Medical Factors Associated With Fracture Nonunion: A Retrospective Study

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Abstract

Background: Nonunion is one of the medical conditions challenging the trauma specialists. Timely identification of people at high risk of nonunion is important to improve the prognosis of patients.

Methods: We retrospectively analyzed the demographic and laboratory hematological characteristics of 338 patients with either clavicle or femoral fractures treated with ORIF in Shandong Provincial Hospital affiliated to Shandong University from January 2010 to May 2019. Descriptive statistics, univariate regression analysis, and multivariate regression analysis were conducted to confirm the independent factors associated with nonunion after ORIF.

Results: The overall nonunion rate among the patients investigated in this study was ~6.8%, while the nonunion rates were 5.6% and 10.3% in clavicle and the femur fractures, respectively. Results of the univariate logistic regression analysis showed that the serum fibrinogen concentration (FIB), the hemoglobin count (HGB), the lymphocyte absolute value (LYMPH), the coefficient of variation of red blood cell distribution width (RDW-CV), the American Society of Anesthesiologists (ASA) classification, and the mechanism of injury were related to the occurrence of nonunion ($p < 0.05$). Results of the multivariate regression analysis showed that FIB (OR = 1.64, 95% CI of 1.14 to 2.36, $p < 0.01$), LYMPH (OR = 0.34, 95% CI of 0.15 to 0.77, $p < 0.01$), ASA classification (OR = 3.52, 95% CI of 1.20 to 10.31, $p = 0.02$), and injury mechanism (OR=3.13, 95% CI of 1.20 to 8.21, $p = 0.02$) were independently associated with the occurrence of nonunion.

Conclusions: Our study has revealed that FIB, LYMPH, ASA classification, and injury mechanism are independently related to the occurrence of nonunion after ORIF, providing important guidance for clinicians to identify patients with high risk of nonunion in time, ultimately improving the prognosis and quality of life of patients.

Background

As one of the most challenging clinical problems in the area of trauma specialty, nonunion is a medical condition with the fractured bone not completely healed. Due to the improvement of the survival rate of patients with fractures, the probability of nonunion after fracture treatment increases gradually [1]. Previous studies have shown that the incidence of nonunion in all fractures ranges from 2–10% [2–4]. The incidence of nonunion varies depending on the anatomical sites. For example, a study with a large sample size conducted by Zara et al. [4] to explore the probability of nonunion of 18 types of bones in human body revealed that metacarpal (1.5%) and radius (2.1%) showed the lowest nonunion rates, while the highest rate of nonunion was identified in scaphoid (15.5%), followed by tibia and fibula (14%) and femur (13.9%).

Open reduction and internal fixation (ORIF) is the most common treatment of fractures [5, 6]. Studies have demonstrated that compared with conservative treatment, ORIF showed a lower rate of nonunion with an increased patient satisfaction [7–9]. A study has shown that non-surgical treatment of the same type of fracture leads to an increased nonunion rate by 30%, while the nonunion rate is reduced to 6% with surgical treatment [10]. However, other study has shown that the rate of postoperative nonunion reached as high as 10% [11]. Therefore, the identification of predictive factors of postoperative nonunion is very important for the prognosis of fracture patients and the improvement of patients' quality of life.

A recent review [12] reported that for the past two decades, people are increasingly interested in and concerned about the incidence of nonunion, while studies have extensively investigated the factors related to nonunion. A study of 56,492 fractures showed that the incidence of nonunion decreased with age [13], while other studies have found that smoking [14–17], obesity [16], and comminuted fractures [17] are risk factors for nonunion.

Although many studies have explored the factors related to nonunion, few studies have investigated the relationship between common hematological indices and the occurrence of nonunion. A study on elderly patients with proximal femoral fracture found that high ratio of preoperative platelet to lymphocyte may be associated with high mortality in patients with proximal femoral fracture surgery [18], while Hesselink et al. showed that the increase of myeloid cells after severe trauma is associated with normal fracture healing [19]. As the routine laboratory examinations, hematological indices are easy to obtain and will not cause significantly increased financial burden to patients, while the analysis of routine hematological indices is beneficial to the diagnostic potential of nonunion.

In this study, we retrospectively analyzed the demographic characteristics and laboratory hematological features of the patients with fractures to identify the independent factors related to nonunion in patients treated with ORIF.

Methods

In our electronic medical record system, we retrospectively identified 438 fracture patients (with 304 of clavicle fracture and 134 of femoral fracture) who received ORIF in the Department of Orthopaedic Trauma, Shandong Provincial Hospital affiliated to Shandong University from January 2010 to May 2019. We excluded patients with pathological fractures and osteogenesis imperfecta, younger than 18 years old, with infection or leukemia, and without hematological examination (Figure 1). The final single-center retrospective cohort included 338 patients, including 251 with clavicle fractures and 87 with femoral fractures. Of these patients, 315 were completely healed and 23 showed nonunion. All patients were followed up for at least one year. This study was approved by the Ethics Committee of Shandong Provincial Hospital affiliated to Shandong University with the informed consent obtained from all patients in this study.

