

Predictors of Non-Union in Long Bone Fractures Following High-Energy Trauma: A Prospective Cohort Study.

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Abstract

Background:

Non-union of long bone fractures is a serious complication of high-energy trauma, resulting in prolonged disability, impaired functional outcomes, and increased healthcare costs. Early identification of predictors of non-union may facilitate timely interventions and improve fracture healing.

Methods:

This prospective cohort study was conducted in the Department of Orthopaedics at Uttar Pradesh University of Medical Sciences, Saifai, Etawah, over 18 months. A total of 72 patients with long bone fractures following high-energy trauma were enrolled. Clinical, radiological, and treatment-related variables were recorded. Patients were followed for 12 months to assess fracture healing. Non-union was defined as the absence of radiological union with persistent clinical symptoms. Univariate and multivariate logistic regression analyses were performed to identify predictors of non-union.

Results:

The mean age of participants was 41.8 ± 13.6 years, and 75.0% (n=54) were males. The tibia was the most commonly affected bone (38.9%). Overall, 17 patients (23.6%) developed non-union. Non-union was significantly associated with open fractures ($p=0.002$), smoking ($p=0.01$), diabetes mellitus ($p=0.03$), postoperative infection ($p<0.001$), and delayed surgery >48 hours ($p=0.01$). Multivariate analysis identified postoperative infection (adjusted OR=5.8, 95% CI: 2.1-15.9; $p<0.001$) and delayed surgery >48 hours (adjusted OR=3.4, 95% CI: 1.2-9.6; $p=0.02$) as independent predictors of non-union.

Conclusion:

Non-union in long bone fractures is strongly associated with modifiable factors, particularly postoperative infection and delayed surgical intervention. Early surgery and effective infection control may significantly improve fracture healing outcomes.

Recommendation:

Early surgical stabilization and stringent infection prevention measures should be prioritized in patients with high-energy long bone fractures to reduce the risk of non-union.

Keywords: Long bone fractures; Non-union; High-energy trauma; Fracture healing; Postoperative infection; Delayed surgery.

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INTRODUCTION

Long bone fractures that do not fuse are a serious complication in orthopedics, especially when they occur

after a high-energy trauma like road traffic accidents and falls from height. It is widely described as the inability of a fracture to fuse in a reasonable period of time, which is

usually six to nine months, and no further development towards healing occurs [1]. Not only does prolongation of patient morbidity result in higher economic cost of healthcare systems since repeated interventions, long-term rehabilitation, and productivity loss are increased by nonunion [2].

The nonunion rate depends on the kind of fracture, the location, and the injury severity, and has been reported to be 5% to 20% in long bone fractures [3]. High-energy trauma is characterized by a high degree of soft tissue destruction, periosteal stripping, and impaired vascularity, all essential factors in bone healing [4]. The tibia is especially vulnerable to nonunion after such injuries due to its subcutaneous nature and small amount of soft tissue coverage [5].

The fracture healing process is a complicated biological mechanism that depends on mechanical stability and the biological environment. The presence of several patient-related factors, including advanced age, smoking, diabetes mellitus, and nutritional status, has been demonstrated to impair osteogenesis and slow down the healing of fractures [6,7]. An example is smoking, which has been linked to vasoconstriction and decreased blood flow to tissues, hence impacting adversely on the callus formation [8]. In a similar way, diabetes mellitus disrupts microcirculation and cellular functioning, heightening the likelihood of delayed union and nonunion [9].

Along with patient factors, the characteristics of injuries like open fractures, comminution level, and contamination are also important. Open fractures, particularly regarding higher grade based on the Gustilo Anderson system, are highly related to infection and impaired healing [10]. Factors associated with treatment, such as the timing of surgery, fixation mode, and sufficiency of reduction, are also significant. Abnormal fixation and poor fixation may cause abnormal micromotion at the fracture site, which inhibits healing [11].

