The Association of Intracranial Pressure Monitoring and Mortality: A Propensity Score-Matched Cohort of Isolated Severe Blunt Traumatic Brain Injury

Rebecka Ahl1,2, Babak Sarani3, Gabriel Sjolin2,4, Shahin Mohseni2,4
1Department of Surgery, Karolinska University Hospital, Stockholm, 2School of Medical Sciences, Orebro University, Orebro, Sweden, 3Department of Surgery, Center for Trauma and Critical Care, George Washington University, Washington, USA, 4Department of Surgery, Division of Trauma and Emergency Surgery, Orebro University Hospital, Orebro, Sweden

Abstract

Background: Intracranial pressure (ICP) monitoring in traumatic brain injury (TBI) is common. Yet, its efficacy varies between studies, and the actual effect on the outcome is debated. This study investigates the association of ICP monitoring and clinical outcome in patients with an isolated severe blunt TBI. Patients and Methods: Patients were recruited from the American College of Surgeons-Trauma Quality Improvement Program database during 2014. Inclusion criteria were limited to adult patients (≥18 years) who had a sustained isolated severe intracranial injury (Abbreviated Injury Scale [AIS] head of ≥3 and Glasgow Coma Scale [GCS] of ≤8) following blunt trauma to the head. Patients with AIS score >0 for any extracranial body area were excluded. Patients’ demographics, injury characteristics, interventions, and outcomes were collected for analysis. Patients receiving ICP monitoring were matched in a 1:1 ratio with controls who were not ICP monitored using propensity score matching. Results: A total of 3289 patients met inclusion criteria. Of these, 601 (18.3%) were ICP monitored. After propensity score matching, 557 pairs were available for analysis with a mean age of 44 (standard deviation 18) years and 80.2% of them were male. Median GCS on admission was 4[3,7], and a third of patients required neurosurgical intervention. There were no statistical differences in any variables included in the analysis between the ICP-monitored group and their matched counterparts. ICP-monitored patients required significantly longer intensive care unit and hospital length of stay and had an increased mortality risk with odds ratio of 1.6 (95% confidence interval: 1.1–2.5, P = 0.038). Conclusion: ICP monitoring is associated with increased in-hospital mortality in patients with an isolated severe TBI. Further investigation into which patients may benefit from this intervention is required.

Keywords: Intracranial pressure monitoring, mortality, traumatic brain injury

INTRODUCTION

Although widely accepted as standard of care and incorporated into several international guidelines, including the Brain Trauma Foundation (BTF) guidelines,[1-3] the use of intracranial pressure (ICP) monitoring in patients suffering severe traumatic brain injury (TBI) has been shown to be inconsistent by several investigators.[4,5] This finding could be due to conflicting results with regard to the effectiveness of ICP monitoring at reducing mortality in the context of severe TBI. While some observational cohort studies have documented a significant reduction in mortality,[6-8] others have found no difference or even an increase in mortality when ICP monitors have been utilized.[9-11] One major critique directed toward the findings suggesting no beneficial effect of ICP monitoring is the potential risk of selection bias which may occur through selection of severely injured patients deemed to have dismal prognosis who, therefore, do not receive ICP monitoring or selection of mildly injured intoxicated patients who had an initial depressed level of consciousness (e.g., Glasgow Coma Scale [GCS] ≤8) and therefore were subjected to ICP monitoring. In addition, several

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previous studies included patients with extracranial injuries or did not account for extracranial injuries if present, both of which could ultimately affect the overall outcome.

In an attempt to control for such confounding factors and to investigate the effect of ICP monitoring on overall outcome, we decided to match patients with an isolated severe TBI from blunt trauma who were ICP monitored with patients with equivalent intracranial injury burden without ICP monitoring using propensity score matching. We hypothesized that patients with an isolated severe TBI who had been monitored for ICP would have a better overall outcome.

Patients and Methods
A retrospective cohort study using the American College of Surgeons (ACS)-Trauma Quality Improvement Program (TQIP) database was performed for the year 2014. All adult patients (≥18 years) who sustained an isolated severe TBI from blunt trauma were included in the study. An isolated severe TBI was defined as an intracranial Abbreviated Injury Scale (AIS) score of ≥3 with a GCS score of ≤8 and an AIS score of zero for all other body areas. Penetrating injuries were excluded since they are usually less common and have more abysmal prognosis. Patients with an AIS score of 6 or those who died within 48 h of admission were also excluded from the study in order to control for unsurvivable injuries.

