

Retrospective Evaluation of Risk Factors Associated with Delayed Union Following Surgical Fixation of Long-Bone Fractures

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Abstract:

Background: Delays in fracture healing are a significant complication of long-bone fractures that may contribute to prolonged healing, loss of function and further treatment. The ascertainment of risk factors can aid in early detection and proper management of high-risk individuals.

Aim: To identify and assess the risk factors for delayed union after surgery in long bone fractures in a retrospective way.

Methodology: This is a retrospective cohort study in Department of orthopaedics, Maulana Azad Medical College and Lok Nayak hospital, New Delhi, India . One hundred forty-five patients with fractures of long bones were included who had surgical fixation of the fractures. Demographic, clinical, injury related and postoperative variables were evaluated. Logistic regression analysis was used to determine factors for delayed union.

Results: 32 (22.1%) patients had delayed union. Smoking (AOR = 3.42), diabetes mellitus (AOR = 2.89), high-energy trauma (AOR = 2.31), open fracture (AOR = 3.76), comminuted fracture (AOR = 2.67) and postoperative infection (AOR = 4.85) were significant risk factors. The age, sex and fixation method were not significant predictors.

Conclusion: Delayed union was related to several patient, injury and postoperative features. Proper management of the factors early may help to improve fracture-healing outcomes.

Keywords: Delayed Union; Long-Bone Fractures; Surgical Fixation; Risk Factors; Fracture Healing; Postoperative Infection.

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Introduction

Long bone fractures make up a significant percentage of orthopaedic trauma and frequently affect the femur, tibia, humerus and other major bones of the body. These injuries often occur in high-energy situations such as road traffic accidents, falls from height, and sports-related injuries, and may occur with low energy trauma in elderly people and in patients with impaired bone quality [1]. Although there have been great achievements in the field of orthopaedic trauma, complications in fracture healing remain a significant clinical problem. Delayed union, especially, is related to continued pain, functional limitation, extended duration of work absence, re-hospitalization, and higher health care costs. The goal of surgical fixation with intramedullary nails, plates, screws or an external fixation is to restore anatomical alignment and ensure appropriate mechanical

stability, but fixation does not always lead to timely fracture healing [2].

The healing of a fracture is a complex biological process in which there is inflammation, angiogenesis, cellular proliferation, callus formation and bone remodelling. A proper balance between the biological and mechanical aspect of the fracture site is crucial to achieving successful union [3]. The “diamond” or “diamond-shaped” model of fracture healing underscores the pivotal role of osteogenic cells, osteoconductive scaffolding, growth factors, vascularity, mechanical stability, and the surrounding biological environment. Any disruption of one or more of these factors will hinder healing and could lead to non-union or delayed union. The definition of 'delayed union' varies in different studies and depends on the anatomical site but

generally refers to a fracture that has failed to achieve union in the predicted timeframe but still shows signs of healing and thus has the potential to achieve union without necessarily needing definitive further treatment [4].

Delayed union and non-union are clinically important. Delayed union is a prolonged or slower-than-expected healing of a fracture, while non-union is a fracture that hasn't healed or is a fracture that is not expected to heal without additional measures. The Food and Drug Administration of the United States has traditionally defined non-union as a fracture that has not demonstrated any consolidation of healing for three consecutive months and is present for at least nine months [5]. But strict scheduling might not capture the complexity of the clinical process of fracture healing. Thus, when assessing healing complications, radiographic results, clinical symptoms, fracture characteristics, and the assessment of the surgeon treating the case are often taken into account together. Delay in union could thus be a significant phase in which early diagnosis and intervention might prevent the development of true non-union [6].

Long bones, such as the tibia, femur and humerus, are bones where the healing complications can be especially serious. These fractures can include large amounts of soft tissue injury, disruption of the local blood supply, comminution and significant mechanical instability. Tibial shaft fractures are particularly prone to delayed fracture healing due to reduced soft-tissue coverage and perhaps impaired blood supply from the high-energy nature of the injury. Likewise, fractures from high-energy trauma may have a significant amount of soft-tissue damage and multiple associated injuries, and humeral fractures can pose difficulties in fracture pattern, stability of fixation, and local biological factors [7].

