Effect of Early Orthopedic Rehabilitation on Development of Complex Regional Pain Syndrome Type 1

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ABSTRACT

Objective: Complex regional pain syndrome (CRPS) is a syndrome usually occurs in one extremity and characterized by pain, tenderness with palpation, and symptoms of autonomic nervous system dysfunction. An essential factor in the etiology of CRPS is immobilization of the extremity as a result of a fracture. Delaying the start of physical medicine and rehabilitation program after removal of the plaster or splint may increase the rates of CRPS development in patients with fractures. This study aims to determine a direct relationship between delay time in rehabilitation and CRPS development.

Materials and Methods: Patients admitted to our physical therapy and rehabilitation outpatient clinic within the last 3 years (January 2016 to January 2018) for orthopedic rehabilitation following fractures were retrospectively analyzed. CRPS development status, the delay time for the rehabilitation program was determined in 38 CRPS patients of 91 patients with fractures. Probit regression was used to reveal the relationship between delay time for rehabilitation and CRPS development.

Results: CRPS development rates were decreased by years (48.71% in 2016, 43.47% in 2017, and 31.03% in 2018). When cases in 2016 were taken as a reference, it was seen that cases in 2017 and 2018 were exposed to CRPS approximately 0.03% and 16.00% lower than the reference year, 2016. A delay of one day exposes the patient to approximately 0.35% more CRPS.

Conclusion: As the delay time for rehabilitation in our clinic decreased, the incidence of CRPS decreased. The awareness of physicians and patients about the importance of early rehabilitation should be improved.

Keywords: Complex regional pain syndrome, fracture, physical and rehabilitation medicine.

Introduction

Complex regional pain syndrome (CRPS) is a disease seen in extremities, mostly in the upper extremity. CRPS is frequently triggered by a trigger stimulus and causes local pain, swelling, vasomotor and sudomotor dysfunctions, and severe loss of function in the affected extremity [1]. CRPS is divided into Type 1 (CRPS-1) and Type 2 (CRPS-2) according to the presence of nerve damage. CRPS-1 does not include a peripheral nerve lesion but CRPS-2 does [2].

Triggering factors in CRPS are mainly major or minor traumas, surgical procedures, and central nervous system disorders; however, sometimes, idiopathic cases occur spontaneously [3]. The most common cause of CRPS is trauma. While 43% of CRPSs are observed following fracture-induced traumas, this rate is 10%-12% in traumas that do not develop fractures, which is sprain [4]. The incidence of CRPS varies from 5.5 to 26.2 per 100 thousand people annually and the prevalence is 20.57 per 100.000 people [5, 6]. CRPS-1 can be seen in every race and geographic area and in all age groups, and it is known that it is seen more in women than men [7].

According to the traditional approach, CRPS-1 has three different stages: acute (stage I), subacute or dystrophic (stage II), and chronic or atrophic (stage III). In another opinion, there are only two stages of the disease-acute/early and chronic/late. It is the symptomatology, treatment approach, and prognosis of the disease that determine the stages of this disease [8, 9]. Although the transition from the acute phase to the chronic phase is not known exactly, it usually takes between 3 and 6 months. Treatment approaches can change this duration [10]. Diagnosis is

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mainly based on clinical signs and symptoms (2003 Budapest diagnostic criteria), as well as diagnostic methods such as X-ray, bone scintigraphy, magnetic resonance imaging (MRI), and thermography [10, 11].

Early diagnosis and treatment of CRPS-1 is of great importance in the prognosis of the disease particularly for providing functionality. Early orthopedic rehabilitation can prevent serious complications such as chronic pain, contractures, and extremity atrophy, even permanent disability [10].

The goal of the treatment is to reduce pain and to provide a functional repair of the extremity with CRPS. The main treatment applications in CRPS are medical treatment for pain, physical therapy and rehabilitation (PTR), psychotherapy, and interventional pain treatments. PTR applications are the basis of the treatment in CRPS [10, 12].

The study aimed to investigate the relationship between the delay time of rehabilitation and CRPS-1 development. To the best of our literature search, this is the first study determining such a direct relationship.

