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Original Article / Özgün Makale

The overlapping roles of neuropathic and nociplastic pain in non-traumatic shoulder disorders: Implications for pain mechanisms and functional loss

Travmaya bağlı olmayan omuz hastalıklarında nöropatik ve nosiplastik ağrının örtüşen rolleri: Ağrı mekanizmaları ve fonksiyonel kayıp açısından çıkarımlar

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ABSTRACT

Background: This study aims to investigate the prevalence of neuropathic pain in shoulder pain, its relationship with nociplastic pain, and the effects of both pain types on functional outcomes.

Materials and Methods: Between May 2024 and December 2024, a total of 73 patients with non-traumatic shoulder pain persisting for more than three months were included in this multi-center, prospective, cross-sectional study. Participants were classified according to diagnoses of rotator cuff disorders, subacromial impingement, adhesive capsulitis, osteoarthritis, or calcific tendinitis. Assessments were performed using the Visual Analog Scale (VAS), the Short Form of the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS-SF), the Central Sensitization Inventory (CSI), and the Shoulder Pain and Disability Index (SPADI).

Results: Of the patients, 28 were male and 45 were female with a mean age of 54.89±10.24 (range, 32 to 70) years. Neuropathic pain was present in 26% of patients, while 28.8% exhibited central sensitization (CS), indicating nociplastic pain. Patients with both neuropathic and nociplastic pain had significantly higher SPADI scores ($p < 0.05$), indicating greater functional impairment. However, nociplastic pain alone was not significantly associated with disability. Patients with CS had higher VAS scores and longer symptom duration ($p < 0.05$), indicating its role in pain chronicity.

Conclusion: In non-traumatic shoulder disorders, neuropathic and nociplastic pain mechanisms overlap; however, their clinical impacts differ. Nociplastic pain increases pain perception, whereas neuropathic pain is more strongly associated with functional impairment. These findings highlight the importance of multidisciplinary treatment strategies that target both pain components rather than focusing solely on CS.

Keywords: Central sensitization, functional impairment, neuropathic pain, nociplastic pain, non-traumatic shoulder pain, pain mechanisms.

ÖZ

Amaç: Bu çalışmada omuz ağrılarında nöropatik ağrının yaygınlığı, nosiplastik ağrı ile olan ilişkisi ve her iki ağrı tipinin fonksiyonellik üzerindeki etkileri araştırıldı.

Hastalar ve Yöntemler: Mayıs 2024 - Aralık 2024 tarihleri arasında bu çok merkezli, prospektif kesitsel çalışmaya üç aydan uzun süredir devam eden travmaya bağlı olmayan omuz ağrılı toplam 73 hasta dahil edildi. Katılımcılar rotator manşet patolojileri, subakromiyal sıkışma sendromu, adeziv kapsülit, osteoartrit veya kalsifik tendinit tanılarına göre sınıflandırıldı. Görsel ağrı skalası (VAS), Leeds Nöropatik Semptom ve Belirti Skalasının Kısa Formu (LANSS-Kısa), Santral Duyarlılık Envanteri (CDI) ve Omuz Ağrısı ve Engellilik İndeksi (SPADI) ile ölçümler yapıldı.

Bulgular: Hastaların 28'i erkek, 45'i kadın olup, ortalama yaş 54.89±10.24 (dağılım, 32-70) yıl idi. Hastaların %26'sında nöropatik ağrı saptanırken, %28.8'inde nosiplastik ağrıyı işaret eden santral sensitizasyon varlığı tespit edildi. Hem nöropatik hem de nosiplastik ağrısı olan hastalarda SPADI skorları anlamlı düzeyde daha yüksekti ($p < 0.05$) ve bu durum daha ciddi fonksiyonel kaybı yansıtmaktaydı. Ancak yalnızca nösiplastik ağrı, fonksiyonel kayıp ile anlamlı ilişki göstermedi. Santral sensitizasyonu olan hastalarda VAS skorları ve semptom süresi daha yüksekti ($p < 0.05$) ve bu da ağrının kronikleşmesindeki rolünü göstermekteydi.

Sonuç: Travmaya bağlı olmayan omuz hastalıklarında nöropatik ve nosiplastik ağrı mekanizmaları örtüşmekle birlikte, klinik etkileri farklıdır. Nosiplastik ağrı, ağrı algısını artırırken, nöropatik ağrı fonksiyonel bozulma ile daha güçlü ilişkilidir. Bu bulgular, yalnızca santral sensitizasyona odaklanmak yerine, her iki ağrı bileşenini de hedefleyen multidisipliner tedavi stratejilerinin önemini ortaya koymaktadır.

Anahtar sözcükler: Santral sensitizasyon, fonksiyonel kayıp, nöropatik ağrı, nosiplastik ağrı, travmaya bağlı olmayan omuz ağrısı, ağrı mekanizmaları.

