Mortality reduction after implementing a clinical practice guidelines–based management protocol for severe traumatic brain injury

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Keywords:
Guidelines; Mortality; Protocol; Severe Head Injury; Trauma; Traumatic Brain Injury

Abstract

Introduction: The objective of this study was to examine the effect of implementing a clinical practice guidelines–based management protocol on the outcome of patients with severe traumatic brain injury (TBI).

Methods: We carried out a pre-post guideline implementation study using previously collected data in the Intensive Care Unit (ICU). All patients older than 12 years with severe TBI, defined as a Glasgow Coma Scale score of 8 or less, from March 1999 to January 2001 (control group) and from February 2001 to December 2006 (protocol group) were identified and included in this study. Patients in the protocol group were managed using a clinical practice guidelines–based management protocol, derived from the guidelines published by the Brain Trauma Foundation. Primary outcome was hospital mortality, whereas the secondary outcome was ICU mortality. To assess whether the ICU protocol might have led to an increase in the number of surviving patients with severe disability, we examined the association of the protocol use and the need for tracheostomies, mechanical ventilation duration, and ICU and hospital length of stay (LOS) among survivors.

Results: During the study period, a total of 434 patients met the inclusion criteria. After adjustment for several prognostic factors, the use of protocol was independently associated with a significant reduction in hospital and ICU mortality (odds ratio, 0.45; 95% confidence interval, 0.24-0.86; and odds ratio, 0.47; 95% confidence interval, 0.23-0.96, respectively). The use of the protocol was not associated with an increase in the need for tracheostomies, mechanical ventilation duration, ICU LOS, and hospital LOS.
1. Introduction

Traumatic brain injury (TBI) is an important public health problem and is the leading cause of mortality, morbidity, and disabilities in children and young adults [1], especially in young males (15-35 years old). Among trauma victims, TBI remains the most common cause of death and disability [2].

In the United States, approximately 95 per 100 000 inhabitants sustain a fatal or severe enough injury to require hospital admission every year [3], leading to approximately 60 000 to 75 000 deaths [4-6] and an estimated 70 000 to 90 000 patients with permanent neurologic disabilities [7-9]. In Europe, 14 to 30 per 100 000 of the population die of TBI, accounting for 2% of overall mortality and 35% to 42% of deaths in people between 15 and 25 years of age [10].

In Saudi Arabia, the incidence of TBI is high [11,12], with an extrapolated incidence rate of 116 per 100 000 population. There, TBI is associated with higher severity and fatality compared with Western countries because of higher driving speed and variable prehospital emergency care. One of the striking epidemiologic features is the high male-female ratio, reaching [13] 13:1 and reflecting the local driving regulations that restricts driving to males.

Various studies showed considerable variation in the care of patients with severe TBI [14-16]. To improve and standardize neurocritical care management, the Brain Trauma Foundation (BTF) has developed evidence-based guidelines [17-19]. Few studies have reported the impact of implementation of these guidelines on patients’ treatment and outcome [20]. The purpose of this study was to examine the effect of the implementation of a clinical practice guidelines–based management protocol on the mortality of patients with severe TBI. To assess whether the Intensive Care Unit (ICU) protocol led to an increase in the number of surviving patients with severe disability, we examined whether the protocol increased the need for tracheostomies or led to prolongation of the duration of mechanical ventilation and ICU and hospital length of stay (LOS).

2. Materials and methods

2.1. Study design

We carried out a retrospective analysis of prospectively collected information, stored in an electronic database. The ICU database included data on all ICU patients and was collected by a full-time data collector. The study was approved by the institutional review board.

2.2. Setting

This study was conducted in a 21-bed, tertiary care medical-surgical ICU in an 800-bed teaching hospital trauma center in Riyadh, Saudi Arabia. The ICU, which admits more than a thousand patients per year, is run as a closed unit 24 hours a day, 7 days a week by in-house, full-time Critical Care Board–certified intensivists with backgrounds in medicine, emergency medicine, and anesthesia [21]. During both periods, before and after the implementation of the protocol, the ICU management for TBI patients was provided by the intensivists, whereas the surgical management, including the decision to place an external ventricular drain (EVD) for intracranial pressure (ICP) monitoring and management, was at the discretion of the neurosurgeons.

