ABSTRACT

Introduction: Over the last decade the beneficial effects of early stabilization of femoral shaft fractures by intramedullary nailing have been challenged. The association between early femoral fixation with reamed nailing and a higher risk of pulmonary complications has been suggested. On the other hand there are other studies showing that early fixation of femoral fractures can decrease the incidence of pulmonary complications in trauma patients. Patients and Methods: During the period from 01/04/2014 to 31/05/2015 100 patients (73 male and 27 females with mean age 34 years) admitted with fracture femur were included in our study patients were divided randomly into 4 groups group A-isolated fracture who went early fixation, B- isolated fracture with late fixation, C-multiple fractures with early fixation D- multiple fractures with late fixation. Results: In this study early stabilization decreased pulmonary complications compared with delayed stabilization, In patients with isolated fracture: Pneumonia: early (group A) 0% (n = 0/27); delayed (group B) 4.5% (n = 1/22), Pulmonary thrombo-embolism: early (group A) 0% (n = 0/27); delayed (group B) 0% (n = 0/22). Fat emboli: early (group A) 1.8% (n = 1/27); delayed (group B) 18.1% (n = 4/22). Adult respiratory distress syndrome: early (group A) 0% (n = 0/27); delayed (group B) 0% (n = 0/22). In patients with multiple fractures: Pneumonia: early (group C) 7.4% (n = 2/27); delayed (group D) 15.1% (n = 5/33). Pulmonary thrombo-embolism: early (group C) 0% (n = 0/27); delayed (group D) 3% (n = 1/27). Fat emboli: early (group C) 18.5% (n = 5/27); delayed (group D) 30.3% (n = 10/33). Adult respiratory distress syndrome: early (group C) 3.7% (n = 1/27); delayed (group D) 12.1% (n = 4/33). Conclusion: Early fixation (>24 hour) of femur fractures with an intramedullary nail (IMN) has been associated with a decreased incidence of pulmonary complication (PC) in stable trauma patients. Key words: femoral fracture, fat embolism ARDS, pneumonia, timing of femoral shaft fractures fixation.

INTRODUCTION

Thirty years ago, the standard of care for the multiply injured patient with fractures was placement of the fractured limb in a splint or skeletal traction, until the patient was considered stable enough to undergo surgery for fracture fixation. This led to a number of complications such as adult respiratory distress syndrome (ARDS), infection, pneumonia, malunion, nonunion and death(1).

Over this past decade, it has been shown that stable, multiply injured patients with musculoskeletal injuries can safely receive definitive treatment of long-bone fractures very soon after their injury (early total care) (2).

In 1989, Bone et al.,(3) published a prospective study indicating that stabilization of femur fractures within 24 hours decreased pulmonary complications (PCs), including adult respiratory distress syndrome (ARDS), fat embolism, and pneumonias. The authors also reported decreases in hospital and intensive care unit (ICU) stays as well as costs. Several other studies reported similar findings (4-6).

Misuse of early total care, however, led to early surgical fracture fixation in some patients whose physiologic state did not tolerate the additional trauma of fracture fixation in the first twenty-four hours(7,8) Patients considered borderline for tolerating fracture surgery, or more appropriately “at risk,” include those who are hemodynamically unstable or hypothermic, have coagulation abnormalities, or have poor oxygenation due to traumatic lung injury Early stabilization of fractures in “patients at risk” was never advocated by authors of early total care studies(9). Early fracture fixation in these “patients at risk” is associated with a potential for higher complication rates. The need for fracture stabilization in these patients combined with the need for less physiologic stress when stabilizing the skeleton led to the introduction of damage control orthopedics, in which external fixators are placed across long-bone fractures for temporary stabilization (10).

This study was designed to determine whether the timing of stabilization of long bone fracture has role in the incidence of respiratory complications.
PATIENTS AND METHODS

During the period from 01/04/2015 to 31/05/2015 100 patient (73 male and 27 females with mean age 34 years) admitted with fracture femur was included in our study after taking a written consent and approval of the ethic committee of the hospital. The study is double blind randomized prospective clinical study; patients were divided randomly into 4 groups group A- patients (n=18) with isolated fracture femur admitted Saturday, Monday and Wednesday(isolated fracture who went early fixation), group B (n=22) isolated fracture femur admitted Sunday, Tuesday and Thursday (isolated fracture with late fixation), C- patients (n=27) with multiple fractures admitted Saturday, Monday and Wednesday, group(multiple fractures with early fixation) D-patients (n=33) with multiple fractures admitted Sunday, Tuesday and Thursday(multiple fractures with late fixation). Patients were randomly allocated in each group according to day of admission and take a number in order not to bias the results while being assessed by the pulmonology consultant (double blind).