Demographic, injury, and surgical data of the patients were obtained from the electronic medical record system of Shandong Provincial Hospital, including age, gender, smoking and drinking habits, systolic blood pressure (SBP), the diastolic blood pressure (DBP), the time from injury to surgery (TIS), the American Society of Anesthesiologists (ASA) Classification, the mechanism of injury, malformation, mobility, and bony crepitus. As for the injury mechanism, the most common injuries were caused by fall, high fall, and traffic accident, while the other types of rare injuries were classified as other injuries. Hematological examinations included blood coagulation test and whole blood routine examination, and the data of related variables were obtained from the LIS system of the Clinical Medical Laboratory Department of Shandong Provincial Hospital. Coagulation tests included the plasma fibrinogen concentration (FIB), the plasma prothrombin time (PT), the plasma activated partial thromboplastin time (APTT), and the plasma D-dimer concentration (D-dimer). The routine examination of whole blood included the white blood cell count (WBC), the red blood cell count (RBC), the hemoglobin concentration (HGB), the platelets count (PLT), the absolute value of lymphocyte (LYMPH), the absolute value of monocytes (MONO), the absolute value of neutrophils (MEUT), standard deviation of red blood cell distribution width (RDW-SD), and coefficient of variation of red blood cell distribution width (RDW-CV). The blood coagulation test was performed on the STA-R Evolution Experts series automatic blood coagulation analyzer (Stago, France) and the full blood routine examination on the XN-9000 automatic blood humoral analyzer (Sysmex, Japan). Hematological examinations of all patients in this study were performed prior to the surgeries on the fractures.

All patients were treated with ORIF. We used clinical and radiological standards to define the fracture healing and nonunion. Specifically, a complete fracture healing was defined as, through follow-up, that no operation was required 12 months after fracture treatment with blurred fracture line shown on the X-ray image (Figure 2). According to FDA criteria, nonunion has been defined as that for at least 9 months after injury and fracture showed no further healing tendency for 3 consecutive months (Figure 3).

In this study, we used numbers or percentages to represent classification variables, with the significant difference evaluated by chi-square test or Fisher exact test, while continuous data were described as average ± standard deviation or median (inter quartile range, IQR) with significant differences detected by Student t test and Kruskal Wallis rank sum test. Univariate logistic regression analysis was performed on each variable to determine the association between the healing and the nonunion groups with the 95% confidence interval (CI) and odds ratio (OR) calculated. Variables showing significant difference identified by the univariate logistic repression analysis with $P \leq 0.05$ were further analyzed to determine the variables playing an independent role in the occurrence of nonunion.

Data analyses were performed using statistical software R (http://www.r-project.org, The R Foundation), EmpowerStats (http://www.empower-stats.com, X&Y Solutions, Inc., Boston, MA), and GraphPad Prism (GraphPad Software; GraphPad, Bethesda, MD, USA). The significant difference was set at the two tailed P value less than 0.05.

Results

A total of 338 patients with fractures were included in this study, including 251 with clavicle fractures and 87 femur fractures. The distributions of patients with clavicle and femur fractures were shown in Figure 4. No significant difference was revealed in the distribution of femur, clavicle, and total nonunion ($p > 0.05$). Among all the patients with fractures, 315 cases were completely healed (with an average age of

44.59 ± 15.56 years old of 221 males and 94 females), while 23 cases developed nonunion (with an average age of 44.13 ± 20.21 years old of 13 males and 10 females). The overall rate of nonunion was ~6.8%.

The demographic, injury, and surgical features of all patients with fractures were summarized in Table 1. Results showed that the TIS in the nonunion group was significantly longer than that in the healing group, while a significant difference in ASA classification was revealed between the healing and nonunion groups. Specifically, the proportion of patients with ASA classification III & IV in the nonunion group was significantly higher than that in the healing group. No significant difference was detected in other variables ($P > 0.05$). The hematological characteristics of all patients were given in Table 2. Results showed that a significant difference was identified in FIB, WBC, HGB, LYMPH, and RDW-CV between the healing and nonunion groups ($P < 0.05$).

Table 1
Demographic, injury, and surgery characteristics of all fracture patients.