2.3. Patients

All consecutive patients older than 12 years with severe TBI, defined as a Glasgow Coma Scale (GCS) [22] score of 8 or less, from March 1999 to January 2001 (control group) and from February 2001 to December 2006 (protocol group) were identified and included in this study. Patients with brain death on admission were excluded.

2.4. Principles of TBI management in the 2001-2006 cohort

Until the introduction of the ICU protocol for severe TBI, patients with severe TBI were managed according to the knowledge and individual experience of the treating intensivists. A clinical practice guidelines–based management protocol was introduced in February 2001 in a preprinted order form that was completed and signed by the admitting intensivist. The protocol was developed by the intensive care team in agreement with the neurosurgical team and was based on the BTF guidelines [17-19]. All patients with a GCS score of 8 or less were included in the protocol. The protocol included the following items:

- Management of airway and breathing with endotracheal intubation and mechanical ventilation, which was
adjusted to maintain a pulse oximetry of 95% or greater and/or PaO2 of 80 mm Hg or greater and to achieve normoventilation (eucapnia) with PaCO2 of 35 to 40 mm Hg. Prophylactic and chronic hyperventilation was avoided; however, for a brief period (15-30 minutes), hyperventilation (PaCO2 30-35 mm Hg) was used to treat acute neurological deterioration reflecting increased ICP. When patients needed to be suctioned through the endotracheal tube, they were preoxygenated with fraction of inspired oxygen 1.0, administered additional sedation, and briefly (<10 seconds) suctioned.

- Maintenance of euvolemia using isotonic crystalloid solutions (normal saline: 0.9% NaCl) as needed to keep central venous pressure equal to 8 to 10 mm Hg and/or pulmonary capillary wedge pressure equal to 12 to 15 mm Hg. Hypotonic and glucose-containing solutions were avoided.

- Maintenance of cerebral perfusion pressure of 70 mm Hg or greater if the patient had an ICP monitoring or a mean arterial pressure of 80 mm Hg or greater if no ICP monitoring was placed. Cerebral perfusion pressure and/or mean arterial pressure was maintained using appropriate fluid management and administration of vasopressor, with norepinephrine being the first choice [23].

- For patients with EVD, an ICP greater than 20 mm Hg was used as the treatment threshold for cerebrospinal fluid drainage.

- Maintenance of analgesia and sedation using appropriate narcotics and sedatives. Nondepolarizing neuromuscular blocking agents were used only for refractory intracranial hypertension not responding to conventional treatment.

- Prevention and treatment of hyperthermia (temperature >36.5°C) using acetaminophen and/or cooling measures.

- Maintenance of the serum osmolarity greater than 290 mOsm with sodium greater that 142 mmol/L (tolerate up to 155 mmol/L) and avoid serum hypo-osmolarity (serum sodium <142 mmol/L).

- Glucose control to keep blood sugar 5 to 10 mmol/L (90-180 mg/dL).

- Early posttraumatic seizure prophylaxis using phenytoin for the first 7 days.

- Osmotic therapy using mannitol and/or hypertonic saline solutions (NaCl 3, 7.5, 3.0%, 7.5%, or 23.4% of NaCl). Osmotherapy was indicated to control raised ICP and to manage transtentorial herniation or progressive neurologic deterioration. Serum osmolarity was to be kept below 320 mOsm, and euvolemia was maintained by adequate fluid replacement.

- Maintenance of the head of the bed elevated at 30° (unless contraindicated) or application of the reverse Trendelenburg position.

- Nutritional support with early enteral feeding being the method of choice and use of a bowel regimen to avoid constipation.

- Stress ulcer prophylaxis using histamine receptor \((H_2)\) blockers.

- Thromboembolic prophylaxis using graduated-compression stockings, sequential pneumatic compression devices, and unfractionated or low-molecular-weight heparin if not contraindicated.