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Shoulder pain is the third most common musculoskeletal complaint and can significantly affect daily function, work performance, and quality of life. Although most patients recover within six months, up to half develop chronic symptoms leading to persistent disability.[1] Non-traumatic shoulder pain is frequently related to degenerative and inflammatory conditions such as rotator cuff disorders, subacromial impingement, adhesive capsulitis, and calcific tendinitis.[2] Although these conditions are typically nociceptive in origin, many patients fail to respond to conventional anti-inflammatory or physical therapy approaches.[3,4]

The International Association for the Study of Pain (IASP) categorizes pain into nociceptive, neuropathic, and nociplastic types. Neuropathic pain arises from a lesion or disease of the somatosensory system, whereas nociplastic pain results from altered nociception without clear evidence of tissue or nerve damage.[5,6] The traditional view that musculoskeletal pain is purely nociceptive is currently outdated.[7,8] Several studies have demonstrated that neuropathic and nociplastic pain mechanisms can coexist and contribute to chronic pain conditions, including shoulder disorders.[6,9-11]

Central sensitization (CS), an amplification of neural signaling within the central nervous system, underlies nociplastic pain and manifests clinically as hyperalgesia, allodynia, and widespread pain.[12] The Central Sensitization Inventory (CSI) is a validated tool to assess such features and has been linked to greater functional impairment in musculoskeletal pain.[5,13]

Despite increasing recognition of these mechanisms, non-traumatic shoulder pain has been relatively underexplored in terms of concurrent neuropathic and nociplastic components.[14-16] Patients with these pain phenotypes often experience more severe disability and poorer quality of life.[17,18] Therefore, understanding the interaction between pain mechanisms is critical for tailoring personalized treatment strategies.

In the present study, we aimed to investigate the coexistence and relative contributions of nociceptive, neuropathic, and nociplastic pain in patients with non-traumatic shoulder pain, and to determine which of these mechanisms is most strongly associated with functional impairment and disability.

PATIENTS AND METHODS

This multi-center, prospective, cross-sectional study was conducted at Başakşehir Çam and Sakura City Hospital, Department of Physical Medicine and Rehabilitation (PMR) between May 2024 and December 2024. Consecutive adult patients presenting with non-traumatic unilateral shoulder pain lasting more than three months were screened. Diagnoses were made by the treating physiatrists based on a combined assessment of clinical examination and imaging findings, including ultrasound, radiographs, or magnetic resonance imaging (MRI) where applicable. Demographic data, as well as pain, functional disability, and sensitization assessment results, were collected from all participants at the time of enrollment. Inclusion criteria were as follows: age between 18 and 70 years with unilateral, non-traumatic shoulder pain persisting for more than three months. Eligible diagnoses consisted of rotator cuff tendinopathy, partial or full-thickness tears, adhesive capsulitis (frozen shoulder), calcific tendinitis, and subacromial impingement syndrome. Patients with traumatic shoulder injuries, cervical radiculopathy, inflammatory arthropathy, prior shoulder surgery, upper extremity entrapment neuropathy, polyneuropathy, diabetes mellitus, or use of centrally acting analgesics (e.g., pregabalin, duloxetine, opioids) were excluded from the study. Patients with uncontrolled symptoms of CS syndromes (e.g., fibromyalgia, migraine) were also excluded. In contrast, those with mild or controlled symptoms were included to maintain ecological validity, as such comorbidities are common in chronic shoulder pain populations. A written informed consent was obtained from each patient. The study protocol was approved by the Başakşehir Çam and Sakura City Hospital Clinical Research Ethics Committee (Date: 06.06.2024, No: 2024-KAEK-11). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Assessments

Shoulder disorders were diagnosed through a combined evaluation of physical examination findings and imaging results. Rotator cuff tendon tears (complete or partial) were identified on MRI by increased signal intensity at the insertion sites of the supraspinatus and infraspinatus tendons. Subacromial impingement syndrome was diagnosed based on both MRI findings and a positive impingement test. The impingement sign was assessed using the Neer and Hawkins maneuvers and was considered positive when either test elicited pain.[2] Frozen shoulder (adhesive capsulitis) was diagnosed in patients with persistent pain and stiffness lasting longer than one month, restricted passive range of motion (ROM),

normal radiographs, and obliteration of the rotator interval or axillary recess on MRI.[19] Osteoarthritis was diagnosed when ≥ 1 osteoarthritic change was observed on anteroposterior radiographs based on the Samilson-Prieto classification.[20] Calcific tendinitis was diagnosed when calcifications were visible in the subacromial region on radiographs.[2]

Shoulder range of motion

The ROM was assessed with the patient seated. Flexion, abduction, and external rotation at 90° elbow flexion were measured in degrees using a goniometer. Internal rotation was evaluated by recording the highest spinal level reached with the thumb and then converting this level into a numerical value, as previously described: T1-T12 segments correspond to 1-12, L1-L5 to 13-17, and the sacral region to 18.[21]

Pain intensity

Pain intensity was evaluated using the Visual Analog Scale (VAS). Patients rated their average pain intensity during the previous month on a 0-10 scale, where 0 indicates no pain and 10 represents the worst imaginable pain.

Outcome measures

The primary outcome of this study was the presence of neuropathic pain, assessed using the Self-Leeds Assessment of Neuropathic Symptoms and Signs Pain Score (S-LANSS). This self-administered tool comprises five symptom-based items and two examination-based items. A total score of ≥ 12/24 indicates a predominant neuropathic pain component.[22] The Turkish version of S-LANSS has demonstrated strong validity and reliability.[23]

As secondary outcomes, CS-related symptoms were evaluated using the CSI. The CSI includes two parts: Part A (25 items) assessing symptoms associated with CS, and Part B evaluating central sensitivity syndromes. A Part A score of ≥ 40 indicates the presence of CS.[24] The Turkish validation of the CSI was performed by Düzce Keleş et al.[25]

Functional limitation was assessed using the Shoulder Pain and Disability Index (SPADI). This self-administered questionnaire evaluates pain (5 items) and disability (8 items) subscales. The total SPADI score is calculated as a weighted sum (50% pain, 80% disability), expressed as a percentage, where higher scores reflect greater disability.[26] The Turkish adaptation and validation were conducted by Bumin et al.[27]

Pain intensity, used as a secondary clinical parameter, was measured with the VAS as described above.

