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Post-traumatic complex regional pain syndrome type 1: Risk factors and the potential clinical relevance of magnesium depletion score

Posttravmatik kompleks bölgesel ağrı sendromu tip 1: Risk faktörleri ve magnezyum deplesyon skorunun olası klinik önemi

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ABSTRACT

Background: This study aimed to evaluate whether the magnesium depletion score (MDS), an indicator of magnesium deficiency, is associated with the development of complex regional pain syndrome type 1 (CRPS-1) in patients with traumatic extremity injuries.

Patients and Methods: Between November 2024 and May 2025, a total of 117 patients who suffered from traumatic extremity injuries were included. Demographic and clinical data of the patients were collected and recorded, and the MDS was calculated. Age, sex, body mass index (BMI), smoking status, alcohol consumption, diabetes, hypertension, duration of immobilization, MDS, and injury-related characteristics were evaluated as potential risk factors for CRPS-1 development.

Results: Of the patients, 40 were male and 77 were female with a mean age of 51.9 ± 15.01 (range, 20 to 91 years). In a total of 42.7% of patients with traumatic extremity injuries, CRPS-1 developed. The female-to-male ratio was higher among patients with CRPS-1 than among those without. The MDS, hypertension, diabetes, smoking, and alcohol consumption were not found to be independent risk factors. However, prolonged immobilization (more than one month) was found to be an independent risk factor for the development of CRPS-1.

Conclusion: Our study results suggest that the MDS score is not a risk factor for developing CRPS-1, but immobilization for more than one month significantly increases the risk. Taken together, these findings indicate that the duration of immobilization following injury may be a more decisive factor in the development of CRPS-1 than demographic and clinical characteristics.

Keywords: Arm injuries, complex regional pain syndromes, immobilization, leg injuries, magnesium deficiency.

ÖZ

Amaç: Bu çalışmada, travmatik ekstremite yaralanması olan hastalarda magnezyum eksikliğinin bir göstergesi olan magnezyum deplesyon skoru (MDS) ile kompleks bölgesel ağrı sendromu tip 1 (CRPS-1) gelişimi arasında bir ilişki olup olmadığı değerlendirildi.

Hastalar ve Yöntemler: Kasım 2024 ile Mayıs 2025 tarihleri arasında travmatik ekstremite yaralanması geçiren toplam 117 hasta çalışmaya dahil edildi. Hastaların demografik ve klinik verileri toplandı ve kaydedildi; MDS hesaplandı. Yaş, cinsiyet, vücut kitle indeksi (VKİ), sigara kullanımı, alkol tüketimi, diyabet, hipertansiyon, immobilizasyon süresi, MDS ve yaralanmaya ilişkin özellikler, CRPS-1 gelişimi açısından muhtemel risk faktörleri olarak değerlendirildi.

Bulgular: Hastaların 40'sı erkek, 77'si kadın olup, yaş ortalaması 51.9 ± 15.01 (aralık, 20-91) yıl idi. Travmatik ekstremite yaralanması olan hastaların toplam %42.7'sinde CRPS-1 gelişti. CRPS-1 gelişen hastalarda kadın-erkek oranı, CRPS-1 gelişmeyen hastalara kıyasla daha yüksekti. Magnezyum deplesyon skoru, hipertansiyon, diyabet, sigara kullanımı ve alkol tüketimi, CRPS-1 gelişimi açısından bağımsız risk faktörleri olarak saptanmadı. Buna karşın, uzamış immobilizasyon süresi (bir aydan uzun), CRPS-1 gelişimi için bağımsız bir risk faktörü olarak belirlendi.

Sonuç: Çalışma sonuçlarımız, MDS'nin CRPS-1 gelişimi için bir risk faktörü olmadığını, buna karşın bir aydan uzun süreli immobilizasyonun riski anlamlı düzeyde artırdığını göstermektedir. Bu bulgular birlikte değerlendirildiğinde, yaralanma sonrası immobilizasyon süresinin, CRPS-1 gelişiminde demografik ve klinik özelliklerden daha belirleyici bir faktör olabileceğine işaret etmektedir.

