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The Relation Between Reflex Sympathetic Dystrophy Syndrome and Trauma Severity in Patients With Distal Tibia Fracture

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Abstract

Background: Reflex sympathetic dystrophy (RSD) syndrome is a multifactorial disorder with clinical features of neurogenic inflammation that causes hypersensitivity to pain or severe allodynia as well as blood flow problems, swelling, skin discoloration and maladaptive neuroplasticity due to vasomotor disorders. Patients with major trauma are prone to homeostasis leading to inflammatory response syndrome and multiple organ distress syndrome. Several studies have investigated the etiology of this condition, but the cause remains unknown. The role of associated factors such as the limb immobilization technique and genetics has been reported in the development of this complication, but, so far, there is no information regarding the effect of trauma severity on the risk of RSD occurrence.

Objectives: Given the importance of diagnosing and treating this condition, we aimed to study the effect of trauma severity on the prevalence of RSD.

Patients and Methods: In this cross-sectional study, we examined patients with distal tibial fracture who visited Rasht Poursina hospital from 2010 to 2013. Exclusion criteria included associated fractures, underlying musculoskeletal diseases and mental and cognitive problems. To assess the severity of the initial injury in patients, the Hannover Fracture Scale 98 (HFS98) scoring checklist was used. The diagnosis of RSD was made on the basis of the IASP criterion. Demographic data, HFS98 scores, and information regarding RSD prevalence were analyzed using SPSS version 20. The Mann Whitney U nonparametric test was used for variables that were not normally distributed; the chi-square test was used to compare the qualitative variables.

Results: Among the 488 patients, 292 (59.83%) were male. The mean age of the study population was 44 $\pm$ 9.82 years. During the 6-month follow-up, RSD occurred in 45 patients, of whom 28 (62.22%) were female and 17 (37.77%) were male; there was thus a significant difference in the prevalence of RSD in terms of gender (P = 0.00; chi square test). The mean HFS98 score in patients without and with RSD was 3.081 $\pm$ 4.083 and 4.080 $\pm$ 4.622, respectively, and the difference was not statistically significant (P = 0.363; Mann Whitney U test). Analyses of the eight items of HFS98 shows that local circulation in patients with RSD is significantly better than that in patients without RDS (0.683 $\pm$ 0.822 vs. 0.528 $\pm$ 0.629, respectively). Statistical analysis showed that the odds ratio for RSD for patients with HFS95 score > 0 was 1.079 (confidence interval [CI]: 0.898 - 1.333). Moreover, the odds ratio for RSD was 1.100 (CI: 795 - 1.531) in patients with an injury severity score higher than the calculated mean score in patients without RSD (> 4.083).

Conclusions: The results suggest no significant relationship between the severity of injury and risk of RSD occurrence, although the mean injury severity score was higher in patients with RSD than in those without RSD in this study population. The lower score of local circulation in patients with RSD than in those without RSD is a statistically significant finding and can be attributed to changes in the antioxidant levels at the injury site, which is one of the main mechanisms for the onset of RSD. Wound contamination was also justifiably higher in patients with RSD, although the difference was not statistically significant. In summary, the severity of injury alone cannot be a determining factor for predicting the probability of RSD.

Keywords: Reflex Sympathetic Dystrophy, RSD, CRPS1, Trauma, Tibia

1. Background

Complex regional pain syndrome (CRPS) is a multifactorial disorder with clinical features of neurogenic inflammation (swelling in the peripheral nervous system) that causes hypersensitivity to pain or severe allodynia. Associated manifestations include blood flow problems, swelling, skin discoloration, and maladaptive neuroplasticity due to vasomotor disorders (1-3).

Reflex sympathetic dystrophy (RSD) has two semi-

inflammatory warm and cold phases. In the warm phase, initial changes in tissue are caused by a microcircular disorder; followed by the cold phase wherein the tissue undergoes secondary developmental changes. RSD is a pain syndrome caused by sensory and motor disorders from an unknown etiology and can have a wide range of manifestations in the affected organs. RSD is typically a self-limiting syndrome but may recur in other joints (1, 4). Patients with major trauma are prone to homeostasis leading to inflammatory response syndrome and multiple organ distress syndrome. Systemic inflammatory response is an exaggerated inflammatory reaction to events such as trauma, burns, or severe infections. These processes appear to be mediated by host-derived inflammatory mediators. The international association of pain study (IASP) has divided CRPS into two subtypes (5).

Type I, is also known as RSD, Sudeck's atrophy, reflex neurovascular dystrophy (RND), or algoneurodystrophy. There is no proven neurological lesion associated with this type. Most cases of CRPS fall into this category, and the literature also mainly refers to type 1 RSD.

Type II, also known as causalgia, is definitely associated with neural injury. CRPS II is more painful and difficult to control (6). In type II, the cause of nerve damage is known or obvious, although the causal mechanism remains unknown, as is in type I.Some retrospective studies have reported a low prevalence of RSD of about 6% (7, 8). In contrast, prospective studies have reported RSD prevalence as high as 40% (9, 10). Several studies have investigated the etiology of this condition, but the cause remains unknown. The role of associated factors such as the limb immobilization technique and genetics has been reported in the development of this complication, but, so far, there is no information regarding the effect of trauma severity on the risk of RSD occurrence.

