Surgical Stabilization of Femur Fractures in Post-Traumatic Hypoxemic Patients: When and Why?

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Background: Post-traumatic hypoxemia can deteriorate during operative manipulations.
Objectives: In the present study, criteria-based approach was applied to determine optimum conditions for femur surgery. The aim of this study was to optimize perioperative management of post-traumatic hypoxemia.
Patients and Methods: In this prospective observational study, post-traumatic adults with $PaO_2 < 70$ mmHg in room air were enrolled. Physiological parameters, O_2 saturation (SO_2), arterial blood gas (ABG) analysis, Schonfeld fat embolism index score (SS), and Murray's lung injury scores (LIS) were assessed. The management protocol was femur surgery when patient was hemodynamically stable with LIS < 2.5 and $PaO_2/FiO_2 > 200$ mmHg ($FiO_2 < 0.5$, PEEP < 8 cm H_2O).
Results: A total of 31 adults (26 males and 5 females) with LIS of 0.1 to 2.5 (26 patients) and > 2.5 (five patients) at admission were recruited. Sixteen patients were admitted within 24 hours and 15 between 24 and 90 hours after injury. Thirteen patients were operated within 24 hours. Post-operative LIS was improved. No adverse sequels or mortality were seen.
Conclusions: Appropriate surgical stabilization can be safely performed during established post-traumatic hypoxemia using a multidisciplinary approach, continuous monitoring, and serial investigations to diagnose fulminant pathology and associated injuries.

Keywords: Post-traumatic hypoxemia; Damage-control surgery

1. Background

Post-traumatic hypoxemia and fat embolism syndrome (FES) can lead to a cascade of events resulting in acute lung injury (1, 2). Although operative stabilization is thought to control the progress of disease (3-6), release of marrow fat at the time of surgical manipulation can deteriorate the pulmonary status of these patients in whom neutrophil activation and adhesions are already causing damage to the alveoli, thus, making a vicious cycle (secondary insult) (7-9). Various surgical techniques have been developed to reduce the extravasation of fat and to block the inflammatory cascade of events (10); however, optimum time of surgery in patients with established hypoxemia has not been determined yet. In this study, all the participants underwent operative stabilization after meeting predefined hemodynamic and respiratory criteria. They were subsequently evaluated for the clinical outcome and adverse events.

2. Objectives

Post-traumatic hypoxemia can deteriorate during operative manipulations. In the present study, criteria-based approach was applied to determine optimum conditions for femur surgery. The aim of this study was to optimize perioperative management of patients with post-traumatic hypoxemia.

3. Patients and Methods

After achieving an approval of the Institute Ethical Committee and obtaining written informed consent from participants, this prospective observational study was performed on patients aged 18 to 45 years with new injury severity score (NISS) (11) of more than nine and significant post-traumatic hypoxemia who were admitted for surgical stabilization of femur fractures. Patients with associated cerebral or thoracoabdominal injuries, systemic illnesses, or chronic smokers were excluded. Patients were labeled as hypoxemic if their PaO2 was less than 70 mmHg in room air and as clinical FES if Schonfeld's fat embolism index score (SS) (12) was more than five. Time intervals between the injury and arrival to the hospital and duration of hypoxemia were recorded. All these patients had an intensive care therapy back-up and received supplemental oxygen using appropriate ventilatory strategy. Electrocardiography, noninvasive and invasive blood pressure monitoring, arterial oxygen saturation (SO_2), end-tidal carbon dioxide ($EtCO_2$), central venous pressure (CVP), temperature, and hourly urine output measurement were used to monitor the patient. Intra-

venous fluids and/or whole blood were administered to maintain the CVP at 12 ± 2 mmHg. Detailed history regarding physical health, coexisting medical problems, current medications, allergies, and previous anesthetic or surgical experience were recorded. Glasgow Coma Score (GCS) and vital signs were determined during this period at regular intervals. Performed standard investigations included arterial blood gas (ABG) analysis, complete hemogram, serum electrolytes, liver and renal function tests, serum lactate, chest roentgenogram and 12-lead ECG. Modified Murray's Lung injury scoring (LIS) (12) was done repeatedly every four hours to quantify the respiratory dysfunction (Appendix 1) (13). Patients were scheduled for operative stabilization as soon as they achieved hemodynamic stability (without vasopressors and/or inotropic support), normothermic status, PaO_2/FiO_2 ratio of more than 200 mmHg at FiO_2 of less than 0.5, positive end-expiratory pressure (PEEP) of less than 8 cm H_2O, and LIS score of more than 2.5. It was hypothesized that carefully performed operative stabilization would not affect clinical severity of hypoxemia, would protect the patient from risk of recurrent embolization, and would improve overall recovery.

