Classification of soft-tissue injuries in open femur fractures: Relevant for systemic complications?

Christian David Weber, MD, Rolf Lefering, PhD, Thomas Dienstknecht, MD, PhD, Philipp Kobbe, MD, PhD, Richard Martin Sellei, MD, Frank Hildebrand, MD, PhD, Hans-Christoph Pape, MD, *and* **TraumaRegister DGU**, *Aachen, Germany*

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BACKGROUND: A broad range of systemic complications has been described to occur in patients with open major fractures. Various causes have been claimed to play a role. We therefore surveyed a nationwide trauma registry to assess risk factors associated with closed and various types of open femur fractures.

METHODS: This was a cohort study in a nationwide population-based prospective database. Inclusion criteria for selection from database are as follows: individuals with femur fracture, age 16 years or older, and survival until primary admission. Main groups included closed and open femur fracture. Patient demographics, injury severity (New Injury Severity Score), surgical fracture management, length of stay, and systemic complications (e.g., multiple organ failure [MOF], sepsis, mortality) were collected and statistically analyzed using SPSS statistics. Multivariate regression analysis was performed to stratify subgroups for the degree of open soft-tissue injury according to Gustilo and Anderson.

RESULTS: Among 32,582 documented trauma victims (January 1, 2002, to December 31, 2010), a total of 5,761 met the inclusion criteria. Main groups: 4,423 closed (76.8%) and 1,338 open femur fractures (23.2%). Open fractures subgroups were divided into I° (334, 28.1%), II° (526, 44.3%), and III° (328, 27.6%). Open fractures were associated with an increased risk of prehospital hemorrhagic shock ($p = 0.01$), higher resuscitation requirements ($p < 0.001$), MOF ($p = 0.001$), and longer in-hospital ($p < 0.001$) and intensive care stay ($p = 0.001$). While New Injury Severity Score values showed a minor increase per subgroup, the prevalence of MOF, sepsis, and mortality multiplied with the degree of open soft-tissue injury. Especially patients with Type III open femur fractures received mass transfusions (28.2%, $p < 0.001$), and mass transfusions were identified as independent predictor for sepsis (odds ratio [OR], 2.393; 95% confidence interval [CI], 1.821–3.143; $p < 0.001$) and MOF (OR, 2.966; 95% CI, 2.409–3.651; $p < 0.001$). Our data also indicate an increased mortality in patients with open femur managed outside Level I trauma centers (OR, 1.358; 95% CI, 1.018–1.812; $p = 0.037$).

CONCLUSION: Open femur fractures are associated with higher in-hospital complications related to incidence of MOF, associated intensive care unit stay, and hospital days when compared with closed femur fractures. For prevention of in-hospital complications, prompt hemorrhage control, surgical fracture fixation, cautious blood management, and triage to a Level I trauma center must be considered. (*J Trauma Acute Care Surg.* 2016;81: 824–833. Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Epidemiologic/prognostic study, level II.

KEY WORDS: Femur fracture; open long-bone fractures; soft-tissue injury; systemic complications; trauma registry.

Open femur fractures usually result from high-energy trauma and are frequently associated with complex fracture patterns and severe soft-tissue injuries. Various concerns in patients with open fractures have been discussed in the literature. Major controversies were focused on patients with open tibial fractures, including the timing of initial debridement, the method of fixation, the risk of infectious complications, nonunion, and amputation.[1–6]

In this context, we acknowledge the Gustilo classification system for open fractures, assisting scientific research and standardization of management.[7]

Furthermore, certain standards have changed in the management of open long-bone fractures in the past decades, such as early antibiotic coverage,[8] tetanus vaccination, prompt debridement, copious irrigation, surgical fracture stabilization, and timely soft-tissue closure or coverage. These key factors, in addition to knowledge of epidemiologic issues,[9] allowed reducing mortality and morbidity dramatically in the vast majority of patients.[1]

In the late 1980s, Brumback et al.[10] evaluated local complications associated with open femur fractures and internal fixation. To date, intramedullary nailing has become the criterion standard of care for a wide spectrum of open femur fractures. These recommendations for the management of open femoral fractures continue to be valid: in the operation room, thorough debridement and stable fixation should be achieved.[11,12]

However, high-energy fractures of the femur are observed in a special entity of patients, typically suffering from multisystem injuries. In this patient subgroup, major systemic complications outweigh the relevance of local infections, poor bone healing, and late revisions.