2. Objectives

Given the importance of diagnosing and treating this condition, we aimed to study the effect of trauma severity on the prevalence of RSD.

3. Patients and Methods

In this cross-sectional study, we recruited patients with distal tibial fracture at the Rasht Poursina hospital from 2010 to 2013, after screening them for inclusion and exclusion criteria.

The inclusion criteria were age over 18 years, operated by a surgeon with at least 5 years' experience in orthopedic surgery and normal levels of anxiety and depression. The exclusion criteria included associated fractures, underlying musculoskeletal diseases and mental and cognitive problems.

To assess the severity of the initial injury in patients, the Hannover fracture scale 98 (HFS98) scoring checklist was used (10). This checklist includes the following eight items:

1- Extent of bone loss
2- Skin injury as a percentage of limb circumference
3- Muscle injury as a percentage of limb circumference
4- Wound contamination
5- Deperiostation
6- Local circulation
7- Systolic blood pressure (systemic circulation)
8- Neurological findings

The total score for these items can range from 0 to 22 based on the severity. Higher scores indicate greater injury severity; amputation is recommended for scores higher than 11. Patients whose severity of trauma was not high to indicate amputation but had undergone surgery, were asked to fill the Spielberger and Beck's anxiety and depression inventory 24 hours after surgery after obtaining consent. Patients with normal levels of anxiety and depression were clinically examined for RSD during the second and sixth weeks and at 3 and 6 months.

The diagnosis of CRPS I or RSD was performed according to the IASP criterion. In brief, the criterion include the following parameters: presence of pain away from the surgical site, which is checked by applying comparative pressure on two organs; and presence of two of these three symptoms, nocturnal pain resulting in insomnia, local or regional inflammatory symptoms, and radiological symptoms suggestive of RSD (spotty osteoporotic demineralization).

Demographic data, HSF98 scores indicating injury severity, and information on the prevalence of RSD were analyzed using SPSS 20.0.

Kolmogorov Smirnov test was used for determining the normality. When the distribution was found to be abnormal, Mann Whitney U test was used for non-parametric data analysis. To compare the qualitative variables, chi square test was used. $P < 0.05$ was considered significant.

4. Results

The study population comprised 488 patients with distal tibial fractures, including 292 (59.83%) male and 196 (40.17%) female. The mean age of the patients was 44 ± 9.82 years. Regarding the cause of fractures, 139 (28.48%) fractures were due to a car accident, 162 (33.19%) due to a motorcycle accident, 86 (17.62%) due to a pedestrian-vehicle accident, and 101 (20.69%) fractures were due to falling from

heights. During the 6-month follow-up period, RSD occurred in 45 patients, of whom 28 (62.22%) were female and 17 (37.77%) were male, showing a significant difference in the prevalence of RSD in terms of gender (P = 0.00; chi square test). The mean total HFS98 score in patients without and with RSD was 3.081 $\pm$ 4.083 and 4.080 $\pm$ 4.622, respectively; the difference was not statistically significant (P = 0.363; Mann Whitney U test). Analysis of the eight items of HFS98 showed that local circulation in patients with RSD was significantly higher than that in patients without RDS (0.683 $\pm$ 0.822 vs. 0.528 $\pm$ 0.629, respectively). The other seven items did not show significant differences on Mann Whitney U test. Furthermore, the odds ratio for RSD was 0.771 (95% confidence interval [CI]: 0.387 - 1.537) in patients with HFS95 score > 0, and was 0.843 (95% CI: 0.455 - 1.559) in patients with a higher injury severity score than the calculated mean score in patients without RSD (> 4.083).

5. Discussion

The RSD prevalence in our study was almost similar to that reported previously (1-6). The greater prevalence of RSD in the female population, about two folds, when compared with the male population was also consistent with previous similar studies (4-6, 8). Several studies have investigated the factors predisposing patients to the development of RSD. However, no study has evaluated the severity of the initial injury and its relationship with the prevalence of RSD (7, 9, 10). Our analyses showed no significant relationship between the severity of injury and the risk of RSD occurrence, although the mean injury severity score was higher in patients with RSD than in those without RSD in this study population. The lower score of local circulation in patients with RSD than in those without RSD is notable and statistically significant, and can be attributed to changes in antioxidant levels at the injury site, which is one of the main mechanisms for the onset of RSD (11, 12). Wound contamination was also justifiably higher in patients with RSD, although the difference was not statistically significant. Even this finding can be attributed to the disease physiopathology based on the effects of oxidants present at the site of injury, but according to this theory, higher severity of injury should result in higher prevalence of RSD by producing higher levels of free radicals and oxidants at the site of injury. However, the study results showed no relationship between the mean injury severity score and prevalence of RSD. Statistical analysis also showed no significant difference in the probability of RSD between patients with a minimal injury HFS98 score (0) and those with scores higher than 0. Furthermore, there was no statistically significant difference in the probability of RSD in patients with injury severity score greater than the mean score obtained in patients without RSD (HFS98 score = 4.083). As the prevalence of this complication is multifactorial, the lack of correlation between the severity of injury and RSD occurrence can be explained. Many studies have proposed theories other than the oxidant theory, (13-15) and it seems the etiology of RSD cannot be completely justified by the oxidant theory. Some studies have considered the effects of genetic differences among people in the prevalence of this condition. Thus, on the basis of the results of this study, the severity of injury alone cannot be a determining factor in predicting the probability of RSD.

