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Correlation of the neuropathic pain and electrodiagnostic tests in earthquake-related peripheral nerve injuries

Depremle ilişkili periferik sinir yaralanmalarında nöropatik ağrı ile elektrodiyagnostik testlerin korelasyonu

Metin Balduz[1] Halit Fidancı[2]

[1]Health Sciences University Adana City Training and Research Hospital, Neurology Clinic, Yüreğir, Adana, Türkiye

[2]Health Sciences University Adana City Training and Research Hospital, Neurology Clinic, Clinical Neurophysiology Unit, Adana, Türkiye

ABSTRACT

Aim: Peripheral nerve injury resulting from being buried under earthquake-related debris can lead to neuropathic pain. This study investigates the relationship between neuropathic pain and electrodiagnostic test findings in patients with peripheral nerve lesions caused by entrapment under debris.

Materials and Methods: This retrospective study included patients who developed peripheral nerve lesions due to entrapment under debris during the Kahramanmaraş-centered earthquakes in February 2023. Abnormalities in compound nerve action potentials (CNAPs) and compound muscle action potentials (CMAPs) were categorized as mild, moderate, or severe.

Results: 62 (34 female, 28 male) patients were included in this study. The mean (min-max) disease duration, time under debris, and Douleur Neuropathique 4 Questions (DN4) scores were 59.4 ± 37.1 (21-180) days, 22.6 ± 29.7 (0.5-130) hours, and 4.9 ± 1.7 (1-9), respectively.

A positive correlation was observed between the number of severe CNAP/CMAP abnormalities and DN4 scores (p=0.024, r=0.287/ p=0.003, r=0.371). Patients with severe CMAP abnormalities in at least one or at least two nerves had higher DN4 scores compared to those without (p=0.039/p=0.009).

Conclusion: This study highlights a relationship between neuropathic pain and severe CNAP/CMAP abnormalities in patients with peripheral nerve lesions due to entrapment under debris.

Keywords: Earthquake, nerve conduction study, neuropathic pain, peripheral neuropathy,

ÖZ

Amaç: *Depremle ilişkili enkaz altında kalmaya bağlı gelişen periferik sinir yaralanmaları nöropatik ağrıya yol açabilir. Bu çalışma, enkaz altında kalma sonucu periferik sinir hasarı olan hastalarda nöropatik ağrı ile elektrodiyagnostik test bulguları arasındaki ilişkiyi araştırmaktadır.*

Gereç ve Yöntem: *Bu retrospektif çalışma, Şubat 2023'te Kahramanmaraş merkezli depremler sırasında enkaz altında kalma sonucu oluşan periferik sinir hasarı gelişen hastaları içermektedir. Bileşik sinir aksiyon potansiyelleri (CNAP) ve bileşik kas aksiyon potansiyellerindeki (CMAP) anormallikler hafif, orta veya şiddetli olarak kategorize edilmiştir.*

Corresponding author: Metin Balduz
Health Sciences University Adana City Training and Research Hospital, Neurology Clinic, Adana, Türkiye
E-mail: *metdical@gmail.com*

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Bulgular: *Bu çalışmaya 62 (34 kadın, 28 erkek) hasta dahil edilmiştir. Ortalama (min-maks) hastalık süresi, enkaz altında kalma süresi ve Douleur Neuropathique 4 soru (DN4) skorları sırasıyla 59,4 ± 37,1 (21-180) gün, 22,6 ± 29,7 (0,5-130) saat ve 4,9 ± 1,7 (1-9) olarak bulunmuştur.*

Şiddetli CNAP/CMAP anormalliklerinin sayısı ile DN4 skorları arasında pozitif bir korelasyon gözlenmiştir (p=0,024, r=0,287 / p=0,003, r=0,371). En az bir veya en az iki sinirde şiddetli CMAP anormallikleri olan hastalar, anormallik bulunmayan hastalara göre daha yüksek DN4 skorlarına sahipti (p=0,039 / p=0,009).

