SMGroup

SM Journal of Arthritis Research

Research Article

Impaired Fracture Healing of the Distal Femur after High Energy Trauma

Karhof S[1]*, Bastian OW[1,2], Olden GDJ van[2], Leenen LPH[1], Kolkman KA[3] and Blokhuis TJ[1,4]

[1]*Department of Traumatology, University Medical Center Utrecht, The Netherlands*
[2]*Department of Surgery, Meander Medisch Centrum Amersfoort, The Netherlands*
[3]*Department of Surgery, Rijnstate Hospital Arnhem, The Netherlands*
[4]*Department of Surgery, Maastricht University Medical Center, The Netherlands*

Article Information

Received date: Oct 03, 2017
Accepted date: Oct 19, 2017
Published date: Oct 23, 2017

***Corresponding author**

Karhof S, Department of Surgery, UMC Utrecht, Heidelberglaan 100, HP G04. 2283508 GA Utrecht, The Netherlands, Tel: +31 302509882;
Email: steffikarhof@gmail.com

Distributed under Creative Commons CC-BY 4.0

Keywords Femur fractures; Fracture healing; Trauma mechanism

Abbreviations HET: High Energy Trauma; LET: Low Energy Trauma

Article DOI 10.36876/smjar.1003

Abstract

Introduction: Nonunion rates of distal femur fractures range between 10 and 20%. Previous studies have tried to identify parameters that predict impaired bone healing. These factors include local changes after major trauma such as open fractures and highly comminuted fractures. In addition to these local factors, increasing evidence suggests that the systemic inflammatory response induced by major trauma also impairs bone regeneration.

We retrospectively studied patients with distal femur fractures and aimed to identify parameters that predict impaired fracture healing.

Patients and methods: All patients with distal femur fractures treated at a level one trauma center and two large teaching hospitals with locked plating techniques between January 2007 and December 2014 were included. Using multivariable logistic regression, we determined which parameters were independent predictors of impaired fracture healing

Results: A total of 58 fractures in 56 patients were analysed. 26 fractures were caused by high-energy trauma (45%) and 26 patients developed impaired healing (45%).

Impaired fracture healing occurred more frequently after High Energy Trauma ($p<0.001$), open fractures ($p<0.001$), comminuted fractures ($p=0.001$) and in younger patients ($p<0.001$).

High Energy Trauma remained an independent predictor of impaired fracture healing when open fractures and comminution were included in the multivariable logistic regression.

Conclusion: High energy trauma, open fractures and comminution were all identified as independent predictors of impaired fracture healing. This indicates that high energy trauma, regardless of the fracture type that results, may negatively affect fracture healing.

Introduction

Fractures of the distal femur account for 3-6% of all femur fractures and less than 1% of all fractures [1-4]. They occur in a bimodal distribution of high-energy trauma in younger patients, mostly men, and low-energy trauma in the elderly, mostly women.

The gold standard in treating distal femur fractures is internal fixation, which yields good functional outcome [4-7]. Internal fixation is achieved through locked plating and to a lesser extent through intramedullary nailing, both preferably performed in a minimally invasive manner to preserve the fracture vascularization and improve outcome in fracture healing [8]. Since the introduction of lateral locked plating this technique has become increasingly popular since the first publications showing promising levels of union ranging between 90-100% [8-14]. However, later studies that include more complex fractures due to High Energy Trauma showed higher nonunion rates of up to 20 % [4,15].

Factors that increase the risk of impaired fracture healing include open fractures, comminuted fractures, diabetes and increased Body Mass Index (BMI) [4,6,16]. The trauma mechanism is another risk factor that has received increasing attention over the last years. Although the impairment of fracture healing as seen in High Energy Trauma is directly related to an increased incidence of open and comminuted fractures, there is increasing evidence that the systemic inflammatory response caused by major injury negatively affects the outcome of fracture healing [17-19].