Nonunion remains a therapeutic challenge in spite of the improved surgical procedures and fixation techniques. The early identification of high-risk patients will enable specific intervention, including biological augmentation and optimal fixation strategies [12]. Despite advances in surgical techniques and fracture management, non-union remains a major therapeutic challenge. Early identification of patients at high risk for non-union may facilitate timely interventions and improve outcomes. Therefore, this study aimed to evaluate clinical, radiological, and treatment-related predictors of non-union among patients with long bone fractures following high-energy trauma treated at a tertiary care center.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based prospective cohort study was conducted in the Department of Orthopedics, Uttar Pradesh University of Medical Sciences (UPUMS), Saifai, Etawah, Uttar Pradesh, India, a tertiary care teaching and referral institution serving patients from Uttar Pradesh and neighboring states. The institute provides comprehensive trauma, orthopedic, emergency, critical care, radiological, and rehabilitation services and caters to both rural and urban populations.

The study was conducted from 1 January 2024 to 30 June 2025 (18 months). Patient recruitment and baseline data collection were performed during the first 12 months, while enrolled participants were subsequently followed for up to 12 months after surgery for assessment of fracture healing.

Study Size

The sample size was estimated using the formula:

$$n = Z^2 P(1-P)/d^2$$

Assuming a prevalence of non-union of 20%, confidence level of 95% ($Z=1.96$), and precision of 10%, the minimum sample size was calculated as 61 participants. Considering potential losses to follow-up, 72 participants were included.

Participant Selection

Consecutive sampling was employed. All eligible patients presenting with long bone fractures following high-energy trauma during the study period were consecutively recruited until the required sample size was achieved.

Bias

Selection bias was minimized by recruiting all eligible patients sequentially. Information bias was reduced by using standardized clinical and radiological assessment criteria for fracture healing. Outcome assessment was performed using predefined criteria for non-union, and multivariable logistic regression analysis was used to control potential confounding factors.

Study Population and Sample Size

A total of 72 patients presenting with long bone fractures following high-energy trauma were included in the study. High-energy trauma was defined as injuries resulting from road traffic accidents, falls from height, or other high-impact mechanisms.

Inclusion Criteria

1. Patients aged ≥ 18 years
2. Patients with fractures of long bones (femur, tibia, humerus)
3. History of high-energy trauma
4. Patients undergoing surgical management
5. Patients are willing to provide informed consent and comply with follow-up

Exclusion Criteria

1. Pathological fractures
2. Patients with metabolic bone disorders
3. Polytrauma patients with life-threatening injuries preclude follow-up
4. Patients lost to follow-up

Data Collection

Detailed clinical, demographic, and radiological data were collected using a predesigned proforma. The following variables were recorded:

- Demographic details, including age and sex
- Mode of injury
- Type of fracture (open or closed)
- Severity of open fractures using Gustilo Anderson classification
- Fracture pattern and site
- Presence of comorbidities such as diabetes mellitus, smoking, and alcohol use
- Time interval between injury and surgical intervention
- Type of surgical fixation used
- Intraoperative and postoperative complications, including infection

All patients were followed up at regular intervals with clinical and radiological assessment.

Outcome Measures

The primary outcome was the occurrence of nonunion. Nonunion was defined as the absence of radiological evidence of healing at 9 months, along with persistent pain and abnormal mobility at the fracture site. Radiological union was assessed by the presence of bridging callus across at least three cortices on orthogonal views.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 21.0. Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were presented as frequency and percentage.

Chi-square test was used for comparison of categorical variables

An independent t-test was used for the comparison of continuous variables

Multivariate logistic regression analysis was performed to identify independent predictors of nonunion

A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

The Institutional Ethics Committee of Uttar Pradesh University of Medical Sciences, Saifai, Etawah, approved the study. Written informed consent was obtained from all participants before inclusion in the study.

RESULTS

During the study period, 86 patients with long bone fractures following high-energy trauma were assessed for eligibility. Six patients did not fulfill the inclusion criteria, and eight patients were excluded because of loss to follow-up. Consequently, 72 patients completed follow-up and were included in the final analysis.

Baseline Characteristics

A total of 72 patients with long bone fractures following high-energy trauma were included in the study. The mean age of the study population was 41.8 ± 13.6 years. The majority were males (54, 75%), while females constituted 18 (25%). The most commonly involved bone was the tibia (38.9%), followed by the femur (34.7%) and humerus (26.4%).