Exclusion criteria:
1- Patients with head injury.
2- Patients with abdominal injuries.
3- Patients with chest injuries.
4- Pulmonary complications before internal fixation
5- Patients complaining of pre-existing cardiac or pulmonary problems.
6- Patients with hemodynamic instability.
7- Patients with hypothermia.
8- Patients with disturbed coagulation profile.
9- Patients who had definitive external fixation, or who had external converted to internal fixation(damage-control orthopedics)

The following investigations were done:
- Trauma series x-rays (chest x-ray, pelvis AP, cervical spine Lateral view and x-rays for the affected limb or any other suspected injured part according to clinical examination)
- CT chest, CT and CT skeletal system as indicated chest with angiography at admission and for follow up as indicated.
- Arterial blood gases (ABG) were measured routinely from the time of admission and for follow up during admission.
- Microbiological investigations when needed for diagnosis of pneumonia.
- Laboratory investigations (liver and kidney functions, coagulation profile, CBC, electrolytes and random sugar).

All patients received thrombo-prophylaxis according to guidelines (11).

New Injury severity score of the studied patients was assessed for all patients according to Baker’s et al (12).

Groups A,C were treated in the first 24 hours and Groups B,D were treated after 24 hours due to surgical theater arrangements. All patients with fracture femur were treated by intramedullary locking nail. Open femoral fractures were also immediately debrided in the operating room fixation was done. Delayed stabilization: stabilization after 24 hour of the injury: Open femoral fractures were initially placed in traction.

Definitions:

Pneumonia: was defined as the presence of “new lung infiltrate plus clinical evidence that the infiltrate is of an infectious origin, which include the new onset of fever, purulent sputum, leukocytosis, and declining oxygenation.” HAP is defined as a pneumonia not incubating at the time of hospital admission and occurring 48 hours or more after admission. VAP is defined as a pneumonia occurring >48 hours after endotracheal intubation (13).

ARDS: ARDS was defined as: 1) \( \text{PaO}_2/\text{FiO}_2 > 300 \text{ mmHg} \) while receiving ≥5 cmH\(_2\)O positive end-expiratory pressure, 2) diffuse parenchymal infiltrates, 3) pulmonary arterial wedge pressure >18 mmHg or lack of clinical evidence of congestive heart failure, and 4) no other obvious diagnosis explaining these findings. ARDS severity was based on the Berlin consensus definition as mild (200 mmHg > \( \text{PaO}_2/\text{FiO}_2 \leq 300 \text{ mmHg} \)) or moderate/severe (\( \text{PaO}_2/\text{FiO}_2 \leq 200 \text{ mmHg} \)) (14,15).

Pulmonary fat embolism: was diagnosed according to Gurd’s criteria (16).

Pulmonary thromboembolism: was confirmed by pulmonary CT angiography.

Statistical analysis

Results are given as numbers, percentage or mean ±SD. Demographic and physiologic characteristics of the studied groups were compared with use of Student’s t-test for continuous data and chi-square test for categorical data. The SPSS version 21 software package (SPSS, Chicago) was used for all analyses. P >0.05 was considered as statistically significant.
RESULTS

During the period from 01/04/2014 to 31/03/2015 100 patients (73 males and 27 females with mean age 34 years) admitted with fracture femur were included in our study after taking a written consent and approval of the ethics committee of the hospital. The study is a double blind randomized prospective clinical study; patients were divided randomly into 4 groups: Group A (n=18) patients with isolated fracture femur admitted Saturday, Monday and Wednesday (isolated fracture who went early fixation), group B (n=22) isolated fracture femur admitted Sunday, Tuesday and Thursday (isolated fracture with late fixation), group C (n=27) patients with multiple fractures admitted Saturday, Monday and Wednesday, group (multiple fractures with early fixation) D (n=33) patients with multiple fractures admitted Sunday, Tuesday and Thursday (multiple fractures with late fixation).

There were no significant differences between the studied early and late groups with isolated fracture (group A and B) and between the early and late groups with multiple fractures (group C and D) as regard to the demographics, physiological, NISS and preoperative ABG parameters as shown in table 1 and 2.