Based on these findings, we hypothesized that High Energy Trauma is an independent predictor of impaired fracture healing, in addition to open and comminuted fractures. We therefore retrospectively studied patients with distal femur fractures and determined which clinical and fracture related parameters correlate with the outcome of bone regeneration.

OPEN ACCESS
ISSN: 2637-8841

Patients and Methods

A retrospective cohort analysis has been performed of all patients aged 18 and older undergoing locked plating for distal femur fractures between January 2007 and December 2014 at one level I trauma center and two level II trauma centers.

Patient demographics, trauma mechanism, fracture characteristics, surgical technique and follow-up were retrieved from the medical records. Exclusion criteria were periprosthetic fractures, pathological fractures or follow-up duration less than 9 months. The primary endpoint was time to fracture healing. Fracture healing was defined as full weight-bearing without pain. Time to healing was defined as the time in weeks between injury and the first documented time at which patients were able to bear full weight without pain. Normal healing was defined as a healing time not exceeding six months. Impaired healing was defined as no healing at six months after injury. Postoperative complications in healing were scored, including deep infections, malunions, and osteosynthesis-related complications requiring secondary surgical intervention.

The trauma mechanism was either defined as High Energy Trauma (HET) or Low Energy Trauma (LET). High-energy trauma included traffic accidents or falls from height. Fractures caused by fall from a standing position or sports injuries not involving motorized vehicles were classified as low-energy trauma. All fractures were classified according to the AO/OTA system [20]. To improve inter-observer agreement fractures were not subdivided beyond A, B and C [21]. The difference between diaphyseal (shaft) and metaphyseal (distal) fractures of the femur was determined by applying the rule of squares as described by Müller [22].

The influence of all parameters on the outcome, fracture healing, was investigated as follows. First, fracture healing was categorized as normal healing (healing within six months after injury) or impaired healing (no healing after six months, both delayed union and non-union). By comparing the characteristics of the two groups (normal *vs.* impaired healing) using the tests described below, those factors that showed a significant difference were selected and subsequently included in a multivariable logistic regression model to determine which parameters were independent predictors of impaired fracture healing.

Statistical analysis was performed with IBM SPSS 22 (IBM SPSS for Windows version 22.0, Armonk, NY). Two-tailed pearsons' Chi-square was used to compare categorical variables and an independent T-test or Mann-Whitney U test were used for continuous variables depending on whether the data had a binomial distribution. A p-value <0.05 was considered statistically significant (Table 1).

Table 1: Statistical analysis performed with IBM SPSS 22.

	Entire cohort n=58	Normal healing n=32 (55%)	Impaired healing n=26 (45%)	p-value
Age (years) Mean (±SD)	59 (20)	69 (17)	47 (17)	<0.001
Gender Male : Female	23:35	9:23	14:12	ns
BMI[a] Mean (±SD)	25.9 (4.9)	25.3 (5)	26.6 (4.7)	ns
Smoking[a] **(%)**	21 (44%)	8 (32%)	13 (57%)	ns
Diabetes[a] **(%)**	7 (13%)	3 (10%)	4 (21%)	ns
High Energy Trauma (%)	26 (45%)	7 (22%)	19 (73%)	<0.001
Low Energy Trauma (%)	32 (55%)	25 (78%)	7 (27%)	
Open (%)	15 (26%)	2 (6%)	13 (50%)	<0.001
Comminuted (%)	33 (57%)	12 (38%)	21 (81%)	0.001
Fracture type (AO-OTA)				
A	28 (48%)	21 (66%)	7 (27%)	0.001
B	3 (5%)	3 (9%)	0	
C	27 (47%)	8 (25%)	19 (73%)	
Treatment type				
LCP	9 (15%)	6 (11%)	3 (11%)	ns
LISS	37 (64%)	17 (53%)	20 (77%)	
95° angled blade plate	5 (9%)	4 (13%)	1 (4%)	
Angular stable plate	7 (12%)	5 (16%)	2 (8%)	
Previous treatment with external fixation (%)	11 (19%)	2 (6%)	9 (35%)	0.008
Complications				
Minor complications	4 (7%)	3 (9%)	1 (4%)	<0.001
Major complications	17 (29%)	1 (3%)	16 (62%)	

[a]Determined by Pearsons' chi-square for categorical values and with t-test for continuous variables.