Characteristics[a]	**Total (n=338)**	**Healing (n=315)**	**Nonunion (n=23)**	***p* value**
AGE (year)	44.56 ± 15.88	44.59 ± 15.56	44.13 ± 20.21	0.89
TIS (day)	2.00 (1.00-4.00)	2.00 (1.00-4.00)	4.00 (2.00-8.50)	0.03*
SBP (mmHg)	132.36 ± 18.94	132.47 ± 19.17	130.83 ± 15.76	0.69
DBP (mmHg)	81.25 ± 12.17	81.34 ± 12.37	79.96 ± 9.03	0.60
Gender				0.17
Male	234 (69.23%)	221 (70.2%)	13 (56.5%)	
Female	104 (30.77%)	94 (29.8%)	10 (43.5%)	
ASA classification				0.02*
I & II	300 (88.76%)	283 (89.84%)	17 (73.91%)	
III & IV	38 (11.24%)	32 (10.16%)	6 (26.09%)	
Smoker				0.12
Yes	53 (15.68%)	52 (16.51%)	1 (4.35%)	
No	285 (84.32%)	263 (83.49%)	22 (95.65%)	
Alcoholism				0.20
Yes	44 (13.02%)	43 (13.65%)	1 (4.35%)	
No	294 (86.98%)	272 (86.35%)	22 (95.65%)	
Mechanism of Injury				0.09
Fall Injury	196 (57.99%)	188 (59.68%)	8 (34.78%)	
Traffic accident injury	90 (26.63%)	79 (25.08%)	11 (47.83%)	
High Fall Injury	10 (2.96%)	9 (2.86%)	1 (4.35%)	
Other injuries	42 (12.43%)	39 (12.38%)	3 (13.04%)	
Malformation				0.46
Yes	123 (36.39%)	113 (35.87%)	10 (43.48%)	

Abbreviations: TIS, time from injury to surgery; SBP, systolic blood pressure; DBP, diastolic blood pressure; ASA, the American Society of Anesthesiologists.

a Data are presented as number (%), mean ± standard deviation, or median (interquartile range, IQR)

*p < 0.05

Characteristics[a]	Total (n=338)	Healing (n=315)	Nonunion (n=23)	*p* value
No	215 (63.61%)	202 (64.13%)	13 (56.52%)	
Mobility				0.64
Normal	190 (56.21%)	176 (55.87%)	14 (60.87%)	
Limited	148 (43.79%)	139 (44.13%)	9 (39.13%)	
Bone Rubbing				0.07
Yes	246 (72.78%)	233 (73.97%)	13 (56.52%)	
No	92 (27.22%)	82 (26.03%)	10 (43.48%)	
Abbreviations: TIS, time from injury to surgery; SBP, systolic blood pressure; DBP, diastolic blood pressure; ASA, the American Society of Anesthesiologists.				
a Data are presented as number (%), mean ± standard deviation, or median (interquartile range, IQR)				
*p < 0.05				

Table 2
Blood characteristics of all fracture patients.

Characteristics[a]	Total(n=338)	Healing (n=315)	Nonunion (n=23)	*p* value
D-dimer (mg/L)	0.76 (0.40-1.72)	0.76 (0.40-1.75)	0.84 (0.40-1.07)	0.72
PT (s)	12.02 ± 1.37	12.00 ± 1.37	12.42 ± 1.35	0.17
APTT (s)	27.82 ± 5.22	27.71 ± 5.17	29.40 ± 5.88	0.14
FIB (g/L)	3.07 ± 0.99	3.03 ± 0.95	3.59 ± 1.43	0.01*
WBC (10^9/L)	8.82 ± 2.82	8.88 ± 2.78	8.01 ± 3.31	0.02*
RBC (10^{12}/L)	4.37 ± 0.70	4.39 ± 0.69	4.15 ± 0.70	0.12
HGB (g/L)	134.52 ± 20.36	135.26 ± 19.92	124.32 ± 23.88	0.02*
PLT (10^9/L)	224.15 ± 63.72	222.77 ± 61.20	242.65 ± 90.83	0.15
LYMPH (10^9/L)	1.74 ± 0.68	1.77 ± 0.69	1.39 ± 0.42	0.01*
MONO (10^9/L)	0.60 (0.44-0.79)	0.60 (0.45-0.79)	0.52 (0.42-0.70)	0.36
NEUT (10^9/L)	6.35 ± 2.67	6.38 ± 2.63	5.95 ± 3.20	0.46
RDW-CV (%)	12.98 ± 1.01	12.95 ± 0.87	13.46 ± 2.13	0.02*
RDW-SD (fl)	42.33 ± 3.14	42.32 ± 3.13	42.49 ± 3.39	0.80

Abbreviations: D-dimer, the plasma D-dimer concentration; PT, prothrombin time; APTT, activated partial thromboplastin time; FIB, the serum fibrinogen concentration; WBC, the white blood cell count; RBC, the red blood cell count; HGB, hemoglobin concentration; PLT, the platelets count; LYMPH, the absolute value of lymphocyte; MONO, the absolute value of monocytes; NEUT, the absolute value of neutrophils; RDW-CV, the coefficient of variation of red blood cell distribution width; RDW-SD, standard deviation of red blood cell distribution width.

a Data are presented as mean ± standard deviation or median (interquartile range, IQR)

*$p < 0.05$

We further analyzed the differences in demography, injury, and surgical and hematological examinations between the healing and nonunion groups by univariate logistic regression analysis (Table 3). Results showed that there was no significant difference in TIS and WBC between the healing and nonunion groups, while significant difference was revealed in FIB (OR = 1.55, 95% CI of 1.09 to 2.20, P = 0.01), HGB (OR = 0.98, 95% CI of 0.97 to 1.00, P = 0.02), LYMPH (OR = 0.35, 95% CI of 0.16 to 0.78, P = 0.01), and RDW-CV(OR = 1.37, 95% CI of 1.03 to 1.82, P = 0.03) between the two groups. Furthermore, the risk of nonunion varied with different ASA classifications (OR = 3.12, 95% CI of 1.15 to 8.48, P = 0.03). Moreover, among the three most common types of injuries, the risk of nonunion caused by traffic accidents increased by 227% in comparison to that of falls (P < 0.05), while no significant difference was detected between falls and other types of injuries. No significant difference was found in other variables between the healing and nonunion groups ($P > 0.05$).

