularly in patients with incomplete recovery at T2, T3 and T4. ROC curve analysis, however, showed that the facial nerve diameter at T1 had a lower predictive value than the facial nerve conduction study for an incomplete clinical recovery at three (T3) and six (T4) months. Still, the facial nerve diameter asymmetry, as assessed with HRUS, had a relatively high negative predictive value (thus indicating a strong association between normal HRUS examination and a good prognosis).
Conclusions: Although HRUS shows abnormally increased facial nerve diameter in patients in the acute phase of Bell's palsy, the predictive value of this technique for incomplete clinical recovery at three and six months is lower than that of the nerve conduction study.
Significance: Nerve ultrasound has a low predictive value for incomplete clinical recovery in patients with Bell's Palsy.

1. Introduction

Bell's palsy is the most common cause of acute peripheral facial palsy (Eviston et al., 2015). The clinical picture is dominated by a rapid-onset, unilateral facial weakness associated with a wide spectrum of signs and symptoms due to the variable degree of facial nerve involvement. Most patients recover within a few months, while up to a third have a residual functional deficit with facial muscle weakness or synkinesis (De Seta et al., 2014; Yoo et al., 2020).

Conventional neurophysiological testing is informative at all stages of Bell's palsy (Valls-Solé, 2007). A preserved amplitude of the compound muscle action potential in the early phase of facial

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nerve palsy is likely the most informative test for determining the prognosis (Gantz et al., 1999). Beyond 20 days after onset, needle EMG recording brings an approximate measure of the intensity of denervation. A large retrospective study showed that spontaneous fibrillation at needle electromyography investigation predicts unfavourable outcomes with an accuracy of 80.8 % (Sittel and Stennert, 2001). Although neurophysiological tests are widely used for the assessment and prognostic evaluation of Bell's palsy (Valls-Solé, 2007), they cannot provide direct information on the structural damage of the facial nerve caused by oedema and inflammation (Kimura et al., 1976; Ozgur et al., 2010; Tawfik et al., 2015a; Valls-Solé, 2007).

High-resolution nerve ultrasound (HRUS) has increasingly been used to investigate peripheral nervous system conditions. HRUS detects nerve oedema and inflammation and has been proven helpful for diagnosing and monitoring entrapment and inflammatory neuropathies (Van den Bergh et al., 2021; Walker et al., 2018; Hsueh et al., 2020). Facial nerve HRUS may provide evidence of nerve oedema spreading distally from the site of facial nerve damage in Bell's palsy (i.e., the intratemporal portion), thus possibly improving how we diagnose this common condition.

Nevertheless, only a few studies have investigated whether HRUS might provide clinically useful information in patients with Bell's palsy. Additionally, these studies provided contradicting findings on the diagnostic usefulness of facial nerve HRUS, probably due to different methodological approaches (Baek et al., 2020; Li et al., 2016; Lo et al., 2010; Tawfik et al., 2015b). Accordingly, the diagnostic value of this technique in patients with Bell's palsy is still unclear. Understanding more about the diagnostic value of facial nerve HRUS and whether this technique is more informative than facial nerve conduction study for predicting recovery in patients with Bell's palsy might improve the clinical management of this common peripheral nervous system disease.

This longitudinal study aims at assessing the predictive value of facial nerve HRUS in patients with Bell's palsy. To do so, we have investigated facial nerve diameter as assessed with HRUS at three different time points and verified if its predictive value for incomplete facial muscle recovery is higher than that of the facial nerve conduction study.

2. Methods

2.1. Study cohort and design

In this longitudinal study, we prospectively screened patients with a definite diagnosis of Bell's palsy, who were referred to the emergency department of our hospital within 48 hours of the onset of Bell's palsy. Exclusion criteria were age under 18 years, bilateral facial palsy, previous cranial neuropathies, a known history of central or peripheral nervous system disease, pregnancy, and signs and/or symptoms of Varicella Zoster Virus infection. At the time of diagnosis, as part of the emergency assessment of acute facial weakness, all the patients underwent a complete neurological and otolaryngological assessment with microscopic examination to magnify both ears' external canal and the tympanic membrane. All patients also underwent a head CT scan to identify possible structural lesions (e.g., stroke or tumours); clinical and CT examinations showed no abnormalities. All the patients diagnosed with Bell's palsy were started on a standardized oral pharmacological treatment with prednisone 1 mg/Kg for 10 days. In all patients included in the study, treatment was started within 24 hours (IQR 23–42) from symptoms onset.

