Incidence and risk factors for complications after definitive skeletal fixation of lower extremity in multiple injury patients: a retrospective chart review [version 1; peer review: 2 approved]

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Abstract

**Background:** The management of multiple injuries is complex. Type and timing of treatment for lower extremity fractures is a controversial subject. Although many studies have demonstrated the safety and effectiveness of early treatment, others have suggested that early definitive stabilization may cause complications, especially with chest and head injuries. The aim of this study was to determine the complications and effects of timing of fixation, and investigate risk factors for complications in multiple injuries patients with lower extremity fractures.

**Methods:** A Retrospective chart review from Khon Kaen Trauma Registry between 2008 and 2015 were collected. All major complications were identified and collected for example acute respiratory distress syndrome (ARDS), acute kidney injury (AKI) and sepsis. The time to definitive skeletal fixation from initial injury was identified and analyzed with multiple logistic regression.

**Results:** 1224 multiple injuries patients with lower extremity fractures were identified. The mean age was 34±19.5 years, 74.4% were male and 25.6% female. The mean time from initial injury to definitive operation was 55.7±53.9 hours. Complications occurred with 178 patients (14.5%), the most common of which were pneumonia, ARDS and AKI. After adjusting for sex, severity of injury, we found that the operation within 24-48 hours complication was 6.67 times less common than in the early treatment group (less than 24 hours) (95% CI: 3.03 to 10.00, P-value< 0.001).

**Conclusions:** About 15% of the multiple injuries patients with lower extremity fracture had major complications. The optimal time for definitive fixation in lower extremity fractures to reduce complications was within 24-48 hours. We found that if we operated too early...
(before 24 hours) or more than 48 hours after the injury it could increase the morbidity and mortality.

Keywords
Trauma registry, emergency medical services, retrospective cohort study, surgery

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Abbreviations

ARDS  Acute respiratory distress syndrome
AKI  Acute kidney injury
MOF  Multiple organ failure
AIS  Abbreviated Injury Score
ISS  New Injury Severity Score
GCS  Glasgow Coma Scale score
PE  Pulmonary embolism
DVT  Deep venous thrombosis
OR  Odds ratio
95% CI  95% confidence interval

Introduction

Management of lower extremity injury in patient with multiple injuries, especially femoral fractures, is a complex situation. The debate on the optimal time to fixation is commonly over two strategies, 1) early definitive fixation where definitive fixation is within 24 hours after the injury, and 2) damage control orthopedics (DCO). The benefits of early definitive fixation are lower pulmonary complications, shorter length of stay and less morbidity1–4. On the other hand, some of evidences suggested that early fixation of long bones have more complications in patient with head and chest injuries5–7 and can induce inflammatory processes, hypoperfusion and “second hit injury”8–10.

DCO involves an initial skeletal stabilization for the patients with multiple injuries and an unstable condition, followed by delayed definitive fixation11–14. DCO has some advantages over early fixation in pulmonary function, pain relief14 and prevents the complication of early definitive fixation from initiating an inflammatory process that may be followed by acute respiratory distress syndrome (ARDS), acute kidney injury (AKI) and multiple organ failure (MOF)13,14. Many sources support the benefits of DCO17. A meta-analysis from Robinson however, showed a protective effect of early definitive fixation from pulmonary complications when compared with DCO (RR 0.30,0.22–0.40 90% CI)17. Further complicating the situation, data has also been reported indicating no difference in morbidity and mortality between early and late definitive fixation of long bones18.

Since there is inconclusive evidence for the optimal time to perform definitive fixation of long bones, we conducted this study to determine the complications and effects of timing of fixation and investigate risk factors for complications in multiple injury patients with lower extremity fractures.

Methods

A retrospective cohort study using data from the Khon Kaen Trauma Registry conducted between January 2008 and November 2015, was performed.

Study participants

A total of 1,224 multiple injury patients with lower extremity fractures treated between 2008 and 2015 were reviewed. Complications were identified from medical records that mentioned ‘major complication’ for example pneumonia, ARDS, AKI, sepsis and multiple organ failure (MOF). Timing to definitive skeletal fixation of lower extremity from initial injury were identified and analyzed with multiple logistic regression.

