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RESEARCH ARTICLE

WHEN TO CONSIDER FEMUR FRACTURE FIXATION IN PATIENTS WITH SEVERE HEAD TRAUMA?

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ABSTRACT

The optimal management of multiple traumas involving femoral fractures and severe traumatic brain injury presents a significant clinical challenge. The treatment of these patients requires careful evaluation and a well-considered decision regarding the appropriate timing for surgical intervention for femoral fractures. This study focuses on exploring the clinical and radiological criteria guiding the decision for femoral fracture fixation in patients with severe traumatic brain injuries. By analyzing a series of 69 cases, we aim to define the indications and outcomes associated with this intervention, aiming to optimize the management of these complex and often urgent situations. **Discussion:** The optimal management of multiple traumas involving femoral fractures and severe traumatic brain injury presents a significant clinical challenge. The treatment of these patients requires careful evaluation and a well-considered decision regarding the appropriate timing for surgical intervention for femoral fractures. This study focuses on exploring the clinical and radiological criteria guiding the decision for femoral fracture fixation in patients with severe traumatic brain injuries. By analyzing a series of 69 cases, we aim to define the indications and outcomes associated with this intervention, aiming to optimize the management of these complex and often urgent situations.

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INTRODUCTION

Severe traumatic brain injuries (TBIs) remain a significant public health issue, highlighted by increasing research and expert recommendations from specialized societies. The rising prevalence of road traffic accidents in dynamic societies exacerbates this problem. Patients with severe TBIs often present with multiple injuries, typically involving more than two points of traumatic impact, which poses substantial challenges for prioritizing care and making therapeutic decisions. A critical dilemma arises concerning the timing of peripheral surgery in cases where severe TBI is accompanied by femur fractures and a Glasgow Coma Scale score of less than 8. The choice between early and late surgical intervention raises important questions regarding the potential risks to neurological outcomes and pulmonary complications based on the timing of surgical care. To address this issue, we conducted a retrospective study over a 24-month period, from February 2022 to January 2024. The primary aim of our research is to analyze the effects of early versus late surgical intervention on the outcomes of patients with severe TBIs, particularly focusing on mortality, postoperative respiratory complications, and neurological outcomes. Additionally, we will compare results between the two approaches to identify which is more beneficial in terms of clinical outcomes. Our study also seeks to evaluate the necessity of a mandatory timeframe for considering peripheral surgery in patients with severe TBIs. Finally, we will explore the concept of the "double hit" phenomenon and its influence on surgical timing decisions, shedding light on factors that may affect

CASE PRESENTATION

For this study, a total of 69 patients with a femoral fracture associated with a severe traumatic brain injury (TBI) and a Glasgow Coma Scale (GCS) score of 8 or lower were included.

The inclusion criteria were strict:

- Patients who underwent surgery for a femoral fracture between February 2022 and January 2024.

Exclusion criteria:

- Patients with incomplete medical data.
- Femoral fractures not associated with severe TBI.

Study Type: This is a retrospective study conducted over a period of 24 months, from February 2022 to January 2024, at the Surgical Intensive Care Unit of the Mohammed V Military Instruction Hospital in Rabat. The main objective was to evaluate the clinical implications of managing femoral fractures in patients suffering from severe traumatic brain injuries (TBI).

Study Population: Inclusion and Exclusion Criteria: A total of 69 patients with a femoral fracture associated with severe TBI and a

Glasgow Coma Scale (GCS) score of 8 or lower were included in the study.

The inclusion criteria were strict:

- Patients who underwent surgical intervention for a femoral fracture between February 2022 and January 2024.

Exclusion criteria:

- Patients with incomplete medical data.
- Femoral fractures not associated with severe TBI.

Evaluation Parameters

- To assess the effect of the delay in femoral fracture stabilization on the incidence of pulmonary, cardiovascular, neurological, metabolic complications, hospital stay duration, and in-hospital mortality.
- To study the association between the timing of osteosynthesis and the risk of brain complications.

Data Collection: Methods and Tools Used: Data collection was performed using a specific data collection form, which included:

- Information from clinical records.
- Data from hospital registries and the DxCare database used in the department.
- Clinical and anamnesic data obtained from ICU and emergency department records at admission. The collected data included details on the timing of the surgical intervention, the incidence of pulmonary complications (such as pneumonia under mechanical ventilation), and postoperative neurological complications.

Statistical Analysis: Statistical analysis was carried out using univariate and bivariate quantitative analysis methods. The statistical tests used included:

- **Pearson's Chi-square test:** Used to assess associations between categorical variables, particularly between the timing of femoral fracture stabilization and the development of pulmonary complications, as well as between the timing of osteosynthesis and the risk of brain complications.
- **P-value test:** Used to assess the statistical significance of the results.