Among the life-threatening complications in these patients are hemorrhagic shock, sepsis, and multiple organ failure (MOF).[4–6] So far, there are only limited data characterizing severely injured patients with open femur fractures and investigating the relevance of the local soft-tissue injury regarding major complications. The clinical relevance of closed versus open soft-tissue damage, the incidence and impact of concomitant injuries, and data on demographics, prehospital and in-hospital resuscitation, surgical treatment reality and major complications remains poorly characterized. Previously evaluated risk factors for systemic complications include male gender, injury severity, Abbreviated Injury Scale (chest) of 3 or greater, the number of red blood cell units transfused, and the number of operative procedures.[2] We hypothesized that these risk factors might apply

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From the Department of Orthopaedics and Trauma, RWTH Aachen University, Aachen, Germany (C.D.W., T.D., P.K., R.M.S., F.H., H.-C.P.); Harald Tscherne Laboratory for Orthopaedic Research, Aachen, Germany (C.D.W.); Institute for Research in Operative Medicine (IFOM), Witten/Herdecke University, Cologne, Germany (R.L.); and Committee on Emergency Medicine, Intensive Care and Trauma Management (Sektion NIS) of the German Trauma Society (DGU), Germany (T.R.).
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Address for reprints: Christian David Weber, MD, Department of Orthopaedics and Trauma, RWTH, Aachen University Hospital, Pauwels St. 30, 52074 Aachen, Germany; email: chrweber@ukaachen.de.

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TABLE 1. Mechanisms of Injury

Mechanism of Injury	Closed Femur Group n = 4,423	Open Femur Group n = 1,338	p
Motor vehicle accident	1,864 (42.1)	555 (41.5)	0.67
Motorcycle accident	838 (18.9)	393 (29.4)	<0.001
Bicycle	181 (4.1)	45 (3.4)	0.23
Pedestrian	295 (6.7)	68 (5.1)	0.036
Low-energy fall <3 m	221 (5.0)	28 (2.1)	<0.001
High-energy fall ≥3 m	724 (16.4)	152 (11.4)	<0.001
Other	300 (6.8)	97 (7.2)	0.56

Values are presented as n (%).

particularly in individuals sustaining open long-bone fractures and therefore addressed the following questions:

(1) Are open femoral fractures associated with different injury patterns and higher overall injury severity, when compared with closed femur fractures?
(2) Do patients with open femur fracture require a different type of resuscitation (e.g., intravenous fluids, blood products) and method of surgical fracture stabilization, when compared with patients with closed fractures?
(3) Are open femur fractures associated with a higher risk of systemic complications and generate more costs related to the number of surgical procedures and length of stay (LOS), when compared with closed fractures?
(4) How relevant is the degree of local soft-tissue damage for systemic complications, when stratifying open fractures for three subgroups according to the Gustilo classification system?

PATIENTS AND METHODS

Trauma Registry and Data Acquisition

The TraumaRegister DGU of the German Trauma Society (Deutsche Gesellschaft für Unfallchirurgie [DGU]) is a standardized prospective, multicenter, and anonymous documentation of severely injured patients, established in 1993. Data are collected prospectively in four consecutive time phases from the site of the accident until discharge from hospital including emergency room (ER), initial surgery, and intensive care unit (ICU) phase. The documentation includes detailed information on demographics, injury pattern, comorbidities, prehospital and in-hospital management, course on ICU, and relevant laboratory findings including data on transfusion and outcome of each individual.

The inclusion criterion is admission via ER with subsequent ICU/intensive care medicine care or death after admission but before admission to ICU. Patients referred from other hospitals are documented as well if their initial trauma severity was according to the inclusion criteria. The infrastructure for documentation, data management, and data analysis is provided by the Academy for Trauma Surgery. The scientific leadership is provided by the Committee on Emergency Medicine, Intensive Care and Trauma Management (Sektion NIS) of the German Trauma Society.[13,14]

The participating hospitals submit their data anonymously into a central database via a Web-based application. Scientific data analysis is approved according to a peer-review procedure established by Sektion NIS. It covers specific requirements of quality control (www.traumaregister.de) and serves as basis for scientific analyses.[2,3,15] The study was approved by the TraumaRegister DGU review board. The present study is in line with the publication guidelines of the TraumaRegister DGU and registered as TR-DGU project ID 2011-040.

Definitions

- Mortality was defined as overall in-hospital death from any cause.
- Prehospital hemorrhagic shock was defined as hypotension with a systolic blood pressure (SBP) equal to or less than 90 mm Hg before admission to the trauma center.
- In-hospital hemorrhagic shock was defined as hypotension with an SBP equal to or less than 90 mm Hg in the ER.
- All injuries were coded according to the Abbreviated Injury Scale (AIS, version 2005), and the Injury Severity Score and the New Injury Severity Score (NISS) were derived accordingly.[16–18]
- Open fractures were classified according to Gustilo and Anderson.[7]
- Organ failure was defined using the Sequential Organ Failure Assessment score[19] where 3 or 4 points were defined as failure, for each organ.
- Multiple organ failure was defined by a simultaneous organ failure of at least two organ systems.[20]
- Sepsis was defined according to the American College of Chest Physicians/Society of Critical Care Medicine consensus.[21]
- Early in-hospital fluid administration was defined as those fluids administered from the time of admission until arrival at the ICU.
- The number of packed RBC (pRBC) units was documented between ER arrival and ICU admission.
- The Trauma Associated Severe Hemorrhage (TASH) score[22] is provided to describe the predicted risk of hemorrhage; the pTASH score indicates the predicted risk of mass transfusion (≥10 pRBCs).
- The Revised Injury Severity Classification (RISC) score[23] was calculated to compare predicted and observed mortality.