Table 3
Univariate logistic regression analysis of all patients.

Variable	OR	95% CI	*p* value
AGE (year)	1.00	0.97-1.03	0.89
TIS (day)	1.03	1.00-1.06	0.06
SBP (mmHg)	1	0.97-1.02	0.69
DBP (mmHg)	0.99	0.96-1.03	0.60
D-dimer (mg/L)	0.97	0.85-1.12	0.72
PT (s)	1.19	0.93-1.53	0.17
APTT (s)	1.06	0.98-1.14	0.15
FIB (g/L)	1.55	1.09-2.20	0.01*
WBC (10^9/L)	0.88	0.74-1.05	0.15
RBC (10^{12}/L)	0.64	0.36-1.12	0.12
HGB (g/L)	0.98	0.97-1.00	0.02*
PLT (10^9/L)	1	1.00-1.01	0.15
LYMPH (10^9/L)	0.35	0.16-0.78	0.01*
MONO (10^9/L)	0.44	0.08-2.56	0.36
NEUT (10^9/L)	0.94	0.79-1.11	0.46
RDW-CV (%)	1.37	1.03-1.82	0.03*
RDW-SD (fl)	1.02	0.89-1.16	0.80
Gender			
Male	reference		
Female	1.81	0.77-4.27	0.18

Abbreviations: D-dimer, the plasma D-dimer concentration; TIS, time from injury to surgery; SBP, systolic blood pressure; DBP, diastolic blood pressure; PT, prothrombin time; APTT, activated partial thromboplastin time; FIB, the serum fibrinogen concentration; WBC, the white blood cell count; RBC, the red blood cell count; HGB, hemoglobin concentration; PLT, the platelets count; LYMPH, the absolute value of lymphocyte; MONO, the absolute value of monocytes; NEUT, the absolute value of neutrophils; RDW-CV, the coefficient of variation of red blood cell distribution width; RDW-SD, standard deviation of red blood cell distribution width; ASA, the American Society of Anesthesiologists.

OR: odds ratio; CI: confidence interval

*P < 0.05

Variable	OR	95% CI	*p* value
ASA classification			
I & II	reference		
III & IV	3.12	1.15-8.48	0.03*
Smoker			
Yes	reference		
No	4.35	0.57-32.98	0.15
Alcoholism			
Yes	1		
No	3.48	0.46-26.47	0.23
Mechanism of Injury			
Fall Injury	reference		
Traffic accident injury	3.27	1.27-8.44	0.01*
High Fall Injury	2.61	0.29-23.19	0.39
Other injuries	1.81	0.46-7.12	0.40
Malformation			
Yes	reference		
No	0.73	0.31-1.71	0.47
Mobility			
Normal	reference		
Limited	0.81	0.34-1.94	0.64
Bony Crepitus			
Yes	reference		

Abbreviations: D-dimer, the plasma D-dimer concentration; TIS, time from injury to surgery; SBP, systolic blood pressure; DBP, diastolic blood pressure; PT, prothrombin time; APTT, activated partial thromboplastin time; FIB, the serum fibrinogen concentration; WBC, the white blood cell count; RBC, the red blood cell count; HGB, hemoglobin concentration; PLT, the platelets count; LYMPH, the absolute value of lymphocyte; MONO, the absolute value of monocytes; NEUT, the absolute value of neutrophils; RDW-CV, the coefficient of variation of red blood cell distribution width; RDW-SD, standard deviation of red blood cell distribution width; ASA, the American Society of Anesthesiologists.

OR: odds ratio; CI: confidence interval

*P < 0.05

Variable	OR	95% CI	*p* value
No	2.19	0.92-5.18	0.08
Abbreviations: D-dimer, the plasma D-dimer concentration; TIS, time from injury to surgery; SBP, systolic blood pressure; DBP, diastolic blood pressure; PT, prothrombin time; APTT, activated partial thromboplastin time; FIB, the serum fibrinogen concentration; WBC, the white blood cell count; RBC, the red blood cell count; HGB, hemoglobin concentration; PLT, the platelets count; LYMPH, the absolute value of lymphocyte; MONO, the absolute value of monocytes; NEUT, the absolute value of neutrophils; RDW-CV, the coefficient of variation of red blood cell distribution width; RDW-SD, standard deviation of red blood cell distribution width; ASA, the American Society of Anesthesiologists.			
OR: odds ratio; CI: confidence interval			
*P < 0.05			

