

Risk factors for complex regional pain syndrome in patients with traumatic extremity injury

Travmatik ekstremitte yaralanması geçiren olgularda kompleks bölgesel ağrı sendromu risk faktörleri

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BACKGROUND

It is not clear why complex regional pain syndrome (CRPS) develops in some patients but not in others, despite similar initiating events. The aim of this study was to investigate risk factors for CRPS in cases who had suffered traumatic upper extremity injury.

METHODS

One hundred sixty-five patients who had suffered a mechanical traumatic injury isolated to their hand or forearm were included in this study. Age, gender, body mass index, tissue types injured, and side of affected forearm/hand were investigated as possible risk factors for CRPS.

RESULTS

CRPS was diagnosed in 84 patients. Female/male ratio was higher in patients with CRPS versus those without. The mean age was higher in patients with CRPS. The affected forearm/hand was the dominant side in 62.9% of patients without CRPS and in 64.2% of patients with CRPS. CRPS incidence was higher in patients with motor nerve injury and in patients with sensory nerve injury. A logistic regression showed that risk for CRPS was higher in patients with motor nerve injury and in females.

CONCLUSION

This study indicates that motor nerve injury and female gender are risk factors for CRPS. The prevention measures should be focused mainly on females and patients with motor nerve injury in order to reduce the risk of CRPS.

Key Words: Complex regional pain syndrome; risk factor.

AMAÇ

Kompleks bölgesel ağrı sendromunun (KBAS), benzer tetikleyici etkenlere maruz kaldığı halde bazı hastalarda geliştiği, bazılarında ise neden gelişmediği konusu açık değildir. Bu çalışmada, üst ekstremitede travmatik yaralanma geçiren kişilerde KBAS risk faktörleri araştırıldı.

GEREÇ VE YÖNTEM

Çalışmaya ünilateral el veya önkoldan mekanik yaralanma geçiren 165 hasta dahil edildi. Yaş, boy, vücut kitle indeksi, yaralanan doku tipi, yaralanan el/önkol olası risk faktörleri olarak incelendi.

BULGULAR

Seksen dört olguya KBAS tanısı kondu. Kadın/erkek oranı KBAS'li hastalarda daha yüksek idi. KBAS'li olguların yaş ortalaması daha yüksek idi. Yaralanan el/önkol KBAS'li olguların %64,2'sinde, KBAS olmayan olguların %62,9'unda dominant taraf idi. KBAS sıklığı duyu sinir yaralanması geçirenlerde ve motor sinir yaralanması geçirenlerde geçirmeyenlere göre daha yüksek idi. Lojistik regresyon analizi KBAS riskinin motor sinir yaralanması geçirenlerde ve kadınlarda yüksek olduğunu gösterdi.

SONUÇ

Bu çalışma, motor sinir yaralanmasının ve kadın olmanın KBAS için risk faktörü olduğunu göstermektedir. KBAS riskini azaltmak için koruyucu önlemlerin bu hastalarda odaklanması yararlı olabilir.

Anahtar Sözcükler: Kompleks bölgesel ağrı sendromu; risk faktörü.

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Complex regional pain syndrome (CRPS) is a disabling chronic pain condition of unknown etiology and underlying mechanisms.^[1] CRPS can be triggered by noxious events like limb trauma with or without nerve lesions, and in very rare cases, it may develop spontaneously.^[2] In type I CRPSs (reflex sympathetic dystrophy), which typically develop after minor tissue trauma or bone fracture, no overt nerve lesion is detectable, whereas in type II disease (causalgia), a peripheral nerve lesion is necessary for diagnosis.^[3] CRPS II may have all the symptoms seen in patients with CRPS I.^[1]

It is not clear why CRPS develops in some patients but not in others, despite similar initiating events. No clear predisposing factors have been identified thus far.^[4] The aim of this study was to investigate risk factors for CRPS in cases who suffered a mechanical traumatic injury to their forearm or hand.

