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Evaluating the Risk Factors of Nonunion in Long Bone Fractures of Patients Referred to Dr Shariati Hospital's Orthopedic Clinic During 2007 - 2013

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Background: Despite improvements in the understanding of fracture repair and treatment techniques, delayed unions and nonunions still occur more frequently than expected. Although the prevalence of these complications is not very high and is reported to be approximately 2 to 7 percent, they are considered costly complications and impose great burden on patients and the health care system.
Objectives: We aimed to evaluate the risk factors associated with nonunion in long bone fractures in order to propose viable methods to control these factors and decrease the prevalence of nonunion.
Patients and Methods: In this retrospective case control study, all the patients with long bone nonunion fractures referring to Shariati Hospital's orthopedic clinic during 2007 - 2013 were included as the case group. With a ratio of 1 to 3, patients matched according to the type of fractured bone were selected as the control group. Required data were gathered from the patients' records in the archives. SPSS software version 20 was used to analyze the data.
Results: Multivariate regression analysis was performed to assess independent risk factors of nonunion. According to this analysis, aging (P value = 0.007), female sex (P value = 0.041), comminuted and segmental fractures (P value = 0.001), higher grades of soft tissue injury (P value < 0.001), smoking (P value < 0.001), and infection (P value < 0.001) were found to be independent risk factors for nonunion in long bone fractures.
Conclusions: Of the assessed risk factors, smoking, and infection can be controlled to decrease the prevalence of nonunion. Therefore, smoking cessation and prophylactic measures against infection might be viable actions for this objective.

Keywords: Risk Factors; Bone; Fractures; Ununited; Abnormal Union

1. Background

Despite improvements in the understanding of fracture repair and treatment techniques, delayed unions and nonunions still occur more frequently than expected (1). Delayed union is, in fact, a clinical diagnosis and is defined as a union that does not occur within the usual time frame. This depends on various factors including fracture type and location and the extent of injury to the bone and soft tissue (2). In physical examination, tenderness, and minor movements at the fracture site are present. Radiographic findings are also indicative of some degree of callus formation with radiolucency at the location of the fracture.

Nonunion is defined as lack of improvements in the healing process of the fractured bone within twice the ordinary time, at least 6 months after trauma. According to the food and drug administration (FDA), nonunion is the failure of complete healing 9 months after the injury or observing no clinical and radiological improvements in the last 3 months (3). However, the time varies according to the fracture site; for example, it is considered to be 3 months for a fracture in neck of femur and 6 months in long bone fractures (1, 4).

Delayed union and nonunion are more common in diaphyseal open fractures. Their incidence is reported to be 16% - 60% in low-grade fractures (Gustilo type I, II and IIIA) and 43% - 100% in high-grade injuries (Gustilo Type IIIB and IIIC) (5, 6).

Multiple local and systemic factors affect the healing process of a fractured bone and can cause nonunion (7, 8). All efforts should be aimed at minimizing the effects of these factors during treatment. Systemic factors include age, nutritional condition, systemic diseases, corticosteroids, metabolic bone disorders, tumors, and anti-neoplastic agents. Effective local factors include blood supply, level of fracture, reduction, immobilization, soft tissue injury, local radiotherapy, and infection (7, 8). Despite controlling for all these factors, nonunion still occurs in some cases, and the exact cause is not yet understood.

Nonunion is an unpleasant complication for both the patient and the responsible physician. Considering the long period of time needed for treatment and the associated financial burden (9, 10), the importance of preventive measures is accentuated.

2. Objectives

We aimed to evaluate the risk factors for nonunion and their prevalence in order to propose plans of action to control these factors.

3. Patients and Methods

This retrospective case-control study included patients with diaphyseal and metaphyseal long bone fractures. Nonunion was regarded as failure of complete healing within 6 months from the injury and no clinical and radiological improvements in the last 3 months.

Data were gathered from the medical records of patients with nonunion of long bone fractures who were referred to Shariati hospital from 2007 to 2013. For each nonunion fracture, 3 patients with normally healed fracture of the same bone were included. The included subjects were chosen from patients who had a medical record with at least a 9-month follow up or those who had been referred to the clinic with signs and symptoms of nonunion including pain and movements at the site of fracture. Therefore, inclusion criteria were as follows:

- Long bone fracture (tibia, femur, humerus, radioulnar)
- Diaphyseal and metaphyseal fractures
- Medical record with at least a 9-month follow up

Exclusion criteria included the following:

- Intra-articular fractures
- Pathological fractures
- Incomplete medical records

Overall, 89 patients met the inclusion criteria for the case group, and our control group, with a ratio of approximately 1 to 3, included 231 subjects.