We further performed multivariate logistic regression analysis based on the significant variables identified in the univariate logistic regression model (Table 4). Results showed that there was no significant difference in HGB and RDW-CV between the healing and nonunion groups (P > 0.05). There was a significant correlation between FIB and the risk of nonunion with the risk of nonunion increased by 64% for every 1 g/L FIB (OR = 1.64, 95% CI of 1.14 to 2.36, P < 0.01). LYMPH was negatively correlated with the occurrence of nonunion with the risk of nonunion decreased as the LYMPH increased (OR = 0.34, 95% CI of 0.15 to 0.77, P < 0.01). In the mechanism of injury, the risk of nonunion in traffic accident fracture was higher than that in fall (OR = 3.13, 95% CI of 1.20 to 8.21, P = 0.02). The risk of nonunion in patients with ASA classification III & IV was 3.52 times higher than that in ASA classification I & II (OR = 3.52, 95% CI of 1.20 to 10.31, P = 0.02).

Table 4
Results of multivariate logistic regression analysis assessing the association between the medical characteristics of patients and the occurrence of nonunion.

Variable	**OR**	**95% CI**	***p* value**
FIB (g/L)	1.64	1.14-2.36	□0.01*
HGB (g/L)	0.98	0.96-1.0	0.06
LYMPH (10^9/L)	0.34	0.15-0.77	□0.01*
RDW-CV (%)	1.32	0.99-1.77	0.06
Mechanism of Injury			
Fall Injury	reference		
Traffic accident injury	3.13	1.20-8.21	0.02*
High Fall Injury	2.98	0.33-27.08	0.33
Other injuries	1.94	0.49-7.76	0.35
ASA classification			
I & II	reference		
III & IV	3.52	1.20-10.31	0.02*
Abbreviations: FIB, the serum fibrinogen concentration; HGB, hemoglobin concentration; PLT, the platelets count; LYMPH, the absolute value of lymphocyte; RDW-CV, the coefficient of variation of red blood cell distribution width; RDW-SD, standard deviation of red blood cell distribution width; ASA, the American Society of Anesthesiologists.			
OR: odds ratio; CI: confidence interval			
*p < 0.05			

Discussion

A total of 338 patients with fracture were included in our study with 23 case showing nonunion, accounting for an overall nonunion rate of ~6.8% with the nonunion rate of clavicle and femur fractures of 5.6% and 10.3%, respectively. In the large-scale study of 309,330 patients conducted by Zura et al. [4], the clavicular nonunion rate (8.6%) and the femoral nonunion rate (13.9%) were higher than those in our study, probably due to the exclusion of patients with nonunion after conservative treatment in our study. A comparable rate of clavicle nonunion (6.1%) to that of our study was previously reported by Jarvis et al. [15].

In this study, the general description and univariate logistic regression analysis were carried out based on the demographic characteristics of fracture patients and the characteristics of laboratory coagulation and blood routine indices. Variables showing significant difference ($p \leq 0.05$) detected by the univariate logistic regression analysis were further analyzed by multivariate logistic regression analysis. Results showed that the risk of nonunion in traffic accident fractures was 3.13 times higher than that of fall ($p < 0.05$), while the risk of nonunion in fracture patients with ASA classification III & IV was 3.52 times higher than that in ASA classification I & II ($p < 0.05$). Furthermore, FIB and LYMPH were independently related to the occurrence of nonunion ($p < 0.05$).

Our study showed that ASA classification played an independent role in the occurrence of nonunion. However, no significant relationship was identified between ASA classification and nonunion in the studies of Lim et al. [20] and Kim et al. [21]. Our results showed that there was no significant difference in the mechanism of injury between the nonunion and healing groups (Table 1), whereas the results of both univariate and multivariate analyses showed that the probability of nonunion in fracture of traffic accident was significantly higher than that in fall. Previous studies have reported conflicting results of the relationship between the nonunion and the injury mechanisms. For example, the results of Kim et al. [21] showed that there was a significant difference in injury mechanism between the healing and nonunion groups, whereas other studies revealed no significant difference in injury mechanism between the healing and nonunion groups [22, 15, 20].

Among the hematological indices, our study showed that there was a negative correlation between LYMPH and the occurrence of bone nonunion. These results were consistent with those previously reported. For example, Hesselink et al. found that the lymphocyte count remained within the range of reference values in patients with healing, while decreased slightly below the reference value in patients with nonunion [19]. Studies have shown that as a type of protein involved in blood coagulation, fibrinogen forms a primitive extracellular matrix to support tissue regeneration, facilitating fibrinogen to promote healing [23, 24]. However, our results showed that the increase of FIB was related to the occurrence of nonunion. For every 1 g/L FIB increased, the risk of nonunion increased by 64% ($p < 0.05$). Similarly, studies of Yuasa et al. [25] and O'Keefe et al. [26] also showed that high FIB was not conducive to fracture healing. Further studies are necessary in the future to evaluate the correlation among these factors, to determine their predictive ability for nonunion, and to establish a predictive model, ultimately providing guidelines for clinical evaluation of the incidence of nonunion and improving the prognosis of patients.