All patients underwent clinical examination, neurophysiological testing, and facial nerve HRUS at three distinct time points: T1 corresponding to 10–15 days from symptoms onset, T2 corresponding to one month (±2 days), T3 corresponding to three months (±2 days) after Bell's palsy onset; the patients who did not experience complete recovery within three months also underwent clinical examination after six months (T4). At T1, all patients had completed the corticosteroid treatment (Supplementary Table 1).

All the patients without a complete recovery within one month from the onset of the symptoms underwent a gadolinium-enhancement brain and maxillofacial MRI (1.5 T) focused on the facial nerve path to rule out other possible alternative causes of peripheral facial nerve palsy. All data were collected in a structured form using standardized protocols by staff members (clinical examination: AT, PM, CDE; neurophysiological testing: GDS, EG, CL; HRUS: GDP, PF).

The primary outcomes of interest included the amplitude of the compound muscle action potential of the facial nerve as assessed with neurophysiological testing and the diameter of the facial nerve as assessed with the HRUS.

The study was approved by the local institutional review board. Written informed consent to participate was obtained from all participants.

2.2. Clinical evaluation

We collected demographic and clinical information, including sex, age, and comorbidities at time points T1, T2, T3, T4. At each point, facial muscle deficit was assessed with the House-Brackmann Facial Grading System (HB) (House and Brackmann, 1985). During the clinical examination, we collected detailed data regarding Bell's palsy-associated symptoms (auricular and retro auricular pain, dysgeusia, hyper lacrimation, dry eye, hyperacusis, and aural fullness).

2.3. Neurophysiological and nerve ultrasound investigation

At time points T1, T2, T3, the patients underwent a complete neurophysiological evaluation. Facial nerve CMAP was recorded bilaterally by stimulating the nerve anterior to the mastoid process (stimulus duration: 0.2 ms; stimulation intensity: 15–50 mA; filters: 20 Hz-2 kHz), with the recording electrodes placed over the nasalis muscle. The percentage of asymmetry of the CMAP amplitude compared to the control side was calculated as: (CMAP amplitude affected - CMAP amplitude control side)/CMAP amplitude control side*100. The blink reflex was recorded bilaterally, stimulating the supraorbital nerve, with surface recording electrodes over the inferior orbicularis oculi muscles (stimulus duration: 0.1 ms; stimulation intensity: 15–40 mA; filters: 20 Hz-2 kHz). Blink reflex responses were defined as presence/absence of the R1 blink reflex response. Needle electromyography (EMG) was performed on the orbicularis oris and orbicularis oculi muscles on the affected side. We collected EMG data regarding presence/absence of denervation and electromyographic voluntary activity (qualitative pattern evaluation with full voluntary force, scored as 0: no activity, 1: discrete recruitment, 2: reduced recruitment, 3: normal recruitment). In the same session dedicated to clinical examination and neurophysiological testing (T1, T2, T3), patients underwent facial nerve HRUS examination with an 18 MHz linear array transducer (Siemens S2000, Virtual Touch IQ). A standardized scanning protocol was applied to ensure the reproducibility of the test (the settings were kept constant during all examinations, depth = 3 cm). With the patient lying supine and the probe placed just under the ear lobule, two operators (GDP, PF) blinded to the neurophysiological data assessed the facial nerve bilaterally.

The nerve was examined along its longitudinal course inside the parotid gland after it emerges from the stylomastoid foramen, where it appears as a thin tubular structure, dividing the superficial and the deep lobe of the gland. The probe was kept perpendic-

ular to the skin with minimal pressure to ensure precise measurements. The facial nerve diameter was measured at the point of maximum enlargement within the epineural rim. The average facial nerve diameter calculated by the two operators was then used as an outcome variable.

The percentage of asymmetry of the diameter compared to the control side was calculated as (diameter affected-diameter control side)/diameter control side*100.

2.4. Statistics

The normality assumption was assessed with the Kolmogorov-Smirnov test.

We used the Cronbach's alpha test to establish an agreement for facial nerve diameter assessment between the two operators (GDP, PF).