Prevalence of Non-Union

Out of 72 patients, 17 (23.6%) developed nonunion, while 55 (76.4%) achieved union within 6 months.

Table 1 presents baseline demographic and fracture characteristics of study participants. The mean age was 41.8 ± 13.6 years, and males accounted for 75.0% of the study population. The tibia was the most commonly fractured bone, while closed fractures constituted 61.1% of injuries.

Table 1: Baseline Characteristics of Study Population (N = 72)

Variable	Frequency	Percentage
Age (years)	Mean $\pm$ SD	41.8 $\pm$ 13.6
Gender		
Male	54	75.0%
Female	18	25.0%
Bone involved		
Tibia	28	38.9%
Femur	25	34.7%
Humerus	19	26.4%
Type of fracture		
Closed	44	61.1%
Open	28	38.9%

Factors Associated with Nonunion

Nonunion was significantly higher in patients with open fractures, smoking history, diabetes mellitus, infection, and delayed surgical intervention (>48 hours).

Table 2 demonstrates factors associated with non-union. Patients with open fractures, smoking history, diabetes mellitus, infection, and delayed surgery showed significantly higher rates of non-union compared with those without these factors.

Table 2: Comparison of Risk Factors Between Union and Non-Union Groups

Variable	Non Union (n = 17)	Union (n = 55)	p value
Open fracture	12 (70.6%)	16 (29.1%)	0.002
Smoking	10 (58.8%)	14 (25.5%)	0.01
Diabetes mellitus	7 (41.2%)	9 (16.4%)	0.03
Infection	11 (64.7%)	8 (14.5%)	<0.001
Delay >48 hours	9 (52.9%)	11 (20.0%)	0.01

Radiological and Treatment Factors

Patients with delayed fixation and postoperative infection had significantly higher rates of nonunion. The type of fixation did not show a statistically significant association.

Table 3 summarizes treatment-related factors. Postoperative infection was significantly associated with non-union, whereas fixation modality did not significantly influence fracture healing outcomes.

Table 3: Treatment Related Factors

Variable	Non Union (n = 17)	Union (n = 55)	p value
Intramedullary nailing	9 (52.9%)	32 (58.2%)	0.68
Plating	8 (47.1%)	23 (41.8%)	0.70
Infection present	11 (64.7%)	8 (14.5%)	<0.001

Multivariate Analysis

On multivariate logistic regression analysis, infection and delayed surgical intervention emerged as independent predictors of nonunion.

Table 4 presents a multivariate logistic regression analysis. After adjustment for confounding variables, postoperative infection and delayed surgery remained independent predictors of non-union.

Table 4: Multivariate Logistic Regression Analysis

Variable	Odds Ratio (OR)	95% CI	p value
Infection	5.8	2.1–15.9	<0.001
Delay >48 hours	3.4	1.2–9.6	0.02
Open fracture	2.1	0.8–5.9	0.11
Smoking	1.9	0.7–5.2	0.14

At 6 weeks, radiological signs of healing were observed in 18 (25.0%) patients. At 3 months, 42 (58.3%) patients demonstrated progressive callus formation. By 6 months, fracture union was achieved in 55 (76.4%) patients. At 9 months, persistent non-union was observed in 17 (23.6%) patients, and similar findings were noted at 12 months, confirming established non-union.

DISCUSSION

The present prospective cohort study identified a non-union prevalence of 23.6% among patients with long bone fractures following high-energy trauma. Open fractures, smoking, diabetes mellitus, infection, and delayed surgery were significantly associated with non-union on univariate analysis. Multivariate analysis revealed postoperative infection (adjusted OR=5.8, 95% CI: 2.1–15.9; $p<0.001$) and delayed surgical intervention beyond 48 hours (adjusted OR=3.4, 95% CI: 1.2–9.6; $p=0.02$) as independent predictors. These findings suggest that both biological and treatment-related factors substantially influence fracture healing.

The nonunion of long bone fractures remains one of the greatest challenges of the orthopedic practice, especially after high-energy trauma, where both the biological and mechanical factors are impaired. In the current research, the non-union rate was 23.6, which is in agreement with other documented instances of high incidence in high-energy injuries with severe soft tissue injury and vascular injury [13]. These injuries precondition the processes of impaired osteogenesis and delayed healing because of the disruption of the fracture microenvironment.