Statistical analysis

Study power analysis and sample size calculation were performed using the G*Power version 3.1.9.7 software (Heinrich Heine University Düsseldorf, Düsseldorf, Germany). Parameters were set as: effect size (Cohen's d) = 0.91, derived from Vrouva et al.,[17] $\alpha = 0.05$, $\beta = 0.05$ (power = 95%). The minimum required sample size was 54 participants (27 per group). Since 73 patients were ultimately included, the achieved power exceeded 0.95, confirming adequate statistical sensitivity for group comparisons.

Statistical analysis was performed using the IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality using the Shapiro-Wilk test. Normally distributed data were presented in mean ± standard deviation (SD), while non-normally distributed data were presented in median and interquartile range (IQR). Categorical variables were presented in number and frequency. Comparisons between two independent groups were conducted using the independent samples t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. Where appropriate, categorical variables were compared using the chi-square test or Fisher exact test. Correlations between continuous variables were assessed using Spearman's rank correlation coefficient. A p value of < 0.05 was considered statistically significant with 95% confidence interval (CI). As multiple comparisons were performed, the potential inflation of type 1 error was evaluated. Bonferroni correction was applied to adjust for multiple testing; however, the statistical significance of the main findings ($p < 0.05$) remained unchanged after correction. In addition, all p-values between 0.05 and 0.10 were interpreted with caution as representing only a trend toward significance.

RESULTS

The study included a total of 73 patients (28 male, 45 female; mean age: 54.89±10.24 years; range, 32 to 70 years). The mean body mass index (BMI) was 28.03±4.40 kg/m^2. Rotator cuff tears (37.0%) and impingement syndrome (32.9%) were the most common shoulder pathologies, followed by frozen shoulder (13.7%), glenohumeral osteoarthritis (12.3%), and calcific tendinitis (4.1%). The mean duration of symptoms was 15.48±19.33 months, and the mean VAS score was 7.16±1.47. The mean SPADI score was 63.78±17.81, S-LANSS 7.29±6.53, and CSI-A 33.55±16.15.

Among comorbidities listed in CSI-B, the most frequently reported were restless leg syndrome (8.2%) and tension-type headache or migraine (8.2%), while neck injury and multiple chemical sensitivity were not reported. Demographic and clinical characteristics are summarized in Table 1.

The primary outcome of this study was the presence of neuropathic pain, as determined using the S-LANSS scale. Totally 19 (26.0%) patients were classified as having neuropathic pain (S-LANSS > 12), while 54 (74.0%) were not (S-LANSS < 12). Neuropathic pain was significantly more frequent among females (84.2% *vs.* 53.7%, $p = 0.019$). Patients with neuropathic pain tended to be younger than those without it (49.89±10.66 *vs.* 56.65±9.58 years, $p = 0.023$), indicating a trend toward statistical significance. In addition, SPADI scores were higher in the neuropathic group ($p = 0.030$), indicating a borderline statistically significant difference and reflecting greater pain-related disability. The CSI-A scores were also higher ($p = 0.005$), indicating a clear association between neuropathic pain and CS. Other clinical parameters, including BMI, symptom duration, VAS pain scores, ROM, and comorbidities such as diabetes mellitus, hypertension, pulmonary disease, and malignancy, did not differ significantly between the groups (Table 2).

The patients were further divided into two groups according to CSI-A scores: Group 1 (no CS, < 40; n = 52) and Group 2 (CS present, ≥ 40; n = 21). Central sensitization was significantly more common among female participants (95.2% *vs.* 48.1%, $p < 0.001$). Hypertension was also more prevalent in the CS group (57.1% *vs.* 21.2%, $p = 0.003$). The CS group also exhibited longer symptom duration ($p = 0.038$), higher VAS scores ($p = 0.011$), and higher S-LANSS scores ($p = 0.018$). While the differences in VAS and S-LANSS scores were statistically significant, the longer symptom duration showed a borderline significance and should be interpreted cautiously.

Table 1. Patient demographics and clinical variables

Variables	n	%	Mean±SD
Age (year)			54.9±10.2
Sex			
Female	45	61.6	
Male	28	38.4	
BMI (kg/m^2)			28±4.4
Shoulder diseases (%)			
Adhesive capsulitis	10	13.7	
Rotator cuff tears	27	37.0	
Glenohumeral osteoarthritis	9	12.3	
Calcific tendinitis	3	4.1	
Impingement syndrome	24	32.9	
Symptom duration (month)			15.48±19.3
VAS pain			7.16±1.5
Total SPADI score			63.8±17.8
S-LANSS			7.3±6.5
CSI-A			33.5±16.1
CSI-B (%)			
Restless leg syndrome	6	8.2	
Chronic fatigue syndrome	5	6.8	
Fibromyalgia syndrome	2	2.7	
TMD	1	1.4	
Tension headaches/migraines	6	8.2	
Irritable bowel syndrome	2	2.7	
Anxiety or panic attacks	2	2.7	
Depression	2	2.7	

SD, standard deviation; BMI, body mass index; VAS, Visual Analog Scale; SPADI, The Shoulder Pain and Disability Index; S-LANSS, Self-Leeds Assessment of Neuropathic Symptoms & Signs Pain Score; CSI, central sensitization inventory; TMD, temporomandibular disorders.