Anahtar sözcükler: Kol yaralanmaları, kompleks bölgesel ağrı sendromu, immobilizasyon, bacak yaralanmaları, magnezyum eksikliği.

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Complex regional pain syndrome type 1 (CRPS-1) is a clinical condition which typically follows trauma or surgery. It is characterized by neuropathic pain, as well as sensory, motor, autonomic, and trophic disorders, affecting quality of life adversely.[1] While its exact pathophysiology still remains unclear, inflammatory and immune responses, vasomotor dysfunction, nervous system changes, and psychosocial factors are believed to contribute to its development.[1,2] Although rare, CRPS-1 can lead to significant limitations in daily living activities and work capacity.[1,3] Various risk factors have been identified in the literature, including female sex, high-energy fractures, nerve damage, carpal tunnel surgery, severe post-traumatic pain, migraine, fibromyalgia, asthma, and rheumatoid arthritis.[4-10]

Abnormal inflammation following trauma, together with peripheral and central sensitization, is usually considered to play a fundamental role in the development of CRPS-I.[11] The increased release of proinflammatory mediators can enhance pain sensitivity in the central nervous system by activating N-methyl-D-aspartate (NMDA) receptors.[12-14] Magnesium is a physiological antagonist that inhibits NMDA receptors and is used as an additional analgesic in the treatment of neuropathic pain.[15] While some studies have reported positive effects of magnesium treatment on pain, function, and quality of life in CRPS-1 patients, these findings have not been consistently demonstrated in chronic cases.[16,17]

It is well established that serum magnesium levels alone are insufficient for determining an individual's actual magnesium status, as they reflect only a small proportion of total body magnesium.[18] Therefore, although the magnesium tolerance test (MTT) is widely recognized as the most reliable method of assessing magnesium status, it is not widely used in clinical practice due to practical difficulties. The Magnesium Depletion Score (MDS), which was developed as an alternative, has been shown to correlate well with MTT-confirmed magnesium deficiency in individuals.[19]

Various neurodegenerative diseases and neuroinflammation have been shown to be associated with magnesium deficiency.[20] However, the literature provides insufficient evidence to determine whether magnesium deficiency plays a role in the development of CRPS-1. In the present study, we hypothesized that magnesium deficiency might be a risk factor in the development of CRPS-1. We, therefore, aimed to investigate whether magnesium deficiency, as assessed by MDS, was associated with the development of CRPS-1 in patients with traumatic extremity injuries and to identify other potential risk factors that may contribute to CRPS-1 development.

PATIENTS AND METHODS

This single-center, cross-sectional, clinical study was conducted at Cemil Taşcıoğlu City Hospital, Department of Physical Medicine and Rehabilitation between November 2024 and May 2025. Eligible patients aged 18 years and older who presented to our clinic for rehabilitation following traumatic extremity injuries were reviewed. Patients who previously experienced CRPS-1, had chronic pain disorders, severe heart/liver failure, cognitive impairment, or were taking vitamin C supplements were excluded. Of a total of 140 patients presenting with traumatic extremity injuries, 117 were included in the study. Twenty-three patients were excluded: 15 due to the absence of renal function tests within the past three months, five due to vitamin C supplementation, one due to a history of fracture and CRPS-1 in the same extremity, and one due to refusal to participate in the study. Finally, a total of 117 patients who met the inclusion criteria were recruited. Medical histories and data relating to the current injury were recorded for all participants. A CRPS-1 diagnosis was made according to the Budapest criteria, which have a high sensitivity (0.99) and specificity (0.68).[21,22] A written informed consent was obtained from each patient. The study protocol was approved by the Medipol University Ethics Committee (Date: 13.12.2024, No. 1222). The study was conducted in accordance with the principles of the Declaration of Helsinki. The study was registered at ClinicalTrials.gov (NCT: 07093424).