The Khon Kaen Trauma Registry collected pre-hospitalization and hospitalization information from medical records (including injury condition, comorbidities, fracture type, treatment type, operations, complications and outcomes)

The inclusion criteria for this study were 1) closed or open diaphyseal fracture of the femur and tibia; 2) multiple injuries in at least 2 body region; 3) underwent a definitive treatment of the long bone fracture with internal fixation. The exclusion criteria were 1) patient with late admission or transferred from other hospitals; 2) pathological fracture caused by neoplasm or malignancy; 3) open fracture grade IIIB or IIIC classified by Gustilo et al.19 or 4) inadequate information in the medical record (Figure 1).

![Figure 1](https://example.com/figure1.png)

**Figure 1.** The flow of included patients from Khon Kaen Trauma Registry.
The information of covariates and potential confounding in the Khon Kaen Trauma Registry were collected to identify the association between time of treatment and complications. The potential confounders included age, sex, comorbidity, type of fracture, type of treatment, Abbreviated Injury Score (AIS) for each of the six anatomical body regions (head/neck, face, chest, abdomen, extremity/pelvis, and skin)\(^5\), New Injury Severity Score (ISS)\(^6\) and Glasgow Coma Scale score (GCS) on admission\(^7\). In order to identify the association between time of definitive fixation of long bone and complications we divided patients with time of definitive fixation into three groups: 1) 24 hours or less, 2) between 24–48 hours, and 3) 48 hours or more from time of admission, based on cut-off points from previous studies\(^8,12,24\). Timing to definitive fixation was recorded in number of days and hours after admission.

Assessment of outcome

The primary outcome analyzed was major complications, including pneumonia, pulmonary embolism (PE), ARDS, sepsis, deep venous thrombosis (DVT), AKI, MOF and mortality.

For diagnosis of ARDS, we defined it as an acute onset of bilateral pulmonary infiltrates on chest radiography and a PaO\(_2\)/FiO\(_2\) 200 mm Hg for four days and had no evidence of pneumonia and cardiogenic pulmonary edema\(^25,26\). Acute kidney injury was defined by renal insufficiency which required hemodialysis\(^2,27\). Multiple organ failure (MOF) was identified as failure of more than one organ system\(^8\).

Data analysis

Baseline characteristics and selected variables were analyzed using descriptive statistical method, categorical variables were presented as number and percent, continuous data were reported as mean, standard deviation (SD), median, minimum value and maximum value (Min: Max). The effect of time to definitive long bone fixation, potential confounding and major complications were analyzed by logistic regression. All significant factors were evaluated with logistic multivariate regression analysis to eliminate the effect of confounding factors. Results are reported with odds ratios (OR) and 95% confidence intervals (CIs). STATA 10 (Stata Corp., College Station, TX, USA) statistical software was used for analysis.

Ethics statement

The current study utilized data from the database of Khon Kaen Trauma Registry between 2008 and 2015 which was conducted in a single hospital in Thailand. Permission for this purpose was obtained from the hospital before receiving an approval from the Institutional Review Board (IRB) of Khon Kaen University with the reference number of HE602122. The data analysis was performed after the permission gained from the registry and approval was obtained from the IRB.

Results

The average age was 34.0 ±19.5 years. 910 patients (77.4%) were male and 314 (25.6%) were female. More than 50% of the patients (n= 785) were treated within 48 hours after admission. The average time to definitive fixation was 55.7±53.9 hours. The median time to definitive fixation was 35.0 hours (1.5–293.1). After categorizing the time to definitive fixation into three groups, it was found the highest proportion was in the group of delayed definitive fixation of more than 48 hours (38.7%). The mean Glasgow coma scale score was 14.3 ± 2.2. The mean Injury Severity Score was 8.5 ± 7.7. The mean Abbreviated Injury Scale was 2.6 ± 0.6. Femur fractures were the most common fractures (57.6%) (Table 1).

Overall, complication were found in 178 patients (13.4%). Most of the complications were pulmonary complications, specifically, pneumonia (6.7%) and ARDS (5.8%). Other complications were acute kidney injury (2.2%) and sepsis/MOF (0.9%). Patients with definitive fixation performed between 24–48 hours had fewer major complications than other groups as shown in Table 2. Pneumonia was found in 82 patients in total, 41 of which had definitive fixation more than 48 hours after injury, 37 in <48 hours group, and only 4 patients in the group were the fixation was performed between 24–48 hours after injury (6.7 per 100 people per year (PPY) (10.3–24.1;95%CI). A similar pattern was found in AKI and ARDS with an incidence of 2.2 per 100 PPY and 5.8 per 100 PPY respectively.