Table 2. Comparison of variables between patients with and without neuropathic pain (LANSS groups)

	S-LANNS < 12 (n = 54)			S-LANNS > 12 (n = 19)			
Variables	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			56.65±9.5			49.89±10.7	**0.023***
Sex							**0.019***
Female	29	53.7		16	84.2		
Male	25	46.3		3	15.8		
BMI (kg/m^2)			28.03±4.4			28.02±4.4	0.855
Comorbidities (%)							
Diabetes mellitus	17	31.5		6	31.6		0.994
Hypertension	16	29.6		7	36.9		0.561
Coronary artery disease	9	16.7		0	0		0,057
Pulmonary disease	4	7.4		2	10.5		0.647
Malignancy	2	3.7		1	5.3		1.000
Symptom duration (month)			16.1±21.6			13.8±10.8	0.267
VAS pain			7.1±1.4			7.4±1.7	0.585
Total SPADI score			61.3±17.1			70.9±18.2	**0.030***
CSI-A			31.1±16.1			40.4±14.6	**0.005***
ROM							
Flexion			153.3±24.6			148.4±26.9	0.467
Abduction			150.6±29.5			147.1±31.1	0.660
External rotation			75.9±17			76.8±14.3	0.847
Internal rotation			9.1±3.9			8.7±3.5	0.761

S-LANSS, Self-Leeds Assessment of Neuropathic Symptoms & Signs Pain Score; SD, standard deviation; BMI, body mass index; VAS, Visual Analog Scale; SPADI, The Shoulder Pain and Disability Index; CSI, central sensitization inventory; ROM, range of motion. Independent-samples t-test or Mann-Whitney U test for continuous data; Chi-square test for categorical data. * $p < 0.05$.

Table 3. Comparison of variables between patients with and without central sensitization (CSI-A groups)

	CSI < 40 (n = 52)			CSI > 40 (n = 21)			
Variables	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			54.7±9.4			55.2±12.4	0.976
Sex							**< 0.001***
Female	25	48.1		20	95.2		
Male	27	51.9		1	4.8		
BMI (kg/m^2)			28.4±4.2			27.1±4.7	0.354
Comorbidities (%)							
Diabetes mellitus	14	26.9		9	42.9		0.185
Hypertension	11	21.2		12	57.1		**0.003***
Coronary artery disease	5	9.6		4	19.0		0.267
Pulmonary disease	4	7.7		2	9.5		1
Malignancy	2	3.8		1	4.8		1
Symptom duration (month)			14.7±20.8			17.3±15.4	**0.038***
VAS pain			6.9±1.4			7.8±1.5	**0.011***
Total SPADI score			62.2±18.7			67.7±15.1	0.166
S-LANSS			6.1±6.1			10.2±6.7	**0.018***
ROM							
Flexion			150.6±24.7			155.7±26.6	0.347
Abduction			147.0±31.1			156.2±25.6	0.263
External rotation			74.9±17.2			79.3±13.3	0.361
Internal rotation			9.3±4			8.2±3.1	0.307

CSI, central sensitization inventory; SD, standard deviation; BMI, body mass index; VAS, Visual Analog Scale; SPADI, The Shoulder Pain and Disability Index; S-LANSS, Self-Leeds Assessment of Neuropathic Symptoms & Signs Pain Score; ROM, range of motion. Independent-samples t-test or Mann-Whitney U test for continuous data; Chi-square test for categorical data. * $p < 0.05$.

These findings indicate a notable overlap between nociplastic and neuropathic pain mechanisms. No statistically significant differences were found in age, BMI, coronary artery disease, pulmonary disease, malignancy, SPADI, or ROM values between the groups (Table 3).

The overall mean SPADI score was 63.78±17.81. Patients with neuropathic pain had significantly higher SPADI scores compared with those without neuropathic pain (p = 0.030). Moreover, the coexistence of neuropathic pain and CS was associated with the highest disability levels; patients with both conditions had significantly higher SPADI scores (69.80±15.43 *vs.* 59.58±18.31, p = 0.011) (Figure 2). A detailed comparison of SPADI values according to pain mechanisms is presented in Table 3.

The mean VAS score in the overall cohort was 7.16±1.47. The patients with CS reported significantly higher VAS pain scores than those without (p = 0.011). No statistically significant difference in VAS was observed between the neuropathic and non-neuropathic pain groups.

The Spearman correlation analysis demonstrated significant associations among the primary clinical variables. The CSI-A scores exhibited moderate positive correlations with S-LANSS (r = 0.38, 95% CI: 0.16-0.56, p = 0.001), VAS (r = 0.33, 95% CI: 0.11-0.52, p = 0.004), and symptom duration (r = 0.38, 95% CI: 0.15-0.54, p = 0.001). The S-LANSS scores showed moderate positive correlations with SPADI (r = 0.31, 95% CI: 0.09-0.50, p = 0.008) and symptom duration (r = 0.26, 95% CI: 0.02-0.48, p = 0.026), while they were weakly and negatively correlated with age (r = −0.27, 95% CI: −0.50 to −0.03, p = 0.024). A strong positive correlation was found between VAS and SPADI scores (r = 0.60, 95% CI: 0.43-0.73,