In the study, age, sex, body mass index (BMI), smoking and alcohol consumption, diabetes, hypertension, proton pump inhibitor (PPI) and diuretic use, affected extremity, injury type and tissue type (fracture, tendon rupture, nerve injury), immobilization duration and factors associated with MDS were recorded. The MDS scoring system evaluated diuretic use (1 point), PPI use (1 point), excessive alcohol consumption (1 point), estimated glomerular filtration rate (eGFR) of ≥ 90 mL/min (0 points), 60- 89 mL/min (1 point), and <60 mL/min (2 points).[19]

Statistical analysis

Power analysis and sample size calculation were performed using the G*Power version 3.1 software

(Heinrich Heine University Düsseldorf, Düsseldorf, Germany). For the one-way logistic regression model, with α set to 0.05, power set to 0.80, an odds ratio (OR) of 2.96 and a probability (P) of 0.20 of Y = 1 given X = 0, the minimum required sample size was calculated to be 67 individuals.[23]

Statistical analysis was performed using the IBM SPSS for Windows version 23.0 software (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was evaluated using the Shapiro-Wilk test and visual methods (histograms and Q-Q plots). Continuous variables were presented in mean ± standard deviation (SD) or median (min-max), while categorical variables were presented in number and frequency. Between-group comparisons of continuous variables were conducted using the independent-samples t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. The distribution of categorical variables between groups was analyzed using the Fisher exact test or the Yate's corrected or Pearson chi-square test, as appropriate. A p value of < 0.05 was considered statistically significant. Logistic regression analysis was used to determine factors associated with CRPS-1. Age, sex, BMI, smoking, alcohol consumption, diabetes, hypertension, diuretic usage, PPI usage, injured extremity, injured tissue types, type of injury, fracture, surgery, tendon rupture, nerve damage, immobilization periods, MDS were the independent variables. Initially, a univariable analysis was performed. Statistically significant independent variables ($p < 0.10$) and potential risk factors reported in the literature for inclusion in the binary logistic regression analysis were entered into the model using forward selection method. The Hosmer-Lemeshow test was used to test the appropriateness of the regression model. Wald statistical analysis was used to determine the significance of the B coefficient. The discriminatory power of the variable was examined using a receiver operating characteristic (ROC) curve analysis of the data. The area under the curve

Table 1. Clinical characteristics and risk factors by CRPS-1 development

	CRPS-1 (–) (n = 67)			CRPS-1 (+) (n = 50)						
Variables	n	%	Mean ± SD	n	%	Mean ± SD	*p*	OR	95% CI	*p*
Age (year)			50.8 ± 15.7			50.5 ± 15.2	0.889*	0.998	0.975-1.002	0.887
BMI (kg/m^2)			27.9 ± 5.0			27.1 ± 5.4	0.379*	0.968	0.901-1.040	0.376
Immobilization duration (days)			34.1 ± 12.3			40.5 ± 15.8	**0.005†**	1.034	1.005-1.064	**0.021**
MDS			0.79 ± 0.91			0.72 ± 0.86	0.715†	0.912	0.601-1.386	0.667
Sex							0.468‡	1.389	0.636-3.035	0.410
Female		42			35					
Male		25			15					
Smoking							0.772‡	0.886	0.406-1.934	0.762
No	46				33					
Yes	21				17					
Alcohol consumption		9				8	0.654‡	0.815	0.290-2.286	0.697
Diabetes		11				6	0.606§	1.440	0.494-4.200	0.504
Hypertension		14				7	0.346§	0.616	0.228-1.663	0.339
Injured extremity							0.793‡	0.893	0.383-2.080	0.793
Upper		51			37					
Lower		6			13					
Fracture		61			42		0.245‡	1.937	0.626-5.989	0.251
Surgery		32			24		0.980‡	0.990	0.476-2.062	0.980
Mechanism of injury							0.855‡	1.131	0.302-4.242	0.855
Blunt trauma		61			46					
Sharp/penetrating		6			4					
Tendon rupture		5			5		0.627‡	1.378	0.376-5.044	0.628
Nerve injury		4			1		0.391§	3.111	0.337-28.728	0.317

CRPS-1, complex regional pain syndrome type 1; SD, standard deviation; OR, Odds ratio; CI, confidence interval; BDI, body mass index; MDS, magnesium depletion score; *, independent samples t-test; †, Mann-Whitney U-test; ‡, Chi-Squared test; §, Fisher exact test. The level of significance was set at $p < 0.05$. Statistical significance is shown in bold.