We note the limitations in our study. First, our investigation was a retrospective study with inevitably inherent biases. For example, the information of height and body weight of patients was not recorded, causing the lack of analysis of the relationship between obesity and nonunion. Second, smoking habit was not identified as a risk factor for nonunion in our study, probably because our data of smoking habit were based on patients at the time of consultation, whereas some patients may have already received smoking cessation therapy. Third, the sample size of this study limited our further stratified analysis, while the results revealed in this study should be further validated by future studies with a larger number of subjects.

Conclusions

The overall nonunion rate in this study was ~6.8%, with the nonunion rates of clavicle and femur as 5.6% and 10.3%, respectively. Results of both univariate and multivariate logistic regression analyses showed that the mechanism of injury, ASA classification, FIB, and LYMPH were independently associated with the occurrence of nonunion after ORIF. Our study provides important guidance for clinicians to identify potential patients with high risk of bone nonunion in time and to ultimately improve the prognosis of patients with nonunion.

Abbreviations

ORIF: Open reduction and internal fixation; SBP: systolic blood pressure; DBP: the diastolic blood pressure; TIS: the time from injury to surgery; ASA: the American Society of Anesthesiologists; FIB: the plasma fibrinogen concentration; PT: the plasma prothrombin time; APTT: the plasma activated partial thromboplastin time; D-dimer: the plasma D-dimer concentration; WBC: the white blood cell count; RBC: the red blood cell count; HGB: the hemoglobin concentration; PLT: the platelets count; LYMPH: the absolute value of lymphocyte; MONO: the absolute value of monocytes ; MEUT: the absolute value of neutrophils; RDW-SD: standard deviation of red blood cell distribution width; RDW-CV: coefficient of variation of red blood cell distribution width; IQR: inter quartile range; CI: confidence interval; OR: odds ratio

Declarations

Ethics approval and consent to participate

All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee. The study was approved by the Ethics Committee of Shandong Provincial Hospital affiliated to Shandong University (Jinan, PR China), and the reference number of the Ethics Committee is SWYX2020-178.

Consent for publication

Not applicable

Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

W-RR and C-Z collected data and wrote the manuscript, W-DW drafted the manuscript, M-JY and W-LL sorted out and explained the research data, W-Y and B-XH helped submit the manuscript. All authors read and approved the final manuscript.