We used the Mann-Whitney test to assess differences between independent groups, Wilcoxon test was used for paired values. Two-way repeated measures analysis of variance (ANOVA) was used to assess facial nerve diameter as assessed with HRUS and CMAP amplitude with the variables time (T1, T2, T3) and side (affected, control). A post hoc multiple comparisons test with Sidak correction was then performed. Categorical variables between independent groups were compared with the chi-squared test and Fisher's exact test as appropriate. A p-value of 0.05 was considered statistically significant.

We used the Receiver Operating Characteristic (ROC) analysis to assess the discriminative ability for incomplete recovery at three and six months from the Bell's palsy onset for nerve conduction study and HRUS data collected at T1. The Youden index assessed the best diagnostic value for nerve conduction study and HRUS; relative sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were then estimated.

Statistical analyses were performed using Prism 9.4 (GraphPad, CA, USA).

3. Results

We consecutively screened 39 patients and excluded five (two due to Varicella Zoster Virus infection and three due to concomitant diabetic neuropathy). We therefore enrolled 34 patients (age 55 years, IQR 40–65; 16 men) with a definite diagnosis of Bell's Palsy (Supplementary Table 1). Three patients were lost at follow-up after the first evaluation (Table 1). The Cronbach's alpha test showed a good inter-operator agreement for facial nerve diameter measurements with HRUS (T1 $\alpha = 0.86$, T2 $\alpha = 0.89$, T3 $\alpha = 0.9$).

At T1, the facial nerve diameter was larger ($p = 0.001$), (Fig. 1) and the CMAP amplitude was lower ($p < 0.0001$) in the affected side than in the normal side. At T1, 24 patients had a preserved R1 blink reflex.

The two-way repeated measure ANOVA for the facial nerve diameter, as assessed with HRUS, showed a significant interaction between time (T1, T2, T3) and side (affected, control side) ($F(2, 120) = 3.088$, $p < 0.05$), (Fig. 2). Post hoc analysis showed a significant difference between facial nerve diameter at T1 and T3 on the affected side ($p = 0.005$, Fig. 2) (Supplementary Tables 2, 3), indicating a progressive reduction in the facial nerve diameter on the affected side.

The two-way repeated measure ANOVA for the facial nerve CMAP amplitude showed a significant interaction between time (T1, T2, T3) and side (affected, control side) ($F(2, 120) = 11.83$, $p < 0.001$). Post hoc analysis showed a significant difference between facial nerve CMAP amplitude at T1 and T3 on the affected side ($p < 0.001$) (Supplementary Tables 2, 3), indicating a progressive increase in the facial nerve CMAP amplitude on the affected side.

One month after symptoms onset (T2) seven patients of the 34 patients enrolled had a complete clinical recovery (i.e., HB = 1). All these seven patients had a preserved R1 blink reflex at T1 and a significantly lower facial nerve diameter at T1, compared to patients with incomplete recovery (i.e., HB > 1), ($p = 0.023$), (Table 2). At three (T3) and six months (T4) after Bell's palsy onset, twenty and twenty-four patients of the 34 enrolled had a complete clinical recovery (i.e., HB = 1). All these patients had a larger facial nerve CMAP and a smaller facial nerve diameter at T1 when compared with patients with incomplete recovery (i.e., HB > 1), ($p < 0.05$), (Tables 3 and 4).

The ROC curve analysis showed that the asymmetry of the CMAP amplitude between the affected and normal side at T1 had a better performance than the facial nerve diameter asymmetry as assessed with HRUS in predicting patients with incomplete recovery (i.e., HB > 1) at three (AUC = 0.88 vs AUC = 0.76, PPV = 88.88 % vs PPV = 58.33 %) and six (AUC = 0.91 vs AUC = 0.79, PPV = 66.66 % vs PPV = 50 %) months (Fig. 3), (Table 5). The optimal trade-off value between sensitivity and specificity corresponded to a facial nerve diameter asymmetry of 25 % (an increase in the diameter on the affected side higher than the 25 % of the control side) and a CMAP amplitude asymmetry of 65 % (a decrease in the CMAP amplitude on the affected side more than the 65 % of the control side).

Table 1
House-Brackmann Score, Neurophysiological and Ultrasound variables across three time points.