Table 2. Logistic regression analysis for CRPS-1 development

Independent variables	B	SE	Wald	df	*p*	OR	95% CI	
							Lower	Upper
Immobilisation duration (days)	0.034	0.015	5.330	1	0.021	1.034	1.005	1.064
Constant	-1.537	0.573	7.198	1	0.007	0.215		

CRPS-1, complex regional pain syndrome type 1; CI, confidence interval; B, regression coefficient; SE, standard error; df, degree of freedom; OR, odds ratio. Omnibus test of model coefficients: $p = 0.022$; Nagelkerke $R^2 = 0.089$; Hosmer-Lemeshow test: $p = 0.147$.

(AUC) was used to assess the test's classification performance. An AUC value greater than 0.5 indicates that the test performs better than random guessing. The optimal cut-off point was determined using the Youden index. A p value of < 0.05 was considered statistically significant with 95% confidence intervals (CIs) were calculated for the OR.

RESULTS

Of a total of 117 patients included in the study, 40 were male and 77 were female with a mean age of 51.9 ± 15.01 (range, 20 to 91 years). Table 1 shows the demographic, clinical and injury-related data of the patients. Accordingly, 91.5% experienced blunt trauma, 8.5% sustained injuries from sharp instruments and 75.2% had upper extremity injuries. Fractures accounted for 88% of injuries, tendon injuries for 8.5% and nerve injuries for 4.3%. Of those with fractures, 57% received conservative treatment. The CRPS-1 developed in 42.7% patients, including 41% with fractures. Localized osteopenia was detected in 50% of these patients.

Logistic regression analysis was performed including the risk factors most commonly associated with CRPS-1 development (i.e., advanced age, female sex, fracture, nerve injury, extremity trauma, surgery, and high BMI), immobilization duration, and MDS (Table 2). The immobilization period was found to be longer in patients who developed CRPS-1 than in those who did not, with prolonged immobilization increasing the risk of CRPS-1 by 1.034 times.

The ROC analysis was performed to determine the threshold value of immobilization duration associated with the development of CRPS-1. As shown in Figure 1, the AUC was 0.651 (95% confidence interval [CI]: 0.549-0.753; p = 0.005). A cut-off value of 28.5 days yielded a sensitivity of 86.0% and a specificity of 28.4%, with a positive likelihood ratio of 1.20 and a negative likelihood ratio of 0.49. These results indicate a limited discriminative ability of immobilization duration alone for predicting CRPS-1.

DISCUSSION

In the present study, we investigated the relationship between MDS, a composite clinical indicator reflecting risk factors for magnesium depletion, and the development of post-traumatic CRPS-1 in patients with traumatic extremity injuries. The main findings of this study were as follows: MDS was not identified as an independent risk factor for CRPS-1 development, while longer immobilization duration was associated with an increased risk of CRPS-1. These findings suggest that MDS may not be an appropriate standalone predictor of post-traumatic CRPS-1 in this patient population, whereas prolonged immobilization remains an important potentially modifiable risk factor.

Although the possible relationship between magnesium status and CRPS-1 is biologically plausible,

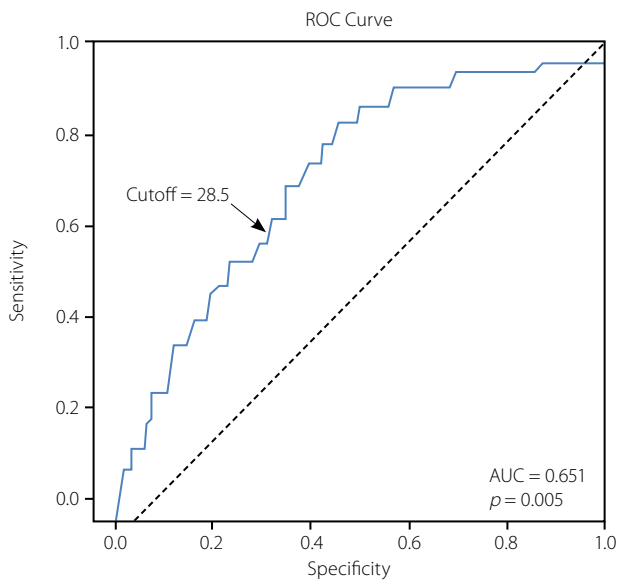

Figure 1. ROC curve for immobilization duration in predicting CRPS-1 development.