In this study, open fractures were identified to be significantly more associated with nonunion. This is attributable to the degree of soft tissue damage, contamination, and impaired blood supply that is usually observed in more open fractures. It has been shown by the previous research that the severity of open fractures as an independent variable is associated with the related increase in the rates of infection and nonunion, which is why close and careful debridement and fixation with stable structures are so important [14].

The most important independent predictor of nonunion that came out in the analysis was infection. Infection interferes

with the cascade of fracture healing processes through stimulating inflammation, hampering the activity of osteoblasts, and bone resorption. Earlier reports have also shown similar results, in which infection greatly enhanced the risk of delayed union and nonunion, which frequently required subsequent surgical procedures [15]. Efficient infection control measures, such as early administration of antibiotics and appropriate wound care, are thus important.

Another significant factor that was linked to non-union was delayed surgery intervention. The non-union rates of patients who were fixed after 48 hours were much higher. The delay of the stabilization may extend the period of inflammation, cause more harm to the soft tissues, and cause the instability at the fracture site. Literature proposes that early fixation is not only more mechanically stable, but also offers more biological healing due to its ability to maintain vascularity and reduce additional tissue damage [16].

Other patient-related factors, like smoking and diabetes mellitus, were also found to be significant on univariate analysis. Smoking has been reported to inhibit the healing of fractures by lowering tissue oxygenation and angiogenesis, and diabetes influences microvascular circulation and cell activity, which is necessary to heal bone [17,18]. These factors did not play an independent role in multivariate analysis, but may not be neglected in terms of clinical implications, and proper counseling and optimization are required.

The kind of fixation was not significantly related to nonunion in our study, which indicates that the effectiveness of the stabilization process and not the technique might be of more significance. This is consistent with other studies that have shown that intramedullary nailing and plating can yield satisfactory results if the correct principles of surgery are adhered to [19].

On the whole, the results of the research indicate that nonunion is a multifactorial phenomenon, infection and late intervention being the most important factors. High-risk patients can be identified early to institute appropriate interventions to ensure better results through enhanced fixation strategies, biological augmentation, and strict measures in controlling infection [20].

Generalizability

Since UPUMS is a major tertiary referral center catering to diverse trauma populations, the findings may be generalizable to similar tertiary care institutions managing high-energy long bone fractures. However, caution should be exercised when extrapolating results to primary care settings or populations with different injury patterns.

CONCLUSION

Nonunion of long bone fractures following high-energy trauma remains a multifactorial problem with significant clinical implications. The present study identified infection and delayed surgical intervention as independent predictors of nonunion, while open fractures, smoking, and diabetes mellitus were important contributing factors. These findings emphasize the critical role of early stabilization, meticulous surgical technique, and aggressive infection control in improving fracture healing outcomes. Identification of high-risk patients at an early stage allows for targeted interventions, which may include optimized fixation, biological augmentation, and close monitoring. Addressing modifiable risk factors such as smoking cessation and glycemic control can further enhance healing potential. Overall, a multidisciplinary and timely approach is essential to reduce the incidence of nonunion and improve patient prognosis.

Limitations

The study was conducted at a single center with a relatively small sample size, limiting external validity. Residual confounding due to unmeasured factors such as nutritional status and fracture severity may have influenced outcomes. In addition, the observational design precludes establishing causality. These limitations may have affected the precision and generalizability of the study findings.

Recommendations

Early fracture stabilization and aggressive infection prevention strategies should be implemented in patients sustaining high-energy trauma. Smoking cessation, optimization of glycemic control, and close monitoring of high-risk patients are recommended to reduce the occurrence of non-union. Future multicenter studies with larger sample sizes are warranted.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Author Contributions

All authors equally contributed.

List of Abbreviations

- OR – Odds Ratio
- CI – Confidence Interval
- SD – Standard Deviation
- UPUMS – Uttar Pradesh University of Medical Sciences
- SPSS – Statistical Package for the Social Sciences

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