Inclusion Criteria

Patients were included when the following criteria were fulfilled:

- femur fracture: coding according to AIS-98 AIS-2005 and/or AO/OTA classification or by keyword ("femur fracture") in free-text description[24]
- age 16 years or older
- hospital admission between January 2002 until December 2010
- fracture stabilization by intramedullary nailing or external fixation (EF) according to the OPS 301 (German version of the International Classification of Procedures in Medicine, version 10) or free-text description

TABLE 2. Patient Demographics

Parameter	Closed Femur Group	Open Femur Group	p
Patients, n (%)	4,423 (76.8)	1,338 (23.2)	–
Gender (male), %	72.0	73.2	0.37
Age, median (IQR), y	37 (22–54)	34 (22–47)	<0.001
NISS, median (IQR), points	27 (19–34)	27 (22–34)	0.99
Head injury (AIS ≥3)	30.7%	27.7%	0.035
Chest injury (AIS ≥3)	45.5%	44.5%	0.52
Abdominal injury (AIS ≥3)	18.4%	16.2%	0.07
Unstable pelvic injury (AIS ≥4)	14.7%	13.0%	0.11

TABLE 3. Indicators of Hemorrhagic Shock and Resuscitation

Parameter	Closed Femur Group	Open Femur Group	*p*
Prehospital shock, n (%)	866 (22.4)	310 (26.0)	0.01
Hemorrhagic shock in ER, n (%)	733 (18.2)	251 (20.3)	0.11
Prehospital volume,* median (IQR), mL	1,250 (500–2,000)	1,500 (1,000–2,250)	<0.001
Volume until ICU admission, median (IQR), mL	2,000 (1,000–4,000)	2,550 (1,297–4,500)	<0.001
pRBCs until ICU admission, mean (SD)	3.2 (6.7)	4.6 (7.8)	<0.001
Mass transfusion (≥10 pRBCs administered), n (%)	467 (10.7)	218 (16.4)	<0.001
Base excess, mean (SD), mmol/L	3.8 (5.2)	4.0 (5.4)	0.60
Quick's value**	75.3%	71.5%	<0.001
TASH score	9.56	10.27	0.003

*Until ER admission.
**Quick's value (100%, normal). A Quick's value of less than 60% is equivalent to a prothrombin time ratio of approximately 1.4.

Exclusion Criteria

- transfers
- incomplete data

The following general parameters were documented: demographics, injury severity, injury pattern and mechanism, and parameters related to complications and outcome.

Endpoints

- mortality
- sepsis
- MOF
- ICU LOS
- hospital LOS

Furthermore, prehospital and in-hospital fluid administration, presence of hemorrhagic shock, requirement of blood products, and ventilator days were documented. All data were assessed regarding the number of surgical procedures performed if they were related to the femur fracture, and surgical wound care was determined as well.

Statistical Analysis

Continuous variables are reported as means and SD, whereas categorical data are presented as frequencies and percentages. If a large SD was calculated, the median value and interquartile range (IQR) are additionally provided.

All data were tested for normal distribution. The χ^2 test was used for comparison of categorical variables. The Mann-Whitney *U* test was applied to test differences in both groups (open vs. closed femur fracture group). Furthermore, the Kruskal-Wallis test was applied for nonparametric data. Multivariate logistic regression analyses were performed for the three subgroups of open femur fractures (I°-III°). Multivariate regression analysis was performed to analyze the effects of open femur fractures on hospital mortality, MOF, and sepsis after adjusting for covariates. The closed femur fracture group was used as reference (odds ratio [OR], 1.0). The mortality analysis was adjusted for age, gender, NISS, AIS head, Glasgow Coma Scale score, partial thromboplastin time, base excess, anemia (<9 mg/dL), hypotension (SBP <90 mm Hg), mass transfusion (>10 pRBCs), cardiac arrest, level of care (three categories), and the year of treatment. We provide two model performance measures for the analysis on mortality: the area under the curve (AUC) was calculated as 0.931 (95% confidence interval [CI], 0.922–0.941), and Nagelkerke R^2 was calculated as 0.579. For the MOF analysis, we measured an AUC of 0.787 (95% CI, 0.774–0.800) and Nagelkerke Nagelkerke value of 0.264. The model performance measures for the regression analysis for sepsis were AUC of 0.757 (95% CI, 0.738–0.776) and Nagelkerke R^2 of 0.149.