ROC, receiver operating characteristic; CRPS-1, complex regional pain syndrome type 1; AUC, area under the curve. ROC curve analysis of immobilization duration for predicting CRPS-1 development. The AUC was 0.651 (95% CI: 0.549–0.753; $p = 0.005$). A cut-off value of 28.5 days yielded a sensitivity of 86.0% and a specificity of 28.4%, with a positive likelihood ratio of 1.20 and a negative likelihood ratio of 0.49.

it remains insufficiently clarified. The CRPS-1 is a multifactorial pain disorder in which peripheral and central sensitization, neurogenic inflammation, autonomic dysregulation, altered microcirculation, and maladaptive neuroplasticity may contribute to symptom development and persistence.[1,11,24,25] Among these mechanisms, NMDA receptor-mediated nociceptive transmission has particular relevance. Experimental and clinical studies have shown that inflammatory processes may increase NMDA receptor activity at both peripheral and central levels, thereby facilitating neuronal hyperexcitability and pain amplification.[12-14,26] Magnesium is a physiological antagonist of NMDA receptors and may modulate nociceptive transmission, neuromuscular excitability, inflammatory responses, oxidative stress, and endothelial function.[15,20] Therefore, magnesium depletion could theoretically contribute to mechanisms involved in CRPS-1, particularly in the early post-traumatic period when inflammatory and sensitization-related processes are more active.

Previous clinical studies have also suggested a potential role for magnesium in CRPS-1 treatment, although the evidence is not definitive. Intravenous magnesium infusion was reported to improve pain and related symptoms in patients with acute CRPS-1 in a pilot study.[16] However, a subsequent study in patients with chronic CRPS-1 did not demonstrate superiority over placebo.[17] This discrepancy may indicate that magnesium-related mechanisms are more relevant in the early phase of CRPS-1 than in the chronic stage, where central reorganization and persistent maladaptive pain mechanisms may be more established. In the present study, the inclusion of both acute and chronic CRPS-1 patients may partly explain why MDS was not independently associated with CRPS-1 development. Since data on the exact interval between trauma and CRPS-1 onset were unavailable, we could not determine whether magnesium depletion risk was more relevant during the early phase of the disease.

To date, no studies have directly evaluated magnesium deficiency or the MDS as risk factors for the development of CRPS-1. Magnesium depletion score has been proposed as a clinical tool reflecting the cumulative burden of factors associated with magnesium depletion, including impaired renal function, diuretic use, PPI use, and alcohol consumption.[19] However, it should be emphasized that MDS is not a direct biochemical measurement of serum or intracellular magnesium concentration. In our study, neither MDS nor its individual components, including eGFR, diuretic use, chronic alcohol consumption, and PPI use, independently increased the risk of CRPS-1 in logistic regression analysis. These findings suggest that although magnesium depletion is mechanistically relevant to pain modulation, MDS alone may not be sufficient to identify patients at increased risk of post-traumatic CRPS-1. Future prospective studies should evaluate MDS together with biochemical magnesium measurements, dietary magnesium intake, and longitudinal clinical follow-up from the early post-traumatic period.

The relationship between medication use and CRPS-1 also deserves consideration. De Mos et al.[27] reported a significant association between chronic angiotensin-converting enzyme (ACE) inhibitor use and the onset of CRPS. One proposed explanation is that ACE inhibitors may influence neuroinflammatory or vascular pathways, and hypomagnesaemia secondary to increased magnesium excretion has also been discussed as a possible contributing mechanism. However, this remains hypothetical. In our study, MDS did not emerge as an independent predictor of CRPS-1, indicating that magnesium depletion risk, as captured by this score, should be interpreted as a potential associated clinical marker rather than a causal or independent risk factor.