The data in Table 3 shows the association between major complications and time to definitive fixation together with other covariates. Time to definitive fixation between 24–48 hours had a statistical significant effect on decreasing the risk of major complications. (OR=0.15; 95% CI: 0.08–0.27; p-value = <0.001) compared with other groups. Factors that significantly increase the risk of major complication are being over 65 years of age (OR=2.36; 95%CI: 1.20–4.67; p-value = 0.010), an Injury Severity Score (ISS) more than 18 (OR=6.24; 95% CI: 4.10–9.50; p-value = <0.001). The Abbreviated Injury Scale (AIS), abdominal injury and lower extremities had a statistical significant effect on decreasing the risk of major complications (Table 3).

Multivariable analysis, with multiple logistic regression and adjusted for potential confounders; GCS, AIS BR and type of fracture, found that the risk factors that are associated with major complications were time to definitive fixation being less than 24 hours, being aged more than 65 years and an ISS of more than 18 (Table 4). Receiving definitive fixation between 24–48 hours following injury led a statistical significant decrease in risk of major complication (Adjusted OR=0.18; 95% CI: 0.10–0.33; p-value = <0.001) when compared with those who received that treatment lower than 24 hours. Those 65 years and older had a statistical significant increased risk of major complication (Adjusted OR=3.3; 95% CI: 1.6–6.5; p-value = <0.001). An Injury Severity Score (ISS) of more than 18 causes a statistical significant increase risk of major complication (Adjusted OR =5.90; 95%CI = 3.80-9.18; p – value = <0.001)
**Table 1. General characteristic of patients.**

| Characteristics                        | Number | Percent |
|----------------------------------------|--------|---------|
| **Age (year)**                         |        |         |
| Children (<15)                         | 151    | 12.3    |
| Adult (15–49)                          | 797    | 65.1    |
| Old age (50–65)                        | 172    | 14.1    |
| Advance age (>65)                      | 104    | 8.5     |
| **Mean ± SD**                          | 34.0 ± 19.5 |
| **Median (Min: Max)**                  | 29 (1:94) |
| **Gender**                             |        |         |
| Male                                   | 910    | 74.4    |
| Female                                 | 314    | 25.6    |
| **Time to operate (hour)**             |        |         |
| <24                                    | 415    | 33.9    |
| 24–48                                  | 335    | 27.4    |
| >48                                    | 474    | 38.7    |
| **Mean ± SD**                          | 55.7 ± 53.9 |
| **Median (Min: Max)**                  | 35.0 (1.5: 293.1) |
| **Glasgow Coma Scale (GCS)**           |        |         |
| <8                                     | 56     | 4.4     |
| ≥8                                     | 1168   | 95.4    |
| **Mean ± SD**                          | 14.3 ± 2.2 |
| **Median (Min : Max)**                 | 15 (3:15) |
| **Injury Severity Score (ISS)**        |        |         |
| <18                                    | 1089   | 89.0    |
| ≥18                                    | 139    | 11.0    |
| **Mean ± SD**                          | 8.5 ± 7.7 |
| **Median (Min : Max)**                 | 5 (0.3:41) |
| **Abbreviated Injury Scale (AIS)**     |        |         |
| <3                                     | 544    | 44.5    |
| ≥3                                     | 679    | 55.5    |
| **Mean ± SD**                          | 2.6 ± 0.6 |
| **Median (Min : Max)**                 | 3 (1:5) |
| **Body Region (BR)**                   |        |         |
| Head/Neck                              | 391    | 40.0    |
| Face                                   | 11     | 0.9     |
| Thorax chest                           | 13     | 1.1     |
| Abdomen and pelviccontents             | 28     | 2.3     |
| Extremities and pelvic girdle          | 797    | 62.7    |
| External and body surface              | 13     | 1.1     |
| **Type of fracture**                   |        |         |
| Femur                                  | 705    | 57.6    |
| Tibia                                  | 519    | 42.4    |
| Multiple fracture                      | 767    | 62.7    |
| **Type of fixation**                   |        |         |
| Nail system                            | 293    | 23.6    |
| Plating system                         | 783    | 64.4    |
| External fixator                       | 148    | 12.1    |
Table 2. The incidence of complications.