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Figures

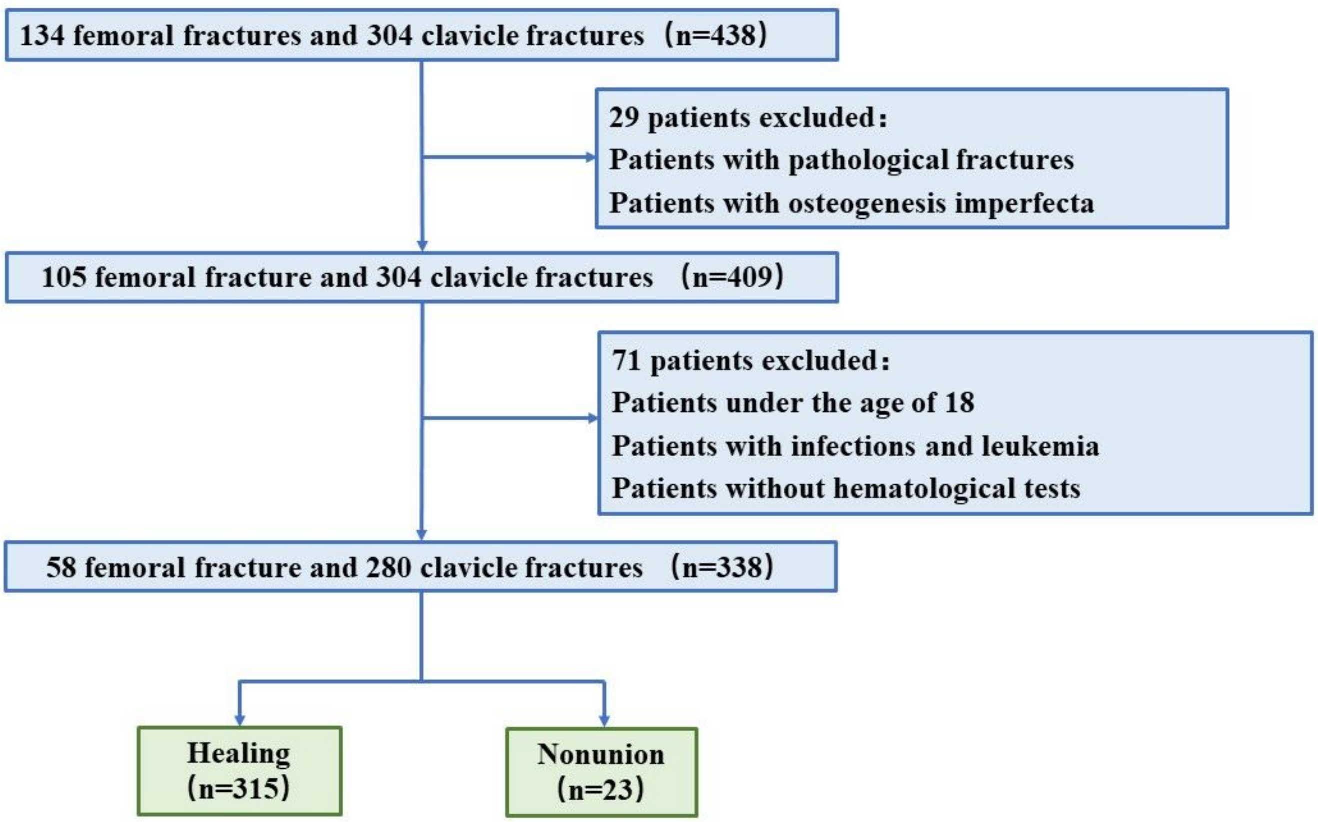

Figure 1

Flowchart of selection of subjects in this study.

Figure 2

The normal healing in a patient with femur fracture. (a) Preoperative femoral fracture on September 03, 2015. (b) After open reduction and internal fixation on September 05, 2015. (c) Postoperative review showing signs of healing on December 15, 2015. (d) Review on February 02, 2016 showing bone suture fuzzy and signs of healing. (e) Review on May 03, 2016 showing bone suture fuzzy and signs of healing. (f) Removal of the internal fixation on July 07, 2016 showing the completely healed fracture.