In general, CRPS-1 develops after direct trauma, particularly following injuries of the hand and wrist, and fractures are among the most frequently reported triggering events.[25,28] Distal radius fractures, in particular, have been widely studied in relation to CRPS-1 development.[7,9] In the present study, fractures constituted the majority of traumatic extremity injuries, and more than half of the patients underwent cast immobilization. Although CRPS-1 developed frequently after fractures, neither fracture presence nor upper extremity injury was identified as an independent risk factor. In contrast, immobilization duration was associated with CRPS-1 development. The ROC curve analysis was conducted to determine the threshold value of this relationship and the AUC value was found to be 0.651, indicating that the variable has limited but statistically significant discriminatory power. The analysis suggested a threshold value of 28.5 days for CRPS-1 development; however, the relatively low specificity indicates that this cut-off alone may have limited value in clinical decision-making.

Several demographic and clinical risk factors for CRPS-1 have been reported in previous studies, including female sex, older age, upper extremity injury, high-energy trauma, intra-articular fracture,

and high early pain intensity.[5,8,10] However, the literature is not entirely consistent. While female sex has frequently been reported as a risk factor, some authors have suggested that this association may partly reflect the higher incidence of wrist fractures among women rather than a direct sex-specific predisposition.[29,30] De Mos et al.[27] reported an increased incidence of CRPS-1 in women with menstrual cycle-related disorders. In our study, female sex was not an independent risk factor. The absence of sex-related differences in our study may be attributed to the fact that most of the women included were postmenopausal. Similarly, age, hypertension, diabetes mellitus, smoking, and alcohol use were not independently associated with CRPS-1 development. These findings are consistent with previous reports showing that demographic and comorbidity-related predictors are not uniformly reproducible across CRPS-1 populations.[5,31,32] Taken together, our results suggest that immobilization duration may be a more clinically relevant and potentially modifiable factor than baseline demographic characteristics in post-traumatic CRPS-1 development.

Nonetheless, this study has several limitations that should be acknowledged. First, the retrospective design limits causal inference. Second, we did not have data on the exact time interval between trauma and CRPS-1 onset; therefore, we could not separately analyse acute and chronic CRPS-1 patients. This is particularly relevant for interpreting the possible role of magnesium depletion, as magnesium-related mechanisms may differ according to disease stage. Third, serum, erythrocyte, or intracellular magnesium levels were not measured, and MDS was used only as a clinical proxy for magnesium depletion risk. Fourth, psychological factors, including anxiety, depression, and personality traits, were not evaluated, although these factors may influence pain perception, recovery, and CRPS-related outcomes. Further prospective longitudinal studies beginning in the early post-traumatic period are needed to clarify whether magnesium depletion, biochemical magnesium status, immobilization duration, and early pain severity interact in the development of CRPS-1.

In conclusion, our study results suggest that MDS is not an independent risk factor for the development of post-traumatic CRPS-1. However, longer immobilization duration can be associated with increased CRPS-1 risk, with a threshold of approximately one month showing limited but statistically significant discriminatory value. Taken together, these findings suggest that early and controlled mobilization during post-traumatic rehabilitation may be clinically important in reducing CRPS-1 risk. Despite the biological plausibility of magnesium depletion in the pathogenesis of CRPS-1, its role should be confirmed in well-designed prospective studies employing direct biochemical measurements of magnesium status and longitudinal follow-up.

Author Contributions

D.E.Z., S.A., E.D., B.Ö., M.Z., İ.K., Ö.K.: Concept; D.E.Z., S.A., E.D., M.Z.: Design; S.A., E.D., M.Z., Ö.K.: Supervision; D.E.Z., M.Z., B.Ö.: Resources, materials, data collection and/or processing; D.E.Z., E.D., M.Z., İ.K.: Analysis and/or interpretation; D.E.Z., B.Ö., M.Z., S.A., İ.K.: Literature review; D.E.Z., B.Ö., M.Z., S.A., E.D., İ.K.: Writing-original draft; D.E.Z., B.Ö., S.A., E.D., M.Z., İ.K., Ö.K.: Critical review.

Conflict of Interest

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Data Sharing Statement

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

AI Disclosure

The authors declare that artificial intelligence (AI) tools were not used, or were used solely for language editing, and had no role in data analysis, interpretation, or the formulation of conclusions. All scientific content, data interpretation, and conclusions are the sole responsibility of the authors. The authors further confirm that AI tools were not used to generate, fabricate, or 'hallucinate' references, and that all references have been carefully verified for accuracy.