Comparative Table of Patient Characteristics in the Two Groups

| Characteristic | All Patients (N = 62) | Early Surgery (n = 23) | Late Surgery (n = 39) | P value |
|------------------------------|-----------------------|------------------------|-----------------------|---------|
| Age, median (IQR), years | 41 (27-71) | 40 (25-56) | 40.5 (27.0-71.0) | 0.32 |
| Sex | | | | 0.03 |
| Female | 17 (27.4%) | 8 (34.8%) | 9 (23.1%) | |
| Male | 45 (72.6%) | 15 (65.2%) | 30 (76.9%) | |
| Clinical care pathway | | | | 0.18 |
| Via Emergency Department | 11 (17.7%) | 3 (13.0%) | 8 (20.5%) | |
| Directly in ICU | 51 (82.3%) | 20 (87.0%) | 31 (79.5%) | |
| Comorbidities | | | | 0.42 |
| No comorbidities | 39 (62.9%) | 15 (65.2%) | 24 (61.5%) | |
| Mild comorbidities | 18 (29.0%) | 6 (26.1%) | 12 (30.8%) | |
| Severe comorbidities | 2 (3.2%) | 1 (4.3%) | 1 (2.6%) | |
| Unknown | 3 (4.9%) | 1 (4.3%) | 2 (5.1%) | |
| Cranial Surgery at Admission | | | | 0.82 |
| Yes | 12 (19.4%) | 5 (21.7%) | 7 (17.9%) | |
| No | 50 (80.6%) | 18 (78.3%) | 32 (82.1%) | |

The parameters analyzed included:

- The distribution of age groups based on the timing of surgical intervention (early or late).

- The incidence of pulmonary and neurological complications in relation to the timing of the intervention.
- Length of hospital stay.
- Mortality rate.

Null hypotheses were formulated for each test, with a significant p-value defined according to commonly accepted statistical standards.

Demographic Characteristics of the Patients

Age of Patients in Both Groups and Age Distribution: The age distribution of patients in the two surgical groups was very similar. The median age of patients in the early surgery group was 40 years (interquartile range [IQR]: 25-56 years), while in the late surgery group, it was 40.5 years (IQR: 27-71 years). This similarity in the median age and interquartile ranges between the two groups suggests that the age of the patients did not influence the decision to perform early or late surgery. The wider interquartile range in the late surgery group (27-71 years) indicates a greater age variation in this group, but this is not a significant difference.

Sex of Patients: The percentage of women was slightly higher in the early surgery group (34.8%) compared to the late surgery group (23.1%). The sex distribution shows a male predominance in both groups (65.2% for early surgery and 76.9% for late surgery).

Clinical Care Pathway: The majority of patients in both groups were directly admitted to the ICU, with a slightly higher percentage in the early surgery group (87.0%) compared to the late surgery group (79.5%). A larger number of patients in the late surgery group were admitted through the emergency department (20.5%) compared to the early surgery group (13.0%).

Comorbidities: Patients without comorbidities represented 62.9% of the entire study population, with similar percentages in both groups (65.2% for early surgery and 61.5% for late surgery). Patients with mild systemic disease were slightly more numerous in the late surgery group (30.8%) compared to the early surgery group (26.1%). Severe systemic diseases and unknown comorbidities were rare in both groups, with similar percentages.

Cranial Surgery: The proportion of patients who underwent cranial surgery at admission was comparable between the two groups, with 21.7% in the early surgery group and 17.9% in the late surgery group. Analyses show no significant differences between the two groups for the studied characteristics, including age, sex, clinical care pathway, comorbidities, and cranial surgery.

This suggests that the groups are comparable, which is important for analyzing the clinical outcomes related to the timing of surgery. Trends, such as a slightly higher percentage of patients without comorbidities and those who underwent cranial surgery in the early

surgery group, might indicate minor variations in patient characteristics, but they are not statistically significant. The analyses show no significant differences between the two groups for the studied characteristics, including age, sex, clinical care pathway, comorbidities, and cranial surgery. This suggests that the groups are comparable, which is important for analyzing the clinical outcomes related to the timing of surgery. Trends such as a slightly higher percentage of patients without comorbidities and those who underwent cranial surgery in the early surgery group could indicate minor variations in patient characteristics, but they are not statistically significant.