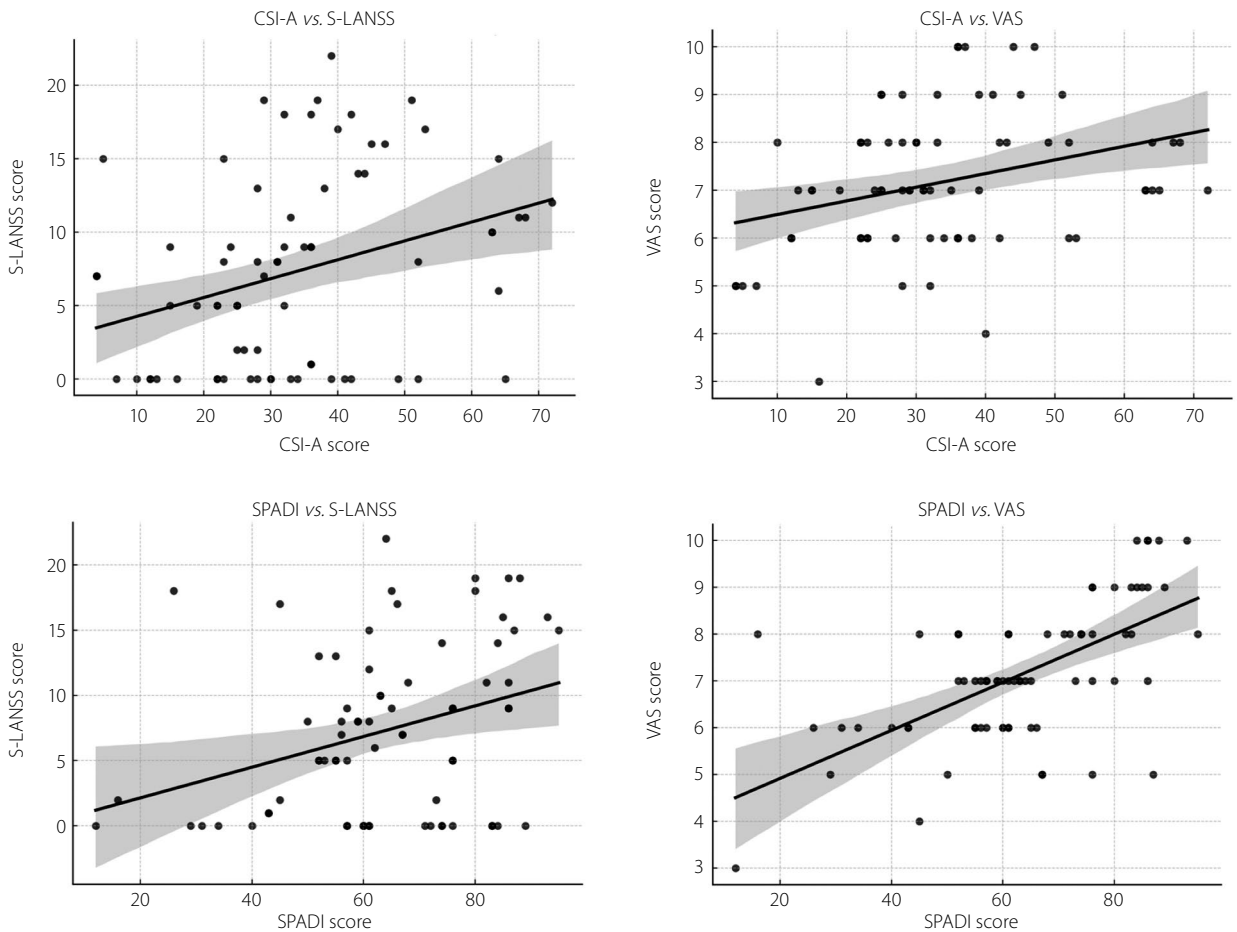

Figure 1. Correlation plots between CSI-A, S-LANSS, VAS, and SPADI scores.

CSI-A, Central Sensitization Inventory-Part A; S-LANSS, Self-Leeds Assessment of Neuropathic Symptoms & Signs Pain Score; VAS, Visual Analog Scale; SPADI, The Shoulder Pain and Disability Index.

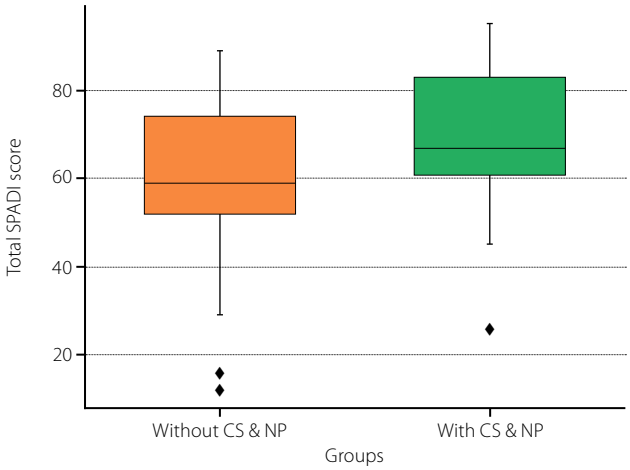

Figure 2. Comparison of SPADI scores between patients with and without CS & NP.

SPADI, The Shoulder Pain and Disability Index; CS, central sensitization; NP, neuropathic pain.

$p < 0.001$). No statistically significant correlations were observed between SPADI and CSI-A (r = 0.20, 95% CI: −0.04-0.41, $p = 0.090$) or between VAS and symptom duration (r = 0.15, 95% CI: −0.09-0.37, $p = 0.198$).