| Time         | Number, Incidence of complications, and 95% CI of incidence | Major complications | Severe complications | *Any complications |
|--------------|-------------------------------------------------------------|---------------------|----------------------|-------------------|
|              |                                                              | Pneumonia | AKI | ARDS | Sepsis/MOF |                          |
| Overall      |                                                              | 82        | 27  | 71   | 26         | 178                       |
|              |                                                              | 6.7       | 2.2 | 5.8  | 0.9        | 14.5                      |
|              |                                                              | (4.1 to 10.3) | (1.4 to 2.6) | (4.5 to 6.3) | (0.5 to 1.0) | (12.5 to 19.2) |
| < 24 hrs     |                                                              | 37        | 11  | 39   | 2          | 87                        |
|              |                                                              | 8.9       | 2.7 | 9.4  | 4.80       | 21.0                      |
|              |                                                              | (6.1 to 11.7) | (1.1 to 4.2) | (6.6 to 12.2) | (1.9 to 11.5) | (17.0 to 24.9) |
| 24 – 48 hrs  |                                                              | 4         | 1   | 8    | 2          | 13                        |
|              |                                                              | 1.2       | 0.3 | 2.4  | 6.0        | 3.9                       |
|              |                                                              | (0.02 to 2.4) | (0.02 to 0.8) | (0.7 to 4.0) | (2.3 to 14.2) | (1.8 to 6.0) |
| > 48 hrs     |                                                              | 41        | 15  | 24   | 3          | 78                        |
|              |                                                              | 8.7       | 3.2 | 5.1  | 6.30       | 16.5                      |
|              |                                                              | (6.1 to 11.2) | (1.6 to 4.7) | (3.1 to 7.0) | (0.8 to 13.4) | (13.1 to 19.8) |

*Acute respiratory distress syndrome (ARDS), acute kidney injury (AKI), multiple organ failure (MOF), hrs = hours

Table 3. The bivariate analysis of covariates with time to operate and treatment group Crude odds ratio (Crude OR).

| Factor                          | Number | % Complication | Crude OR | 95% CI          | p-value |
|---------------------------------|--------|----------------|----------|-----------------|---------|
| **Time to operate (hours)**     |        |                |          |                 |         |
| <24                             | 415    | 20.9           | 1        |                 |         |
| 24–48                           | 335    | 3.9            | 0.15     | 0.08-0.27       | <0.001  |
| >48                             | 474    | 16.5           | 0.74     | 0.53-1.04       | 0.085   |
| **Age increase with 1 year**    |        |                |          |                 |         |
| <15                             | 151    | 11.2           | 1        |                 |         |
| 15–49                           | 797    | 14.1           | 1.23     | 0.75-2.22       | 0.360   |
| 50–65                           | 172    | 14.5           | 1.34     | 0.69-2.59       | 0.380   |
| >65                             | 104    | 23.1           | 2.36     | 1.20-4.67       | 0.010   |
| **Gender**                      |        |                |          |                 |         |
| Male                            | 910    | 14.8           | 1        |                 | 0.620   |
| Female                          | 314    | 13.7           | 0.91     | 0.63-1.32       |         |
| **Glasgow Coma Scale (GCS)**    |        |                |          |                 | <0.001  |
| <8                              | 56     | 65.3           |          |                 |         |
| ≥8                              | 11167  | 11.6           | 0.07     | 0.04-0.14       |         |
| **Glasgow Coma Scale increase 1 score** |        |              | 0.73     | 0.69-0.77       | <0.001  |
| **Injury Severity Score increase 1 score** |        |              | 1.07     | 1.05-1.09       | <0.001  |
| **Injury Severity Score (ISS)** |        |                |          |                 | <0.001  |
| <18                             | 1115   | 11.6           |          |                 |         |
| ≥18                             | 109    | 45.0           | 6.24     | 4.10-9.50       |         |
| **Abbreviated Injury Scale (AIS) increase 1 score** |        |                | 3.30     | 2.52-4.35       | <0.001  |
| **Abbreviated Injury Scale (AIS)** |        |                |          |                 | <0.001  |
## Table 4. The multivariable analysis of the time to operate and complication after adjusted for age and injury severity score (Adjusted OR).