	Side	T1 (n = 34)	T2 (n = 31)	T3 (n = 31)
House-Brackmann score	Affected	4 (3–4)	2 (2–3)	1 (1–2)
Neurophysiological variables				
CMAP latency (ms)	Affected	3.6 (3.1–4.4)	3.6 (3.2–4)	3.3 (3–3.8)
	Control	3 (2.6–3.3)	3.2 (2.8–3.6)	3.1 (2.8–3.6)
CMAP Amplitude (mV)	Affected	1.2 (0.8–1.75)	1.7 (0.9–2)	2 (1.5–2.5)
	Control	2.5 (2–3)	2.5 (2–3)	2.6 (2–3)
R1 blink reflex preserved	Affected	23	27	27
EMG denervation	Affected	1	4	0
High Resolution Nerve Ultrasound				
Facial nerve diameter (mm)	Affected	0.8 (0.7–1.1)	0.8 (0.6–1)	0.7 (0.6–1)
	Control	0.7 (0.6–1)	0.7 (0.5–0.9)	0.7 (0.6–1)

CMAP: compound muscle action potential.
CMAP and ultrasound variables are expressed as median and (IQR); R1 blink reflex and EMG denervation are expressed as absolute number of patients.

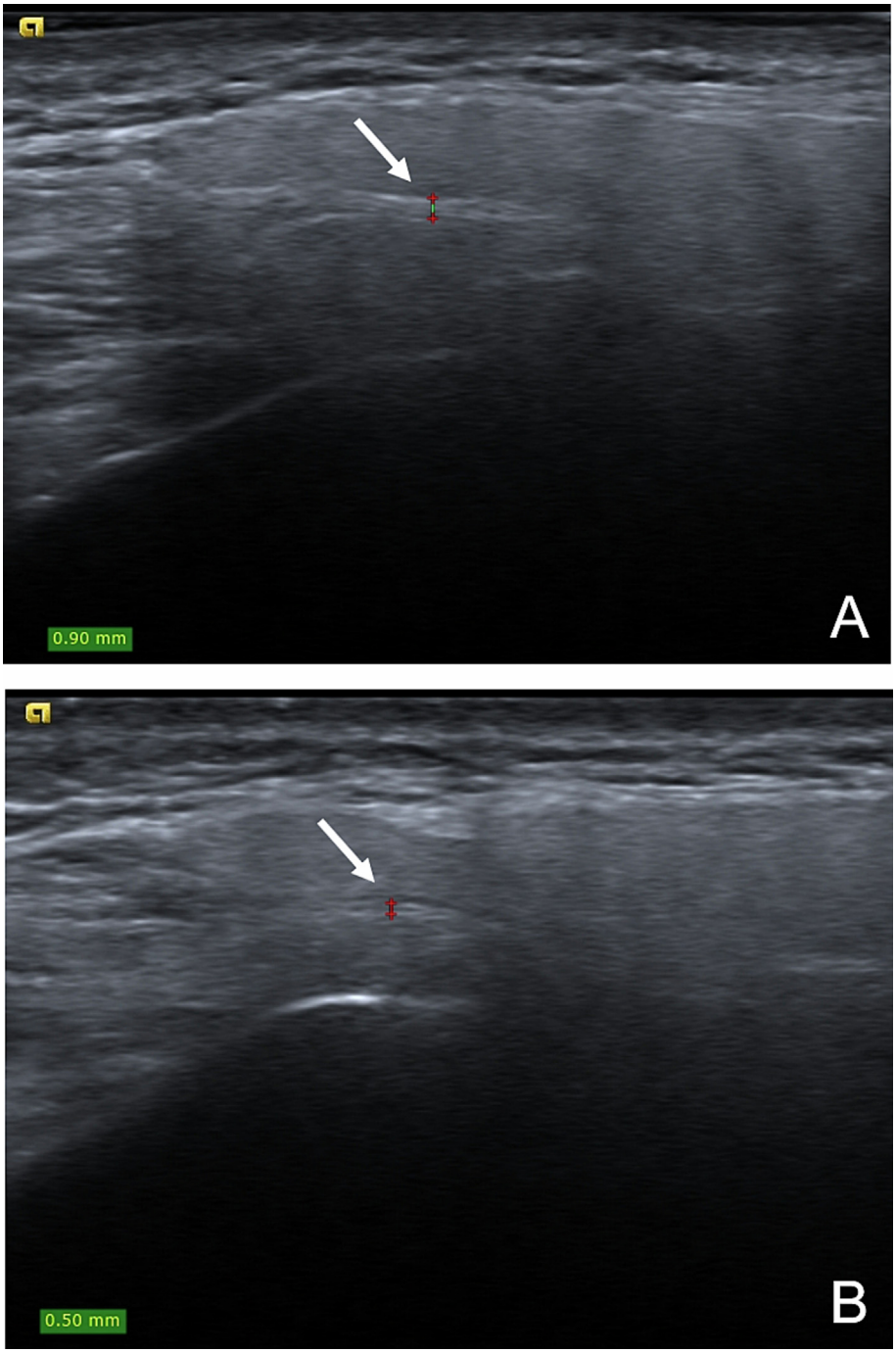

Fig. 1. Facial Nerve Ultrasound at T1 in a representative patient: A. Affected side, B. Control side.

4. Discussion

Our longitudinal study found that although the HRUS showed an increased facial nerve diameter during the first days of Bell's palsy onset, the predictive value for the incomplete recovery of this HRUS variable is lower than that of CMAP amplitude.

Predicting facial muscle recovery in patients with Bell's palsy relies on clinical and neurophysiological findings (Yoo et al., 2020). In particular, the predictive value of CMAP amplitude asymmetry between the affected and normal side is an established approach for estimating axonal loss and providing prognostic information. Previous observations indicated that a 90 % facial nerve CMAP reduction is associated with incomplete clinical recovery (grade III HB or higher), (Valls-Solé, 2007; Ozgur et al., 2010; Halvorson et al., 1993; Gantz et al., 1999).