There are several patient related factors that have been involved in impaired fracture healing. Smoking is an easily recognized modifiable risk factor and there is evidence that it is associated with delayed union or non-union. Cigarette smoke contains nicotine and other substances that can negatively influence angiogenesis, tissue oxygenation, and osteoblast function, and hence the biologic mechanisms that can promote bone healing. The other diseases that have been linked to diabetes mellitus are impaired healing, possibly due to microvascular dysfunction, inflammatory responses, and bone metabolism changes. Other factors mentioned in the literature are multiple medical conditions, alcohol consumption, obesity, poor nutritional status and advanced age [8]. The proportion of individual patient characteristics, however, may differ depending on the location of the fracture, the severity of the injury and the treatment.

Delayed unions may be as much injury related as to surgery. Increased risk of healing complications has been linked to open fractures, severe soft-tissue injury, high-energy trauma, comminution, segmental fracture patterns and fracture displacement. Furthermore, infection is a significant hindrance to a good fracture healing as it can impair vascularity, destroy bone and soft tissue and may require additional surgery [9]. How well fractures are reduced and fixed is also crucial. Poor stability allows too much movement at the fracture site, while too much rigidity may hinder movement under certain circumstances, and thus, the mechanical stimulation needed for secondary bone healing. Thus, the type of fixation and characteristics of the implant, surgical technique, and restoration of alignment all may have an impact on the subsequent sequence of union.

Many studies on fracture-healing complications have concentrated on non-union, various definitions and measurements have been used, and some have examined singular fracture sites with comparative smaller numbers of patients. Such methodological distinctions make comparative analyses between studies challenging and may reduce the applicability of published risk factors [10]. In addition, delayed union is clinically important in that it can significantly extend treatment and rehabilitation even if union occurs. Factors associated with increased union time after surgical fixation could thus be useful to help identify high-risk patients for whom postoperative monitoring should be more closely tailored to the healing process; to help patients modify preventable risk factors; and to help clinicians consider timely interventions if healing isn't progressing normally.

This retrospective assessment can be used to review routinely collected clinical, radiological, demographic and injury and treatment-related information from patients undergoing surgery for long-bone fracture fixation. This could be useful to establish a relationship between age, sex, smoking status, diabetes, mechanism of injury, fracture characteristics, open versus closed injury, fixation method, infection and any other peri-operative variables and delayed union. It is especially important to understand these associations in environments where delayed union is associated with longer disability and higher healthcare resource utilization. The goal of the present study is to therefore to assess retrospectively the risk factors for delayed union after surgical fixation of long bone fractures. The study analyses patient-related, injury-related, and treatment-related factors to determine if any are associated with delayed fracture healing and to provide evidence to help guide risk stratification, postoperative monitoring and management of patients with a higher risk of delayed fracture healing.

Methodology

Study Design: This study was designed as a retrospective cohort study to evaluate the risk factors associated with delayed union following surgical fixation of long-bone fractures. Retrospective medical records of eligible patients who underwent surgical management for long-bone fractures were reviewed. The study compared demographic, clinical, injury-related, and treatment-related characteristics between patients who developed delayed union and those who achieved fracture union within the expected healing period.

Study Area: The study was conducted at Department of orthopaedics, Maulana Azad Medical College and Lok Nayak hospital, New Delhi, India

Study Duration: The study was conducted over a period of one year.

Sample Size: A total of 145 patients (N = 145) who fulfilled the eligibility criteria were included in the study. The sample comprised patients with long-bone fractures who underwent surgical fixation and for whom adequate clinical, operative, and follow-up records were available for assessment of fracture healing outcomes.

Sample Population: The study population consisted of patients treated at Lok Nayak Hospital, New Delhi, with surgically managed fractures involving major long bones, including the humerus, femur, and tibia. Both male and female patients were included. Patients were categorised according to the occurrence or absence of delayed union during the postoperative follow-up period. Delayed union was identified based on the treating orthopaedic surgeon's clinical assessment and available serial radiological evidence showing slower-than-expected progression of fracture healing.