Gathered information included demographic characteristics (age and gender), the fractured bone, type of fracture, soft tissue injury, treatment, and possible risk factors of smoking, diabetes, and infection. Based on the type of fracture, patients were categorized into 3 groups: simple transverse, segmental, and comminuted. To evaluate the severity of injury, Gustilo classification was applied. Patients with closed fractures were classified into 1 group, and the subjects with open fractures were classified into 3 groups according to wound size: Group I, less than 1 cm; Group II, 1 to 10 cm; and Group III, more than 10 cm. Based on the treatment, patients were categorized into 5 groups: closed or cast, intramedullary nailing (IMN), open reduction internal fixation (ORIF), bridging, and external fixator.

Data were entered into SPSS software version 20. First, normality tests were used to assess the distribution of quantitative variables. Univariate analysis was performed to evaluate the correlation of each predictor variable with nonunion. Independent samples T-test for quantitative variables and chi-square test for qualitative variables were utilized. Finally, independent risk factors for nonunion were assessed through multivariate logistic regression, and adjusted odds ratios with 95% confidence intervals were reported. Pvalue < 0.05 was regarded as statistically significant.

4. Results

A total of 320 patients were included in this survey; 231 (72.2%) were in the union group, and 89 (27.8%) were in the nonunion group. The mean age of the participants was 36.75 ± 17.11 years with a minimum of 6 and a maximum of 88 years; 71.3% of the participants were male.

The mean age of the 89 nonunion patients was 42.08 ± 16.05, and this figure among the 231 subjects of the union group was 34.70 ± 17.10. The differences between the 2 groups were analyzed via Independent Samples T-test and found to be statistically significant (Pvalue = 0.001).

Table 1 presents the differences between the union and nonunion groups regarding the evaluated variables of the survey. As demonstrated, the differences were insignificant considering gender, fracture location, and medical history of diabetes.

The prevalence of nonunion in comminuted fractures was higher than that in the other 2 types of fracture, and the differences were found to be significant (P-value < 0.001). The higher the severity of soft tissue injury, the greater was the prevalence of nonunion (P value < 0.001). External fixator and bridging were accompanied with the highest rates of nonunion, and the total differences between the 2 groups regarding treatment method were also significant (Pvalue < 0.001).

Rate of smoking was significantly higher in the nonunion group, and according to the odds ratio calculated for this correlation, smoking increases the risk of nonunion by 2.8 times (Pvalue < 0.001, OR = 2.83, 95%CI = 1.71 - 4.69).

Infection of the fracture site was also significantly higher among the patients in the nonunion group, and according to the computed odds ratio, subjects who develop infection at their fracture site are 11.6 times more at risk for nonunion (Pvalue < 0.001, OR = 11.6, 95%CI = 4.49 - 29.85).

Finally, to assess the independent risk factors for nonunion, a multivariate regression analysis was performed, and according to the yielded results, the following factors were found to significantly increase the risk of nonunion as its independent risk factors: old age (P-value = 0.005, OR = 1.03, 95%CI = 1.01 - 1.06), female sex (P-value = 0.037, OR = 2.44, 95%CI = 1.05 - 5.62), segmental fractures (Pvalue = 0.001, OR = 6.01, 95%CI = 2.11 - 17.11), and comminuted fractures (P-value < 0.001, OR = 8.19, 95%CI = 2.60 - 25.76), higher severity of soft tissue injuries (P-value < 0.001, OR = 2.72, 95%CI = 1.78 - 4.13), smoking (P-value < 0.001, OR = 4.17, 95%CI = 1.93 - 9.03), and fracture site infection (Pvalue < 0.001, OR = 9.43, 95%CI = 2.78 - 31.99). The fractured bone, type of treatment, and medical history of diabetes yielded Pvalues higher than 0.05.