2.5. Data collection

The following data were extracted from the ICU electronic database: patients’ age and sex; Acute Physiology and Chronic Health Evaluation (APACHE) II [24] score; GCS score; Injury Severity Score; the absence or presence of associated injuries, including abdomen, chest, orthopedic/soft tissue, other head/neck, spinal, and vascular; surgical interventions; and the use of ICP monitoring.

2.6. Outcome measures

We compared the outcomes of the protocol group with those of the control group. The primary outcome considered in the study was hospital mortality, whereas the secondary outcomes were ICU mortality, duration of mechanical ventilation, need for tracheostomy, ICU LOS, and hospital LOS.

2.7. Statistical analysis

Descriptive statistics were carried out to describe patients’ baseline characteristics. Continuous variables were described as mean and SD and compared using Student \(t\) test. Categorical variables were expressed as absolute and relative frequencies and compared using \(\chi^2\) test. We used stepwise multiple logistic regression models to assess the effect of the protocol on the categorical outcomes (hospital and ICU mortality and need for tracheostomy). Odds ratio (OR) and 95% confidence interval (CI) were calculated. Moreover, we used stepwise multiple linear regression models to assess the effect of the protocol on the continuous outcomes (duration of mechanical ventilation, ICU LOS, and hospital LOS). The following variables were entered in both models: age, APACHE II score, GCS score, the presence or absence of associated injuries, operative status, and ICP monitoring. The \(\beta\) estimates were calculated for the association, as well as 95% CI. A \(P\) value less than .05 was considered to indicate statistical significance. All statistical analyses were performed using SAS software (version 8.0; SAS Institute, Cary, NC).

3. Results

3.1. Baseline characteristics

During the study period, a total of 434 patients were included (control group, \(n = 72\) patients; protocol group, \(n =\)
Patients in the protocol group, compared with patients in the control group, had slightly higher APACHE II scores and lower GCS scores (19.8 ± 5.4 vs 18.4 ± 5.4, \( P = .06 \); and 4.9 ± 1.8 vs 5.3 ± 1.9, \( P = .06 \); respectively) and were less likely to have ICP monitoring (8.6% and 34.7%, respectively, \( P < .001 \)) (Table 1).

### 3.2. Hospital mortality

Crude hospital mortality was 27.8% in the control group vs 18.8% in the protocol group. After adjustment, the use of protocol was independently associated with a reduction in hospital mortality (OR, 0.45; 95% CI, 0.24-0.86; \( P = .02 \)) (Table 2).

### 3.3. Secondary outcomes

Crude ICU mortality was 20.8% in the control group and 13.8% in the protocol group. As shown in Table 2, after adjustment for several prognostic factors, the use of protocol was associated with a significant reduction in ICU mortality (OR, 0.47; 95% CI, 0.23-0.96; \( P = .04 \)).

The use of protocol was not associated with an increase in the need for tracheostomies or in the duration of mechanical ventilation, ICU LOS, and hospital LOS among survivors. The reduction in hospital mortality after implementing the protocol was more significant for the groups of patients with admission GCS scores of 3 to 5 (25.1% vs 50% in the protocol vs control group, respectively; \( P = .003 \)), patients without ICP monitoring (17.8% vs 29.8% in the protocol vs control group, respectively; \( P = .05 \)), and in patients with isolated TBI (16.5% vs 39.1% in the protocol vs control group, respectively; \( P = .02 \)) (Table 3).

### 4. Discussion

Our study shows that the implementation of a clinical practice guidelines–based management protocol for the management of severe TBI is associated with a significant