Footnote

Authors' Contribution: Study concept and design: Ahmadreza Mirbolook; acquisition of data: Ahmadreza Mirbolook; analysis and interpretation of data: Reza Bahador; drafting of the manuscript: Amirmohammad Gholizadeh; critical revision of the manuscript for important intellectual content: Sayyed Hassan Karbasi; statistical analysis: Sara Arbab; administrative, technical, and material support: Ahmadreza Mirbolook; study supervision: Pooya Derakhshan.

References

1. Cazeneuve JF, Leborgne JM, Kermad K, Hassan Y. [Vitamin C and prevention of reflex sympathetic dystrophy following surgical management of distal radius fractures]. *Acta Orthop Belg.* 2002;**68**(5):481–4. [PubMed: 12584978].
2. Stanton-Hicks M, Janig W, Hassenbusch S, Haddox JD, Boas R, Wilson P. Reflex sympathetic dystrophy: changing concepts and taxonomy. *Pain.* 1995;**63**(1):127–33. [PubMed: 8577483].
3. Veldman PH, Reynen HM, Arntz IE, Goris RJ. Signs and symptoms of reflex sympathetic dystrophy: prospective study of 829 patients. *Lancet.* 1993;**342**(8878):1012–6. [PubMed: 8105263].
4. Merskey H, Bogduk N. Classification of chronic pain. Descriptions of chronic pain syndromes and definitions of pain terms. Prepared by the International Association for the Study of Pain, Subcommittee on Taxonomy. *Pain Suppl.* 1986;**3**:S1–226. [PubMed: 3461421].
5. Zollinger PE, Tuinebreijer WE, Kreis RW, Breederveld RS. Effect of vitamin C on frequency of reflex sympathetic dystrophy in wrist fractures: a randomised trial. *Lancet.* 1999;**354**(9195):2025–8. doi: 10.1016/s0140-6736(99)03059-7. [PubMed: 10636366].
6. Manicourt DH, Brasseur JP, Boutsen Y, Depreseux G, Devogelaer JP. Role of alendronate in therapy for posttraumatic complex regional pain syndrome type I of the lower extremity. *Arthritis Rheum.* 2004;**50**(11):3690–7. doi: 10.1002/art.20591. [PubMed: 15529370].
7. Atkins RM, Duckworth T, Kanis JA. Features of algodystrophy after Colles' fracture. *J Bone Joint Surg Br.* 1990;**72**(1):105–10. [PubMed: 2298766].
8. Besse JL, Gadeyne S, Galand-Desme S, Lerat JL, Moyen B. Effect of vitamin C on prevention of complex regional pain syndrome type I in foot and ankle surgery. *Foot Ankle Surg.* 2009;**15**(4):179–82. doi: 10.1016/j.fas.2009.02.002. [PubMed: 19840748].

9. Bruehl S, Harden RN, Galer BS, Saltz S, Bertram M, Backonja M, et al. External validation of IASP diagnostic criteria for Complex Regional Pain Syndrome and proposed research diagnostic criteria. International Association for the Study of Pain. *Pain.* 1999;**81**(1-2):147–54. [PubMed: 10353502].
10. Krettek C, Seekamp A, Kontopp H, Tscherne H. Hannover Fracture Scale '98–re-evaluation and new perspectives of an established extremity salvage score. *Injury.* 2001;**32**(4):317–28. [PubMed: 11325369].
11. Field J, Warwick D, Bannister GC, Gibson AG. Long-term prognosis of displaced Colles' fracture: a 10-year prospective review. *Injury.* 1992;**23**(8):529–32. [PubMed: 1286904].
12. Holder LE, Cole LA, Myerson MS. Reflex sympathetic dystrophy in the foot: clinical and scintigraphic criteria. *Radiology.* 1992;**184**(2):531–5. doi: 10.1148/radiology.184.2.1620860. [PubMed: 1620860].
13. Colton AM, Fallat LM. Complex regional pain syndrome. *J Foot Ankle Surg.* 1996;**35**(4):284–96. [PubMed: 8872750].
14. Harris J, Fallat L, Schwartz S. Characteristic trends of lower-extremity complex regional pain syndrome. *J Foot Ankle Surg.* 2004;**43**(5):296–301. doi: 10.1053/j.jfas.2004.07.004. [PubMed: 15480404].
15. van der Laan L, Kapitein PJ, Oyen WJ, Verhofstad AA, Hendriks T, Goris RJ. A novel animal model to evaluate oxygen derived free radical damage in soft tissue. *Free Radic Res.* 1997;**26**(4):363–72. [PubMed: 9167941].