<p>| Table (1) Demographics and Characteristics of the Early and Late Groups (All Patients) |</p>
<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A (n= 18 )</th>
<th>Group B (n=22 )</th>
<th>P</th>
<th>Group C (n= 27)</th>
<th>Group D(n=33)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(mean±SD)</td>
<td>35.1±5.2</td>
<td>33.16±4.3</td>
<td>P&gt;0.05</td>
<td>35.16±4.6</td>
<td>33.32±7.4</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>GENDER</td>
<td>Male(n %)</td>
<td>14(77.8 %)</td>
<td>17 (73.3 %)</td>
<td>P&gt;0.05</td>
<td>19 (70.4 %)</td>
<td>23 (69.7 %)</td>
</tr>
<tr>
<td></td>
<td>Female(n%)</td>
<td>4 (22.2%)</td>
<td>5(22.7%)</td>
<td>P&gt;0.05</td>
<td>8 (29.7%)</td>
<td>10 (30.3%)</td>
</tr>
<tr>
<td>Respiratory rate(mean±SD)</td>
<td>22.4±3.2</td>
<td>23.1±2.7</td>
<td>P&gt;0.05</td>
<td>22.5±3.5</td>
<td>24.4±2.1</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Heart rate(mean±SD)</td>
<td>114.2±8.6</td>
<td>113.4±8.7</td>
<td>P&gt;0.05</td>
<td>115.4±7.8</td>
<td>114.7±4.7</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Systolic blood pressure(mean±SD)</td>
<td>100.2±10.5</td>
<td>98.6±11.7</td>
<td>P&gt;0.05</td>
<td>100.8±9.6</td>
<td>111.6±13.6</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Diastolic blood pressure(mean±SD)</td>
<td>70.6±5.1</td>
<td>73.6±5.5</td>
<td>P&lt;0.05</td>
<td>71.5±4.9</td>
<td>69.7±6.1</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>SPO2(mean±SD)</td>
<td>97.1±1.8</td>
<td>96.9±1.1</td>
<td>P&gt;0.05</td>
<td>96.3±1.2</td>
<td>97.1±2.1</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>GCS(mean±SD)</td>
<td>15</td>
<td>15</td>
<td>P&gt;0.05</td>
<td>15</td>
<td>15</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>NISS(mean±SD)</td>
<td>9±1.1</td>
<td>9±1.4</td>
<td>P&gt;0.05</td>
<td>21±2.3</td>
<td>20±2.7</td>
<td>P&gt;0.05</td>
</tr>
</tbody>
</table>

GCS: Glasgow Coma Score, NISS: Injury Severity Score

<p>| Table (2) Blood gas analysis (preoperative) of the studied groups |</p>
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A (n= 18 )</th>
<th>Group B (n=22 )</th>
<th>P</th>
<th>Group C (n= 27)</th>
<th>Group D(n=33)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.39±0.02</td>
<td>7.38±0.08</td>
<td>P&gt;0.05</td>
<td>7.38±0.07</td>
<td>7.39±0.04</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>PaO2 (mmHg)</td>
<td>81.1±3.2</td>
<td>82.3±2.2</td>
<td>P&gt;0.05</td>
<td>79.7±4.2</td>
<td>80.2±2.1</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>PaCO2 (mmHg)</td>
<td>35.6±3.3</td>
<td>36.2±2.5</td>
<td>P&gt;0.05</td>
<td>335.7±4.2</td>
<td>37.3±4.1</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>HCO3_ (mmol/L)</td>
<td>25.3±2.1</td>
<td>27.1±1.1</td>
<td>P&gt;0.05</td>
<td>24.6±2.5</td>
<td>26.4±3.2</td>
<td>P&gt;0.05</td>
</tr>
</tbody>
</table>

PaCO2: arterial partial pressure of carbon dioxide; PaO2 :arterial partial pressure of oxygen:HCO3 bicarbonate.

The mean time (in hours) between the admission and the operation was 9.5±3.1 for group A ,56.7±6.4 for group B,9.7±3.6 for group C and 55.9±7.6 for group D table(3).