A multiple linear regression analysis was conducted to identify independent predictors of functional disability (SPADI). The model included S-LANSS, CSI-A, VAS, and sex (coded as 1 = female, 2 = male) as independent variables. The overall model was statistically significant ($p < 0.001$) and explained 43.2% of the variance in SPADI scores (adjusted $R^2 = 0.432$).

The VAS (β = 0.59, $p < 0.001$) and S-LANSS (β = 0.26, $p = 0.005$) were independent positive predictors of higher disability, whereas CSI-A (β = −0.29, $p = 0.008$) showed an inverse relationship with SPADI scores. Sex (β = −0.31, $p = 0.004$) also remained significant, indicating higher SPADI scores among female participants. These findings showed that pain intensity, neuropathic pain features, and sex were significant determinants of shoulder-related disability, whereas the contribution of CS appeared inverse and weaker (Table 4).

DISCUSSION

In the present study, we investigated the prevalence of neuropathic pain in patients with shoulder pain, its associated clinical factors, and its potential relationship with nociplastic pain, as assessed through CS. Our study findings showed that neuropathic pain was common among patients with non-traumatic shoulder disorders and was significantly associated with nociplastic pain. However, disability was found to be more strongly related to neuropathic pain than to nociplastic pain. These results suggest that although these pain mechanisms overlap, they have distinct clinical implications. Nociplastic pain appears to amplify pain intensity, while neuropathic pain contributes more directly to functional impairment. Vrouva et al.[17] previously reported a positive correlation between neuropathic pain and SPADI scores, indicating that patients with neuropathic pain tend to have higher disability scores. Similarly, our study found that patients with neuropathic pain exhibited higher disability scores, whereas no significant relationship was observed between nociplastic pain and functional impairment.

Previous studies have shown an association between neuropathic pain and rotator cuff tears in shoulder disorders.[9,11] In a study by Sasaki et al.,[10] the prevalence of neuropathic pain among patients with non-traumatic shoulder disorders was reported to be 7.6%, based on an assessment of neuropathic pain characteristics. In contrast, our study found a

Table 4. Multiple linear regression analysis predicting SPADI scores

Predictor	B	β	t	*p* value	95% CI (Lower-Upper)	VIF
Constant	33.435	-	3.022	0.004	11.356 to 55.514	-
S-LANSS	0.696	0.255	2.869	0.005	0.212 to 1.179	1.126
CSI-A	−0.315	−0.286	−2.734	0.008	−0.545 to −0.085	1.557
VAS	7.151	0.591	6.640	<0.001	5.002 to 9.301	1.131
Sex	−11.126	−0.306	−3.009	0.004	−18.505 to −3.746	1.475

SPADI, The Shoulder Pain and Disability Index; B, unstandardized regression coefficient; β, standardized regression coefficient; t, test statistic for the null hypothesis that B = 0; 95% CI, confidence interval for the regression coefficient; VIF, variance inflation factor indicating multicollinearity. Multiple linear regression analysis with SPADI as the dependent variable. S-LANSS, Self-Leeds Assessment of Neuropathic Symptoms & Signs Pain Score; CSI, central sensitization inventory; VAS, Visual Analog Scale.

prevalence of 26%, which may be attributed to the higher proportion of frozen shoulder and rotator cuff tear patients in our sample, conditions that are more likely to present with neuropathic pain. Additionally, Sasaki et al.[10] did not assess comorbidities such as diabetes, smoking, or alcohol consumption, which may have influenced their findings. In contrast, our study evaluated these variables and found no significant differences between patient groups regarding these factors.

The reported prevalence of CS in patients with chronic non-traumatic shoulder pain varies significantly in the literature. Studies using the CSI have estimated the prevalence of CS in shoulder pain to be 47.5% in one study and 15.6% in another.[3,16] A study conducted in the Turkish population reported a CS prevalence of 57.5% among patients presenting with shoulder pain.[18] In our study, CS was identified in 28.8% of patients. The finding that female patients had higher CSI scores is consistent with the experimental study by Guekos et al.,[28] which demonstrated that women are more prone to CS than men, possibly due to differences in spinal and supraspinal mechanisms. Key contributing factors to higher CS prevalence in women included increased excitability of dorsal horn neurons, less effective serotonergic and noradrenergic inhibitory pathways, and hormonal modulation of pain perception. These neurobiological factors contribute to enhanced pain sensitivity and explain the sex-related variation in nociplastic pain expression.

Although nociplastic pain and CS are closely related, they represent distinct concepts. According to the IASP 2021 criteria, CS refers to the neurophysiological amplification of pain signaling within the central nervous system, whereas nociplastic pain represents the clinical manifestation of this process in the absence of clear tissue or nerve damage.[5,6] In chronic shoulder pain, repetitive nociceptive input and low-grade inflammation may trigger CS, which over time can lead to a nociplastic pain phenotype. This transition explains why some patients continue to experience pain and disability even after the resolution of local pathology or completion of conventional treatment.

Peripheral sensitization may also serve as a biological bridge between nociceptive, neuropathic, and nociplastic mechanisms. Persistent peripheral input can enhance dorsal horn excitability and disrupt descending inhibitory control, facilitating the spread of pain sensitivity beyond the initial site of injury. This interaction between peripheral and central processes supports the view that chronic shoulder pain represents a mechanistic continuum rather than distinct categories.