In our study, we investigated the clinical usefulness of HRUS for predicting clinical recovery in patients with Bell's palsy. Compared with MRI, HRUS is less expensive, easy to perform and allows serial studies of the distal portion of the facial nerve after its emergence at the stylomastoid foramen.

The cross-sectional area is the most widely used ultrasound parameter in assessing peripheral nerve conditions. Conversely, in our study, we used the diameter of the facial nerve as the main outcome measure, given that the facial nerve is a tiny nerve in the

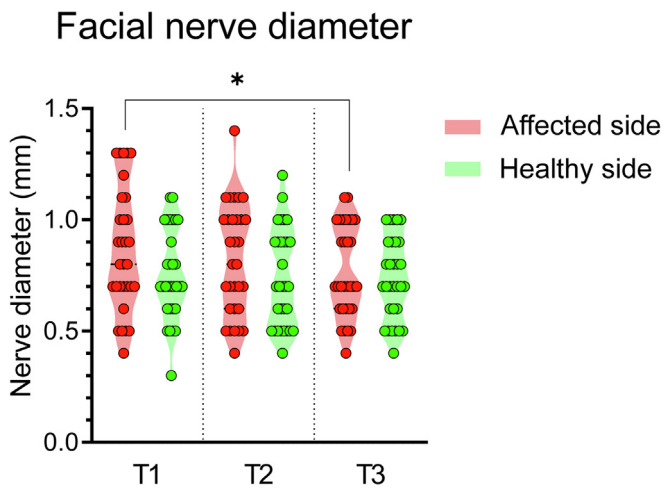

Fig. 2. Two-way repeated measure ANOVA, for the facial nerve diameter. The asterisks indicate a significant difference (post hoc analysis with Sidak correction) between facial nerve diameter at T3 and T1 (p = 0.005).

relatively isoechoic salivary gland tissue. Accordingly, an isolated axial view of the facial nerve is often technically challenging (Tawfik et al., 2015b).

We found that in the first days after Bell's palsy onset, the diameter of the affected facial nerve is increased compared with the normal side, a finding in line with previous observations (Tawfik et al., 2015a). Facial nerve swelling may be due to the spreading along the nerve of oedema and inflammation secondary to nerve entrapment in the facial canal (Liston and Kleid, 1989; Michaels, 1990). Remarkably, all the patients who had complete recovery within one month from symptoms onset (i.e., having an HB 1) had a smaller facial nerve diameter at T1 (10–15 days after the Bell's palsy onset) compared with patients with incomplete recovery. Moreover, all these patients had a preserved R1 blink response. A less prominent nerve enlargement associated with a preserved R1 blink reflex response may therefore reflect a negligible axonal loss and inflammation after nerve injury in this subgroup of patients, regardless of the clinically evident severity (as assessed with HB) and the facial CMAP amplitude reduction.