Patient demographics and clinical characteristics collected for analysis were level of admitting trauma center, age, gender, blood pressure and GCS on admission, intracranial AIS, intracranial specific injury, ICP monitoring, neurosurgical intervention (craniotomy/craniectomy), intensive care unit (ICU) length of stay (LOS), hospital LOS, and in-hospital mortality. The main outcome of interest was in-hospital mortality, and the secondary outcomes of interest were complications including acute respiratory distress syndrome (ARDS), deep vein thrombosis (DVT), sepsis, acute kidney injury, and unplanned return to the operating room or ICU, as well as ICU and hospital LOS.

Statistical analysis
Cases receiving ICP monitoring were matched in a 1:1 ratio with controls who did not receive such therapy using propensity score matching. Propensity scores (predicted probability of receiving ICP monitoring) were calculated for all patients with an isolated severe TBI using binary logistic regression. Variables included in the propensity score model were level of admitting trauma center, age, gender, type of intracranial injury, GCS on admission, intracranial AIS, and neurosurgical intervention. These variables were chosen to cover the indication for ICP monitoring set by the BTF, i.e., GCS ≤8 after resuscitation with an abnormal brain computed tomography (CT), and known factors affecting the outcome in patients suffering severe TBI. Each patient receiving ICP monitoring was matched with a control who did not receive ICP monitoring within a 0.026 caliper of propensity without replacement. The caliper was equal to one-fifth of a standard deviation (SD) of the logit of the propensity score. ICP-monitored patients for whom no suitable match could be found were excluded from analysis.

Demographics and clinical characteristics between the matched cohorts were compared using univariate analysis. Group differences were tested for significance using McNemar’s test for categorical variables and paired Student’s t-test or Wilcoxon signed-rank test for continuous variables wherever appropriate. Odds ratios (OR) with 95% confidence intervals (CI) and P value, with statistical significance set to <0.05, were derived for mortality. Values were reported as percentages for categorical variables and as mean (SD) or median (upper quartile, lower quartile) for continuous variables. The analysis was performed using the Statistical Package for the Social Science (SPSS Windows®) version 21.0 (SPSS Inc., Chicago, IL, USA).

Results
A total of 3289 patients met inclusion criteria. There were no missing values for the variables included in the current study. Almost half of the total cohort was admitted to an ACS-verified Level 1 trauma center. A total of 601 (18.3%) patients were subjected to ICP monitoring. Patients who received an ICP monitor were significantly younger (43.6 [SD 17.7] years vs. 53.1 [SD 20.3] years, P < 0.001), male (79.4% vs. 71.3%, P < 0.001), had more severe intracranial injuries (intracranial AIS 5 in 42.6% vs. 25.3%, P < 0.001), and underwent craniectomy/craniotomy more commonly (35.9% versus 16.8%, P < 0.001) [Table 1]. Before matching, ICP-monitored patients demonstrated a significant increase in the incidence of ARDS (4.3% vs. 2.3%, P = 0.015), DVT (8.0% vs. 2.8%, P < 0.001), and sepsis (3.0% vs. 1.3%, P = 0.006). This subgroup also showed a higher rate of unplanned return to the operating room (2.2% vs. 1.1%, P = 0.048), ICU LOS (12 [6, 18] days vs. 5 [3, 10] days, P < 0.001), and hospital LOS (16 [9, 27] days vs. 8 [4, 16] days, P < 0.001), as well as in-hospital mortality (27.5% vs. 21.9%, P = 0.004) [Table 2]. The unadjusted risk for mortality was 30% higher in patients who had ICP monitoring (OR: 1.3, 95% CI: 1.1–1.6, P = 0.004).

After propensity matching, 557 matched pairs were available for analysis. Table 1 delineates demographic and clinical characteristics of the ICP-monitored cases and their respective nonmonitored controls. The average age of the matched cohorts was 44 (SD 18) years and 926 (80.2%) were male. The median GCS on admission was 4 [3, 7]. Five hundred and sixty-six (49.0%) patients suffered a traumatic subarachnoid hemorrhage, 396 (34.3%) patients sustained a subdural hemorrhage, 75 (6.5%) had an epidural hemorrhage, and 165 (14.2%) demonstrated intracranial contusions. A total of 383 (33.2%) patients underwent neurosurgical intervention. In-hospital mortality was 24.8% (n = 286). After matching, there were no statistical differences in any variables included in the analysis between the two cohorts. No discrepancies were noted with regard to patient characteristics, GCS on
admission, intracranial injury severity, the occurrence of specific types of intracranial injury, or required neurosurgical interventions [Table 1].