| Factor                        | Number | % Complication | Crude OR | Adjusted OR | 95% CI    | p-value |
|-------------------------------|--------|----------------|----------|-------------|-----------|---------|
| **Time to operate (hour)**    |        |                |          |             |           |         |
| <24                           | 415    | 20.9           | 1        | 0.18        | 0.10-0.33 | <0.001  |
| 24-48                         | 335    | 3.9            | 0.15     | 0.85        | 0.53-1.05 | 0.100   |
| >48                           | 474    | 16.5           | 0.74     | 1.34        | 0.69-2.59 | 0.380   |
| **Age (year)**                |        |                |          |             |           |         |
| <15                           | 151    | 11.2           | 1        |             |           |         |
| 15-49                         | 797    | 14.1           | 1.23     | 1.43        | 0.80-2.55 | 0.030   |
| 50-65                         | 172    | 14.5           | 1.34     | 1.65        | 0.81-3.33 | 0.170   |
| >65                           | 104    | 23.1           | 2.36     | 3.30        | 1.56-6.5  | <0.001  |
| **Injury Severity Score (ISS)**|       |                |          |             |           |         |
| >18                           | 1115   | 11.6           | 1        |             |           |         |
| ≥18                           | 109    | 45.0           | 6.24     | 5.90        | 3.80-9.18 | <0.001  |

### Discussion

Earlier studies have demonstrated the advantage of early definitive treatment of long bone fractures, especially in femoral fractures, over delayed fixation\(^5,6\). The DCO developed as a treatment option for multiple injury patients with long bone fractures, combines the advantages of early fixation and decreases the physiologic and inflammatory process after the major orthopedic procedure\(^1,2,15,29\). Despite DCO being associated with a shorter operative time and less blood loss than definitive fixation (IMN or plating), the retrospective study of 97 severe multiple injured patients with ISS more than 25 showed no difference in complication of ARDS and MOF when compared with early definitive fixation\(^14\).

We found that delayed treatment of more than 48 hours after admission significantly increased the risk of complications
compared with treatment within 24 hours or 24–48 hours. In some situations, the definitive treatment may be delayed more than two weeks after admission due to an unstable condition and is associated with further complications. These findings reflect the effect of the timing of definitive long bone fixation, especially in femoral shaft fractures in patients with multiple trauma, and care should be taken to avoid delay of treatment of more than 48 hours from admission, similar to the study of Morshed et al.\(^23,30\). In a large cohort study among multiple injury patients with an ISS of more than 15 with femoral shaft fractures where they studied the effect of timing of definitive fixation of femoral shaft fractures, they showed an increased length of stay for patients treated within 48 to 120 hours compared with other groups, especially in patients with chest trauma (AIS > 2). This study found that patients treated within 24 hours have lower length of stay\(^31\). In our study, we found performing definitive fixation 24 to 48 hours after admission to the hospital, has improved outcomes and survival rates.

In the study of multiple injury patients with femoral shaft fractures (ISS >18) definitive fixation between 2 to 4 days after injury was associated with higher inflammatory conditions and an increased rate of multi-organ failure compared with fixation 5 to 8 days after the injury\(^10\). Other studies, however, have shown different results, with higher mortality when the operation is performed within the 2 to 5 days after injury; both of these resulted in high morbidity. Our study results found that performing fixation within 24–48 hours decreased the complications\(^39\).

Many studies have supported this evidence that patients with multiple injuries namely head injuries\(^9,11\), chest injuries\(^3\) or abdominal injuries\(^40\) have higher morbidity and a higher risk of complications. For multivariate analysis with associated severe head injury, chest injury, abdominal injury and lower extremity injury, especially femoral fractures, after adjusting for confounding, show a decreased morbidity rate if fixation is performed within 24 to 48 hour.

In our study, for patients with an unstable conditions who received early definitive fixation within 24 hours had increased inflammation which has the effect of increasing mortality rate\(^22,33\).

A study on early fixation of femoral shaft fractures (less than 24 hours) with a hypoperfusion state (serum lactate, > 2.5 mmol/L) demonstrated a similar number of postoperative complications to our study.\(^8\) Multiple injury without appropriate resuscitation produces a hypoperfusion state and increases the inflammatory response leading to end-organ injury\(^34\). Damage control orthopaedics (DCO) involves temporary fixation of the fracture until resuscitation of the patient is adequate and patients are stable for definitive fixation\(^5,35,36\). For this study we found the benefits of delaying definitive long bone fixation for at least 24 hours until patients were stable and then performing the definitive fixation within 24–48 hours after admission to prevent second hit injury.

The retrospective chart review has limitation were selection bias and information bias. Variation in the time from the injury scene to hospital, lack of data for patients transferred from other hospital, the accurate time to operate?, and in some cases the data for DCO being incomplete contribute to information bias. This study has no investigation of blood chemistry, inflammatory mediators due to the fact it was a retrospective review. Complex femoral fractures, especially in proximal femoral fractures and distal femoral fractures, are not be clearly identified as a which may be lead to delayed fixation due to the fracture configuration and not by patient’s condition, which may affect the data. Furthermore there was a large number of patients who were transferred from other hospitals and therefore were not included in the study.