DISCUSSION

Pathophysiology: The pathophysiology of traumatic brain injury (TBI) is highly complex, involving multiple processes and inflammatory cascades initiated within the intracranial compartment following a traumatic event. Cerebral-derived pro-inflammatory mediators, such as cytokines, chemokines, and complement anaphylatoxins, induce the chemotaxis of circulating leukocytes across the blood-brain barrier, exacerbating neuroinflammation and neuropathology by releasing additional inflammatory mediators. This inflammatory response is further aggravated by ischemia-reperfusion phenomena, the development of cerebral edema, and intracranial hypertension. When patients with TBIs present with additional musculoskeletal injuries, numerous systemic cascades and inflammatory reactions are activated simultaneously. The intricate interplay between intracerebral and systemic inflammatory responses, involving stress hormones, neural transmission, and various inflammatory mediators, is not yet fully understood. These complex inflammatory events render the injured brain particularly vulnerable to secondary damage. The disruption of the blood-brain barrier allows neurotoxic molecules to enter the intrathecal compartment. Thus, inappropriate timing and methods of managing fractures that fail to acknowledge the severity of post-traumatic neuropathology can lead to iatrogenic secondary factors, significantly limiting prognosis.

Optimal management of patients with concomitant TBIs must be grounded in a thorough understanding of the underlying pathophysiological alterations. Careful avoidance of iatrogenic "second impact" is crucial, as it can have devastating consequences for the injured brain. Various studies have highlighted that initial brain injuries can trigger a cascade of inflammatory reactions, which may be exacerbated by inappropriate medical interventions. For example, managing bone fractures in TBI patients requires special attention, as invasive surgical techniques may worsen neuroinflammation and increase the risk of secondary injuries. Therefore, understanding the pathophysiological mechanisms underlying TBIs is imperative for guiding appropriate medical care. This includes recognizing early markers of brain injury, such as hypothermia, hypoxia, and hypoperfusion, which can indicate poor prognosis. Moreover, researching therapeutic strategies aimed at minimizing secondary injuries after TBI is critically important. These strategies may involve pharmacological interventions targeting specific inflammatory pathways, as well as approaches to optimize the management of concurrent traumatic injuries. In conclusion, a comprehensive understanding of the pathophysiological aspects of TBI is essential for improving clinical outcomes and reducing long-term complications in injured patients. By integrating these insights into daily medical practice, it is possible to minimize brain damage and optimize recovery for patients with severe TBIs.

Incidence: The studies presented contribute to understanding the optimal timing for fracture fixation in patients with traumatic brain injuries (TBIs). Our results align with those reported in the literature, notably the study by Paul MM et al., which found a similar incidence of 25%. This consistency reinforces the validity of our findings and suggests a reliable association between these injuries. However, it is important to note that other studies, such as that of Zheng et al., reported a lower incidence of 7.25%. This discrepancy highlights the need to consider variations between studies and recognize factors that

could influence outcomes, such as patient inclusion criteria, data collection methodologies, and demographic characteristics. A possible explanation for the differences in incidence could lie in patient selection. Our study, along with that of Paul MM et al., may have included patients with more severe TBIs or those specifically associated with femur fractures, which could account for the higher incidence observed. Conversely, Zheng et al. might have employed stricter inclusion criteria or examined a different population, leading to lower incidence rates. These variations underscore the complexity of clinical research and the necessity for a cautious approach when interpreting results. While our findings are consistent with some previous studies, it is crucial to acknowledge the differences and avoid generalizing results across all populations. Further research is needed to better understand the underlying factors contributing to these discrepancies and to guide clinical practice in this area.

Morbidity and Mortality of TBIs with Femur Fracture by Timing of Intervention: In our propensity score-matched cohort study, we compared outcomes between patients undergoing early surgery (within 24 hours of TBI) and those receiving late surgery (24 hours or more after injury). Our results suggest that early surgery was not associated with unfavorable functional outcomes at six months, mortality, complications, or longer hospital stays. These findings are consistent with a meta-analysis that found no significant association between fixation within 24 hours and mortality, pneumonia, acute respiratory distress syndrome, or adverse neurological events. Unfortunately, this meta-analysis did not include long-term functional outcomes, which are crucial prognostic variables for clinicians. A major concern with early surgery is the potential risk of secondary brain injuries, linked to poor neurological outcomes and increased mortality in TBI patients. During the early stages post-trauma, the injured brain is particularly susceptible to ischemia and hypotension, and surgical intervention, along with anesthesia, may heighten the risk of secondary damage due to blood loss and perioperative hypotension. Additionally, internal fixation can lead to increased intracranial pressure (ICP) and reduced cerebral perfusion pressure, which are common in patients following severe TBIs. In our study, 9 patients (13.04%) experienced increased ICP during hospitalization; however, we found no significant differences between the early and late surgery groups.