MATERIALS AND METHODS

From April 2003 to June 2006, among patients admitted to our Departments of Orthopedic Surgery and Plastic and Reconstructive Surgery, 165 patients (43 female, 122 male) who had suffered a unilateral mechanical traumatic injury isolated to their hand or forearm were included in this study. These patients underwent general physical and neurological examinations and were questioned regarding their medical history. Patients with chemical injury or burn of the upper extremity or history of peripheral polyneuropathy, peripheral nerve entrapment, dermatological disease or arthritis of the upper extremity, psychiatric diseases, vascular disease such as stroke and myocardial ischemia, and metabolic or endocrine disease such as diabetes mellitus and uremia were excluded.

The CRPS was diagnosed according to the International Association for the Study of Pain criteria.^[5] These criteria are: 1) Presence of an initiating noxious event, or a cause of immobilization, 2) Continuing pain, allodynia, or hyperalgesia with which the pain is disproportionate to any inciting event, 3) Evidence at some time of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of pain, and 4) Exclusion of this diagnosis by the existence of conditions that would otherwise account for the degree of pain and dysfunction.

In this observational study, gender, age, body mass index (BMI), tissue types injured (fracture, tendon rupture, sensory nerve injury or motor nerve injury), and side of affected forearm/hand (dominant or non-dominant side) were investigated as the possible risk factors for CRPS. The data about the tissue types injured were obtained from the surgeons who treated the patients. Injury to the nervus digitalis, a sensory nerve, was accepted as a sensory nerve injury, while injury to

the nervus medianus, ulnaris or radialis, which have both motor and sensory functions, was accepted as both motor and sensory nerve injury.

Statistical Analysis

Descriptive statistics (arithmetic means \pm standard deviation, frequency) were used. To detect the influence of various demographic (age, gender, BMI) and injury-related variables (type of injury, period after the trauma and side of affected forearm/hand) on the occurrence of CRPS, univariate association between the variables was tested using chi-square tests for categorical variables and two-tailed t tests for normally distributed continuous variables. Normal distribution was verified with Kolmogorov-Smirnov test. Tissue types injured were dichotomous variables: fracture (0: absent, 1: present), tendon rupture (0: absent, 1: present), sensory nerve injury (0: absent, 1: present), and motor nerve injury (0: absent, 1: present). Next, a multivariate analysis was performed to find independent predictors for the occurrence of CRPS by using a binary logistic regression analysis and to find confounding effects between potentially independent predictors. Variables with p values less than 0.1 in univariate analyses were considered as potentially independent variables in a multivariate analysis. Forward stepwise selection was used to derive the final model for which significance levels of 0.1 and 0.05 were chosen to remove and add terms, respectively. To determine whether the regression model adequately described the data, the Hosmer-Lemeshow goodness-of-fit test was used. If the significance value is less than 0.05, the Hosmer-Lemeshow statistic indicates a poor fit. Results were expressed as an adjusted odds ratio (aOR) and B coefficients. Crude odds ratio (cOR) was calculated with univariate analysis. Ninety-five percent confidence interval (95%CI) was used to evaluate significance of OR. Wald test was used to evaluate significance of individual B coefficients. A p value of less than 0.05 was considered statistically significant. The data management software package SPSS version 10.0 for Windows was used.

RESULTS

The mean age was 39.3 ± 13.6 (16-79) years. One hundred fifty-two patients (94.5%) were right-handed (patients-deleted). In 105 patients (63.6%), the dominant side forearm or hand was affected by trauma. The mean period after the trauma was 3.05 ± 2.30 months.

Complex regional pain syndrome was diagnosed in 84 patients. Frequency of CRPS was 69.7% in females and 44.2% in males. The female/male ratio was significantly higher in the CRPS group. The mean age was higher in patients with CRPS than those without CRPS. There were no significant differences in BMI or the period after trauma between patients with and

Table 1. Demographic and injury-related variables associated with CRPS in univariate analyses

	CRPS (-)	CRPS (+)	p
Age (yrs)	36.7±12.2	41.7±14.2	0.016
Female / Male	13/68	30/54	0.007
BMI (kg/m ²)	25.5±4.7	25.7±4.4	0.850
Affected forearm/hand (dominant/nondominant)	51/30	54/30	0.860
Period after the trauma (months)	3.4±3.2	2.7±1.2	0.176

without CRPS. The affected forearm/ hand was the dominant side in 62.9% of patients without CRPS and in 64.2% of patients with CRPS (Table 1).