Sonuç: *Bu çalışma, enkaz altında kalmaya bağlı periferik sinir hasarı olan hastalarda nöropatik ağrı ile şiddetli CNAP/CMAP anormallikleri arasındaki ilişkiye dikkat çekmektedir.*

Anahtar Sözcükler: *Deprem, sinir ileti çalışması, nöropatik ağrı, periferik nöropati*

INTRODUCTION

Abnormalities in the peripheral nervous system can lead to the development of weakness, sensory abnormalities, and neuropathic pain (1, 2). These issues can range from mild impairment to disability in affected patients. Traumas, alongside chronic systemic diseases, are known to cause disorders involving the peripheral nervous system, including peripheral nerve damage, plexopathy, or radiculopathy (1-4). Nerve conduction studies and needle electromyography are valuable tools not only for diagnosing peripheral nerve lesions but also for providing insights into differential diagnosis and prognosis (5, 6). Peripheral nerve lesions may result from traumas such as being trapped under debris caused by earthquakes (4, 7-9). Moreover, individuals affected by earthquakes may develop neuropathic pain (10). This study investigates the potential relationship between neuropathic pain and nerve conduction study findings in peripheral nerve lesions resulting from individuals being trapped under debris due to earthquakes centered in Kahramanmaraş.

MATERIALS AND METHODS

Subjects

This retrospective study included patients who suffered peripheral nerve lesions due to being trapped under debris in the Kahramanmaraş-centered earthquakes on February 6, 2023. The study was conducted at Adana City Training and Research Hospital's Neurology Clinic and Clinical Neurophysiology Laboratory between February 2023 and June 2023. Ethics committee approval for the study was obtained from Adana City Training and Research Hospital Clinical Research Ethics Committee (number: 129/2669, date: 2023). Patients exhibiting clinical features and electrodiagnostic findings consistent with single or multiple nerve lesions, plexopathy, and/or radiculopathy were included. Exclusion criteria comprise individuals with conditions predisposed to polyneuropathy, neurodegenerative diseases, or a history of radiculopathy/plexopathy or nerve lesions. Douleur Neuropathique 4 Questions (DN4) pain scale was applied to the patients. The cut-off point for DN4 score was considered as 4 points (11, 12).

Electrodiagnostic tests

Nerve conduction study and needle electromyography were performed with the Cadwell Sierra Summit EMG unit (Cadwell Laboratories, Kennewick, Washington, USA). Recommended methods and reference values for nerve conduction study and needle electromyography were used. Considering the clinical findings of the patients', recommended methods were and reference values for nerve conduction study and needle electromyography were performed on the median, ulnar, radial, superficial radial, medial antebrachial cutaneous, lateral antebrachial cutaneous, posterior tibial, peroneal, and sural nerves. The normal values for these nerve conduction studies are as follows: Posterior tibial CMAP: 4.2 µV, Median CMAP: 4.3 µV, Median CNAP: 10.3 µV, Ulnar CMAP: 6.4 µV, Ulnar CNAP: 7.1 µV, Peroneal CMAP: 3.7 µV, Sural CNAP: 5.1 µV, Superficial peroneal CNAP: 5.3 µV, Superficial radial CNAP 10 µV, Medial antebrachial cutaneous (MAC):3 µV, Lateral antebrachial cutaneous (LAC): 6 µV (13-16).

For motor and sensory nerve conduction studies, upper and lower band filters were set as 20 Hz-10kHz and 20Hz-2Khz, respectively. In sensory and motor nerve conduction studies, the sweep speed was 1 ms/division and 5 ms/division, respectively. Sensitivity in sensory and motor nerve conduction studies was set as 10 uV/division and 2 mV/division, respectively.

Compound muscle action potential (CMAP) and compound nerve action potential (CNAP) amplitudes were calculated from peak to peak. Considering clinical findings of the patients, nerve conduction studies of the median, ulnar, radial, superficial radial, medial antebrachial cutaneous, lateral antebrachial cutaneous, posterior tibial, peroneal, and sural nerves were performed on the patients. CMAP or CNAP were classified according to their amplitudes as follows (17): 1) Mild nerve injury: CNAP / CMAP amplitude is less than 50% of the normal value 2) Moderate nerve injury: CNAP / CMAP can be obtained but the amplitude is between 50-100% 3) Severe nerve injury: CMAP/CNAP cannot be obtained.

Concentric needle electrodes (length=50mm, 26 G, Natus, Galway, Ireland; length=50mm, diameter=0.46mm, Bionen Medical Devices, Florence, Italy) were used for needle electromyography (EMG). Band filter 10 Hz It was set to -10 kHz. Positive sharp waves and fibrillation potentials at rest were carefully examined. When the motor unit action potential (MUAP) amplitude was >3.5 mV and/or duration was >15 ms, this MUAP was considered neurogenic. Muscles with positive sharp wave/Fibrillation potentials were divided into two groups according to whether MUAP could be obtained or not. Muscle selection for needle EMG was made according to the clinical characteristics of the patient.