Data Collection: Data were collected retrospectively from the medical records of eligible patients treated at Lok Nayak Hospital, New Delhi. Information was obtained from orthopaedic admission records, patient case files, operation theatre registers, discharge summaries, radiological records, and outpatient follow-up documentation. A structured data collection proforma was used to extract demographic variables, including age and sex; patient-related factors such as smoking status, diabetes mellitus, and other comorbidities; injury-related characteristics, including the affected long bone, fracture location and pattern, mechanism of injury, and open or closed fracture status; and treatment-related variables, including the method of surgical fixation and postoperative complications. Serial clinical and radiological follow-up records were reviewed to assess fracture-healing progression, and the occurrence of delayed union was recorded as the primary outcome. Patients were

subsequently classified into delayed union and non-delayed union groups for comparative analysis.

Inclusion Criteria

Patients were included in the study if they met the following criteria:

1. Patients of either sex treated for a fracture of a major long bone, including the humerus, femur, or tibia.
2. Patients who underwent surgical fixation for the fracture.
3. Patients with adequate medical, operative, radiological, and follow-up records available for review.
4. Patients in whom the postoperative fracture-healing outcome could be assessed.
5. Patients who developed delayed union as well as those who demonstrated normal progression of fracture healing.

Exclusion Criteria

The following patients were excluded from the study:

1. Patients with pathological fractures, including fractures associated with metastatic bone disease.
2. Patients managed exclusively by conservative or non-operative treatment.
3. Patients with incomplete, missing, or inadequate medical and follow-up records.
4. Patients in whom the fracture-healing outcome could not be determined from the available clinical and radiological documentation.
5. Patients with fractures outside the selected long-bone sites included in the study.
6. Patients with multiple records representing duplicate admissions for the same fracture episode.

Procedure: After obtaining ethical approval and the required institutional permission, a retrospective review of records was undertaken to identify 145 eligible patients who underwent surgical fixation for long-bone fractures. Each record was screened according to the predetermined inclusion and exclusion criteria, and eligible cases were included in the study. Relevant demographic, clinical, injury-related, and surgical information was extracted using a structured proforma and entered into a database. Postoperative follow-up records and serial radiographs were reviewed to evaluate the progression of fracture healing. Delayed union was determined on the basis of documented clinical and radiological evidence indicating slower-than-expected progression towards fracture union for the respective fracture site. Patients were then categorised into those with delayed union and those without delayed union, and the distribution of potential risk factors was compared between the two groups.

Statistical Analysis: The collected data were entered into a spreadsheet and analysed using appropriate statistical software. Descriptive statistics were used to summarise demographic, clinical, injury-related, and treatment-related characteristics of the study population. Continuous variables were expressed as mean $\pm$ standard deviation or median with interquartile range, depending on the distribution of the data, whereas categorical variables were presented as frequencies and percentages. Differences between patients with delayed union and those without delayed union were assessed using the Chi-square test or Fisher's exact test for categorical variables and the student's t-test or Mann-Whitney U test for continuous variables, as appropriate. Univariable logistic regression analysis was performed to identify factors potentially associated with delayed union, and variables with a preliminary significance level of $p < 0.25$, along with clinically important variables, were included in the multivariable logistic

regression model. Adjusted odds ratios (AORs) with 95% confidence intervals were calculated to identify independent risk factors associated with delayed union, and a two-sided p value of <0.05 was considered statistically significant".

Result

Table 1 presents the demographic characteristics of the study population. Among the 145 patients included in the study, delayed union was observed in 32 (22.1%) patients, while 113 (77.9%) patients did not develop delayed union. The majority of the participants were male (70.3%). The mean age was slightly higher among patients with delayed union (42.8 ± 14.6 years) compared with those without delayed union (39.7 ± 15.2 years); however, the difference was not statistically significant ($p = 0.298$). Similarly, no significant association was observed between sex and the occurrence of delayed union ($p = 0.521$).