We acknowledge that a multi-institutional study design involves a possible institutional bias (cluster effect). We partially controlled for patient clustering within levels of care, adjusting multivariate analyses for the type of trauma center (Levels I, II, and III).

TABLE 4. Clinical and Outcome Variables

Parameter	Closed Femur Group	Open Femur Group	*p*
Surgical procedures,* mean (SD)	1.3 (1.1)	2.2 (2.3)	<0.001
External fixation, n (%)	1,371 (31)	768 (57.4)	<0.001
In-hospital LOS, median (IQR), d	24 (13–39)	28 (16–46)	<0.001
Intensive care days, median (IQR)	5 (2–15)	6 (2–17)	0.001
Ventilator days, mean (SD)	6.6 (11.6),	7.0 (12.3),	0.001
Multiple organ failure, n (%)	1,067 (24.3%)	385 (28.8%)	0.001
Sequential Organ Failure Assessment score abnormality (>2), n (%)	1,651 (37.7)	575 (43.0)	<0.001
Renal failure, n (%)	231 (5.3)	92 (6.9)	0.026
Pulmonary failure, n (%)	866 (19.8)	309 (23.1)	0.008
Sepsis, n (%)	428 (9.8)	135% (10.1)	0.73
Mortality, n (%)	626 (14.2)	158 (11.8)	0.028

*Related to femur fracture and associated soft-tissue injury.

TABLE 5. Data Stratified for the Degree of Open Soft-tissue Injury

	I° Open	II° Open	III° Open	Total*	*p*
n (%)	334 (28.1)	526 (44.3)	328 (27.6)	1,188 (88.8)	—
NISS, median (IQR)	26 (17–34)	27 (22–34)	27 (22–37)	27	<0.001
External fixation, % (n)	45.8 (153)	58.0 (305)	71.3 (234)	58.2 (692)	<0.001
Prehospital shock, % (n)	19.5 (59)	27.8 (133)	29.7 (85)	26.0 (277)	0.009
Shock in ER, % (n)	12.9 (40)	20.2 (98)	28.3 (86)	20.4 (224)	<0.001
pTASH,** mean (SD)	15.4 (18.7)	20.4 (22.5)	28.4 (26.4)	21.2 (23.2)	<0.001
Mass transfusion (≥10 pRBCs), % (n)	8.4 (28)	13.2 (69)	28.2 (92)	16 (189)	<0.001
Sepsis, %, (n)	6.0 (20)	9.5 (50)	16.2 (53)	10.4 (123)	<0.001
MOF, % (n)	22.2 (74)	30.2 (159)	36.0 (118)	29.5 (351)	<0.001
Predicted mortality (RISC score), %	10.2	13.5	17.9	13.7	<0.001
Observed mortality, % (n)	8.1 (27)	9.9 (52)	17.1 (56)	11.4 (135)	<0.001

*One hundred fifty of 1,338 (11.2%) nonclassified open femur fractures excluded.
**Predicted risk of mass transfusion (%).

Odds ratios were calculated with 95% CI. Results were considered statistically significant if $p < 0.05$. The analysis was performed with SPSS for Windows (version 20; IBM Inc., Armonk, New York).

Of 39,556 patients from the database, 6,974 patients (17.6%) were excluded because of incomplete data (missing at random). No imputation or any form of missing data treatment was performed.

RESULTS

Patient Characteristics

A total of 32,582 patients were documented in the TR-DGU between 2002 and 2010. Among these, we identified 5,761 individuals (17.6%) with femoral fracture, who met the inclusion criteria; 4,423 fractures were closed (77.8%), and 1,338 fractures were open (23.2%). The overall demographic data for patients with open fractures were as follows: median age, 34 years (22–54 years); median NISS, 27.[22–34] Most common trauma mechanisms (Table 1) for both groups were motor vehicle accidents and other high-energy mechanisms including motorcycle accidents and high falls. Patients were predominantly male (72.3%) in both patient groups. Table 2 also lists all demographic data.

Injury Patterns and Severity

A significantly higher incidence of head injuries was observed in closed femur fracture patients ($p = 0.035$). All common sites for major hemorrhage, including severe chest, abdominal, and unstable pelvic injuries, were distributed equally (Table 2). General injury severity was comparable: the median NISS was 27 points for both groups.

Hemodynamic Status and Resuscitation

Despite a clinically comparable general injury severity and a similar pattern of concomitant injuries, except for head trauma, the incidence of hemorrhagic shock (SBP ≤90 mm Hg) in the prehospital setting was significantly higher in the open femur group (26.0% vs. 22.4%, $p = 0.01$). Likewise, these patients required significantly more intravenous fluids, received significantly more pRBCs (closed: 3.2 vs. open group: 4.6; $p < 0.001$), and required mass transfusions more often (closed: 10.7% vs. open group: 16.4%, $p < 0.001$). While the base excess was comparable for both groups, the Quick's value showed significant differences ($p < 0.001$) during resuscitation in the ER. The risk of severe trauma-associated hemorrhage was indicated by an elevated TASH score (Table 3) in the open fracture group ($p = 0.003$).