Despite many limitations, our study has a large sample size of patients with multiple injuries and lower extremity fractures. The data has been collect from the Khon Kaen Trauma Registry, a referral and level I trauma center. The large cohort size supports the generalizability of our findings. The Khon Kaen Trauma Registry also has significant data on potential confounders, which was used for analytical multivariate methods.

**Conclusion**

Nearly 20% of multiple injuries patients with lower extremity fractures had major complications. We found that the timing of definitive fixation of lower extremity fracture (especially with femoral fracture) in multiple injury patients is associate with major complications.

The optimal time for definitive skeletal fixation in lower extremity fractures with the least complications based on our analysis appears to be within 24–48 hours. Performing operation too early (before 24 hours) or too late (after 48 hours) is associated with an increase in complication rate and should be considered in patient management for improved outcome.

The results support a delayed or “damage control orthopedics” management over definitive fixation of long bone fracture in multiple injuries patients. In patients who are unstable, adequate resuscitation at least 24 hours to 48 hours before undergo definitive fracture fixation is necessary, due to the systemic inflammatory response and to avoid “second hit” from a major surgical procedure. The trauma center hospitals should manage their resources to guarantee time to definitive fixation and proper management of multiple injuries patients.

**Data availability**

Dataset 1: Raw data obtained from the Khon Kaen Trauma Registry between 2008 and 2015. 10.5256/f1000research.14825.d203372\(^37\)

**Competing interests**

No competing interests were disclosed.