A pure tissue injury or combined tissue injury was determined in our patients (Fig. 1). Comparing the types of injury, CRPS incidence was the highest in motor nerve injury (Fig. 2).

Univariate analyses indicated the potentially independent variables in a multivariate analysis to be gender, age, sensory nerve injury, and motor nerve injury. cORs of all independent variables are shown in Table 2.

A multivariate logistic regression model showed that CRPS was not associated with age or sensory nerve injury. This model also indicated that risk for CRPS was found to be higher in patients with motor nerve injury compared to those without (aOR, 4.53; 95%CI, 1.52 to 13.45), and in female patients (aOR, 3.56; 95%CI, 1.66 to 7.62) (Hosmer-Lemeshow test, p=0.972) (Table 3).

DISCUSSION

A wide range of conditions have been known to precede CRPS. Trauma is the commonest cause in most series, accounting for 30-77% of cases, the majority following minor insults of an extremity.^[6,7] In this study, we sought to determine why one traumatic

insult should give rise to CRPS in one patient while the identical insult in another patient does not. Thus, we investigated risk factors for CRPS in cases who had suffered a mechanical traumatic injury isolated to their forearm or hand. We found that motor nerve injury and being female were important risk factors for CRPS. Traumatic tendon rupture, fracture, sensory nerve injury, and the side of affected forearm/hand were not significant concerning the development of CRPS.

It is commonly believed that gender influences the frequency of CRPS and that it is twice as common in females as in males.^[7,8] Similar to the previous studies, in this study, CRPS developed more frequently in females (69.7%) than in males (44.2%). Logistic regression analysis also showed that the risk of the development of CRPS was 3.56 times higher in females than in males. De Mos et al.^[9] reported that CRPS was more common in patients having preexisting menstrual cycle-related disorders. They suggested that sex hormones, such as estrogens, may be important for developing CRPS. In this study, menstrual cycle-related disorders were not questioned.

The incidence of CRPS has been studied retrospectively and prospectively in clinical settings after a certain precipitating event, most frequently after distal radius fracture. Fracture was the most common precipitating event, accounting for 44% of the CRPS

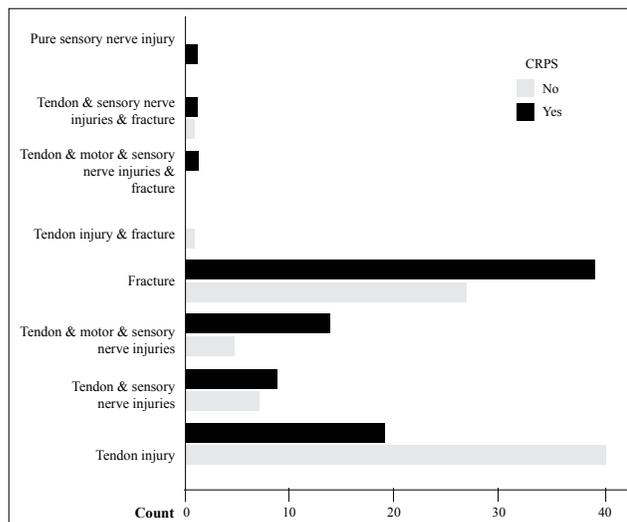


Fig. 1. The pure or combined tissue injuries and CRPS frequency.

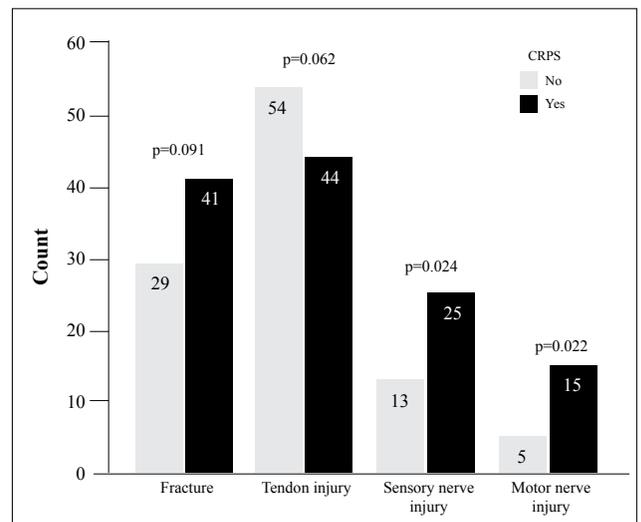


Fig. 2. Association between tissue type injured and CRPS in univariate analyses.