General anesthesia with endotracheal intubation was performed to maintain the $EtCO_2$ between 30 to 35 mmHg. ABG analysis was done 30 minutes after surgical incision and regularly towards the end of surgery. The surgical stabilization of fractures was done by standard techniques of unreamed intramedullary nailing with distal venting and plating according to the fracture patterns. Surgery time was restricted to the minimum possible time for appropriate stabilization. Patients who were hemodynamically stable with $PaO2/FiO2$ ratio of more than 300 mmHg were reversed and extubated. Patients who were preoperatively on mechanical ventilation or hemodynamically unstable were electively ventilated. In the post-operative period, GCS, vital parameters, CVP, and SO_2 were recorded at regular intervals. ABG and SO_2 were assessed every twelve hours until the patients were weaned off the oxygen therapy (maintaining $PaO_2 > 80$ mmHg on $FiO_2 < 0.28$). Chest roentgenogram and LIS were assessed daily; persistent rise in LIS value by more than 0.5 or reduction in $PaO2/FiO2$ ratio to less than 200 mmHg were considered as deterioration and persistent fall in LIS by 0.5 was considered as improvement after surgery. Number of patients requiring mechanical ventilatory support, type of ventilatory strategy used, need for high PEEP (> 8 cm H_2O), and duration of mechanical ventilation were recorded. Total hospital stay, length of ICU stay, and morbidity and mortality during hospitalization were also determined. Perioperative adverse events like frank pulmonary edema, hypotension or hypertension requiring inotropes or vasoactive substances, respectively, excessive blood loss, and neurological or respiratory deterioration, ie, rise in LIS score by more than one, were recorded.

The data were analyzed with SPSS (v.10.1, SPSS Inc., Chicago, IL, USA). Patient characteristics were analyzed by the Chi square test for nominal data. Parametric data was analyzed using the independent-samples t-test. To evaluate anesthetic and surgical data, the independent-samples t-test or the Mann Whitney U-test were used. The occurrence of postoperative events were analyzed with the Chi square test or the Fisher's exact test where appropriate. All the values were expressed as mean $\pm$ SD, range, or number (%). A P value of less than 0.05 was considered statistically significant.

4. Results

Over a period of two years, 31 patients (26 males and five females with mean age of 27.48 ± 7.69 years and mean weight of 50.87 ± 5.38 kg) with significant hypoxemic changes (SS ≥ 5; Appendix 2) indicating classical FES were observed preoperatively. Eleven patients had isolated femur fracture another 20 had one or two associated musculoskeletal injuries (NISS > 16). Time intervals between injury and presentation to the institute were shorter than six hours in ten, six to 24 hours in six, 24 to 48 hours in ten, and 48 to 72 hours in five patients. Respiratory discomfort was observed in 23 patients (74.2%) at the time of admission and in the remaining eight patients (25.8%) after hospitalization. Petechial hemorrhages were seen in 14 patients (45.2%). Cerebral symptoms were predominant in five patients while head computed tomographic scan findings were normal in all except one patient in whom it was suggestive of cerebral FES on the second post-operative day. Patent foramen ovale (5 mm) was detected in one patient. This patient was operated 18 hours after admission and required mechanical ventilatory support with high PEEP for two weeks. At admission, 21 patients (67.8%) had raised serum lactate levels (> 22 mg/dL). The values stabilized back to normal range over next three to five days. Preoperative Murray's LIS was > 2.5 and 0.1 to 2.5 in 5 (16.1%) in 26 patients (83.9%), respectively. The LIS scores are shown in Figures 1-3.