Table 1: Demographic Characteristics of the Study Population (N = 145)

Variable	Delayed Union (n = 32)	No Delayed Union (n = 113)	Total (N = 145)	p-value
Age (years), Mean $\pm$ SD	42.8 $\pm$ 14.6	39.7 $\pm$ 15.2	40.4 $\pm$ 15.1	0.298
Male	24 (75.0%)	78 (69.0%)	102 (70.3%)	0.521
Female	8 (25.0%)	35 (31.0%)	43 (29.7%)	0.521
Age $\leq$ 40 years	17 (53.1%)	68 (60.2%)	85 (58.6%)	0.476
Age >40 years	15 (46.9%)	45 (39.8%)	60 (41.4%)	0.476

Table 2 shows the association between patient-related risk factors and delayed union. Smoking history was significantly more common among patients with delayed union (56.3%) than among those without delayed union (24.8%) ($p = 0.001$). Similarly, diabetes mellitus was present in 28.1% of patients with delayed union compared with 11.5% of

patients without delayed union ($p = 0.018$). The presence of other comorbidities was also significantly higher among the delayed union group ($p = 0.049$). These findings indicate that smoking, diabetes mellitus, and the presence of comorbidities may contribute to an increased risk of delayed fracture healing.

Table 2: Distribution of Patient-Related Risk Factors According to Delayed Union

Risk Factor	Delayed Union (n = 32)	No Delayed Union (n = 113)	Total (N = 145)	p-value
Smoking history	18 (56.3%)	28 (24.8%)	46 (31.7%)	0.001
Diabetes mellitus	9 (28.1%)	13 (11.5%)	22 (15.2%)	0.018
Other comorbidities	12 (37.5%)	23 (20.4%)	35 (24.1%)	0.049
No comorbidity	11 (34.4%)	77 (68.1%)	88 (60.7%)	0.001

Table 3 presents the relationship between injury-related factors and delayed union. High-energy injuries were significantly more frequent among patients with delayed union (71.9%) compared with those without delayed union (46.0%) ($p = 0.011$). Open fractures were also significantly associated with delayed union, occurring in 43.8% of delayed union cases compared with 16.8% of patients

without delayed union ($p = 0.002$). In addition, comminuted fractures were significantly more common in the delayed union group (59.4%) than in the non-delayed union group (30.1%) ($p = 0.004$). These findings suggest that severe injury characteristics may adversely affect the fracture-healing process.

Table 3: Association of Injury-Related Factors with Delayed Union

Variable	Delayed Union (n = 32)	No Delayed Union (n = 113)	Total (N = 145)	p-value
High-energy injury	23 (71.9%)	52 (46.0%)	75 (51.7%)	0.011
Open fracture	14 (43.8%)	19 (16.8%)	33 (22.8%)	0.002
Closed fracture	18 (56.3%)	94 (83.2%)	112 (77.2%)	0.002
Comminuted fracture	19 (59.4%)	34 (30.1%)	53 (36.6%)	0.004
Multiple injuries	11 (34.4%)	21 (18.6%)	32 (22.1%)	0.062

Table 4 demonstrates the distribution of fracture location and treatment-related factors among patients with and without delayed union. Tibial fractures constituted the highest proportion of delayed union cases (53.1%), followed by femoral fractures (31.3%) and humeral fractures (15.6%); however, the association between fracture site and delayed union was not statistically significant.

Similarly, no significant association was observed between the method of surgical fixation and delayed union. In contrast, postoperative infection was significantly more common among patients with delayed union (25.0%) compared with those without delayed union (6.2%) ($p = 0.003$), indicating that postoperative infection may be an important contributor to impaired fracture healing.

Table 4: Distribution of Fracture and Treatment-Related Factors

Variable	Delayed Union (n = 32)	No Delayed Union (n = 113)	p-value
Fracture site			
Humerus	5 (15.6%)	27 (23.9%)	0.318
Femur	10 (31.3%)	38 (33.6%)	0.811
Tibia	17 (53.1%)	48 (42.5%)	0.295
Method of fixation			
Intramedullary nailing	19 (59.4%)	61 (54.0%)	0.596
Plate fixation	13 (40.6%)	52 (46.0%)	0.596
Postoperative infection	8 (25.0%)	7 (6.2%)	0.003
Implant/fixation-related complication	6 (18.8%)	8 (7.1%)	0.058

Table 5 presents the multivariable logistic regression analysis of factors independently associated with delayed union. After adjustment for potential confounding variables, smoking history (AOR = 3.42, 95% CI: 1.45–8.07, $p = 0.005$), diabetes mellitus (AOR = 2.89, 95% CI: 1.03–8.11, $p = 0.044$), high-energy injury (AOR = 2.31, 95% CI: 1.01–5.31, $p = 0.047$), open fracture (AOR =

3.76, 95% CI: 1.48–9.58, $p = 0.005$), comminuted fracture (AOR = 2.67, 95% CI: 1.12–6.39, $p = 0.027$), and postoperative infection (AOR = 4.85, 95% CI: 1.52–15.48, $p = 0.008$) remained significantly associated with delayed union. Among these variables, postoperative infection showed the strongest association with delayed union, followed by open fractures and smoking history.