The ROC curve analysis showed that the optimal trade-off between sensitivity and specificity for the facial nerve asymmetry assessed with HRUS at T1 corresponded to 25 % (an increase in the diameter on the affected side higher than 25 % of the control side). This threshold, however, had a lower sensitivity and specificity for predicting the incomplete recovery at three (T3) and six (T4) months than the facial nerve CMAP asymmetry. This finding may reflect the different diagnostic characteristics of neurophysiological testing and nerve HRUS (Kerasnoudis et al., 2015). HRUS explores only the distal portion of the facial nerve, while

Table 2
Comparison between patients with complete (HB = 1) and incomplete (HB > 1) recovery at one month (T2).

	Complete recovery HB = 1 (n = 7)	Incomplete recovery HB > 1 (n = 24)	p
Age (years)	45 (23; 70)	55.5 (42.25; 63)	0.72
Sex (M:F)	1:6	12:12	0.19
HB at T1	4 (3; 4)	4 (3; 4)	0.27
Preserved R1 blink reflex at T1	7	14	0.06
CMAP on the affected side at T1 (mV)	1.6 (1.2; 2.2)	1.15 (0.62; 1.85)	0.17
Facial nerve diameter on the affected side at T1 (mm)	0.6 (0.5; 0.8)	0.9 (0.7; 1.22)	0.023
CMAP amplitude asymmetry at T1 (%)	−40 (-45; −27.27)	−55 (-77.62; −25.95)	0.19
Facial nerve diameter asymmetry at T1 (%)	0 (-19.64; 9.37)	24 (0; 34.3)	0.035

HB: House-Brackmann score.
Values are expressed as: Median (IQR).
p assessed by Mann-Whitney test and chi-squared test and Fisher's exact test as appropriate.
Preserved R1 blink reflex is expressed as absolute number of patients.
CMAP: compound muscle action potential.
CMAP amplitude asymmetry: (CMAP amplitude affected - CMAP amplitude control side)/CMAP amplitude control side*100.
Facial nerve diameter asymmetry: (diameter affected-diameter control side)/diameter control side*100.

Table 3
Comparison between patients with complete (HB = 1) and incomplete (HB > 1) recovery at three months (T3).

	Complete recovery HB = 1 (n = 20)	Incomplete recovery HB > 1 (n = 11)	p
Age (years)	45 (23; 70)	60 (55; 68)	0.02
Sex (M:F)	7:13	6:5	0.44
HB at T1	4 (3; 4)	4 (4; 6)	0.03
Preserved R1 blink reflex at T1	16	5	0.1
CMAP on the affected side at T1 (mV)	1.6 (1.2; 2.15)	0.6 (0.5; 1)	<0.001
Facial nerve diameter on the affected side at T1 (mm)	0.75 (0.62; 1)	0.9 (0.7; 1.3)	0.16
CMAP amplitude asymmetry at T1 (%)	−35.8 (-49.4; -23.43)	−77.78 (-84;-62.9)	<0.001
Facial nerve diameter asymmetry at T1 (%)	0 (0; 27.5)	30 (14.29; 50)	0.014

HB: House-Brackmann score.
Values are expressed as: Median (IQR).
p assessed by Mann-Whitney test and chi-squared test and Fisher's exact test as appropriate.
Preserved R1 blink reflex is expressed as as absolute number of patients.
CMAP: compound muscle action potential.
CMAP amplitude asymmetry: CMAP amplitude affected - CMAP amplitude control side/CMAP amplitude control side*100.
Facial nerve diameter asymmetry: diameter affected-diameter control side)/diameter control side*100.

Table 4
Comparison between patients with complete (HB = 1) and incomplete (HB > 1) recovery at six months (T4).