[b]Missing data: BMI in 7, smoking in 10 and diabetes in 4 patients unknown.

Table 2: Binary logistic regression analysis.

	Odds ratio	p-value
Open	14.9	0.001
Comminution	7	0.002
Trauma mechanism	9.7	<0.001
Multivariate Analysis		
Open	4	0.149
Comminution	3.4	0.08
Trauma mechanism	4.3	0.043

Results

Between January 2007 and December 2014, 96 patients with a distal femur fracture were treated with locked plating in the three participating centers. Two patients suffered bilateral distal femur fractures after high-energy trauma. Forty patients were excluded; 19 patients were excluded since their fractures were periprosthetic, 9 patients due to pathological fractures, 1 patient due to a lower leg amputation, 1 patient due to paraplegia, 1 patient moved abroad, 1 patient was lost to follow up and 8 patients died within 6 months after injury and were therefore excluded.

A total of 56 patients with 58 fractures were available for final analysis. Thirty-two fractures were caused by low-energy trauma (55%) and 26 fractures (45%) followed high-energy trauma. Thirty-three fractures were comminuted (57%) and 15 fractures were open fractures (26%). Prior to definitive treatment; an external fixator was used for temporary stabilization in 11 cases. In all patients the external fixator was replaced by definitive fixation within 14 days after injury. When classified by the AO-OTA system there were 28 type A, 3 type B and 27 type C fractures.

Thirty-two fractures healed adequately within 6 months after injury (55%). The 26 fractures that did not heal within 6 months (45%) included 9 delayed unions and 17 nonunions. The mean healing time was 8 months (±7.6) for the entire cohort. Patients following high-energy trauma healed significantly longer than those after low-energy trauma (11 *vs.* 6 months, p=0.030).

There were no postoperative complications in 37 of the patients (64%). In the remaining patients, 17 patients required secondary surgery due to non- or malunion, 2 patients suffered from leg-length discrepancies, one developed a loose screw without malalignment and one temporary loss of peroneal nerve function.

Open fractures occurred more frequently in the impaired healing group compared to fractures that healed adequately within 6 months after injury (50% *versus* 6%, p<0.001). Comminuted fractures were also more prevalent in the impaired healing group (81% *versus* 38%, p=0.001). Within the impaired healing group 19 fractures were caused by high energy trauma, compared to 7 following Low Energy Trauma (73% *versus* 27%, p<0.001).

Patients with impaired fracture healing were significantly younger than patients with normal fracture healing (47 years *versus* 69 years, p<0.001).

Binary logistic regression analysis showed that when including comminution, open fractures and trauma mechanism in the model, high-energy trauma remained an independent predictor of impaired fracture healing with an odds ratio of 4.3 (Table 2).

Discussion

We found that high-energy trauma remained an independent predictor of impaired fracture healing of the distal femur when open fractures and comminution were added to the multivariable logistic regression with an odds ratio of 4.3. Of the fractures that were analyzed, 45% showed impaired healing. Factors that were associated with impaired fracture healing were age (p<0.001), open fractures (p<0.001), comminuted fractures (p=0.001) and high-energy trauma (p<0.001).

Since High Energy Trauma was identified in this study as an independent predictor of impaired healing, besides comminuted fractures and open fractures, it is tempting to speculate that the role of the trauma mechanism could be more significant than previously thought. There is increasing evidence that major trauma not only impairs fracture healing through local changes at the fracture sites, but also by inducing a detrimental systemic inflammatory response. In animals it has been shown that blunt experimental chest injury or intraperitoneal injection of polysaccharides, which are both models of systemic inflammation, impairs bone regeneration [23,24]. Moreover patients with multiple injuries who suffered impaired fracture healing of the tibia were shown to have a different systemic inflammatory response compared to patients with normal healing [17].