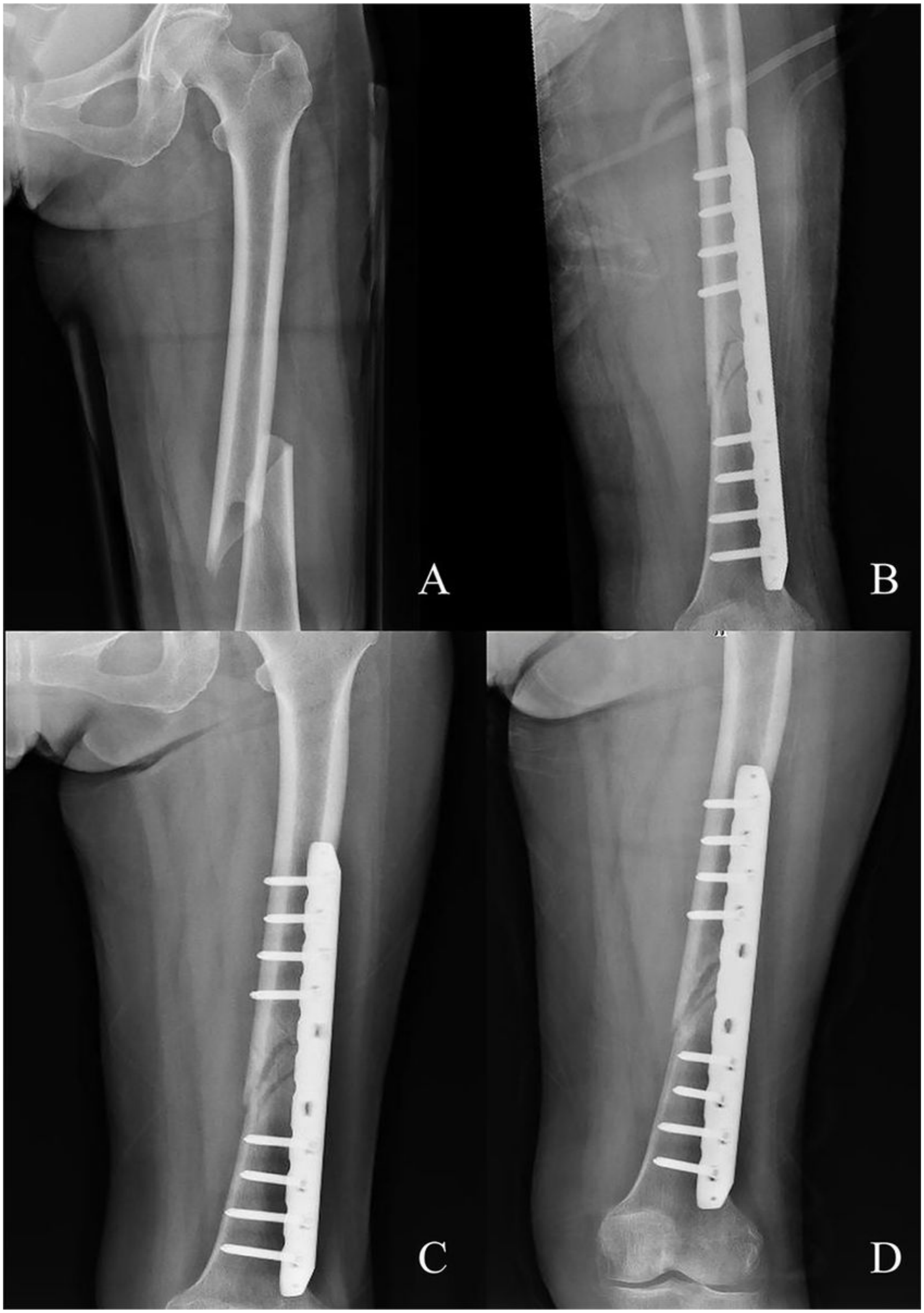

Figure 3

The nonunion in a patient with a femur fracture. (a) Preoperative femur fracture on August 10, 2015. (b) After open reduction and internal fixation on August 15, 2015. (c) Postoperative review showing no signs of healing on October 19, 2015. (d) Review showing evident bone sutures and no signs of healing on March 06, 2016.

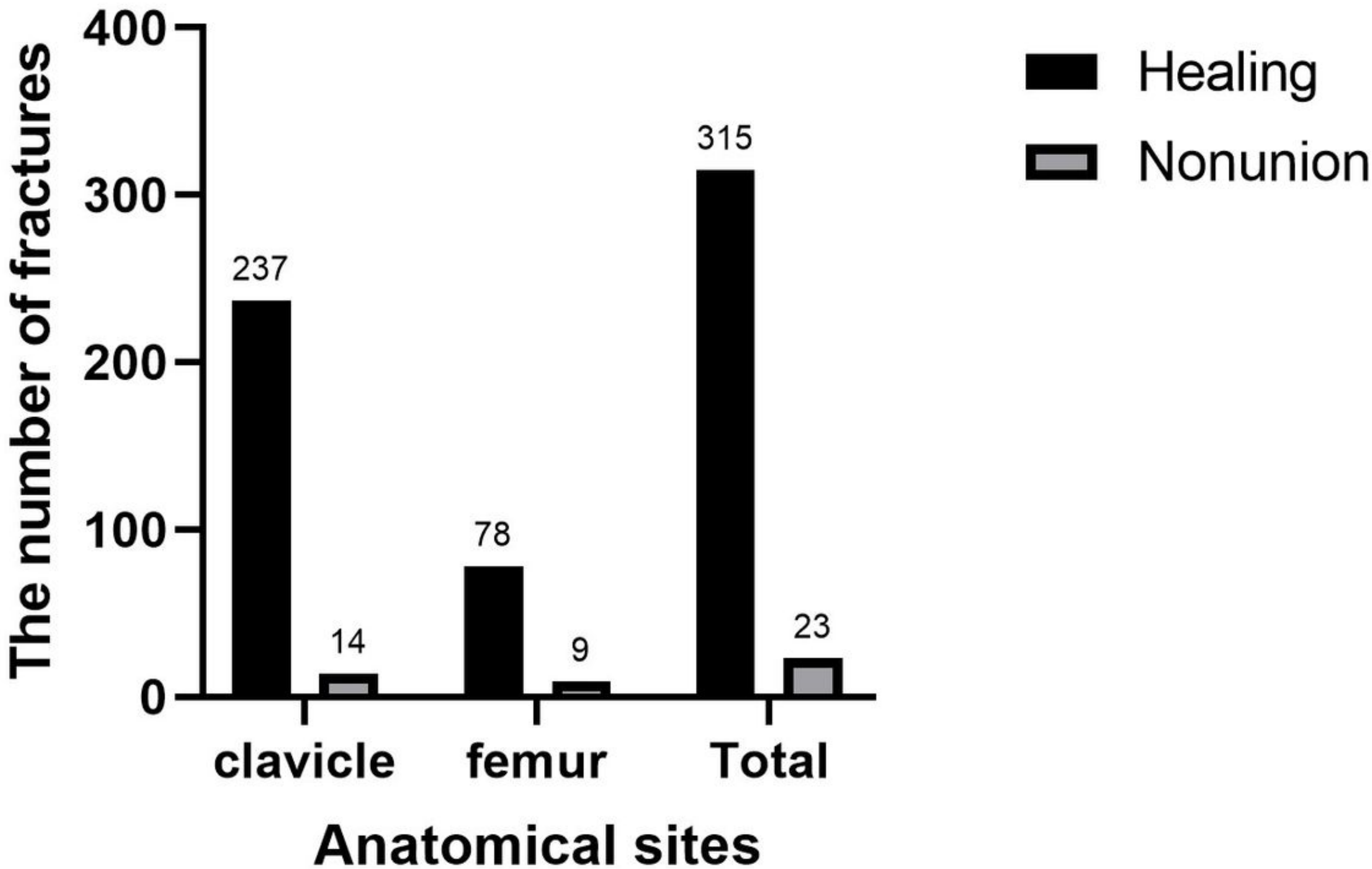

Figure 4

Distribution of the clavicle and femur fractures in the healing and nonunion groups in this study.