	Complete recovery HB = 1 (n = 24)	Incomplete recovery HB > 1 (n = 7)	p
Age (years)	48 (35.7; 63)	55 (60; 73)	0.03
Sex (M:F)	8:16	5:2	0.1
HB at T1	4 (3;4)	4 (4; 6)	0.008
Preserved R1 blink reflex at T1	19	2	0.02
CMAP on the affected side at T1 (mV)	1.45 (1.12; 1.97)	0.6 (0.4; 0.9)	<0.001
Facial nerve diameter on the affected side at T1 (mm)	0.8 (0.7; 1)	0.9 (0.7; 1.3)	0.23
CMAP amplitude asymmetry at T1 (%)	−38.33 (-57.5; −24.4)	−77.78 (-84; −71.88)	<0.001
Facial nerve diameter asymmetry at T1 (%)	0 (0; 27.5)	30 (28.57; 50)	0.016

HB: House-Brackmann score.
Values are expressed as: Median (IQR).
p assessed by Mann-Whitney test and chi-squared test and Fisher's exact test as appropriate.
Preserved R1 blink reflex is expressed as absolute number of patients.
CMAP: compound muscle action potential.
CMAP amplitude asymmetry: CMAP amplitude affected - CMAP amplitude control side/CMAP amplitude control side*100.
Facial nerve diameter asymmetry: diameter affected-diameter control side)/diameter control side*100.

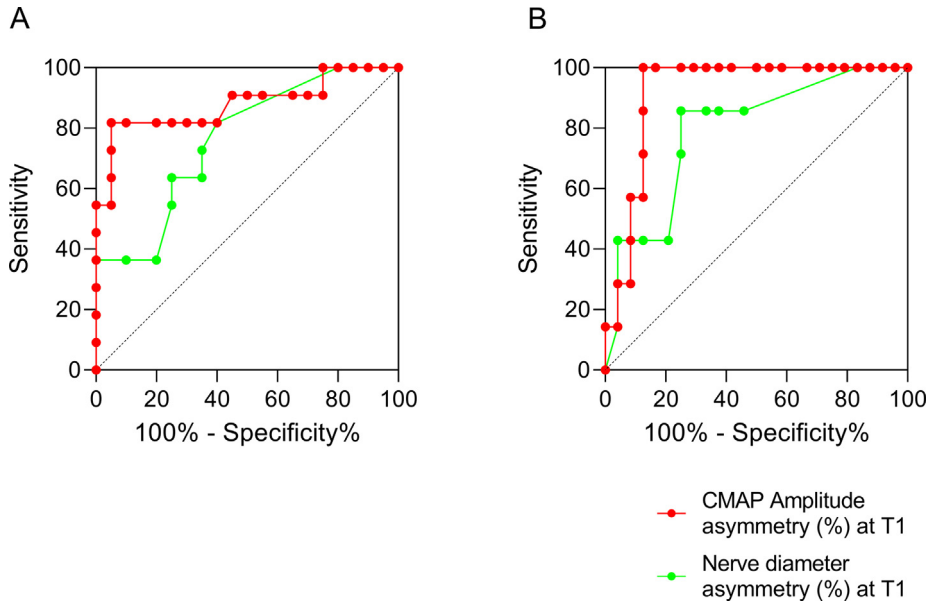

Fig. 3. ROC curve analysis after three (A) and six (B) months from symptoms onset. Red dots: side-to-side facial nerve compound muscle action potential (CMAP) amplitude asymmetry using the contralateral side as reference. Green dots: side-to-side facial nerve diameter asymmetry using the contralateral side as reference. Optimal trade-off value between sensitivity and specificity corresponded to a facial nerve diameter asymmetry of 25% (an increase in the diameter on the affected side higher than the 25% of the control side) and a CMAP amplitude asymmetry of 65% (a decrease in the CMAP amplitude on the affected side more than the 65% of the control side).

Table 5
Predicting values of nerve conduction and ultrasound variables after three and six months.

	Sensitivity (%)	Specificity (%)	Youden-index	PPV (%)	NPV (%)
Prognosis at 3 months					
CMAP amplitude asymmetry at T1 (>65 %**)	82 (52–96)	95 (76–99)	0.77	88.88	86.36
Nerve diameter asymmetry at T1 (>25 %**)	63 (35–85)	75 (53–89)	0.38	58.33	78.94
Prognosis at 6 months					
CMAP Amplitude asymmetry at T1 (>65 %**)	100 (64–100)	87 (69–95)	0.87	66.66	95.45
Nerve diameter asymmetry at T1 (>25 %**)	85 (48–99)	75 (55–88)	0.6	50	94.73