Materials and Methods

Study Design and Ethical Approval

The study was designed as retrospective analysis and approved by the local ethics committee.

Patients and Methods

The study was conducted by retrospective analysis of patients admitted to our PTR outpatient clinic within the last 3 years (January 2016 to January 2018) for orthopedic rehabilitation following fractures. Patients who had CRPS-1 on more than one extremity were excluded. The fracture site, the immobilization time (duration of plaster or splint), the number of days from the end of immobilization to the start of rehabilitation, and the total number of days from fracture to rehabilitation were determined. CRPS-1 was developed in 38 of 91 patients who had fractures. The study design and patient selection criteria are shown in a flowchart (Figure 1).

Main Points

- Patients should be closely monitored for CRPS development following fractures.
- Rehabilitation should be started as early as possible in patients with fractures. A delay of one day exposes the patient to approximately 0.35% more CRPS.
- Complications can be reduced by early rehabilitation.

Statistical Analysis

The data were analyzed using the current version (3.6.1) of the R program. The relationship between delay time and CRPS-1 occurrence was determined by the probit regression model. We investigated whether there was a relationship between the operative status and the development of CRPS-1. Patients who have fractures for more than 1 year and who have been reoperated because the fracture did not merge were excluded.

Probit regression, one of the binary choice models, was used to reveal such a relationship. Probit regression is derived from the inverse normal distribution and is widely used as an alternative to the logit regression model in binary selection models. The presence or prevalence of CRPS is associated with the risk factors mentioned above, and the probit regression was used to achieve such aim. Therefore, it is coded as 1, otherwise 0 as numerical values for characterizing the presence of CRPS. Since the factors affecting the probability of CRPS are not linear in the model, their impact on the probability should be measured separately with their corresponding standard errors. We have measured these unitary (marginal) effects along with their standard errors. Before discussing such marginal impacts on the likelihood of CRPS, the Wald test was conducted to determine whether the factors used as explanatory variables in the regression could adequately explain the variation in the probability of CRPS.

Results

A total of 91 patients (51 male, 40 female) with fracture history were included in the study. Number of patients by years were as follows: 39 (22 male, 17 female) patients in the year 2016, 23 (12 male, 11 female) patients in year the 2017, and 29 (17 male, 12 female) patients in the year 2018. CRPS-1 development percentages by years among these patients are shown in Figure 2. Demographic (age, sex) and some clinical properties (mean delay time of rehabilitation, time after frac-