Although previous studies have reported a direct association between CS and functional impairment,[16,18] this relationship was not observed in our study. Several factors may explain this discrepancy. The SPADI measures both pain intensity and functional impairment, but it may be more sensitive to peripheral mechanisms than to CS, thereby weakening its correlation with CS. While CS amplifies pain perception, it does not always lead to overt functional deficits, which may explain the lack of a significant correlation between SPADI scores and CS. Furthermore, psychosocial variables such as depression, anxiety, kinesiophobia, and pain catastrophizing, factors known to influence CS, were not evaluated in this study. Their absence may have contributed to the observed findings and represents a potential limitation.

The introduction of nociplastic pain into pain research has led to a paradigm shift in understanding and managing chronic pain. This shift enables clinicians to view pain not only as a local musculoskeletal condition, but also as a manifestation of altered central processing. The finding that patients with both neuropathic and nociplastic pain exhibited significantly higher SPADI scores compared to those without these mechanisms suggests that the coexistence of these two pain mechanisms has a greater impact on functional impairment. Furthermore, the significant differences in VAS scores and symptom duration between patients with and without CS indicate that CS may enhance pain perception and contribute to pain chronicity. Prolonged pain experience, particularly in patients with a nociplastic component, may reinforce central pain mechanisms and lead to increased subjective pain intensity, highlighting the importance of considering both peripheral and central mechanisms in the evaluation and management of chronic shoulder pain.[18]

One of the main limitations of this study is the use of only the CSI for evaluating CS. Given the fluctuating nature of CS-related symptoms, a cross-sectional design with a single cut-off value may lead to false-positive or false-negative classifications.[6] In addition, the cross-sectional nature of the study prevents causal inferences regarding the observed relationships between pain mechanisms and clinical outcomes. Another limitation is the incomplete representation of all subtypes of shoulder pain in the sample, which may

restrict the generalizability of the findings. Despite these limitations, the main strengths of this study include its focus on the most common non-traumatic shoulder pain subtypes encountered in clinical practice, an adequate sample size in each subgroup, and a comprehensive evaluation of neuropathic and nociplastic pain-related characteristics in chronic pain populations.

In conclusion, our study results suggest that neuropathic and nociplastic pain mechanisms are frequently observed in patients with non-traumatic shoulder pain and are associated with both pain intensity and functional limitation. The presence of CS is significantly related to higher VAS scores and longer symptom duration. However, functional impairment appears to be more closely associated with neuropathic pain than with nociplastic pain. These findings suggest that neuropathic and nociplastic pain may coexist and interact in complex ways, contributing to the overall burden of chronic shoulder pain. While the study design does not allow for conclusions about causality, the observed associations highlight the importance of assessing both peripheral and central pain mechanisms in clinical practice. A multidisciplinary and mechanism-based approach that considers neuropathic components, nociplastic features, and psychosocial factors may be beneficial for optimizing patient outcomes. Interventions aimed at modulating CS should be complemented by strategies that address functional restoration and quality of life.

Author Contributions

D.F., Z.R.Y.T.: Conception; Z.R.Y.T., T.Ş.: Design; D.F., E.K.: Supervision; Z.R.Y.T., E.K., D.F., B.S: Materials; B.S., D.F., E.K.: Data collection and/or processing; T.Ş.: Analysis and/or interpretation; D.F., T.Ş.: Literature review; D,F., B.S.: Writer; D.F., T.Ş., B.Ş.: Critical review.