Table 5: Multivariable Logistic Regression Analysis of Risk Factors Associated with Delayed Union

Variable	Adjusted Odds Ratio (AOR)	95% Confidence Interval	p-value
Smoking history	3.42	1.45–8.07	0.005
Diabetes mellitus	2.89	1.03–8.11	0.044
High-energy injury	2.31	1.01–5.31	0.047
Open fracture	3.76	1.48–9.58	0.005
Comminuted fracture	2.67	1.12–6.39	0.027
Postoperative infection	4.85	1.52–15.48	0.008
Age >40 years	1.34	0.58–3.12	0.494
Male sex	1.21	0.48–3.06	0.681

Discussion

This was a retrospective study aimed at assessing risk factors for delayed union after surgery of fractures of long bones at Lok Nayak Hospital, New Delhi in 145 patients. Thirty-two patients (22.1%) in the study population showed delayed union, and 113 patients (77.9%) showed no delayed union. This

relatively large proportion in the present study could be due to the fact that delayed union was included and not just established non-union. By contrast, Zura et al. did a comprehensive epidemiological study on 18 human bones and found a global rate of non-union of about 4.9%, but with a wide range of frequency depending on the fracture site and characteristics of the patient. The delayed union rate

in the present study was therefore higher (22.1%) than that reported in these other studies, which may be due to the differences in how union was defined and the inclusion of long bone fractures treated surgically". (Zura et al., 2016) [11].

In the current study, smoking was a significant associated factor of delayed union. Smoking was reported in 56.3% of patients with delayed union and 24.8% of patients without delayed union ($p = 0.001$); smokers had 3.42 times higher adjusted odds of delayed union (AOR = 3.42, 95% CI: 1.45–8.07; $p = 0.005$). A similar association has been reported by Pearson et al., who in a systematic review and meta-analysis found that smokers had about a 2.2-fold increased risk of delayed union and/or non-union. Both results in the present study and the previous study report a significant association between smoking and poor fracture healing, with the magnitude of the association being greater in the present study. These discrepancies in risk estimates may be due to differences in fracture types, surgical techniques and definition of delayed healing. (Pearson et al., 2016) [12].

Delayed union was also found to be significantly associated with diabetes mellitus in the present study. Diabetes was found in 28.1% of patients with delayed union vs 11.5% of those without delayed union ($p = 0.018$) and diabetes was associated with a 2.89-fold risk of delayed union (AOR = 2.89, 95% CI: 1.03–8.11; $p = 0.044$). In a systematic review and meta-analysis of surgically treated traumatic diaphyseal fracture, Santolini et al. found that diabetes was a risk factor for non-union (pooled OR, 1.6; 95% CI, 1.3–2.0). Thus, the present results indicate the same general direction of association but higher magnitude of risk in our study. It could mean that metabolic and microvascular changes associated with diabetes have a clinically relevant effect on the healing of fractures. (Santolini et al., 2020) [13].

Delays in union were highly associated with patients having a high energy trauma in the current study (71.9% vs. 46.0% ($p = 0.011$)). High energy injury was also an independent predictor of delayed union after adjustment with an AOR of 2.31 times (AOR = 2.31, 95% CI: 1.01–5.31; $p = 0.047$). Makaram et al. studied risk factors for delayed union after intramedullary nailing of tibial diaphyseal fractures and found that high-energy mechanism was one of the risk factors with the odds ratio of 1.81 (with a P value of 0.030). The present finding is thus similar, but a somewhat stronger association was seen in our population. This relationship may be because of the increased soft-tissue trauma, vascular disruption and complexity of fractures in these high-energy injuries. (Makaram et al., 2021) [14].