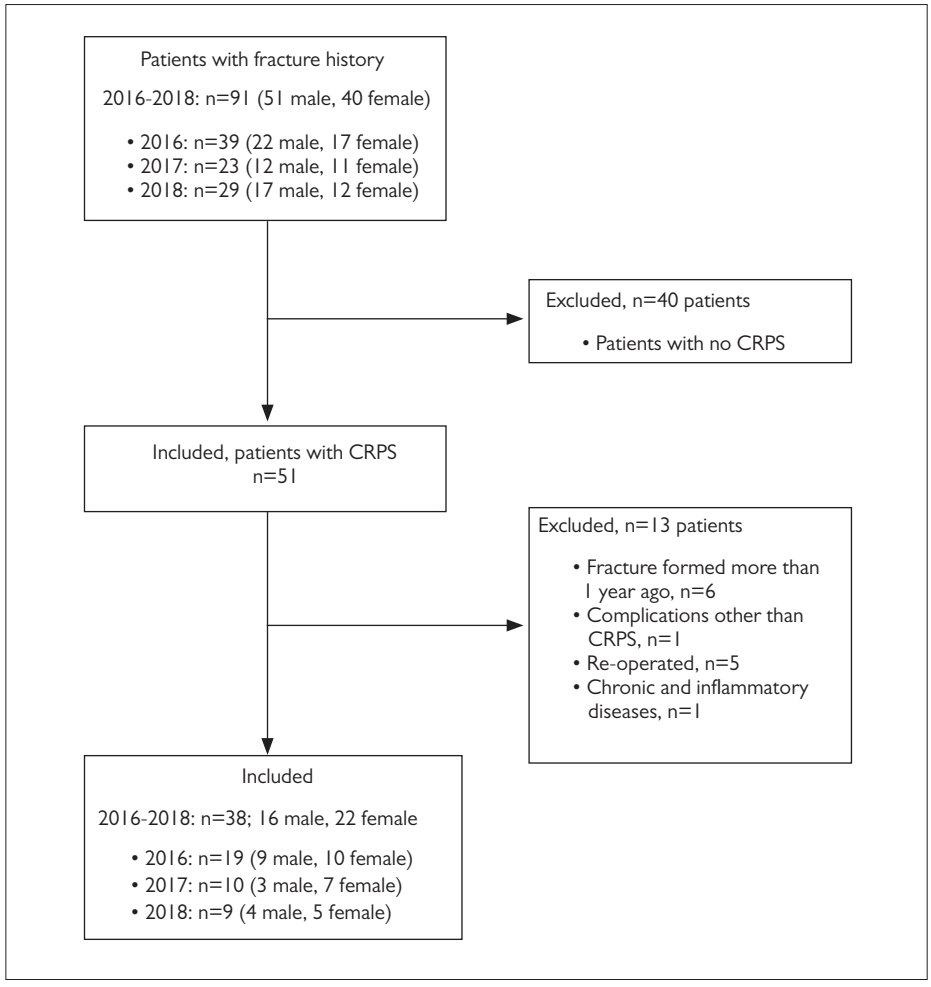

Figure 1. Study design

Table 1. Characteristics of CRPS-1 patients

	Years			
Characteristics	2016-2018	2016	2017	2018
Number of patients, n (male/female)	38 (16/22)	19 (9/10)	10 (3/7)	9 (4/5)
Age, years (mean±SD)	44.87±16.88	43.16±11.44	44.80±24.59	48.56±17.91
Delay time of rehabilitation, days (mean±SD)	37.32±50.39	51.32±66.05	10.50±14.23	37.56±18.27
Time after fracture, days (mean±SD)	88.42±61.61	99.32±78.19	60.30±27.86	96.67±39.76
İmmobilization time, days (mean±SD)	52.82±31.08	48.26±30.12	55.80±26.11	59.11±39.44
Operation status, if yes, n (%)	15 (39.5%)	7 (36.8%)	5 (50%)	3 (33.3%)

SD: standard deviation; CRPS: complex regional pain syndrome

Table 2. Estimates of a probit model and their corresponding marginal effects

	Probit model			Marginal effects		
Variable	Estimate	Standard error	p value	Estimate	Standard error	p
Constant	-2.6778	0.7595	0.0006	-78.3810	19.2010	0.0000
Sex	0.6464	0.3564	0.0728	20.0350	9.4690	0.0370
Age	0.0226	0.0080	0.0057	0.6620	0.2150	0.0030
Region 1	0.3629	0.6527	0.5795	10.5420	16.6350	0.5280
Region 2	1.1586	0.6136	0.0620	31.9980	14.2630	0.0270
Region 4	1.3024	0.6385	0.0441	35.8770	15.0560	0.0190
Delayed time	0.0118	0.0047	0.0143	0.3460	0.1060	0.0010
Operation	0.6655	0.3510	0.0609	19.4660	9.4650	0.0420
Year 2017	-0.0009	0.3811	0.9981	-0.0260	9.8080	0.9980
Year 2018	-0.5422	0.3893	0.1668	-15.6830	9.7240	0.1100