Table 2 outlines the clinical outcomes following isolated severe TBI. After propensity score matching, ICP-monitored patients had a higher incidence of DVT (7.8% vs. 3.1%, P = 0.001). There was a trend toward more ARDS (4.3% vs. 2.3%, P = 0.073) and sepsis (3.1% vs. 1.4%, P = 0.076) in the ICP-monitored cohort.

Both ICU LOS (12 [6, 18] days vs. 6 [3, 12] days, P < 0.001) and hospital LOS (16 [9, 26] days vs. 10 [5, 19] days, P < 0.001) were longer in the ICP-monitored group. The overall mortality rate was significantly lower in patients not subjected to ICP monitoring compared to those who were (22.2% [95% CI: 18.9–25.8] vs. 27.4% [95% CI: 23.8–31.2], P = 0.038) [Table 2]. Patients subjected to ICP monitoring had an increased mortality OR of 1.6 (95% CI: 1.1–2.5, P = 0.038).

### Table 1: Demographics and clinical characteristics between intracranial pressure monitored and unmonitored cohorts before and after propensity score matching

|                      | No ICP monitoring (n=2688) | ICP monitoring (n=601) | P     | No ICP monitoring (n=577) | ICP monitoring (n=577) | P     |
|----------------------|---------------------------|------------------------|-------|---------------------------|------------------------|-------|
| Level-1 Trauma center, n (%) | 1304 (48.5) | 352 (58.6) | <0.001 | 309 (53.6) | 337 (58.4) | 0.110 |
| Male gender, n (%) | 1917 (71.3) | 477 (79.4) | <0.001 | 470 (81.5) | 456 (79.0) | 0.175 |
| Age years, mean (SD) | 53.1 (20.3) | 43.6 (17.7) | <0.001 | 44 (18.5) | 44.3 (16.5) | 0.668 |
| Age ≥55 years, n (%) | 1315 (48.9) | 171 (28.5) | <0.001 | 181 (31.4) | 171 (29.6) | 0.395 |
| GCS, median (LQ, UQ) | 4 (3,7) | 4 (3,6) | 0.250 | 4 (3,7) | 4 (3,6) | 0.320 |
| GCS 3, n (%) | 1329 (49.4) | 300 (49.9) | 0.857 | 285 (49.4) | 288 (49.9) | 0.905 |
| GCS 4, n (%) | 118 (4.4) | 32 (5.3) | 0.330 | 29 (5.0) | 32 (5.5) | 0.798 |
| GCS 5, n (%) | 146 (5.4) | 38 (6.3) | 0.378 | 28 (4.9) | 37 (6.4) | 0.314 |
| GCS 6, n (%) | 360 (13.4) | 90 (15.0) | 0.325 | 74 (12.8) | 86 (14.9) | 0.356 |
| GCS 7, n (%) | 420 (15.6) | 82 (13.6) | 0.234 | 91 (15.8) | 76 (13.2) | 0.245 |
| GCS 8, n (%) | 315 (11.7) | 59 (9.8) | 0.201 | 70 (12.1) | 58 (10.1) | 0.290 |
| AIS head 3, n (%) | 371 (13.8) | 25 (4.2) | <0.001 | 23 (4.0) | 25 (4.3) | 0.754 |
| AIS head 4, n (%) | 1636 (60.9) | 320 (53.2) | 0.001 | 333 (57.7) | 315 (55.3) | 0.275 |
| AIS head 5, n (%) | 681 (25.3) | 256 (42.6) | <0.001 | 221 (38.3) | 233 (40.4) | 0.346 |
| SAH, n (%) | 1066 (39.7) | 290 (48.3) | <0.001 | 290 (50.3) | 276 (47.8) | 0.333 |
| SDH, n (%) | 832 (31.0) | 216 (35.9) | 0.020 | 194 (33.6) | 202 (35.0) | 0.594 |
| EDH, n (%) | 88 (3.3) | 48 (8.0) | <0.001 | 35 (6.1) | 40 (6.9) | 0.620 |
| Contusion, n (%) | 262 (9.7) | 94 (15.6) | <0.001 | 79 (13.7) | 86 (14.9) | 0.582 |
| Multiple intracranial injuries | 630 (23.4) | 222 (36.9) | <0.001 | 196 (34.0) | 207 (35.9) | 0.491 |
| Cranieotomy/craniotomy, n (%) | 451 (16.8) | 216 (35.9) | <0.001 | 190 (32.9) | 193 (33.4) | 0.865 |