The findings of the current study are in line with another study in which an increased incidence of impaired fracture healing after major trauma was found [25]. However, to our knowledge this has not yet been determined in distal femur fractures treated with plating. Many other studies have examined risk factors for impaired healing after locked plating. A prospective multicenter study performed by Schutz et al. [13] analyzed healing in 52 patients with 55 distal femur fractures. They observed an impaired healing rate of 15%, and found no significant influence of age, fracture type, soft-tissue injuries, trauma-mechanism or the interval between accident and surgery. The distribution of patients in their study was different from ours, and their statistical analysis was primarily aimed at analyzing mechanical outcome. Henderson et al. [15] performed a retrospective review among 70 distal femur fractures. They found a nonunion rate of 20%, and one of the significant predictors for nonunion was comminution, which is in line with our findings. Rodriguez et al. [26] found a nonunion rate of 10% in 283 fractures. In their retrospective analysis the only significant factors increasing nonunion rates were obesity (BMI>30), open fractures, infection and stainless steel implants. In a retrospective review by Ricci et al. [27] a nonunion rate of 19% was found in 335 distal femur fractures. They identified diabetes and open fractures as independent predictors of nonunion. Although some of these studies have identified open fractures and comminution as risk factors for impaired healing, trauma mechanism was identified as an independent risk factor in our study following binary logistic regression. This increases the likelihood of a causal relationship between High Energy Trauma and impaired healing. In the interpretation of the results of the current study several limitations must be kept in mind. Firstly, the small study population of 58 fractures increases the risk of a type II error. Due to our small study population we were unable to include all 4 parameters into the logistic regression that were significantly different between normal

Citation: Karhof S, Bastian OW, van Olden GDJ, Leenen LPH, Kolkman KA and Blokhuis TJ. Impaired Fracture Healing of the Distal Femur after High Energy Trauma. SM J Arthritis Res. 2017; 1(1): 1003.
https://dx.doi.org/10.36876/smjar.1003

and impaired fracture healing. We therefore excluded age from the regression since we believed that this parameter represented or closely correlated with trauma mechanism (e.g. young men are seen more often in de HET group and older women mostly within the LET group). Poor fracture healing in younger patients also seems counter-intuitive from a biological perspective. Ricci et al. [27] also found a higher incidence of nonunion in closed fractures in patients younger than 65 years and they also suggested this was due to the severity of the trauma, since younger patients represent a large part of the high-energy trauma group. In addition, the limited number of cases from 3 different centers is also a form of selection bias.

Secondly, the retrospective design of the study increases the risk of bias. Most of the patients were seen in the outpatient clinic at standard follow-up times of 6 weeks, 3, 6 and 12 or 15 months after surgery. This may have influenced the reported healing rates since the majority of the patients healed between 6 and 12 months. In addition, we defined healing as the first documented moment of pain-free full weight bearing. This may explain the difference in healing time mentioned in other studies, where other types of healing were defined. Defining healing from a patient's perspective was deliberately chosen as this reflects patient's activities rather than, for example, radiological healing.

Lastly, a remarkable finding in this study is the high number of patients with impaired fracture healing. The nonunion rates previously reported range from 10-20% [13,15,25,27] whereas in our study population 45% of the fractures resulted in impaired fracture healing. To our knowledge this might be due to the following: (1) our wide definition of fracture healing combined with the retrospective design of the study (information bias), (2) the wide definition of impaired fracture healing in which not only non-union but also delayed union is included and (3) the rigid fixation generated by locking plates might as well cause a higher number of delayed- or nonunion [30].

In conclusion, our study shows that factors associated with impaired fracture healing of the distal femur are age, open fractures, comminuted fractures and high-energy trauma. Logistic regression analysis showed that high-energy trauma remains an independent predictor of impaired fracture healing when open and comminuted fractures are added to the same model. Major trauma may therefore impair bone healing through an additional mechanism other than increased incidence of open and comminuted fractures, for instance by inducing a detrimental systemic inflammatory response.