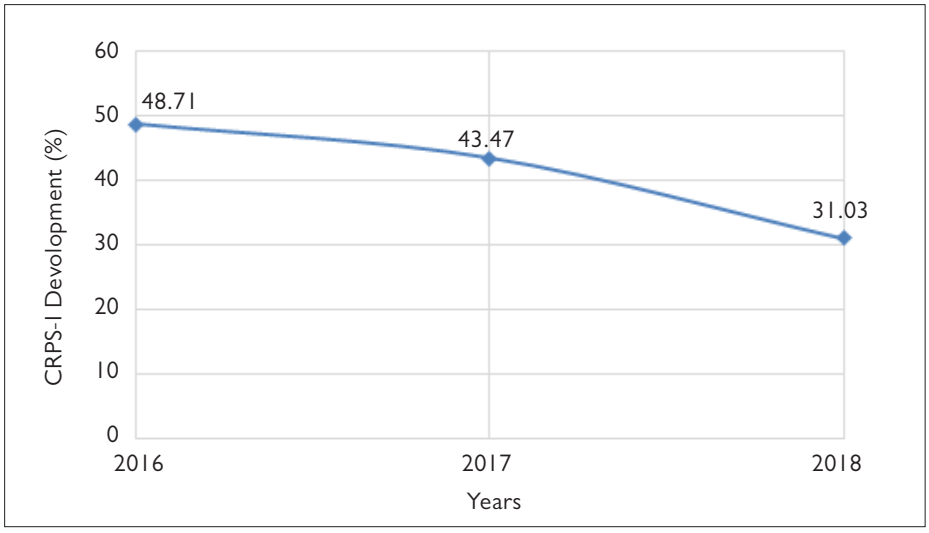

Figure 2. CRPS-1 development percentages by years

ture, immobilization time, and operation status) of patients with CRPS-1 are determined and results are given in Table 1.

Fracture regions of CRPS patients were categorized into four groups as follows: first, from proximal to upper extremity (including the proximal and distal humerus); second, distal to upper extremity (including ulna, radius, and hand); third, from proximal to lower limb (including the femur); and fourth, from distal to lower limb (including the tibia, the fibula bone, and the foot). Similarly, the regions of CRPS-1 of patients were categorized into four groups as follows: first, from proximal to upper extremity (including the humerus); second, distal to upper extremity (elbow and hand); third, from proximal to lower limb (including femur); and fourth, from distal to lower limb (including the tibia, the fibula, and the foot).

The fracture region and the CRPS region distributions of patients with CRPS-1 are shown in Figure 3.

CRPS was examined to have a relationship with explanatory risk factors such as age, sex, delay time (time to stay in cast or delay in starting physical therapy after the cast), whether the patient had undergone surgery, and differences between years.

The probit regression analysis results showed that the explanatory variables had sufficient power to explain the variation simultaneously in the likelihood of CRPS (Wald=20.001, df=9, $p<0.005$). Results of the probit model are given in Table 2 and are shown in Figures 4 and 5.

Discussion

In this study, we determined the relationship between the delay time of rehabilitation and CRPS-1 development by using the probit regression model. Additionally, we determined that CRPS incidence increases with age, women's gender and has been operated.

Geographical Factors

Our region is located in Eastern Anatolia where winter season is long and winter conditions are severe. Therefore, fractures, especially caused by falls, are very common in our region. Considering that fracture and immobilization is one of the important causes of CRPS development, our study brings an additional contribution to the awareness of physicians about early diagnosis and treatment of CRPS.

Sex

As evaluating the probit regression results, marginal effects of the explanatory variables used in the regression on the CRPS probability show that women are exposed to about 20% points more risk than men. This result is consistent with the literature findings. Studies reporting higher CRPS incidences in women than in men suggest that this difference may be attributed to the hormonal differences in men and women [4, 13]. A population-based study conducted in the Netherlands has reported that the incidence of CRPS in women was more than three-fold higher than in men [4]. Authors have reported that the majority of CRPS cases have developed after the menopausal period (in the age category of 61-70 years) [4] among women.