Table 2. Crude odds ratios (cOR) of the variables in univariate analyses

	cOR	95%CI for cOR	
		Lower	Upper
Gender (female)	2.906	1.383	6.105
Age	1.029	1.005	1.054
BMI	1.007	0.941	1.077
Period after the trauma	0.863	0.702	1.060
Affected forearm/hand (dominant)	0.944	0.501	1.781
Fracture (present)	1.710	0.916	3.191
Tendon rupture (present)	0.550	0.293	1.033
Sensory nerve injury (present)	2.345	1.105	4.975
Motor nerve injury (present)	3.304	1.141	9.569

CI: Confidence interval; BMI: Body mass index.

cases.^[10] In this study, of all CRPS patients, 32.5% had a fracture.

Although fracture is reported to be the most common precipitating event of CRPS, CRPS incidence is relatively low in patients with fracture. Specifically, after Colles' fractures, the CRPS incidence ranges from 1% to 37%.^[11] We found that of all patients with forearm/hand fracture, 58.6% had CRPS. Interestingly, this study also showed that fracture was not an important risk factor for CRPS. Briefly, according to our study findings, CRPS developed in patients with fracture, whereas fracture was not a risk factor. Data of these patients were re-analyzed, and it was found that of these cases, 60.9% had one of the risk factors for CRPS (female gender or motor nerve injury).

This study showed that motor nerve injury was an important risk factor for CRPS. Undue immobilization has been proposed as a cause of CRPS, and CRPS features, except pain, are seen after cast immobilization.^[7] Early mobilization and functional rehabilitation of the operative limb, facilitated by effective analgesia, is vital for the prevention and treatment of CRPS.^[12] In this study, after the trauma, all patients were placed in a cast to immobilize their hand. Motor nerve injury also leads to immobilization. It may exacerbate abnormal changes related to cast immobilization and thus may increase the risk for CRPS.

Cheng et al.^[13] showed that diffuse spontaneous electromyographic activity in the distal muscles of the paralyzed upper extremity might be a good predictor

of the future development of clinical CRPS in stroke patients. The fibrillation and decrement of motor unit number can be seen in the hemiplegic side especially in distal and intermediate muscles. These changes were reported to be due to the transsynaptic degeneration secondary to an upper motor neuron lesion.^[14,15] Our finding that motor nerve injury may be a risk factor for CRPS is in agreement with Cheng's finding.

There were several limitations to the current study. The first was that this was an observational retrospective study. Patients were questioned regarding their medical history. Although patients having history of peripheral polyneuropathy, peripheral nerve entrapment, dermatological disease or arthritis in the upper extremity, psychiatric diseases, vascular disease such as stroke and myocardial ischemia, and metabolic or endocrine disease such as diabetes mellitus and uremia were questioned and excluded from this study, it can not be stated unequivocally that our patients did not have these diseases. Several laboratory tests such as plasma glucose level, etc. should be performed. The second limitation was that we had no knowledge about medical complication rate, multiple surgical procedures and period of plaster cast. Well-designed future studies are needed that address these points.

In conclusion, our study indicates that when comparing types of injury, only motor nerve injury may be an important risk factor for CRPS. This study also showed that risk of CRPS may be higher in females than males. Based on this finding, it is suggested that

Table 3. B coefficients and adjusted odds ratios of significant variables in multivariate analyses

	B	SE	Wald	df	p	aOR	95%CI for aOR	
							Lower	Upper
Gender (female)	1.270	0.388	10.691	1	0.001	3.562	1.663	7.626
Motor nerve injury (present)	1.512	0.555	7.428	1	0.006	4.535	1.529	13.451
Constant	-0.458	0.202	5.142	1	0.023	0.633		

B: Coefficients; SE: Standard error; df: Degree of freedom; aOR: Adjusted odds ratio; CI: Confidence interval.

the prevention measures should be focused mainly on female patients and patients with motor nerve injury in order to reduce the frequency of CRPS.

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