There is no significant differences between the studied early and late groups with isolated fracture and between the early and late groups with multiple fractures as regard of the operation time(mean ± SD in hours) as showed in table(3) as it was 53.3 in group A, 52.5 in group B, 165.2 in group C and 165.2 in group D.
Table (3) Preoperative and operative time of the studied groups

<table>
<thead>
<tr>
<th>Time</th>
<th>Group A (n=18)</th>
<th>Group B (n=22)</th>
<th>Group C (n=27)</th>
<th>Group D (n=33)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative time (hours, mean±SD)</td>
<td>9.5±3.1</td>
<td>56.7±6.4</td>
<td>9.7±3.6</td>
<td>55.9±7.6</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Operation time (hours)</td>
<td>53.3</td>
<td>52.5</td>
<td>165.2</td>
<td>165.2</td>
<td>P&gt;0.05</td>
</tr>
</tbody>
</table>

In this study early stabilization inpatients with isolated fracture significantly decreased pneumonia and fat embolism but there was no significant difference as regard to thromboembolism and ARDS, and in patients with multiple fracture early stabilization significantly decreased pneumonia, fat embolism and ARDS as shown in table (4) and figure 1.

In patients with isolated fracture:
Pneumonia: early (group A) 0% (n = 0/18); delayed (group B) 4.5% (n = 1/22), pulmonary thrombo-embolism: early (group A) 0% (n = 0/18); delayed (group B) 0% (n = 0/22). Fat emboli: early (group A) 5.5% (n = 1/18); delayed (group B) 18.1% (n = 4/22), Adult respiratory distress syndrome: early (group A) 0% (n = 0/18); delayed (group B) 0% (n = 0/22).

In patients with multiple fractures:
Pneumonia: early (group C) 7.4% (n = 2/27); delayed (group D) 15.1% (n = 5/33) Pulmonary thrombo-embolism: early (group C) 0% (n = 0/27); delayed (group D) 3% (n = 1/27). Fat emboli: early (group C) 18.5% (n = 5/27); delayed (group D) 30.3% (n = 10/33). Adult respiratory distress syndrome: early (group C) 3.7% (n = 1/27); delayed (group D) 12.1% (n = 4/33).

Table (4): Pulmonary complications in the studied groups

<table>
<thead>
<tr>
<th>Pulmonary complications</th>
<th>Group A (n=18)</th>
<th>Group B (n=22)</th>
<th>P value</th>
<th>Group C (n=27)</th>
<th>Group D (n=33)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia (n%)</td>
<td>0 (0%)</td>
<td>1 (4.5%)</td>
<td>0.042</td>
<td>2 (7.4%)</td>
<td>5 (15.1%)</td>
<td>0.022</td>
</tr>
<tr>
<td>Pulmonary thrombo-embolism (n%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.1</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
<td>0.034</td>
</tr>
<tr>
<td>Fat embolism</td>
<td>1 (5.5%)</td>
<td>4 (18.1%)</td>
<td>0.0453</td>
<td>5 (18.5%)</td>
<td>10 (30.3%)</td>
<td>0.025</td>
</tr>
<tr>
<td>ARDS (n%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.1</td>
<td>1 (3.7%)</td>
<td>4 (12.1%)</td>
<td>0.033</td>
</tr>
</tbody>
</table>

PC: Pulmonary complications, ARDS: Acute respiratory distress syndrome.

Figure (1) Pulmonary complications according to each group of patients.
DISCUSSION

Over the last decade the beneficial effects of early stabilization of femoral shaft fractures by intramedullary nailing have been challenged. The association between early femoral fixation withthemednailing and a higher risk of ARDS/MOF has been suggested (4,14). On the other hand there are other studies showing that early fixation of femoralfractions can decrease the incidence of ARDS and multiple organ failure (MOF). The study conducted by Pape et al 2002, concluded that early total care of femoral shaft fracture leads to better outcomes and less pulmonary complications (17). Other multiple studies by Anwar et al 2004(18), Scalea et al 2000(19) and Nowotarski et al 2000(20), concluded that early external fixation of fracture femur and conversion to definitive fixation leads to less pulmonary complications .Pape HC et al 2005,2002 O’Toole RV et al 2009, three studies comparing early versus late fixation of femoral shaft fractures and pulmonary complications and they found that early fixation leads to less pulmonary complications (21,22,23).

This study was designed to determine whether the timing of stabilization of long bone fracture has role in the incidence of respiratory complications.

This study included100 patient (73males and 27females with mean age 34 years) admitted with fracture femur. Patients with head, chest or abdominal injuries were excluded from this study as numerous studies have supported the notion that there are particular subgroups of polytrauma patients defined by severe associated head (24,25) chest (26) or abdominal (27)injuries whose survival or morbidity experience may be particularly sensitive to timing of fixation.