Table 1. Differences Between the Union and Nonunion Groups Regarding the Evaluated Variables [a]

Variables	Healing Condition		P Value
	Union	Nonunion	
Gender			0.682
Male	166 (71.9)	62 (69.7)	
Female	65 (28.1)	27 (30.3)	
Bone			0.482
Femur	57 (24.7)	27 (30.3)	
Tibiofibula	90 (39.0)	37 (41.6)	
Radioulnar	49 (21.2)	13 (14.6)	
Humerus	35 (15.2)	12 (13.5)	
Type of Fracture			< 0.001
Simple transverse	88 (38.1)	5 (5.6)	
Segmental	103 (44.6)	46 (51.7)	
Comminuted	40 (17.3)	38 (42.7)	
Soft tissue injury			< 0.001
Closed fracture	159 (68.8)	27 (30.3)	
Gustilo type I	57 (24.7)	32 (36.0)	
Gustilo type II	12 (5.2)	17 (19.1)	
Gustilo type III	3 (1.3)	13 (14.6)	
Treatment			< 0.001
Closed or cast	32 (13.9)	6 (6.7)	
IMN	89 (38.5)	17 (19.1)	
ORIF	104 (45.0)	49 (55.1)	
Bridging	5 (2.2)	3 (3.4)	
External fixator	1 (0.4)	14 (15.7)	
Diabetes			0.179
No	197 (85.3)	70 (78.7)	
Yes	34 (14.7)	19 (21.3)	
Smoking			< 0.001
No	152 (65.8)	36 (40.4)	
Yes	79 (34.2)	53 (59.6)	
Infection			< 0.001
No	225 (97.4)	68 (76.4)	
Yes	6 (2.6)	21 (23.6)	

[a] Data are presented as No. (%).

5. Discussion

Delayed union and nonunion still occur more frequently than expected in spite of the vast improvements in fracture treatment methods. Although the prevalence of these complications is not very high and is reported to be approximately 2 to 7 percent, they are considered costly complications and impose great burden on patients and the health care system. Therefore, understanding the causes and risk factors for nonunion is of utmost importance so that preventive measures can be suggested to decrease the incidence of this complication.

In the present study, we evaluated the effects of age, gender, fractured bone, type of fracture, severity of soft tissue injury, provided treatment, smoking, medical history of diabetes, and infection at the injury site on incidence of nonunion in long bone fractures.

As presented in the results, no significant difference was found between the 2 groups regarding the fractured bone, which is compatible with the results of earlier studies such as the survey conducted by Boyd et al. (11); recent studies have reported a significantly higher prevalence of nonunion in fractures of the tibia (1, 4). Female gender was found to be an independent risk factor for nonunion, which was congruent with the results of surveys conducted by Kyro et al. (12) and Robinson et al. (13).

Similar to the results of previous surveys (13-15), the mean age was found to be significantly higher in the nonunion group, and old age was reported as an independent risk factor for this complication. Comminuted fractures were reported as risk factors for nonunion in studies conducted by Kyro et al. (12), Mathog et al. (16), Karladani et al. (17), and Robinson et al. (13), an observation that was also confirmed by the results of our study. Higher severity of soft tissue injury was also a risk factor in our survey that was reported by many other studies (15, 17-20).

In our raw analysis, we found significant differences considering the treatment provided for the patients, but when the effects of other variables were controlled, none of the treatment methods were found to be independent risk factors. Most previous studies had evaluated a specific type of fracture and a unique treatment method, so comparison of different treatments similar to our survey was not performed.

Smoking was found to be an independent risk factor for nonunion, confirming the results of many other studies (12, 14-17, 21). Infection of the fracture site was found to increase the risk of nonunion by 11.6 times. The adverse effects of infection on the healing process of fractures were also pointed out in the surveys conducted by Harley et al. (18) and Mathog et al. (16).

Of the variables found to be independent risk factors for nonunion in the multivariate regression analysis, smoking and infection at the site of infection are the ones that can be controlled; therefore, smoking cessation and prophylactic measures against infection might be effective preventive actions for nonunion in long bone fractures. However, further investigations are needed to elaborate on this matter.

Putting it altogether, aging, female gender, comminuted and segmental fractures, higher grades of soft tissue injury, smoking, and infection were found to be independent risk factors for nonunion in long bone fractures. Among the risk factors, smoking and infection can be controlled to decrease the prevalence of nonunion. Therefore, smoking cessation and prophylactic measures against infection might be viable actions for this objective.

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