Statistical analysis

Categorical variables were expressed as frequency and percentage, while numerical data were presented as mean ± standard deviation (SD) and range. Statistical analysis employed the Mann-Whitney U test for numerical data comparison between groups and the Pearson-Chi Square test for categorical variables. Spearman correlation analysis assessed correlations. A p-value < 0.05 was deemed statistically significant. SPSS 22.0 was used for statistical analysis.

RESULTS

The findings of 97 patients were reviewed. There were 22, eight and five patients with a history of diabetes mellitus, polyneuropathy and radiculopathy, respectively. These patients were excluded from the study. Finally, 62 patients (34 female, 28 male) were included in the study. The mean age of the patients was 35.3±14.3 years. The time interval between the time the lesion occurred and the time the clinical/electrodiagnostic examination was performed was 59.4±37.1 (min-max 21-180) days. The mean time spent under debris is 22.6±29.7 (0.5-130) hours. The clinical features of the patients are given in Table-1. When patients were grouped according to lesion localization, there were 24 (38.7%), 18 (29.1%) and two (3.1%) patients with only peripheral nerve lesion, plexopathy and radiculopathy, respectively. Eighteen patients had at least two of these three types of injuries.

The mean DN4 score of the patients was 4.9±1.7 (min-max 1-9). There were 40 (64.5%) patients with a DN4 score > 4. DN4 scores of individuals with one extremity affected and more than one extremity were 4.5±1.8 (min-max 1-9) and 5.6±1.3 (min-max 3-8), respectively (p=0.007). The numbers of mild, moderate, and severely affected CNAP/CMAPs in patients are shown in Table-2. Table-3 shows the correlation between the number of mildly, moderately, and severely affected nerves / disease duration / time under debris and DN4 scores. Figure 1 shows the correlation between DN4 scores and the number of nerves with severe CMAP abnormality in each patient. The comparison of disease duration/time in debris/DN4 scores between the groups formed by separating the patients according to the presence of MUAP and the number of severe CNAP/CMAP abnormalities is available in Table-4. Correlation between DN4 scores and the number of nerves with severe CMAP abnormality in patients with and without severe CMAP abnormality in at least two nerves shows in Figure 2.

Table-1. The clinical features of the patients.

Clinical feature	**Number of patients (%)**
Median / Ulnar nerve	7 (11.2) / 10 (16.1)
Radial / Axillary nerve	6 (9.6) / 1 (0.01)
Peroneal / Posterior tibial / Sural nerve	15 (24.1) / 3 (0.04) / 2 (0.03)
Superficial / Sciatic nerve	1 (0.01) / 15 (24.1)
Brachial / Lumbosacral / Sacral plexus	9 (14.5) / 4 (0.06) / 10 (16.1)
Cervical / Lumbosacral radiculopathy	1 (0.01) / 4 (0.06)
Affected extremity	
Only one extremity / >1 extremity	18(29.1)/ 24 (38.7)
Right / Left / Bilateral	23(37.1)/21(33.9)/18(29.0)
Upper / Lower / Both	20(32.3)/34(54.8)/8(12.9)

Table-2. The numbers of mild, moderate and severely affected CNAP/CMAPs in patients.

Electrodiagnostic abnormality	**Number of patients**				
CNAP	Abnormality in one nerve	Abnormality in two nerves	Abnormality in three nerves	Abnormality in four nerves	Abnormality in five nerves
Mild	13	4	2	-	-
Moderate	1	-	-	-	-
Severe	18	16	8	-	3
CMAP					
Mild	16	4	2	-	-
Moderate	14	2	-	-	-
Severe	15	15	9	10	2

Table-3. The correlation between the number of mild, moderate and severely affected nerves /disease duration/ time under debris and DN4 scores.