The study is double blind randomized prospective clinical study in which Patients were randomly allocated in 4 groups according to day of admission in order not to bias the results while being assessed by the pulmonology consultant (double blind).

There were no significant differences between the studied early and late groups with isolated fracture(group A and B) and the early and late groups with multiple fractures (group C and D) as regarding to the demographics,physiological, ISS and preoperative ABG parameters as shown in table 1 and 2.

The mean time ( in hours ) between the admission and the operation was 9.5±3.1 for group A ,56.7±6.4 for group B,9.7±3.6 for group C and 55.9±7.6 for group D table(3).

There is no significant differences as regard of the operation time for patients with isolated fracture (between early and late groups) (mean ± SD in hours) as it was 53.3 in group A, 52.5 in group B, and for patients with multiple fracture (between early and late groups) as it was 165.2 in group C and 165.2 in group D as showed in table (3).

Trauma patients are at higher risk for developing pneumonia in comparison with the medical ICU patients. In trauma patients, additional variables such as injury severity score, and the critical need for prehospital intubation in the field increase the risk of developing a pneumonia. Multiple studies also show that trauma factors such as pulmonary contusion, rib fracture, sternal fracture, spinal cord injury, and traumatic brain injury increase the risk of developing pneumonia (28).

Incidence of fat embolism vary between 0.25 % to 0.35% in trauma patients and this may be explained by authors use of different diagnostic criterias. The actual incidence of FES is not known, as mild cases often go unnoticed. Bulger et al(29)in their retrospective study, reported an incidence of > 1%, while Fabian et al. in their prospective study, reported an incidence of 11–29%.(30).

Fat embolism syndrome typically affects the young, muscular victims of high-energy trauma, following multiple long bone fractures. The multiple injuries not only initiate the influx of marrow fat into the systemic and pulmonary vasculature, but also induce a systemic inflammatory response that produces cytokines capable of causing pulmonary damage. The number of clinically evident cases of clamant respiratory distress in such a scenario only represents the tip of the iceberg, with a large number of lung injury remaining clinically inapparent(31).

In this study early stabilization decreased pulmonary complications compared with delayed stabilization as shown in table (4).

In patients with isolated fracture:
Pneumonia: early (group A) 0 % (n = 0/18); delayed (group B) 4.5% (n = 1/22) with significant difference p>0.05, Pulmonary thrombo-embolism: early (group A ) 0% (n=0/18); delayed (group B) 0% (n =0/22) with no significant difference . Fat emboli: early (group A) 5.5% (n = 1/18); delayed (group B) 18.1% (n = 4/22) with significant difference
p>0.05, Adult respiratory distress syndrome: early (group A) 0% (n = 0/18); delayed (group B) 0% (n = 0/22 with no significant difference.

In patients with multiple fractures:
Pneumonia: early (group C) 7.4% (n = 2/27); delayed (group D) 15.1% (n = 5/33) with significant difference p>0.05. Pulmonary thromboembolism: early (group C) 0% (n=0/27); delayed (group D) 3% (n = 1/27) with no significant difference. Fat emboli: early (group C) 18.5% (n = 5/27); delayed (group D) 30.3% (n = 10/33) with significant difference p>0.05. Adult respiratory distress syndrome: early (group C) 3.7% (n = 1/27); delayed (group D) 12.1% (n = 4/33) with significant difference p>0.05.

These findings are in agreement with previous studies showing a benefit of early total care in patients stable enough for IMN. Bone et al(5), reported 2 PCs [(4.3%) (1ARDS and 1 pneumonia)] in the early stabilization group with multiple injuries compared with 17 PCs (50%) in the delayed stabilization group with multiple injuries. Charash et al(6), reported a 1.9% incidence of ARDS in patients with an ISS of greater than 17 undergoing early, primary IMN and 9.1% in the delayed group. Early stabilization eliminates the need for supine position for skeletal traction, it improves pulmonary function, prevents atelectasis and lead to early stabilization of the fractured bone. Early fixation is in accordance with the "two-hit" hypothesis, that is, an increase in proinflammatory markers during Days 3 to 5 after injury, increases the risk of developing a PC. It is hypothesized that early IMN fixation of femur fractures would be associated with a decreased incidence of PC(3-6).

CONCLUSION
Early fixation (>24 hour) of femur fractures with an intramedullary nail (IMN) has been associated with a decreased incidence of pulmonary complication (PC) in stable trauma patients.

REFERENCES