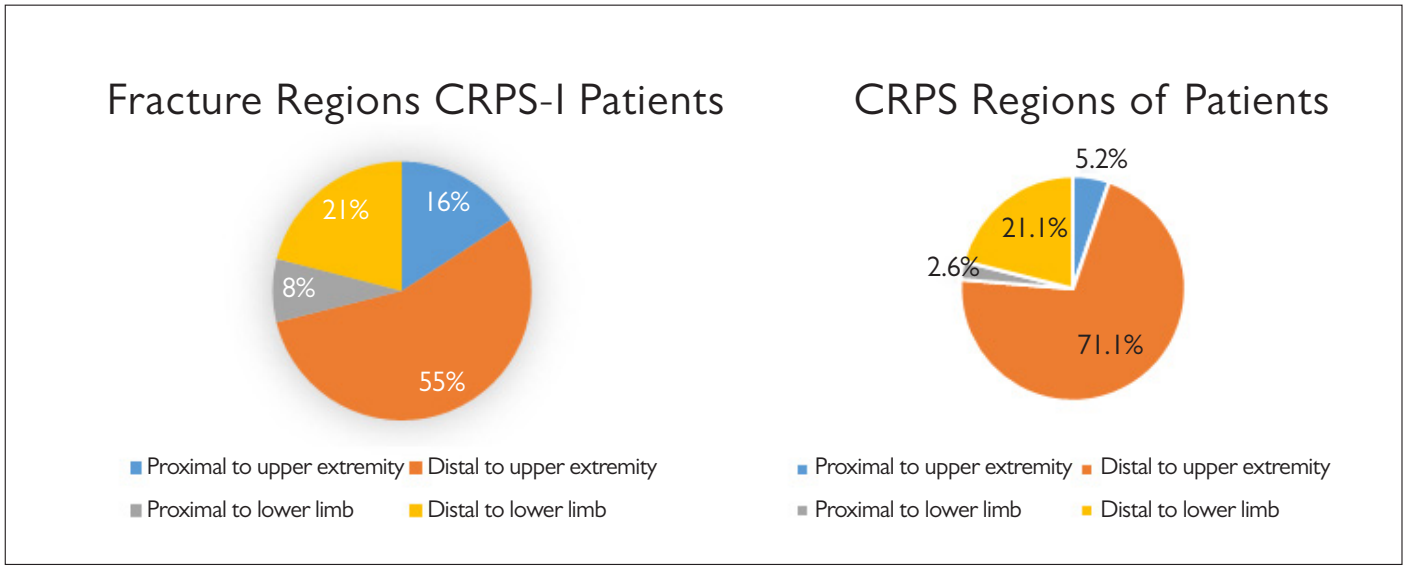

Figure 3. Fracture regions and CRPS regions of patients with CRPS-I

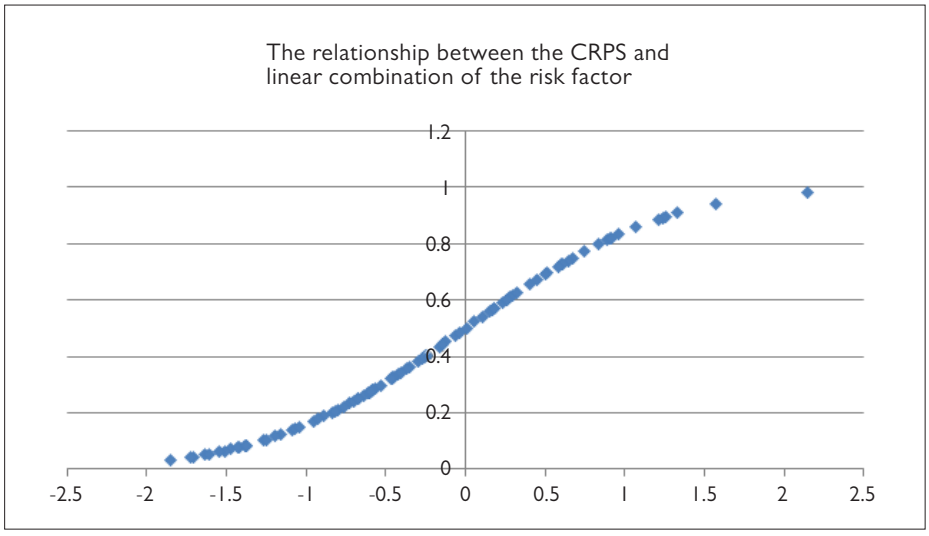

Figure 4. The relationship between CRPS and linear combination of the risk factors