Skeletal Fixation

While the majority of open fractures were primarily stabilized with EF (57.4%), the open fracture group required twice the number of surgical procedures related to the femoral fracture (closed: 1.3 vs. open: 2.2).

The rate of EF increased from 45.8% in grade I, up to 71.3% in grade III open injuries.

Intensive Care and Complications

Open femur fractures were associated with a significantly longer duration of mechanical ventilation and longer stay in the hospital and the ICU and had a higher incidence of MOF (Table 4). While the median NISS values were the same for Types II° and III° patients, significant differences regarding systemic complications were evident: in contrast to Types I° and II° open injuries, approximately a third of all patients with Type III° open femur were exposed to a prolonged state of shock in the prehospital and ER phase (29.7% and 28.3%). In this patient

TABLE 6. Multivariate Regression Analysis*: In-hospital Mortality

Variable	Coefficient	*p*	OR	95% CI
Closed femur fracture			1.0	Reference
Open femur (NFS)	0.090	0.796	1.094	0.555–2.155
Open femur Type I	−0.106	0.718	0.899	0.505–1.601
Open femur Type II	−0.189	0.398	0.828	0.534–1.282
Open femur Type III	0.353	0.114	1.423	0.919–2.204
Other than Level I center	0.306	0.037	1.358	1.018–1.812
Surgical fracture fixation	−1.813	<0.001	0.163	0.119–0.224

*Adjusted for age, gender, NISS, AIS head, Glasgow Coma Scale score, partial thromboplastin time, base excess, anemia (<9 mg/dL), hypotension (SBP <90 mm Hg), mass transfusion (>10 pRBCs), cardiac arrest, level of care (three categories), and year of treatment.
NFS, not further specified open femur fracture (n = 150).

TABLE 7. Multivariate Regression Analysis*: MOF

Variable	Coefficient	p	OR	95% CI
Closed femur fracture			1.0	Reference
Open femur (NFS)	−0.249	0.290	0.780	0.502–1.213
Open femur Type I	−0.105	0.497	0.900	0.665–1.219
Open femur Type II	0.055	0.636	1.056	0.842–1.326
Open femur Type III	0.143	0.307	1.154	0.877–1.518
Advanced age (>59 y)	0.683	0.001	1.980	1.554–2.523
Male gender	0.135	0.085	1.145	0.982–1.335
NISS	0.032	0.001	1.032	1.025–1.039
AIS head ≥3	0.649	0.001	1.914	1.636–2.239
AIS chest ≥3	0.325	0.001	1.384	1.193–1.607
AIS abdomen ≥3	0.212	0.017	1.236	1.039–1.470
Any blood transfusions	0.686	0.001	1.987	1.706–2.313
Mass transfusion (≥10 pRBCs)	1.087	0.001	2.966	2.409–3.651

*Adjusted for age, gender, NISS, AIS (head, chest, and abdomen) of 3 or greater, blood transfusion, mass transfusion, cardiac arrest, level of care (three categories), and year of treatment.

group, the pTASH score very precisely predicted the risk of mass transfusion (predicted: 28.4%, observed: 28.2%).

Subgroup Analysis

For subgroup analysis (Table 5), open fractures were subdivided into I° (334 [28.1%]), II° (526 [44.3%]), and III° (328 [27.6%]). While median NISS values showed a minor increase per subgroup, the prevalence of MOF, sepsis, and mortality multiplied with the degree of open soft-tissue injury. The mortality rate increased from 8.1% in grade I, to 9.9% in grade II, and up to 17.1% in grade III open fractures. The adjusted OR for Type III open fractures was calculated with 1.423. However, the observed in-hospital mortality was in all three groups lower when compared with the predicted mortality (RISC score). The regression analysis (Table 6) indicates an increased mortality patients with open femur managed outside Level I trauma centers (OR, 1.358; 95% CI, 1.018–1.812; p = 0.037) and clearly shows that surgical fracture fixation is associated with patient survival (OR, −1.813; 95% CI, 0.119–0.224; $p < 0.001$).

Regression analyses for MOF and sepsis (Tables 7 and 8) identified mass transfusions as independent predictor for MOF (OR, 2.966; 95% CI, 2.409–3.651; $p < 0.001$) and sepsis (OR, 2.393; 95% CI, 1.821–3.143; $p < 0.001$).