Another significant factor of delayed union was open fracture. 43.8% of patients with delayed union

had open fractures in the present study, and only 16.8% of patients without delayed union ($p = 0.002$). Open fractures increased the adjusted odds of delayed union by 3.76 times (AOR = 3.76, 95% CI: 1.48–9.58; $p = 0.005$). Dai et al. did a retrospective case-control study of 669 patients and found that open fractures were independently associated with postoperative non-union with an odds ratio of 2.71 (95% CI: 1.72–4.27; $p < 0.001$). The current study thus showed a similar relationship but of a higher degree of risk. This may be explained by the variance in severity of injury, location of fracture and considering delayed union as the primary outcome. (Dai et al., 2021) [15].

Delayed union was also found to be significantly associated with comminuted fracture patterns in the present study. Delayed union was seen in 59.4% of patients with comminuted fractures; 30.1% without delayed union ($p = 0.004$); and patients with comminuted fractures had 2.67 times greater adjusted odds of delayed union (AOR = 2.67, 95% CI: 1.12–6.39; $p = 0.027$). Fracture complexity and mechanical and biological factors at the fracture site were identified by Calori et al. as significant factors in poor fracture healing and non-union. They commented that severe fracture patterns, loss of bone contact and loss of vascularity could have a negative impact on union. The results of the present study thus support this evidence and indicate that comminution should be regarded as an important injury related factor when evaluating the risk for delayed union. (Calori et al., 2007) [16].

Delayed union was most strongly independently associated with postoperative infection in the current study. A higher incidence of infection was found in patients with delayed union (25.0%) than in patients without delayed union (6.2%) with a p value of 0.003, and the adjusted OR was 4.85 (95% CI: 1.52–15.48; $p = 0.008$). Metsemakers et al. identified fracture related infection to be a significant complication that can hinder bone regeneration due to chronic inflammation, tissue loss, and the need for multiple surgeries. The current results corroborate this and underscore the need for prevention, detection, and early intervention in the case of infection after surgical fixation. (Metsemakers et al., 2018) [17].

In the present study, there was no significant association between delayed union and age and sex. The mean age was 42.8 ± 14.6 years in the delayed union group and 39.7 ± 15.2 years in the non-delayed union group ($p = 0.298$), while male sex was not an independent predictor (AOR = 1.21; $p = 0.681$). In contrast to the epidemiological study by Mills and Simpson who showed that the incidence of non-union was different between age and fracture location, with the middle-aged adults having a higher incidence of non-union for certain fracture types. Any discrepancies with their results and the

current study could be due to the lower number of patients, inclusion of certain fractures that had undergone surgery and use of delayed union as a criterion. (Mills & Simpson, 2013) [18].

In summary, the current study suggests that delayed union after surgical fixation of long bone fractures is related to mainly modifiable patient factors and injury severity. Smoking (AOR = 3.42), diabetes mellitus (AOR = 2.89), high-energy trauma (AOR = 2.31), open fractures (AOR = 3.76), and comminuted fractures (AOR = 2.67) and postoperative infection (AOR = 4.85) independently correlated with delayed union. Nicholson et al. also highlighted in a review that there are multiple factors involved in complications after long-bone healing, including severity of injury, patient comorbidities, mechanical factors, and infection. The current results corroborate this multifaceted model and indicate that early identification of high-risk patients could help to stop smoking, optimise metabolic parameters, prevent infections, and more closely monitor the postoperative period to enhance fracture healing.

Conclusion

In the current retrospective study, delayed union was seen in 22.1% of 145 patients with long-bone fractures treated with surgical fixation and was dependent on a variety of patient-, injury-, and treatment-related factors. Smoking, diabetes mellitus, high energy trauma, open fractures, comminuted fracture patterns and postoperative infection were significantly associated with an increased risk of delayed union, with postoperative infection having the strongest independent association. However, age and sex and method of fixation had no significant effect on delayed union. These findings highlight the need for early identification and careful monitoring of high-risk patients, optimisation of modifiable risk factors like smoking and diabetes, careful management of severe and open fractures, and effective prevention and timely treatment of postoperative infection. In summary, a combined biological and mechanical strategy could be favourable for the reduction of delayed union and fracture healing after surgical fixation of long bone fractures.

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