Out of 16 patients who presented within 24 hours of injury, 13 (81.3%) could be operated during the hypoxemia phase or during the hot phase of FES. Other three patients had fulminant FES manifestation and required hemodynamic support prior to definitive stabilization. Remaining 15 patients who were referred 24 hours after injury with hypoxemic manifestations were operated at the earliest time after ensuring stable respiratory and hemodynamic parameters according to the protocols. Thus, two groups could be defined based upon the timing of surgery after injury, ie, immediate and early surgery group. Patient's demographic characteristics, pattern of injury, perioperative management, and outcome were comparable in these two groups. Except for two patients in early surgery group and three patients in delayed surgery group, all other patients underwent nailing for femur fractures; plating was also performed wherever associated injury was present. Standard techniques of unreamed intramedullary nailing with distal venting and appropriate type of plate fixation was chosen by the operating surgeon.
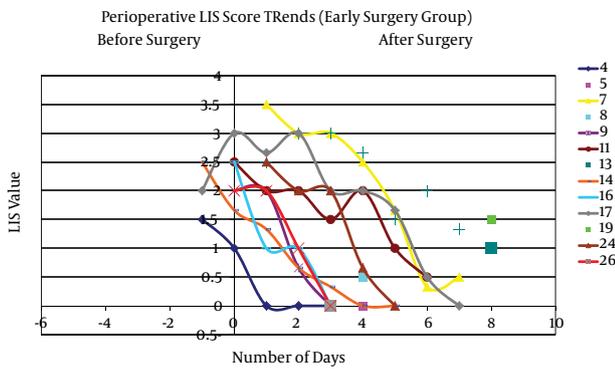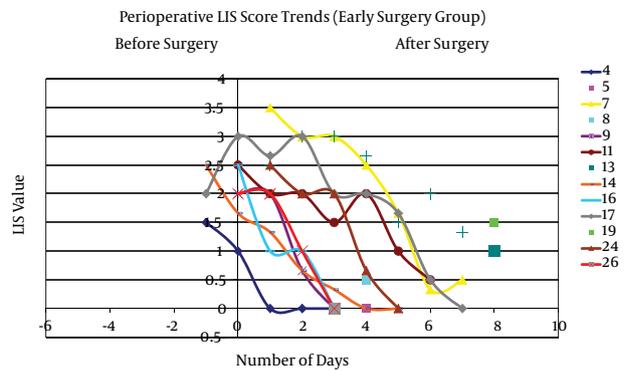
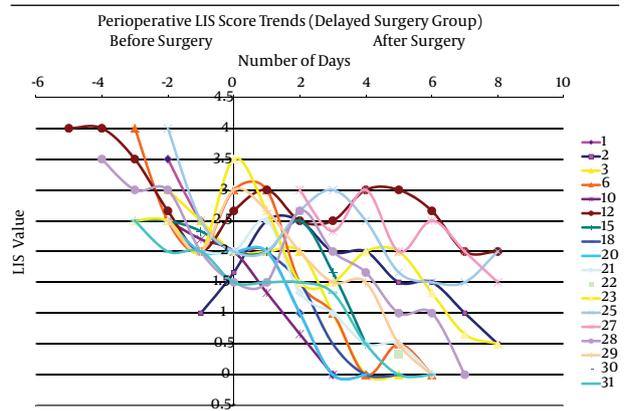**Figure 1.** Perioperative Lung Injury Score Trends (Early Surgery Group)

Figure 2. Perioperative Lung Injury Score Trends (Delayed Surgery Group)

Figure 3. Perioperative Lung Injury Score Trends (All Patients)

Thus, surgery time varied from 80 to 230 minutes. The LIS improved consistently in all patients in the post-operative period. The total ICU stay was 8.7 ± 4.8 days and 4.3 ± 1.56 days in XXX and YYY groups, respectively. Post-operative ICU stay had no significant difference between early and delayed surgery groups. Duration of hospitalization was 5.2 ± 1.9 days and 17.6 ± 3.9 days in early and delayed surgery groups, respectively (Table 1).

5. Discussion

Trauma is a leading cause of morbidity and mortality. In recent years, therapeutic strategies to manage trauma patients have significantly progressed; however, further research to examine different aspects of trauma is still necessary (14). Although the earliest possible surgery is the standard for stabilizing femur fractures (15, 16), surgical trauma elicits a stress response of combined endocrine and inflammatory origin (2, 17). Thus, surgical interventions needed to fix fractures can increase the patient's embolic burden of marrow fat. This can further influence major organ functions including alveolar gas exchange and the clinical outcome (secondary insult) (7-9). The incidence of clinically manifesting FES reported in literature is 11% to 29% (18, 19). There is a paucity of data regarding the optimum timing of surgical stabilization in otherwise healthy patients who become significantly hypoxemic.