DISCUSSION

A frequency of 11.5 per 100,000 persons per year has been reported for open long-bone fractures.[26] Open femur fractures are common high-energy injuries in patients with multiple trauma and are associated with a high incidence of major complications.[27–30] The socioeconomic impact of severely injured lower extremities is considered to be significant.[31]

Our study has both strengths and limitations: Two limitations are related to the classification of the soft-tissue injury. First, the classification of closed soft-tissue injuries was not performed consistently, which is why subgroups analysis for closed

TABLE 8. Multivariate Regression Analysis*: Sepsis

Variable	Coefficient	p	OR	95% CI
Closed femur fracture			1.0	Reference
Open femur (NFS)	−0.476	0.136	0.621	0.332–1.162
Open femur Type I	−0.552	0.024	0.576	0.356–0.931
Open femur Type II	−0.304	0.69	0.738	0.532–1.024
Open femur Type III	0.088	0.614	1.092	0.777–1.534
Advanced age (>59 y)	0.786	<0.001	2.194	1.615–2.982
Male gender	0.563	<0.001	1.756	1.400–2.202
NISS	0.017	<0.001	1.017	1.008–1.026
AIS head ≥3	0.186	0.089	1.204	0.972–1.491
AIS chest ≥3	0.408	<0.001	1.503	1.221–1.851
AIS abdomen ≥3	0.217	0.061	1.242	0.990–1.558
Any blood transfusions	0.603	<0.001	1.827	1.473–2.267
Mass transfusion (>10 pRBCs)	0.872	<0.001	2.393	1.821–3.143

*Adjusted for age, gender, NISS, AIS (head, chest, and abdomen) of 3 or greater, blood transfusion, mass transfusion, cardiac arrest, level of care (three categories), and year of treatment.

soft-tissue injuries could not be performed. Among the drawbacks is also the fact that the timing and quality of initial debridement are not documented. Moreover, we are unable to provide follow-up data, especially regarding healing and the requirements of late revisions. Furthermore, data on antibiotic coverage, microbiological findings, and laboratory values (procalcitonin, C-reactive protein, interleukin 6) are also not provided in the registry.

Among the strengths is that fact that we are able to provide large patient groups, as this appears to be the largest study involving open femur fractures to date. Moreover, the quality of data acquisition has been proven to be very reliable.[2,3,15,22,23]

In this light, we feel that the main conclusions drawn from our study are reliable. Our results can be summarized as follows:

First, both patient groups demonstrated similar demographic characteristics, injury patterns, and injury severity distributions (chest, abdomen, and pelvic ring), except for severe head trauma.

Second, increased resuscitation requirements (e.g., intravenous fluids, number of pRBC units) were found in the open femur group. The TASH score[22] seems to be a helpful instrument, especially in Type III open fractures, predicting severe hemorrhage very precisely. Our data are suggest that a relevant proportion of the subgroup with Type III open femur fracture was exposed to a prolonged state of hemorrhagic shock despite higher resuscitation efforts for patients with open fractures documented for the prehospital and ER phase.

Patients with open femur therefore required an increased time spent in the ICU and overall hospital stay. In addition, the number of surgical procedures related to the femoral fracture and associated soft-tissue injury was significantly higher in the open femur group.

Third, open fractures were associated with a higher incidence of MOF despite a comparable overall injury severity; however, the mortality rate was even higher in the closed femur fracture group. Risk factors for an increased mortality in the closed fracture group include advanced age and a higher prevalence of severe head injuries.

Finally, we tested for differences regarding injury severity, resuscitation, surgical management, prevalence of complications, and mortality in the subgroup analysis, after stratifying for the degree of open soft-tissue injury.

While the NISS demonstrated only a minor increase per subgroup (Type I°, 26; Type II°, 27; Type III°, 27 points), the prevalence of MOF, sepsis, and mortality multiplied with the degree of open soft-tissue injury. While the median NISS was identical for Types II° and III° open fractures, clinically relevant differences regarding systemic complications were evident: in contrast to Types I° and II° open injuries, the same proportion of patients with Type III° open femur fractures remained in a state of shock, when comparing prehospital and ER phase (29.7% and 28.3%). In types I° and II° open fractures, the proportion of patients in shock was reduced substantially between the prehospital and emergency phases (Type I, 19.5%–12.9%; Type II, 27.8%–20.2%). A prolonged state of shock despite a threefold higher transfusion rate, combined with an extended local tissue damage and host factors, might attribute to the higher risk of systemic complications in the (Type III) open fracture group.[32,33] In this patients group, the pTASH score very precisely predicted the risk of mass transfusion (predicted, 28.4%; observed, 28.2%). This instrument might be a feasible method to predict severe hemorrhage and to estimate blood product requirements. Striking was also the rate of EF, which increased from 45.8% in grade I, up to 71.3% in grade III open injuries. The current treatment practice in Germany stands in contrast with the latest literature: Gandhi et al.[4] published the recommendation for early definitive fracture stabilization in the majority of patients in the *Journal of Trauma* in 2014. However, the strength of evidence was considered low.