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References
1. Nahm NJ, Como JJ, Wilber JH, et al.: Early appropriate care: definitive stabilization of long bone fractures within 24 hours of injury is safe in most patients with multiple injuries. J Trauma. 2011; 71(1): 175–85. PubMed Abstract | Publisher Full Text
2. Pape HC, Auf'mKolk M, Paffrath T, et al.: Primary intramammary femur fixation in multiple trauma patients with associated lung contusion—a cause of posttraumatic ARDS? J Trauma. 1993; 34(4): 540–7; discussion 547–8. PubMed Abstract | Publisher Full Text
3. Meek RN, Vinoda EE, Pirier D: Comparison of mortality of patients with multiple injuries according to type of fracture treatment—a retrospective age- and injury-matched series. Injury. 1986; 17(1): 2–4. PubMed Abstract | Publisher Full Text
4. Brenneman FD, Boulanger BR, McLellan BA, et al.: Influence of thoracic trauma and primary femoral intramammary nailing on the incidence of ARDS in multiple trauma patients. Injury. 1993; 24 Suppl 3: S82–103. Publisher Full Text | Publisher Full Text
5. Crowl AC, Young JS, Kahler DM, et al.: Occult hyperperfusion is associated with increased morbidity in patients undergoing early femur fracture repair. J Trauma. 2000; 48(2): 260–7. PubMed Abstract | Publisher Full Text
6. Giannoudis PV, Smith RM, Bellamy MC, et al.: Stimulation of the inflammatory system by reamed and unreamed nailing of femoral fractures. An analysis of the second IHI. J Bone Joint Surg Br. 1999; 81(2): 356–61. PubMed Abstract | Publisher Full Text
7. Pape HC, Schmidt RE, Rice J, et al.: Biochemical changes after trauma and skeletal surgery of the lower extremity: quantification of the operative burden. Crit Care Med. 2000; 28(10): 4441–8. PubMed Abstract | Publisher Full Text
8. Scales TM, Boswell SA, Scott JD, et al.: External fixation as a bridge to intramammary nailing for patients with multiple injuries and with femur fractures: damage control orthopedics. J Trauma. 2000; 48(4): 613–21; discussion 621–3. PubMed Abstract | Publisher Full Text
9. Nowotarski PJ, Turen CH, Brumback RJ, et al.: Conversion of external fixation to intramammary nailing for fractures of the shaft of the femur in multiply injured patients. J Bone Joint Surg Am. 2000; 82(6): 781–8. PubMed Abstract | Publisher Full Text
10. Tuttle MS, Smith HR, Williams AE, et al.: Safety and efficacy of damage control external fixation versus early definitive stabilization for femoral shaft fractures in the multiple-injured patient. J Trauma. 2005; 59(2): 409–16; discussion 417. PubMed Abstract | Publisher Full Text
11. Taeger G, Ruchholtz S, Waydhas C, et al.: Damage control orthopedics in patients with multiple injuries is effective, time saving, and safe. J Trauma. 2005; 59(2): 409–16; discussion 417. PubMed Abstract | Publisher Full Text
12. O’Toole RV, O’Brien M, Scales TM, et al.: Resuscitation before stabilization of femoral fractures limits acute respiratory distress syndrome in patients with multiple traumatic injuries despite low use of damage control orthopedics. J Trauma. 2009; 67(5): 1013–21. PubMed Abstract | Publisher Full Text
13. Bosse MJ, MacKenzie EJ, Riemer BL, et al.: Adult respiratory distress syndrome, pneumonia, and mortality following thoracic injury and a femoral fracture treated either with intramedullary nailing with reaming or with a plate. A comparative study. J Bone Joint Surg Am. 1997; 79B(6): 793–809. PubMed Abstract
14. Robinson CM: Current concepts of respiratory insufficiency syndromes after fracture. J Bone Joint Surg Br. 2001; 83(6): 781–91. PubMed Abstract | Publisher Full Text
15. Rien D, Grass G, Sauerdank S, et al.: Evaluation of criteria for temporary external fixation in risk-adapted damage control orthopedic surgery of femoral shaft fractures in multiple trauma patients: “evidence-based medicine” versus “reality” in the trauma registry of the German Trauma Society. J Trauma. 2006; 59(6): 1375–94; discussion 94–5. PubMed Abstract | Publisher Full Text
16. Gustilo RB, Anderson JT: Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. J Bone Joint Surg Am. 1976; 58B(4): 453–8. PubMed Abstract | Publisher Full Text
17. MacKenzie EJ, Sternwachs DM, Shankar B: Classifying trauma severity based on hospital discharge diagnoses. Validation of an ICD-9CM to AIS-85 conversion table. Med Care. 1989; 27(4): 412–22. PubMed Abstract | Publisher Full Text
18. Gill M, Windemuth R, Steele R, et al.: A comparison of the Glasgow Coma Scale score to simplified alternative scores for the prediction of traumatic brain injury outcomes. Ann Emerg Med. 2000; 48(1): 37–42. PubMed Abstract | Publisher Full Text
19. Oster T, Baker SP, Long W: A modification of the injury severity score that both improves accuracy and simplifies scoring. J Trauma. 1997; 43(6): 922–5; discussion 925–6. PubMed Abstract | Publisher Full Text
20. Blakely JD, Kontaxis DN, Thomson NL, et al.: Timing of Femoral Shaft Fracture Fixation Affects Length of Hospital Stay in Patients with Multiple Injuries. Open Orthop J. 2015; 9: 324–31. PubMed Abstract | Publisher Full Text | Free Full Text
21. Brundage SI, McGahan R, Jurkovich GJ, et al.: Timing of femur fracture fixation: effect on outcome in patients with thoracic and head injuries. J Trauma. 2002; 52(2): 299–307. PubMed Abstract | Publisher Full Text
22. Dushianthan A, Grocott MP, Postle AD, et al.: Acute respiratory distress syndrome and acute lung injury. Postgrad Med J. 2011; 87(1031): 612–22. PubMed Abstract | Publisher Full Text
23. Konstantinides SV, Torbicki A, Agnelli G, et al.: 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. Eur Heart J. 2014; 35(43): 3303–69, 309a–309p. PubMed Abstract | Publisher Full Text | Free Full Text
24. Dorfman DL, Grable Jr WR, Zuckerman JD, et al.: Multiple organ failure in trauma patients. J Trauma. 2005; 59(4): 608–16. PubMed Abstract | Publisher Full Text | Free Full Text
25. Durham RM, Moran JJ, Mazuski JE, et al.: Multiple organ failure in trauma patients. J Trauma. 2003; 56(1): 7–13. PubMed Abstract | Publisher Full Text
26. Pape HC, Grimme K, Van Griensven M, et al.: Influence of thoracic trauma and primary femoral intramammary nailing on the incidence of ARDS in multiple trauma patients. Injury. 1993; 24 Suppl 3: S82–103. Publisher Full Text | Publisher Full Text
27. Taeger G, Ruchholtz S, Waydhas C, et al.: Damage control orthopedics in patients with multiple injuries is effective, time saving, and safe. J Trauma. 2005; 59(2): 409–16; discussion 417. PubMed Abstract | Publisher Full Text
28. Tuttle MS, Smith HR, Williams AE, et al.: Safety and efficacy of damage control external fixation versus early definitive stabilization for femoral shaft fractures in the multiple-injured patient. J Trauma. 2009; 67(3): 602–5. PubMed Abstract | Publisher Full Text
29. O’Toole RV, O’Brien M, Scales TM, et al.: Resuscitation before stabilization of femoral fractures limits acute respiratory distress syndrome in patients with multiple traumatic injuries despite low use of damage control orthopedics. J Trauma. 2009; 67(5): 1013–21. PubMed Abstract | Publisher Full Text
30. Bosse MJ, MacKenzie EJ, Riemer BL, et al.: Adult respiratory distress syndrome, pneumonia, and mortality following thoracic injury and a femoral fracture treated either with intramedullary nailing with reaming or with a plate. A comparative study. J Bone Joint Surg Am. 1997; 79B(6): 793–809. PubMed Abstract
31. Liu XY, Jiang M, Yi CL, et al.: Early intramedullary nailing for femoral fractures in patients with severe thoracic trauma: A systemic review and meta-analysis.
32. Hofmann S, Huemer G, Kratochwill C, et al.: [Pathophysiology of fat embolisms in orthopedics and traumatology]. Orthopade. 1995; 24(2): 84–93. PubMed Abstract