Various pharmacological and surgical techniques have been developed to block inflammatory cascade of events and to reduce intravasation of fat during surgery. In the present study, physiological parameters such as heart rate, blood pressure, SO_2, perioperative GCS, ABG, SS, PaO_2/FiO_2 ratio, and LIS were continually recorded till the patient were off oxygen therapy. The LIS (9) indicates severity of lung injury. It is aggregate sum of four components, ie, hypoxemia, chest-X-ray, compliance, and PEEP scores. A LIS of zero, 0.1 to 2.5, and larger than 2.5 stand for no lung injury, moderate lung injury, and severe lung injury, respectively. The PaO_2/FiO_2 ratio or oxygenation ratio quantifies extent of lung injury. Values less than 300 mmHg indicate acute lung injury and values less than 200 mmHg with bilateral chest infiltrates and noncardiogenic pulmonary edema suggest acute respiratory distress syndrome. In the present study, stable hemodynamics without inotropes, serum hemoglobin of more than 10 gm/dL, normal serum electrolytes, coagulation profile, hepatorenal parameters, and PaO_2/FiO_2 of larger than 200 mmHg ($FiO_2 < 0.5$, PEEP < 8 cm H_2O) with LIS values between 0.5 and 2.5 were ensured. Patients with associated cerebral or thoracoabdominal trauma, myocardial insufficiency (myocardial infarction or congestive heart failure), diabetes mellitus, allergy to colloids, hepatorenal disorders, pathological fractures, and pregnancy were not enrolled. The outcome of surgical stabilization was evaluated in patients who were operated after meeting these predefined hemodynamic and respiratory criteria. Satisfactory results were observed using this defined protocol. None of the patients had worsening in their clinical status and there was no readmission/mortality within six weeks and subsequent follow-up after six months.

In conclusion, appropriate surgical stabilization could be safely performed during established post-traumatic hypoxemia when serial assessments had ruled out fulminant pathology and associated injuries. A predefined multidisciplinary criteria-based approach to maintain hemodynamics and respiratory parameters might improve patient satisfaction and final outcome.

Table 1. Characteristics and Perioperative Details of Patients Enrolled in the Study [a, b, c]

Patients Parameters	Early Surgery (Surgery Within 24 Hours)	Delayed Surgery (Surgery After 24 Hours)
Age, y	27.48 ± 7.69	28.93 ± 6.94
Weight, kg	50.87 ± 5.38	51.20 ± 4.86
Gender		
Male	12	14
Female	2	4
Mean NISS	20 ± 3.7	21.9 ± 4.2
Onset of FES after injury, h	18.615 ± 3.33	37.11 ± 19.00
Mean SS	10.15 ± 2.192	12.28 ± 2.02
LIS after admission		
0.5-2.5	10	13
> 2.5	03	06
Type of surgery		
Nailing	6	5
Plating	2	3
Combined (femur nailing & plating for associated injury)	5	10
Type of Anesthesia		
GA	11	13
GA + RA	2	5
Mode of ventilation with PEEP > 10 cm H$_2$O		
NIV	4	2
IPPV	7	12
IPPV	2	4
Ventilator, d	5.0 ± 3.08 (1-10)	6.41 ± 3.66 (2-15)
ICU stay, d	5.77 ± 2.92	9.0 ± 4.9
Hospital stay, d	5.2 ± 1.9	17.6 ± 3.9
Mortality	nil	nil

[a] Abbreviations: NISS, new injury severity score; SS, Schonfeld's fat embolism index score; LIS, lung injury score; GA, general anesthesia; RA, regional anesthesia; NIV, noninvasive ventilation; IPPV, intermittent positive pressure ventilation; PEEP, positive end-expiratory pressure.
[b] Data are presented as mean ± SD or number of patients and/or interquartile range.
[c] P < 0.05 was considered significant.

Appendix 1. Murray's Lung Injury Score (13) [a, b]

Parameters	0	1	2	3	4
CXR score (consolidation), quadrant	none	1	2	3	4
Hypoxemia (Pao$_2$/Fio$_2$), mmHg	> 300	225-299	175-224	100-174	< 100
PEEP, cm H$_2$O	< 5	6-8	9-11	12-14	> 15
Compliance (cm H$_2$O), mL	> 80	60-79	40-59	20-39	< 19

[a] Lung injury score is the aggregate sum of components divided by the number of components: 0, no lung injury; 0.1-2.5, moderate lung injury; and > 2.5, severe lung injury.
[b] Abbreviations: CXR, chest roentgenogram; and PEEP, positive end-expiratory pressure.

Appendix 2. Schonfeld's Fat Embolism Index (12) [a]

Symptoms	Score
Petechiae	5
Diffuse alveolar infiltrates	4
Hypoxemia (PaO$_2$ < 9.3 Kpa)	3
Confusion	1
Fever > 38°C	1
Heart rate > 120/min	1
Respiratory rate > 30/min	1

[a] Patients were labeled as hypoxemic if PaO$_2$ in room air was less than 70 mmHg and as clinical fat embolism syndrome if Schonfeld's fat embolism index score was more than five.

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