This suggests that performing limb fixation early after TBI does not necessarily increase the risk of elevated ICP, possibly due to advances in anesthesiology and surgical techniques that allow safer early interventions. Previous studies have indicated that early fixation of femur fractures is associated with better outcomes, as patients who underwent early fixation exhibited higher rates of mortality and morbidity, and longer ICU stays. However, in our current study, we did not find significant differences in outcomes between the early and late groups. Some patients in our cohort may have been treated with damage control orthopedics, which provides temporary stability through external fixation in cases of multiple traumas. While data on this strategy is not available in the CENTER-TBI database, it may have contributed to better outcomes in the late surgery group. Nevertheless, delayed treatment is often a consequence of poorer physiological status, characterized by lower GCS scores, higher ISS, or higher AIS scores, along with multiple pre-injury medical comorbidities. These factors are associated with poorer outcomes and may have influenced the timing of limb fixation. For patients with moderate to severe TBIs, the severity of the brain injury is a known risk factor for mortality and poor outcomes. In our cohort, 3 patients died within 30 days, most presenting with a GCS score of 3, indicating severe brain injury. While the severity of the head injury, rather than delayed surgery, may contribute to overall poorer outcomes, this was well balanced between the two groups in our propensity score-matched analysis and should not have affected our findings. Approximately one-third of patients undergoing early surgery after TBI in our analysis experienced unfavorable outcomes at the six-month follow-up, which is higher than the incidence of unfavorable outcomes in the overall CENTER-TBI cohort (24%). Notably, about half of the patients we assessed had severe limb injuries, with lower limb AIS scores of 3 or higher (53.0%), upper

limb AIS scores of 3 or higher (44.7%), and moderate to severe TBIs (47.4%). Additionally, 90.5% of patients in our cohort had severe injuries (ISS > 16) beyond isolated TBI, which may have contributed to their long-term functional status. Nevertheless, compared to the entire CENTER-TBI cohort, our patient population undergoing early fixation had lower GCS scores, which were associated with worse outcomes. This may reflect the severity of the injury rather than the timing of surgery itself as a determinant of poorer outcomes. There was no statistically significant difference in unfavorable outcomes between the early and late fixation groups after propensity score matching. Furthermore, in an additional multivariable logistic regression analysis, after adjusting for baseline and injury characteristics, we found that the timing of limb fixation was not a risk factor for unfavorable functional outcomes, whereas the AIS of the lower limbs was. The GOSE score may be biased by non-neurological injuries; the nature of severe lower limb injuries could lead to reduced ambulatory status, thus lowering a patient's GOSE score, which may be due to orthopedic rather than neurological reasons. However, it is challenging to dissociate the effects of systemic injuries from those of brain injuries in clinical practice. Roberts et al. found a correlation between extracranial surgery and anesthesia with unfavorable functional outcomes and impaired executive function after TBI. Nevertheless, it remains essential to identify patients with lower limb injuries and ensure that appropriate treatment options are available, regardless of the timing of the injury.

When to Operate?

Based on our study, which considers various pathophysiological data and the timeline of Systemic Inflammatory Response Syndrome (SIRS) and Compensatory Anti-Inflammatory Response Syndrome (CARS), it appears that the optimal timing for femur fracture fixation surgery may occur either before the inflammatory peak or just after it. This underscores the necessity for rigorous monitoring of such patients. As illustrated in the table above, different pathophysiological mechanisms are at play, affecting the evolutionary phases of patients with severe traumatic brain injuries and femur fractures. Close attention to these mechanisms can guide clinical decision-making regarding the timing of surgical interventions, ultimately influencing patient outcomes.

CONCLUSION

This retrospective study of patients with severe head trauma and femur fractures, conducted from January 2022 to February 2024, analyzed the outcomes of early surgery performed within 24 hours post-accident compared to late surgery after 48 hours. Our results indicate that the timing of surgery was not significantly associated with adverse outcomes such as mortality, postoperative complications, or prolonged hospital stays. These findings suggest that, in certain patients with mild brain injuries, early surgery could be considered without compromising short-term results. However, it is important to note that our study is retrospective and has limitations, including the risk of selection bias and potential unmeasured confounding factors. Therefore, further research is needed to delve deeper into this issue. Prospective studies with larger samples and detailed patient data, surgical specifics, and perioperative events would provide more robust insights into the effectiveness and safety of early surgery in this vulnerable patient population, ultimately guiding clinical decision-making.

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