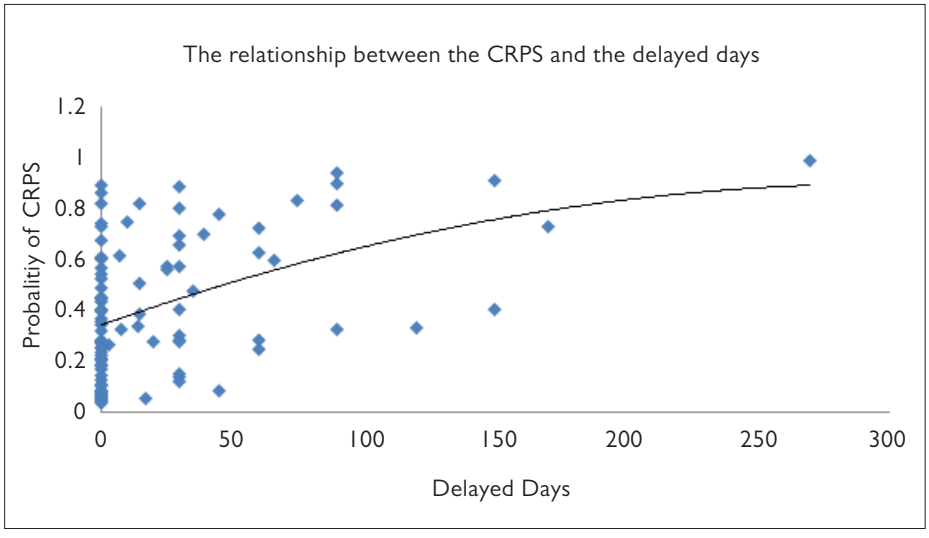

Figure 5. The relationship between CRPS and delayed days

Our study has a limitation being retrospective, and we had not questioned the menopausal status of patients. However, because the mean age of women with CRPS-I in our study was 51.14±16.22 years, we can speculate that most of the women were in the post-menopausal period, thereby explaining the high incidence of CRPS in women.

Age Factor

Another factor that may affect CRPS development is age. In our study, there is a positive correlation between the patient's age and the likelihood of CRPS. The probability of CRPS increases by approximately 0.66% point as a result of aging of the patient for an additional year. Similar to our study, a study [4] has reported that CRPS incidence increases with age, being highest in the age group of 61-70 years. Such results are expected in the elderly because of the difficulties inherent in the age, for example, due to joint and cartilage deterioration, bone resorption intensity, and increased oxidative stress.

CRPS Region

Situations in the second and fourth regions are about 11% and 32% more likely to have CRPS than the referenced region (third region). The most important finding of this study was the positive correlation between CRPS and the duration of the arm or leg stay in the cast and the delay in the starting of physical therapy after the cast, that is, an additional delay of one day exposes the patient to approximately 0.35% more likelihood of having CRPS. A study aimed to provide an overview of CRPS has remarked that late diagnosis and, thus, late rehabilitation

(approximately 6-26 weeks) of CRPS are common [14]. Further, the study [14] stated that significant morbidity occurred in about 50% of patients in whom treatment was delayed for longer than 12 months.

Operation Status

If the patient has undergone any operation due to the case, there exists a positive linear relationship with the likelihood of CRPS. Operated patients are exposed to about 20% points more chance of having CRPS than their untouched counterparts. Our finding is in accordance with the suggestion that the operation itself is an additional morbidity factor for CRPS occurrence and prognosis [15].

In our study, cases in 2016 were taken as a reference to reveal the difference between the probability of CRPS and years. Cases in 2017 and 2018 were, respectively, exposed to CRPS approximately 0.03% and 16% lower than those in the reference year, 2016. As long as patients are reminded of the importance of starting physical therapy as soon as they are cast or after the removal of the cast, the likelihood of exposure to CRPS decreases. In conclusion, we recommend starting a PTR program immediately after from the end-up of immobilization.

Ethics Committee Approval: Ethics committee approval was received for this study from the Clinical Trials Ethics Committee of Ataturk University School of Medicine (26.09.2019/426).

Informed Consent: Informed consent was obtained from patients who participated in this study.

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Conflict of Interest: Authors have no conflicts of interest to declare.

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