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The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Struyf F, Geraets J, Noten S, Meeus M, Nijs J. A multivariable prediction model for the chronification of non-traumatic shoulder pain: A systematic review. Pain Physician 2016;19:1-10.
2. Hodgetts C, Walker B. Epidemiology, common diagnoses, treatments and prognosis of shoulder pain: A narrative review. Int J Osteopath Med 2021;42:11-9.
3. Bilika P, Nijs J, Fandridis E, Dimitriadis Z, Strimpakos N, Kapreli E. In the shoulder or in the brain? Behavioral, psychosocial and cognitive characteristics of unilateral chronic shoulder pain with symptoms of central sensitization. Healthcare (Basel) 2022;10:1658. doi: 10.3390/healthcare10091658.
4. Şirin Ahısha B, Paker N, Kesiktaş N, Buğdayci ND, Ahısha YC. Evaluation of inadequate response to ultrasound-guided subacromial corticosteroid injection in shoulder impingement syndrome: Treatment failure or central sensitization? Arch Phys Med Rehabil 2025;106:1227-37. doi: 10.1016/j.apmr.2025.01.469.
5. Kosek E, Clauw D, Nijs J, Baron R, Gilron I, Harris RE, et al. Chronic nociplastic pain affecting the musculoskeletal system: Clinical criteria and grading system. Pain 2021;162:2629-34. doi: 10.1097/j.pain.0000000000002324.
6. Fitzcharles MA, Cohen SP, Clauw DJ, Littlejohn G, Usui C, Häuser W. Nociplastic pain: Towards an understanding of prevalent pain conditions. Lancet 2021;397:2098-110. doi: 10.1016/S0140-6736(21)00392-5.
7. Kosek E, Cohen M, Baron R, Gebhart GF, Mico JA, Rice ASC, et al. Do we need a third mechanistic descriptor for chronic pain states? Pain 2016;157:1382-6. doi: 10.1097/j.pain.0000000000000507.
8. Kosek E. The concept of nociplastic pain-where to from here? Pain 2024;165:S50-7. doi: 10.1097/j.pain.0000000000003305.
9. Karasugi T, Ide J, Kitamura T, Okamoto N, Tokunaga T, Mizuta H. Neuropathic pain in patients with rotator cuff tears. BMC Musculoskelet Disord 2016;17:451. doi: 10.1186/s12891-016-1311-5.
10. Sasaki T, Shitara H, Tajika T, Ichinose T, Hamano N, Kamiyama M, et al. Relationship between nontraumatic shoulder disorders and neuropathic pain: Retrospective observational analyses of clinical features and background factors. Anesthesiol Res Pract 2023;2023:6046746. doi: 10.1155/2023/6046746.
11. Ko S, Choi C, Kim S, Chae S, Choi W, Kwon J. Prevalence and risk factors of neuropathic pain in patients with a rotator cuff tear. Pain Physician 2018;21:E173-80.
12. Nijs J, Lahousse A, Kapreli E, Bilika P, Saraçoğlu İ, Malfliet A, et al. Nociplastic pain criteria or recognition of central sensitization? Pain phenotyping in the past, present and future. J Clin Med 2021;15:3203. doi: 10.3390/jcm10153203.
13. Tanaka K, Murata S, Nishigami T, Mibu A, Manfuku M, Shinohara Y, et al. The central sensitization inventory predict pain-related disability for musculoskeletal disorders in the primary care setting. Eur J Pain 2019;23:1640-8. doi: 10.1002/ejp.1443.
14. Sanchis MN, Lluch E, Nijs J, Struyf F, Kangasperko M. The role of central sensitization in shoulder pain: A systematic literature review. Semin Arthritis Rheum 2015;44:710-6. doi: 10.1016/j.semarthrit.2014.11.002.
15. Smart KM, Blake C, Staines A, Doody C. Self-reported pain severity, quality of life, disability, anxiety and depression in patients classified with 'nociceptive', 'peripheral neuropathic' and 'central sensitisation' pain. The discriminant validity of mechanisms-based classifications of low back (±leg) pain. Man Ther 2012;17:119-25. doi: 10.1016/j.math.2011.10.002.
16. Walankar PP, Panhale VP, Patil MM. Psychosocial factors, disability and quality of life in chronic shoulder pain patients with central

sensitization. Health Psychol Res 2020;8:8874. doi: 10.4081/hpr.2020.8874.

17. Vrouva SD, Sopidou VK, Chanopoulos KP, Bakalidou DF, Papatsimpas VC, Sorras N, et al. Is shoulder pain and disability index a prognostic factor for neuropathic shoulder pain? Cureus 2021;13:e19173. doi: 10.7759/cureus.19173.
18. Yücel FN, Sanal-Toprak C. Central sensitization-related symptoms and their relationship to disability in prevalent chronic musculoskeletal pain: A cross-sectional study. Musculoskelet Sci Pract 2024;73:103147. doi: 10.1016/j.msksp.2024.103147.
19. de Angelis Guerra Dotta T, Assunção JH, Baptista E, E Silva FBA, Gracitelli MEC, Neto AAF, et al. Diagnostic accuracy of non-contrast MRI in frozen shoulder. Arch Orthop Trauma Surg 2024;144:1149-59. doi: 10.1007/s00402-023-05184-3.
20. Elsharkawi M, Cakir B, Reichel H, Kappe T. Reliability of radiologic glenohumeral osteoarthritis classifications. J Shoulder Elbow Surg 2013;22:1063-7. doi: 10.1016/j.jse.2012.11.007.
21. Hamano N, Yamamoto A, Shitara H, Ichinose T, Shimoyama D, Sasaki T, et al. Does successful rotator cuff repair improve muscle atrophy and fatty infiltration of the rotator cuff? A retrospective magnetic resonance imaging study performed shortly after surgery as a reference. J Shoulder Elbow Surg 2017;26:967-74. doi: 10.1016/j.jse.2016.10.016.
22. Bennett M. The LANSS Pain Scale: The Leeds assessment of neuropathic symptoms and signs. Pain 2001;92:147-57. doi: 10.1016/s0304-3959(00)00482-6.
23. Koc R, Erdemoglu AK. Validity and reliability of the Turkish Self-administered Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) questionnaire. Pain Med 2010;11:1107-14. doi: 10.1111/j.1526-4637.2010.00837.x.
24. Neblett R, Hartzell MM, Mayer TG, Cohen H, Gatchel RJ. Establishing clinically relevant severity levels for the central sensitization inventory. Pain Pract 2017;17:166-75. doi: 10.1111/papr.12440.
25. Düzce Keleş E, Birtane M, Ekuklu G, Kılınçer C, Çalıyurt O, Taştekin N, et al. Validity and reliability of the Turkish version of the central sensitization inventory. Arch Rheumatol 2021;36:518-26. doi: 10.46497/ArchRheumatol.2022.8665.
26. Roach KE, Budiman-Mak E, Songsiridej N, Lertratanakul Y. Development of a shoulder pain and disability index. Arthritis Care Res 1991;4:143-9.
27. Bumin G, Tüzün EH, Tonga E. The Shoulder Pain and Disability Index (SPADI): Cross-cultural adaptation, reliability, and validity of the Turkish version. J Back Musculoskelet Rehabil 2008;21:57-62.
28. Guekos A, Saxer J, Salinas Gallegos D, Schweinhardt P. Healthy women show more experimentally induced central sensitization compared with men. Pain 2024;165:1413-24. doi: 10.1097/j.pain.0000000000003144.