REFERENCES

1. Ferraro MC, O'Connell NE, Sommer C, Goebel A, Bultitude JH, Cashin AG, et al. Complex regional pain syndrome: Advances in epidemiology, pathophysiology, diagnosis, and treatment. Lancet Neurol 2024;23:522-33. doi: 10.1016/S1474-4422(24)00076-0.
2. Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, et al. Chronic pain as a symptom or a disease: The IASP classification of chronic pain for the International Classification of Diseases (ICD-11). Pain 2019;160:19-27. doi: 10.1097/j.pain.0000000000001384.
3. Lee J, Lim YH, Hong SJ, Jeong JH, Choi HR, Park SK, et al. Multicenter survey of symptoms, work life, economic status, and quality of life of complex regional pain syndrome patients. Korean J Pain 2021;34:288-303. doi: 10.3344/kjp.2021.34.3.288.
4. Wiemann M, Zimowski N, Blendow SL, Enax-Krumova E, Naegel S, Fleischmann R, et al. Evidence for converging pathophysiology in complex regional pain-syndrome and primary headache disorders: Results from a case-control study. J Neurol 2024;271:1850-60. doi: 10.1007/s00415-023-12119-w.
5. Xu W, Liu Y, Zhang B, Ma J. Dynamic risk factors for complex regional pain syndrome after distal radius fracture surgery: Multivariate analysis and prediction. BMC Musculoskelet Disord 2024;25:899. doi: 10.1186/s12891-024-07948-3.