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### Table 1 Baseline characteristics of patients included in the study, stratified by the group (control vs protocol)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control group (n = 72)</th>
<th>Protocol group (n = 362)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>69 (95.8)</td>
<td>343 (94.8)</td>
<td>.7</td>
</tr>
<tr>
<td>Age, mean ± SD (y)</td>
<td>31.8 ± 14.3</td>
<td>29.5 ± 14.0</td>
<td>.20</td>
</tr>
<tr>
<td>APACHE II, mean ± SD</td>
<td>18.4 ± 5.4</td>
<td>19.8 ± 5.4</td>
<td>.06</td>
</tr>
<tr>
<td>GCS, mean ± SD</td>
<td>5.3 ± 1.9</td>
<td>4.9 ± 1.8</td>
<td>.06</td>
</tr>
<tr>
<td>ISS, mean ± SD</td>
<td>33.1 ± 11.5</td>
<td>31.6 ± 11.5</td>
<td>.33</td>
</tr>
<tr>
<td>Isolated TBI, n (%)</td>
<td>23 (31.9)</td>
<td>91 (25.1)</td>
<td>.23</td>
</tr>
<tr>
<td>Postoperative status, n (%)</td>
<td>14 (19.4)</td>
<td>66 (18.2)</td>
<td>.81</td>
</tr>
<tr>
<td>ICP monitoring, n (%)</td>
<td>25 (34.7)</td>
<td>31 (8.6)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

**Associated injuries, n (%)**

- Chest: 33 (45.8) vs 160 (44.2), \( P = .80 \)
- Abdomen: 16 (22.2) vs 40 (11.1), \( P = .01 \)
- Ortho/soft tissue: 27 (37.5) vs 156 (43.1), \( P = .38 \)
- Other head/neck: 11 (15.3) vs 126 (34.8), \( P = .001 \)
- Spinal: 5 (6.9) vs 76 (21.0), \( P = .005 \)
- Vascular: 1 (1.4) vs 4 (1.1), \( P = 1.0 \)

**ISS indicates Injury Severity Score.**

### Table 2 Main outcomes in patients in the control and protocol groups and the results of multivariate analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control group (n = 72)</th>
<th>Protocol group (n = 362)</th>
<th>Adjusted OR</th>
<th>95% CI</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Categorical outcomes</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Hospital mortality, n (%)</td>
<td>20 (27.8)</td>
<td>68 (18.8)</td>
<td>0.45</td>
<td>0.24 to 0.86</td>
<td>.02</td>
</tr>
<tr>
<td>ICU mortality, n (%)</td>
<td>15 (20.8)</td>
<td>50 (13.8)</td>
<td>0.47</td>
<td>0.23 to 0.96</td>
<td>.04</td>
</tr>
<tr>
<td>Tracheostomies, n (%)</td>
<td>28/52 (53.9)</td>
<td>123/294 (41.8)</td>
<td>0.66</td>
<td>0.34 to 1.28</td>
<td>.22</td>
</tr>
</tbody>
</table>

**Continuous outcomes**

- Mechanical ventilation duration, mean ± SD \( \text{a} \) (d): 10.4 ± 6.9 vs 11.2 ± 7.4, \( P = 1.56 \)
- ICU LOS, mean ± SD \( \text{a} \) (d): 11.5 ± 7.3 vs 11.9 ± 7.9, \( P = 1.28 \)
- Hospital LOS, mean ± SD \( \text{a} \) (d): 82.3 ± 78.9 vs 71.4 ± 79.1, \( P = 2.98 \) to 21.62

\( \text{a} \): Among survivors.
reduction in ICU and hospital mortality. The use of the protocol was not associated with an increase in the need for tracheostomy or in prolonging the duration of mechanical ventilation, ICU LOS, or hospital LOS among survivors.

It is now clear that only part of the damage to the brain during head trauma occurs at the moment of impact, the so-called primary brain injury. Numerous secondary brain insults (SBIs), both intracranial (hematoma, vasospasm, edema, and hydrocephalus) and extracranial or systemic SBI, complicate the initial damage in the ensuing hours and days and lead to secondary brain injury.

The primary clinical objective after severe TBI is to prevent secondary brain injury, a common sequel to the primary mechanical impact. In the ICU, the mainstay of treatment of patients with TBI is the prevention of systemic SBI such as hypoxemia, hypotension, ischemia, hypercapnia, hypocapnia, hyperthermia, acute anemia, hypertension, hyperglycemia, hypoglycemia, and hyponatremia.