33. Nast-Kolb D, Waydhas C, Gipper-Steppert C, et al.: Indicators of the posttraumatic inflammatory response correlate with organ failure in patients with multiple injuries. J Trauma. 1997; 42(3): 446–54; discussion 454–5. PubMed Abstract

34. Harwood PJ, Giannoudis PV, van Griensven M, et al.: Alterations in the systemic inflammatory response after early total care and damage control procedures for femoral shaft fracture in severely injured patients. J Trauma. 2005; 58(3): 446–52; discussion 452–4. PubMed Abstract | Publisher Full Text

35. Pape HC, Hildebrand F, Pertschy S, et al.: Changes in the management of femoral shaft fractures in polytrauma patients: from early total care to damage control orthopedic surgery. J Trauma. 2002; 53(3): 452–61; discussion 461–2. PubMed Abstract

36. Bernhard M, Becker TK, Nowe T, et al.: Introduction of a treatment algorithm can improve the early management of emergency patients in the resuscitation room. Resuscitation. 2007; 73(3): 362–73. PubMed Abstract | Publisher Full Text

37. Sangkomkamhang T, Thinkhamrop W, Thinkhamrop B, et al.: Dataset 1 in: Incidence and risk factors for complications after definitive skeletal fixation of lower extremity in multiple injury patients: a retrospective chart review. F1000Research. 2018. Data Source
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The authors reviewed large number of multiple injuries patients with lower extremity fracture and, in the abstract, concluded that the optimal time for definitive fixation to reduce complications was within 24-48 hours.

1. However, the authors did not clarify the reason for the delay surgery which could be unstable patient condition or operation room availability or other reasons. Complications in these groups could be different and affected the patient outcome. Do we really need to speed up the improvement process of the patient condition to get fracture fixed in 24-48 hours?

2. Can we conclude from this paper that definite fracture treatment before 24 hours is not recommended? For patients whose conditions are stable before 24 hours, should we wait until we get into 24-48 hours period to reduce the inflammatory process?

3. For the conclusion “optimal time for definitive fixation to reduce complications was within 24-48 hours”, are the severity of the injuries, type of injuries, pre-operative conditions of patients, fracture configuration and operative time in this group similar when compare to those of <24 hours and > 48 hours groups? Should the authors do subgroup analysis on this point?

4. The percentage of multiple injuries patients with lower extremity fracture who had major complications in the abstract is not equal those on the main manuscript, please correct.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Partly
If applicable, is the statistical analysis and its interpretation appropriate?
I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 29 May 2018
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As the authors mentioned, selection bias was an issue. Type, classification, and fracture geometry, those were not recorded, also the important factors associated with postoperative complications. Different experience of multiple surgeons should be mentioned for the information bias. The reasons of delayed definitive operations should be classified, such as, patient condition, surgeon intension, randomisation, or hospital facilities etc. Exactly, “time from the injury scene to definitive fixation” is more concerned duration and more appropriate than “time from admission”.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
I cannot comment. A qualified statistician is required.
Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Hip and knee surgery, lower extremities' orthopaedic trauma

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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