References

1. Court-Brown CM, Caesar B. Epidemiology of adult fractures: a review. Injury. 2006; 37: 691-697.

2. Forster MC, Komarsamy B, Davison JN. Distal femoral fractures: a review of fixation methods. Injury. 2006; 37: 97-108.

3. Hanschen M, Aschenbrenner IM, Fehske K, Kirchhoff S, Kil L, Holzapfel BM, et al. Mono-versus polyaxial locking plates in distal femur fractures: a prospective randomized multicenter clinical trial. Int Orthop. 2014; 38: 857-863.

4. Hoffmann MF, Jones CB, Sietsema DL, Tornetta P, Koenig SJ. Clinical outcomes of locked plating of distal femoral fractures in a retrospective cohort. J Orthop Surg Res. 2013; 8: 43-52.

5. Jeon IH, Oh CW, Kim SJ, Park BC, Kyung HS, Ihn JC. Minimally invasive percutaneous plating of distal femoral fractures using the dynamic condylar screw. J trauma. 2004; 57: 1048-1052.

6. Kao FC, Tu YK, Su JY, Hsu KY, Wu CH, Chou MC. Treatment of distal femoral fracture by minimally invasive percutaneous plate osteosynthesis: comparison between the dynamic condylar screw and the less invasive stabilization system. J Trauma. 2009; 67: 719-726.

7. Zlowodzki M, Bhandari M, Marek DJ, Cole PA, Kregor PJ. Operative treatment of acute distal femur fractures: systematic review of 2 comparative studies and 45 case series (1989-2005). J Orthop Trauma. 2006; 20: 366-371.

8. Hartin NL, Harris I, Hazrawala K. Retrograde nailing versus fixed-angle blade plating for supracondylar femoral fractures: a randomized controlled trial. ANZ J Surg. 2006; 76: 290-294.

9. Fankhauser F, Gruber G, Schippinger G, Boldin C, Hofer HP, Grechenig W, et al. Minimal-invasive treatment of distal femoral fractures with the LISS (Less Invasive Stabilization System) a prospective study of 30 fractures with a follow-up op 20 months. Acta Orthop Scand. 2004; 75: 56-60.

10. Kayali C, Agus H, Turgut A. Successful results of minimally invasive surgery for comminuted supracondylar femoral fractures with LISS: comparative study of multiply injured and isolated femoral fractures. J Orthop Sci. 2007; 12: 458-465.

11. Kregor PJ, Stannard JA, Zlowodzki M, Cole PA. Treatment of distal femur fractures using the less invasive stabilization system: surgical experience and early clinical results in 103 fractures. J Orthop trauma. 2004; 18: 509-520.

12. Markmiller M, Konrad G, Sudkamp N. Femur-LISS and distal femoral nail for fixation of distal femoral fractures: are there differences in outcome and complications? Clin Orthop Relat Res. 2004; 426: 252-257.

13. Schutz M, Muller M, Regazzoni P, Hontzsch D, Krettek C, van der Werken C, et al. Use of the less invasive stabilization system (LISS) in patients with distal femoral (AO33) fractures: a prospective multicenter study. Arch Orthop Trauma Surg. 2005; 125: 102-108.

14. Vallier HA, Immler W. Comparison of the 95-degree angled blade plate and the locking condylar plate for the treatment of distal femoral fractures. J Orthop Trauma. 2012; 26: 327-332.

15. Henderson CE, Lujan TJ, Kuhl LL, Bottlang M, Fitzpatrick DC, Marsh JL. 2010 mid-America Orthopaedic association physician in training award: healing complications are common after locked plating for distal femur fractures. Clin Orthop Relat Res. 2011; 469: 1757-1765.

16. Reikerås O, Shegarfi H, Wang JE, Utvåg SE. Lipopolysaccharide impairs fracture healing: an experimental study in rats. Acta Orthop. 2005; 76: 749-753.