Clinical and electrodiagnostic features	**DN4 scores**
Disease duration (day)	p=0.044, r=0.257
Time under debris (hour)	p=0.865, r=0.022
Number of nerves with CNAP/CMAP abnormality in patients	
CNAP abnormality	
Mild	p=0.574, r=0.073
Moderate	p=0.125, r=-0.197
Severe	**p=0.024, r=0.287**
CMAP abnormality	
Mild	p=0.480, r=-0.091
Moderate	p=0.331, r=-0.126
Severe	**p=0.003, r=0.371**

CMAP: compound muscle action potential; CNAP: compound nerve action potential; DN4: Douleur Neuropathique 4 Questions.

Table-4. The comparison of clinical features / DN4 scores between the patients with and without the electrodiagnostic abnormalities.

Electrodiagnostic feature	Disease duration (day) mean±SD(IQR)	Time under debris (hour) mean±SD	DN4 scores mean±SD
Severe CNAP abnormality in at least one nerve +			
+ (n=45)	59.4±40.0(45)	25.7±29.9(19.5)	5.2±1.6(2)
- (n=17)	59.3±29.17(45)	14.0±28.2(9.5)	4.3±1.8(3)
P value	0.585	**0.006**	0.106
Severe CNAP abnormality in at least two nerves			
+ (n=27)	63.3±42.1(77)	25.4±26.6(14)	5.3±1.7(2)
- (n=35)	56.3±33.2(36)	20.3±32.1(9)	4.6±1.7(2)
P value	0.749	**0.046**	0.110
Severe CMAP abnormality in at least one nerve +			
+ (n=51)	60.2±38.7(55)	23.5±28.8(17)	5.1±1.6(2)
- (n=11)	55.3±29.8(34)	17.9±34.6(9)	4.0±1.9(3)
P value	0.861	0.068	**0.039**
Severe CMAP abnormality in at least two nerves			
+ (n=36)	62.9±40.3(54)	27.1±33.3(41.8)	5.4±1.5(2)
- (n=26)	54.4±32.3(36)	16.2±23.1(14.5)	4.2±1.7(2.2)
P value	0.488	0.387	**0.009**
Absence of MUAP in at least one muscle			
+ (n=35)	57.9±36.4(40)	30.7±36.3(53)	5.1±1.6(2)
- (n=24)	60.5±35.2(50	12.1±12.4(8.8)	4.7±1.9(2.7)
P value	0.676	**0.049**	0.315

CMAP: compound muscle action potential; CNAP: compound nerve action potential; DN4: Douleur Neuropathique 4 Questions; MUAP: motor unit action potential; SD: standard deviation.

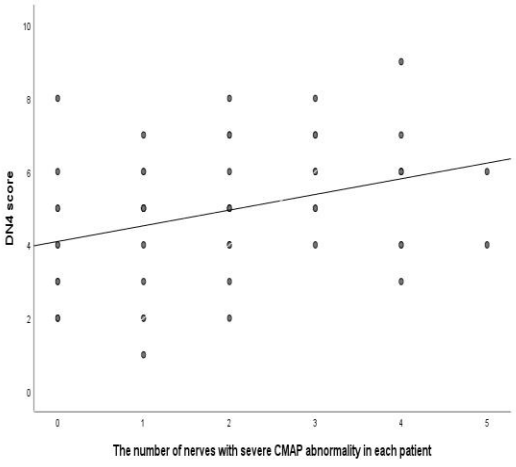

Figure-1. The correlation between DN4 scores and the number of nerves with severe CMAP abnormality in each patient
CMAP: compound muscle action potential; DN4: Douleur Neuropathique 4 Questions.

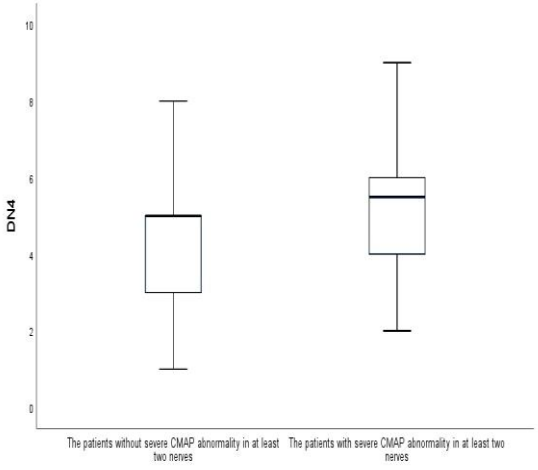

Figure-2. The comparison of DN4 scores between the patients with and without severe CMAP abnormality in at least two nerves
CMAP: compound muscle action potential; DN4: Douleur Neuropathique 4 Questions.