**ROC curve analysis indicated a threshold of 65% (decrease of the CMAP amplitude on the affected side more than the 65% of the control side) and 25% (increase of the nerve diameter on the affected side higher than the 25% of the control side) as optimal trade-off between sensitivity and specificity.
CMAP: compound muscle action potential.
CMAP amplitude asymmetry: (CMAP amplitude affected - CMAP amplitude control side)/CMAP amplitude control side*100.
Facial nerve diameter asymmetry: (diameter affected-diameter control side)/diameter control side*100.
PPV: positive predictive value.
NPV: negative predictive value.

histopathological studies demonstrated that in patients with Bell's palsy oedema and inflammation affect the nerve mainly in the facial canal of the temporal bone (Michaels, 1990). Nevertheless, the negative predictive value of a facial nerve diameter asymmetry of 25 % was relatively high (i.e., 94.73 %). Accordingly, we may speculate that an asymmetry lower than this threshold might be sensitive in detecting patients with a high probability of complete recovery.

Our findings on the predictive value of facial nerve HRUS in patients with Bell's palsy are in line with a previous study that in a relatively small sample of patients with Bell's palsy (Baek et al., 2019) demonstrated that the facial nerve diameter does not correlate with the HB at two months after the onset of Bell's palsy (Baek et al., 2020). Our longitudinal study extends this knowledge and provides previously unreported findings, given that we have now precisely analysed how facial nerve HRUS predicts the recovery in patients with Bell's palsy and provided the sensitivity and specificity of this technique for the incomplete recovery at three and six months after this facial nerve palsy.

Although the predictive value of facial nerve HRUS is lower than that of facial nerve conduction study, we believe that it may represent a potentially useful diagnostic tool in the diagnostic pathway of facial palsy. Ultrasound investigation offers a relatively low-cost, easy-to-perform, non-invasive tool for rapidly evaluating the distal portion of the facial nerve. Furthermore, a less prominent nerve enlargement after 10–15 days is associated with a good outcome at one month from disease onset (regardless of clinical and CMAP amplitude impairment).

4.1. Limitations

Admittedly our study has some limitations. Facial nerve HRUS is an operator-dependent procedure, therefore the reproducibility of this technique is still an open issue; this limitation may affect our findings. However, in our study we used a standardized ultrasound protocol to improve the reproducibility of this technique and demonstrated a good inter-rater reliability between the two operators. An additional limitation is that we have excluded patients with concomitant peripheral nervous system conditions (e.g., diabetes). It follows that our findings on the relatively low predictive value of facial nerve HRUS may have a poor validity for the different patient's categories.

Our study investigated the facial nerve at a single anatomical point. We may hypothesize that a multiple-point assessment might increase the reliability of facial nerve HRUS. Further studies, including larger samples of patients assessing the nerve diameter at multiple points, are needed to provide reliable reference values and support conclusive information on the predictive value of facial nerve HRUS in patients with Bell's palsy. Moreover, the combination of nerve ultrasound and neurophysiological data in larger samples of patients with Bell's palsy may potentially improve prognostication in patients with Bell's Palsy.

In our participants, the difference in the facial nerve diameter median values between the affected and healthy sides is relatively small. This observation is in line with previous studies (Baek et al., 2020; Tawfik et al., 2015a) and reflects the large variability of facial nerve diameter in the affected side of patients with Bell's palsy (some patients had a mild/negligible increase of the diameter). In our study, we have therefore used the facial nerve diameter asymmetry parameter ((diameter affected-diameter control side)/diameter control side*100), which is probably more reliable for the assessment at a single subject level.

The first neurophysiological and nerve ultrasound evaluations were performed after 10–15 days after the diagnosis, after the corticosteroid treatment. We cannot exclude that treatment may impact our findings (e.g., a persistent post-treatment nerve enlargement may reflect more severe facial nerve damage).

5. Conclusions

Our longitudinal study shows that facial nerve HRUS demonstrates an increased facial nerve diameter in the acute phase of Bell's palsy, thus potentially improving patients' evaluation.

The negative predictive value of facial nerve HRUS examination in the acute phase of facial nerve palsy is relatively high, thus potentially supporting the usefulness of this technique in the diagnostic pathway of Bell's palsy. However, facial nerve HRUS examination has a poorer prognostic value than facial nerve conduction study in patients with Bell's palsy.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clinph.2023.11.020.

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