17. Bastian O, Kuijer A, Koenderman L, Stellato R, Solline WW van, Leenen LPH, et al. Impaired bone healing in multitrauma patients is associated with altered leukocyte kinetics after major trauma. J Inflamm Res. 2016; 9: 69-78.

18. Bastian O, Pillary J, Alblas J, Leenen L, Koenderman L, Blokhuis T. Systemic inflammation and fracture healing. J Leukoc Biol. 2011; 89: 669-673.

19. Karladani AH, Granhed H, Kärrholm J, Styf J. The influence of fracture etiology and type on fracture healing: a review of 104 consecutive tibial shaft fractures. Arch Orthop Trauma Surg. 2001; 121: 325-328.

20. Recknagel S, Bindl R, Kurz J, Wehner T, Ehrnthaller C, Knöferl MW, et al. Experimental blunt chest trauma impairs fracture healing in rats. J Orthop Res. 2011; 29: 734-739.

21. Recknagel S, Bindl R, Kurz J, Wehner T, Schoengraf P, Ehrnthaller C, et al. C5aR-antagonist significantly reduces the deleterious effect of a blunt chest trauma on fracture healing. J Orthop Res. 2012; 30: 581-586.

22. Ricci WM, Streubel PN, Morshed S, Collinge CA, Nork SE, Gardner MJ. Risk factors for failure of locked plate fixation of distal femur fractures: an analysis of 335 cases. J Orthop Trauma. 2014; 28: 83-89.

23. Browner BD, Levine A, Jupiter J, Trafton P, Krettek C. Skeletal trauma. 4th edn. Saunders/Elsevier. 2009.

Citation: Karhof S, Bastian OW, van Olden GDJ, Leenen LPH, Kolkman KA and Blokhuis TJ. Impaired Fracture Healing of the Distal Femur after High Energy Trauma. SM J Arthritis Res. 2017; 1(1): 1003.
https://dx.doi.org/10.36876/smjar.1003

24. Meling T, Harboe K, Enoksen CH, Aarflot M, Arthursson AJ, Søreide K. How reliable and accurate is the AO/OTA comprehensive classification for adult long-bone fractures? J Trauma Acute Care Surg. 2012; 73: 224-231.

25. Muller ME, Nararin S, Koch P, Schatzker J. Comprehensive Classification of Fracture of Long Bones. 1st edn. Berlin Heidelberg: Springer-Verlag. 1990.

26. Muckart DJ, Bhagwanjee S. American College of chest physicians/society of critical care medicine consensus conference definitions of the systemic inflammatory response syndrome and allied disorders in relation to critically injured patients. Crit Care Med. 1997; 25: 1789-1795.

27. Mizuno K, Mineo K, Tachibana T, sumi M, Matsubara T, Hirohata K. The osteogenic potential of fracture hematoma. Subperiosteal and intramuscular transplantation of the hematoma. J Bone Joint Surg Br. 1990; 72: 822-829.

28. Park SH, Silva M, Bahk WJ, McKellop H, Lieberman JR. Effect of repeated irrigation and debridement on fracture healing in an animal model. J Orthop Res. 2002; 20: 1197-1204.

29. Rodriguez EK, Boulton C, Weaver MJ, Herder LM, Morgan JH, Chacko AT, et al. Predictive factors of distal femoral fracture nonunion after lateral locked plating: a retrospective multicenter case-control study of 283 fractures. Injury. 2014; 45: 554-559.

30. Kubiak EN, Fulkerson E, Strauss E, Egol KA. The evolution of locked plates. J Bone Joint Surg Am. 2006; 88: 189-200.

Citation: Karhof S, Bastian OW, van Olden GDJ, Leenen LPH, Kolkman KA and Blokhuis TJ. Impaired Fracture Healing of the Distal Femur after High Energy Trauma. SM J Arthritis Res. 2017; 1(1): 1003.
https://dx.doi.org/10.36876/smjar.1003