Many surgeons seem to prefer a risk- and soft-tissue–adapted approach with (temporary) EF. This dilemma reflects the need for prospective data and implementation into surgical practice.[34–37]

The mortality rate increased with the degree of soft-tissue injury, from 8.1% in grade I, to 9.9% in grade II, and up to 17.1% in grade III open fractures. However, the observed in-hospital mortality was in all three groups lower when compared with the predicted mortality (RISC score).

The femur is surrounded by the largest soft-tissue envelope of all long bones. A femur fracture is usually caused by a substantial trauma load; therefore, the systemic impact is considered significant. The associated soft-tissue injury was discussed to imply systemic changes.[38] In our data, the prevalence of sepsis, MOF, and mortality did increase with the degree of soft-tissue injury.

In our study, we observed a significant proportion of open femur fractures (23.2%). This fact may be related to the nature of TraumaRegister DGU, which includes only those trauma patients who require treatment in an ICU. Other registries, such as TARN,[39] include all patients with injuries that are admitted to a hospital. Likewise, Enninghorst et al.[40] characterized the population-based epidemiology of femur shaft fractures and found significantly fewer open femur fractures. Of 126 patients, 11 (9%) were found to have an open fracture. This may be related to the inclusion criteria in the Australian database including individuals, who sustained low-energy trauma and with low overall injury severity.

Our median NISS is comparable with that in other studies. Schreiber et al.[41] compared polytraumatized patients with major fractures from the Unites States and Germany. We also preferred to use the NISS for measuring injury severity, because complex and multiple extremity injuries are potentially underestimated with the Injury Severity Score. Australian and US orthopedic surgeons also recommended the use of the NISS as a more precise indicator for extremity injuries in blunt trauma.[42,43]

One of our most striking data is the increased resuscitation requirements for open fractures. Our data demonstrated that patients with open femur fracture more often received a diagnosis of hemorrhagic shock in the prehospital setting. During the first 24 hours after hospital admission, a significant proportion of patients with open fractures do even require a mass transfusion, which may be related to the local degree of injury. A detailed analysis cannot be performed in this database. However, in view of the even numbers of AIS values found in other body regions, this may be a likely cause. The higher number of pRBCs administered, the number of surgical procedures related to the femur fracture, and the higher prevalence of MOF also may represent a hint toward an open fracture as a risk factor.

The increased length of ICU and hospital stay might be of special importance especially in view of the lower incidence of traumatic brain injuries in this group. Traumatic brain injury is usually associated with an increased duration of ventilation and all associated complications, such as higher rates of pneumonia.[44]

Overaggressive volume resuscitation has not been recommended,[45] as it may contribute to hypothermia and coagulopathy. We feel that this factor does not play a role in our database, as these recommendations are usually followed in Germany. The increased LOS and the higher number of surgical procedures associated with open fractures may be considered as surrogates for the increased hospital costs and require special attention.

CONCLUSION

Open femur fractures are associated with higher in-hospital complications related to incidence of MOF, associated ICU stay, and hospital days when compared with closed femur fractures. For prevention of in-hospital complications, prompt hemorrhage control, surgical fracture fixation, cautious blood management, and triage to a Level I trauma center must be considered.

AUTHORSHIP

All authors have made substantial contributions to all of the following: (1) the conception and design of the study, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version.

DISCLOSURE

The authors declare no conflicts of interest.

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DISCUSSION

Dr. Sharon Henry (Baltimore, Maryland): There are many papers describing the outcome and demographics of patients with tibial fractures, but far fewer focusing on femur fractures. This is certainly the largest I am aware of.

This paper grapples with which aspect of injury plays a larger role in the patient's outcome. Is it their overall injury severity or is it the magnitude of the soft tissue injury that has occurred?

For more than 40 years attempts have been made to correlate the degree or severity of injury with survival and morbidity. Early descriptors utilized primarily anatomic measures of injury severity but found this did not correlate with outcomes. ISS and now NISS are the gold standard for accounting for the impact of global injury.

Here you found a statistical but minor difference in overall injury severity as measured by ISS and no difference in NISS between patients with closed and open femur fractures.

Closed femur fracture patient had increased mortality but fewer blood transfusions, less fluid administration, and prehospital shock. Open femur fracture patients had longer hospital stays, longer ICU stays, and spent more time on the ventilator and had more organ failure and sepsis. These morbidity measures increased slightly with Gustillo grades.

I have a few questions for you.

Do you know whether these patients had other fractures? We know they had their femur fracture but did they have upper extremity fractures or lower extremity fractures as well? And how was this distributed between the groups?