DISCUSSION

Neuropathic pain was prevalent in approximately 65% of the patients in this study, indicating its significant impact on individuals with peripheral nerve lesions resulting from being trapped under earthquake debris. Unlike acute nerve injuries seen in typical trauma, entrapment under debris causes prolonged compression and ischemic damage, leading to more severe axonal degeneration and delayed recovery. This mechanism distinguishes earthquake-related nerve injuries from standard traumatic neuropathies. A noteworthy finding was the positive correlation observed between DN4 scores, indicative of neuropathic pain severity, and the presence of severe CNAP abnormalities. This suggests that as the degree of axonal degeneration in sensory nerves increases, the severity of neuropathic pain may also escalate (18-21). Interestingly, a similar relationship was observed between severe CMAP abnormalities and DN4 scores, implying that in patients trapped under debris, not only the sensory branches of the peripheral nerves are affected, but also the motor and sensory branches more proximally. Another explanation for this situation may be in the pathophysiology of neuropathic pain. Both peripheral and central mechanisms are involved in the pathophysiology of neuropathic pain (18-20). Affecting Damaged to motor fibers may have affected the motor cortex, which is known to be related to the somatosensory cortex (22, 23), and thus may have led to the development of neuropathic pain in these patients. Entrapment duration (time under debris) did not correlate with DN4 scores but correlated with CNAP abnormalities in patients with one or two CNAP abnormalities. Neuropathic pain is a progressive condition, and its severity is influenced by the duration of nerve injury rather than the initial entrapment duration. While entrapment duration objectively correlates with the degree of nerve damage (reflected by CNAP abnormalities), subjective pain perception (DN4) is influenced by multiple factors, including central sensitization and the chronicity of the injury. In this study, neuropathic pain was present in more than half of the patients. It shows that neuropathic pain is an important problem in patients with disorders in the peripheral nervous system as a result of being trapped under earthquake-related debris (10). Similarly, patients without detectable MUAP, indicative of more severe nerve injury, tended to have longer exposure durations under debris compared to those with detectable MUAP. As the time spent under debris increases, the severity of axonal degeneration in the peripheral nerve may gradually increase, or the peripheral nerve may be completely damaged, or an event such as compartment syndrome may damage the peripheral nerve (8, 24). These findings underscore the importance of timely rescue efforts to prevent or mitigate severe peripheral nerve damage in individuals trapped under debris following earthquakes.

Although some studies suggest that the lower extremities are more affected in those trapped under earthquake debris, some studies have reported the opposite (4, 7, 25, 26). In this current study, peripheral neuropathy was more common in the lower extremities. Although lower extremity neuropathy was more common in our study, with ulnar nerve damage prevalent in the upper extremity and sciatic and peroneal nerve damage in the lower extremity, the specific distribution of nerve injuries varied. This variability may be attributed to anatomical vulnerabilities. Peripheral nerves become more superficial or susceptible to neuropathy as they pass through some parts of the extremities. The ulnar nerve is more prone to injury across the elbow segment and the peroneal nerve at the head of the fibula (27-29). Contrary to this situation, the deeper located sciatic nerve is also affected. The most common causes of sciatic nerve neuropathy are hip fractures/dislocations and hip surgery (17). Similarly, there are reports that suggest that approximately 45% of the patients injured in the earthquake had tibia/fibula or femur fractures (4). Therefore, sciatic nerve neuropathy may have been observed more frequently in patients trapped under debris due to traumatic hip and knee injuries.

This study had some limitations. In addition to being a retrospective study, the disease durations of the patients were different. It is known that electrodiagnostic tests are affected by disease duration (6, 30). The low number of patients can also be considered a limitation, but the criteria for inclusion of patients in the study were strict. The nerve conduction studies examine myelinated nerve fibers rather than the A delta and C fibers associated with pain (6). This was also one of the limitations.

CONCLUSION

This study highlights the significant burden of neuropathic pain in individuals with peripheral

nerve lesions following earthquake-related entrapment under debris. The observed correlations between neuropathic pain severity and CNAP/CMAP abnormalities underscore the importance of early detection and intervention in mitigating the impact of such injuries. Further research is warranted to elucidate optimal management strategies for neuropathic pain and peripheral nerve injuries in disaster settings.

Conflicts of interest: Authors declared no conflict of interest.

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