6. Beerthuizen A, van 't Spijker A, Huygen FJ, Klein J, de Wit R. Is there an association between psychological factors and the Complex Regional Pain Syndrome type 1 (CRPS1) in adults? A systematic review. Pain 2009;145:52-9. doi: 10.1016/j.pain.2009.05.003.
7. Jo YH, Kim K, Lee BG, Kim JH, Lee CH, Lee KH. Incidence of and risk factors for complex regional pain syndrome type 1 after surgery for distal radius fractures: A population-based study. Sci Rep 2019;9:4871. doi: 10.1038/s41598-019-41152-x.
8. Pons T, Shipton EA, Williman J, Mulder RT. Potential risk factors for the onset of complex regional pain syndrome type 1: A systematic literature review. Anesthesiol Res Pract 2015;2015:956539. doi: 10.1155/2015/956539.
9. Lorente A, Mariscal G, Lorente R. Incidence and risk factors for complex regional pain syndrome in radius fractures: Meta-analysis. Arch Orthop Trauma Surg 2023;143:5687-99. doi: 10.1007/s00402-023-04909-8.
10. Demir SE, Ozaras N, Karamehmetoğlu SS, Karacan I, Aytekin E. Risk factors for complex regional pain syndrome in patients with traumatic extremity injury. Ulus Travma Acil Cerrahi Derg 2010;16:144-8.
11. Schwartzman RJ, Alexander GM, Grothusen J. Pathophysiology of complex regional pain syndrome. Expert Rev Neurother 2006;6:669-81. doi: 10.1586/14737175.6.5.669.
12. Xie RG, Xu GY, Wu SX, Luo C. Presynaptic glutamate receptors in nociception. Pharmacol Ther 2023;251:108539. doi: 10.1016/j.pharmthera.2023.108539.
13. Yang X, Yang HB, Xie QJ, Liu XH, Hu XD. Peripheral inflammation increased the synaptic expression of NMDA receptors in spinal dorsal horn. Pain 2009;144:162-9. doi: 10.1016/j.pain.2009.04.005.
14. Carlton SM, Coggeshall RE. Inflammation-induced changes in peripheral glutamate receptor populations. Brain Res 1999;820:63-70. doi: 10.1016/s0006-8993(98)01328-6.
15. Shin HJ, Na HS, Do SH. Magnesium and Pain. Nutrients 2020;12:2184. doi: 10.3390/nu12082184.
16. Collins S, Zuurmond WW, de Lange JJ, van Hilten BJ, Perez RS. Intravenous magnesium for Complex Regional Pain Syndrome type 1 (CRPS 1) patients: A pilot study. Pain Med 2009;10:930-40. doi: 10.1111/j.1526-4637.2009.00639.x.
17. Fischer SG, Collins S, Boogaard S, Loer SA, Zuurmond WW, Perez RS. Intravenous magnesium for chronic Complex Regional Pain Syndrome type 1 (CRPS-1). Pain Med 2013;14:1388-99. doi: 10.1111/pme.12211.
18. Simşek E, Karabay M, Kocabay K. Assessment of magnesium status in newly diagnosed diabetic children: Measurement of erythrocyte magnesium level and magnesium tolerance testing. Turk J Pediatr 2005;47:132-7.
19. Fan L, Zhu X, Rosanoff A, Costello RB, Yu C, Ness R, et al. Magnesium Depletion Score (MDS) predicts risk of systemic ınflammation and cardiovascular mortality among US adults. J Nutr 2021;151:2226-35. doi: 10.1093/jn/nxab138.
20. Maier JAM, Locatelli L, Fedele G, Cazzaniga A, Mazur A. Magnesium and the brain: A focus on neuroinflammation and neurodegeneration. Int J Mol Sci 2022;24:223. doi: 10.3390/ijms24010223.
21. Harden NR, Bruehl S, Perez RSGM, Birklein F, Marinus J, Maihofner C, et al. Validation of proposed diagnostic criteria (the "Budapest Criteria") for complex regional pain syndrome. Pain 2010;150:268-74. doi: 10.1016/j.pain.2010.04.030.
22. Harden RN, Oaklander AL, Burton AW, Perez RS, Richardson K, Swan M, et al. Complex regional pain syndrome: Practical diagnostic and treatment guidelines, 4th edition. Pain Med 2013;14:180-229. doi: 10.1111/pme.12033.
23. Toda K. Risk factor for complex regional pain syndrome. JOJ Orthoped Ortho Surg 2018;2:21-4. doi: 10.19080/JOJOOS.2018.02.555579.
24. Candan B, Gungor S. Current and evolving concepts in the management of complex regional pain syndrome: A narrative review. Diagnostics (Basel) 2025;15:353. doi: 10.3390/diagnostics15030353. .
25. Taylor SS, Noor N, Urits I, Paladini A, Sadhu MS, Gibb C, et al. Complex regional pain syndrome: A comprehensive review. Pain Ther 2021;10:875-92. doi: 10.1007/s40122-021-00279-4.
26. Wen B, Zhu H, Xu J, Xu L, Huang Y. NMDA receptors regulate oxidative damage in keratinocytes during complex regional pain syndrome in HaCaT cells and male rats. Antioxidants (Basel) 2024;13:244. doi: 10.3390/antiox13020244.
27. de Mos M, Huygen FJPM, Dieleman JP, Koopman JSHA, Stricker CBH, Sturkenboom MCJM. Medical history and the onset of Complex Regional Pain Syndrome (CRPS). Pain 2008;139:458-66. doi: 10.1016/j.pain.2008.07.002.
28. Diepold J, Deininger C, Von Amelunxen BC, Deluca A, Siegert P, Freude T, et al. Comparison of epidemiological data of Complex Regional Pain Syndrome (CRPS) patients in relation to disease severity-a retrospective single-center study. Int J Environ Res Public Health 2023;20:946. doi: 10.3390/ijerph20020946.
29. Atkins RM, Duckworth T, Kanis JA. Features of algodystrophy after Colles' fracture. J Bone Joint Surg Br 1990;72:105-10. doi: 10.1302/0301-620X.72B1.2298766.
30. Bickerstaff DR, Kanis JA. Algodystrophy: An under-recognized complication of minor trauma. Br J Rheumatol 1994;33:240-8. doi: 10.1093/rheumatology/33.3.240.
31. Zyluk A. Complex regional pain syndrome type I. Risk factors, prevention and risk of recurrence. J Hand Surg Br 2004;29:334-7. doi: 10.1016/j.jhsb.2004.01.003.
32. Gong H, Zhao G, Liu Y, Lu Z. Determinants of complex regional pain syndrome type I in patients with scaphoid waist fracture- a multicenter prospective observational study. BMC Musculoskelet Disord 2022;23:34. doi: 10.1186/s12891-021-04977-0.