You found the frequency of shock in the ED and in the field, sepsis, ICU at length of stay, and hospital length of stay increased with increasing Gustillo classification and suggest this is likely directly related to the soft tissue injury rather than the overall severity.

We know the deleterious effect of crystalloid on these very factors and it appears these patients received substantial amounts of crystalloid fluid resuscitation, both in the field and in the emergency department. Can you comment on the role you feel this amount of crystalloid fluid might have had on these outcome measures?

Do you know how much time patients spent in the field and in the ED? Can you also comment on the resuscitation protocol and whether it changed during the study period, which was a rather long time?

A strong predictor of infection is time to final closure of open fractures. Have you any information on this aspect of the patients' care? What was the philosophy regarding fracture fixation timing? And you already answered the question I had about antibiotic administration – that you don't have that information.

I think this was a very interesting and unique study and I really enjoyed reading it and reviewing it. Thank you, again.

Dr. Weidun Alan Guo (Buffalo, New York): Dr. Weber, this is a nice study and I really enjoyed your presentation.

From your presentation I did not see the time from injury to the femoral fracture fixation. I think it is a piece of important information. Previous studies have shown that early fixation of femoral fracture would decrease the complications, especially the pulmonary one.

Is it true that in your open group, abdominal injury or TBI took precedence over femoral fracture, so you delayed the femoral fixation resulting in a higher complication rate?

Dr. David Blake (Norfolk, Virginia): Interesting study. I do have just one question, and perhaps I missed the information in your data presentation. Were there associated lower extremity/ipsilateral lower extremity injuries with any of these patients, such as a vascular injury, that may have confounded some of this data and contributed to some of the other underlying morbidity and mortality? Thank you.

Dr. Christian D. Weber (Aachen, Germany): Thank you very much for the privilege of the podium, the stimulating discussion, and your insightful questions.

Of course, we very carefully looked for concomitant injuries of the torso and extremities. However, except for severe head trauma, we did not find significant differences between both groups. As a well-known source of major hemorrhage, we also included unstable pelvic injuries into analysis, but this type of injury was also distributed equally. Furthermore, we decided to provide the New ISS, in order to depict multiple extremity injuries. In fact, both groups had very similar NISS values (29.8 vs. 29.5 points), reflecting a highly comparable impact of global injury.

From the trauma registry, we did get very precise data for the pre- and in-hospital interval. The pre-hospital time was comparable for both groups, probably because of the same rate of motor vehicle accidents and the need for complex extrication efforts. Also, the interval for in-hospital resuscitation until surgical fracture care or ICU admission was comparable: 75 minutes for closed fractures, and 72 minutes for open fractures, respectively, to answer Dr. Guo's question.

I share the same concerns with Dr. Henry, with respect to the amount of crystalloid fluid resuscitation and its well-known deleterious effects. While the optimal resuscitation protocol for hypotensive trauma patients remains undefined, our data shows that the treatment reality during the study period included aggressive fluid resuscitation, in order to achieve or maintain hemodynamic stability. There is no uniform resuscitation protocol which is valid for all participating centers, but the pre-hospital volumes of 1434 and 1645 mL are in line with the American College of Surgeons' Advanced Trauma Life Support® protocol, which is widely propagated within Germany.

We know that an approach that includes high volumes of crystalloids might be harmful, especially in the setting of uncontrolled hemorrhage, by contributing to dilutional coagulopathy. Our subgroup analyses indicate that the hemodynamic status of patients with type I and II open injuries might stabilize between the pre-hospital setting until emergency room admission; in contrast to patients with type III open injuries, since around 30% remain hemodynamically unstable in both settings, despite aggressive volume resuscitation.

While the optimal resuscitation protocol for hypotensive trauma patients needs to be defined by future studies, we can conclude that emergent bleeding control remains a primary life-saving intervention for patients with open femur fractures, also in the view of subsequent in-hospital complications like multiple organ failure.

Dr. Guo asked the question if open fracture fixation was delayed by the management of other, e.g. abdominal injuries. I do not think so, as we did not find more associated injuries in patients with open femur fractures! Furthermore, the rate of external fixation was twice as high in the open femur group. Also, the rate of external fixation increased with the degree of open soft-tissue injury. Therefore, primary or temporary fracture stabilization by external fixation might be achieved even earlier, since we all know external fixation is done quicker than primary intramedullary nailing, with the prerequisite of a meticulous debridement and lavage. However, the exact duration of the procedures are not documented within the registry, why we cannot conclude this from our data.

Dr. Blake finally asked if vascular injuries might have contributed to the underlying morbidity and mortality? I am sure that vascular injuries, especially in the type III open femur group, contributed to massive hemorrhage and increased the requirements for blood products and mass transfusions, and consecutively the risk for systemic complications.

Once again, I would like to thank the program committee for the honor and opportunity of the podium and for presenting here at the AAST. Thank you!