Despite the enormous progress in the understanding of TBI and the establishment of evidence-based guidelines for its management, studies have demonstrated considerable variations in the care of patients with severe TBI [13,14]. In 1991, Ghajar et al [14] conducted a survey of trauma centers in the United States to determine their management of patients with severe TBI and revealed a considerable variability in the care among centers. Bulger et al [16] conducted a study in academic trauma centers across the United States and demonstrated the persistence of considerable institutional variability in the management of patients with severe TBI despite the availability of clinical practice guidelines. Although one may expect differences in management surrounding areas with low quality or conflicting evidence (such as ICP use and mannitol), such variations were also observed in areas with stronger levels of evidence (such as hyperventilation) [16,25].

It has been suggested that the establishment of guidelines for the management of TBI based on existing scientific data may lead to improvement in the standard of care [14]. Moreover, the development of protocol-based management algorithms, based on the guideline recommendations, may also help to reduce the variability in care.

Few studies have evaluated the impact of these guidelines on the outcome of trauma patients [20]. Published data shows that significant reduction in mortality and morbidity can be achieved in patients with severe TBI by using intensive care management protocols. Vukic et al [20] have assessed the effect of implementation of guidelines for the management of severe TBI on patients’ treatment and outcome. They concluded that “the implementation of Guidelines in the treatment of severe head injury reduces death and disability rates in patients with severe head injury.” Bulger et al [16] evaluated the correlation between the level of care received by patients with severe TBI and the outcome. The authors demonstrated that an “aggressive” management strategy at aggressive centers (defined as those placing ICP monitors in >50% of patients meeting the BTF criteria for ICP monitoring) was associated with a significant reduction in the risk of mortality (hazard ratio, 0.43; 95% CI, 0.27-0.66). There was no statistically significant difference in functional status at the time of discharge for survivors. Elf et al [26] reported significant improvement in favorable outcome in patients with a GCS score greater than 4 from 40% in the preneurosurgical intensive care to 68% in the period of “basic neurointensive” unit to 84% in neurointensive care unit in which an organized protocol to prevent secondary insult was implemented.

Nevertheless, one must not look at mortality reduction as the only outcome measure because this may result in salvaging a greater number of surviving patients with severe disability. Our study showed that the use of protocol was associated with a reduction in hospital and ICU mortality without an increase in the need for tracheostomy and without an increase in duration of mechanical ventilation, ICU LOS, and hospital LOS in survivors, indicating that the improvement in survival was not at the expense of salvaging more surviving patients with severe disability.

Our study demonstrated that the use of a standardized protocol was associated with a significant reduction in mortality in the setting of decreased use of ICP monitor placement. The impact of ICP monitoring in TBI remains to be demonstrated because studies have yielded inconsistent results [27-29]. The practice of EVD placement changed over time in our ICU because of changes in neurological staffing, with different thresholds for this procedure. Nevertheless, the improvement in outcome was observed despite a reduction in EVD placement. In addition, we adjusted to this difference in EVD placement using 2 methods, multivariate analysis and stratification, and found consistent improvement of outcomes.

This study has a number of strengths, including the prospective nature of data collection by a full-time dedicated data collector, the inclusion of all consecutive patients with severe TBI before and after implementing the protocol, and the large sample size. As a potential limitation, the study was conducted in a single center and is a retrospective cohort in nature. Similar to other reported studies, our observational pre-post design of this study does not allow to definitively exclude the possibility that the observed difference is related to change in general ICU care. However, given the magnitude of the observed change, this possibility is unlikely; nevertheless, it cannot be excluded entirely without a randomized controlled trial. In addition, the functional status of survivors and long-term outcome after discharge were not directly examined because these were not standard parts of our ICU database. However, indirect surrogates were used to reflect the functional status. Although the use of such measures can be confounded by other variables such as concomitant injuries of other systems, we adjusted for these confounding factors using multivariate analysis and stratification.
5. Conclusion

The implementation of a clinical practice guidelines—based management protocol in patients with severe TBI was associated with a significant reduction in hospital and ICU mortality without increasing the need for tracheostomy or prolonging the duration of mechanical ventilation and ICU and hospital LOS, suggesting that the improved survival was not associated with the increased number of surviving patients with severe disability and that the functional status might have also improved. We recommend the implementation of ICU management protocol based on the published guidelines for the management of patients with severe TBI.

References

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