ICP: Intracranial pressure, GCS: Glasgow coma scale score, AIS: Abbreviated injury scale, SAH: Subarachnoid hemorrhage, SDH: Subdural hemorrhage, EDH: Epidural hemorrhage, SD: Standard deviation, LQ: Lower quartile, UQ: Upper quartile

### Table 2: Complications and outcomes between intracranial pressure monitored and unmonitored cohorts before and after propensity score matching

|                      | No ICP monitoring (n=2688) | ICP monitoring (n=601) | P     | No ICP monitoring (n=577) | ICP monitoring (n=577) | P     |
|----------------------|---------------------------|------------------------|-------|---------------------------|------------------------|-------|
| ARDS, n (%) | 61 (2.3) | 25 (4.2) | 0.015 | 13 (2.3) | 25 (4.3) | 0.073 |
| DVT, n (%) | 75 (2.8) | 48 (8.0) | <0.001 | 18 (3.1) | 45 (7.8) | 0.001 |
| Sepsis, n (%) | 35 (1.3) | 18 (3.0) | 0.006 | 8 (1.4) | 18 (3.1) | 0.076 |
| Kidney injury, n (%) | 26 (1.0) | 11 (1.8) | 0.085 | 5 (0.9) | 11 (1.9) | 0.210 |
| Unplanned return to ICU, n (%) | 47 (1.7) | 15 (2.5) | 0.244 | 14 (2.4) | 15 (2.6) | 1.000 |
| Unplanned return to OR, n (%) | 30 (1.1) | 13 (2.2) | 0.048 | 9 (1.6) | 11 (1.9) | 0.824 |
| ICU LOS, mean (SD) days | 7.6 (7.6) | 13.5 (9.4) | <0.001 | 8.9 (8.7) | 13.6 (12.2) | <0.001 |
| ICU LOS, median (LQ, UQ) days | 5 (3,10) | 12 (6,12) | 0.004 | 6 (3,12) | 12 (6,18) | 0.004 |
| Hospital LOS, mean (SD) days | 12.5 (13.9) | 19.7 (15.7) | <0.001 | 14.6 (16.1) | 19.6 (21.8) | <0.001 |
| Hospital LOS, median (LQ, UQ) days | 8 (4,16) | 16 (9,27) | 10 (5,19) | 16 (9,26) | 128 (22.2) | 158 (27.4) | 0.038 |

ICP: Intracranial pressure, ARDS: Acute respiratory distress syndrome, DVT: Deep vein thrombosis, ICU: Intensive Care Unit, LOS: Length of stay, SD: Standard deviation, LQ: Lower quartile, UQ: Upper quartile


**Discussion**

The effects of raised ICP on clinical outcome following severe TBI have been known for decades.[5] In theory, monitoring of the ICP allows physicians to treat any increases in ICP promptly in order to maintain adequate cerebral perfusion pressure. Early treatment of rising ICP is believed to lead to reduced risk of secondary brain injury and subsequent improvement in overall survival and neurological functional outcome. This has led to support for ICP monitoring in different guidelines, most notably the BTF guidelines, which are used to establish the standard of care for the management of TBI. The latest version of BTF guidelines recommends ICP monitoring with a pressure aim of below 22 mmHg (20 mmHg in the former version from 2007) in all salvageable patients with a severe TBI (GCS ≤8 after resuscitation and an abnormal brain CT). Further, patients with GCS ≤8 and no CT-verified intracranial lesion with two out of the following three findings present – age ≥40 years, unilateral/bilateral posturing, or the presence of hypotension – should be considered as candidates for ICP monitoring.[1,14]

Lately, several observational studies have shown varying degrees of compliance with the use of ICP monitoring in the context of neurocritical care for patients who meet BTF criteria for such intervention.[6,11,15] Bulger et al. found an average rate of 33% with a range of 0%–100% for ICP monitoring at 34 academic trauma centers in the United States.[13] A National Trauma Databank analysis done by Shafi et al. noted ICP monitoring in 43% of patients with a severe TBI and meeting BTF monitoring requirements.[4] The equivalent number was 47% in a prospective observational study by Talving et al., where patients who were moribund or assessed to have a grim prognosis were excluded from the study. Interestingly, the main given reason for not receiving an ICP-monitoring device was at the discretion of the neurosurgical attending.[10] One possible reason for this could be due to a low confidence in the idea that routine monitoring truly leads to improvements in outcome following severe TBI by practicing neurosurgeons.[16] In the current study, which only includes patients with an isolated severe TBI who survived beyond 48 h after admission, the overall prevalence of ICP monitoring was 18.3%.

One reason for the noncompliance with clinical guidelines could be the inadequate evidence and conflicting results with regard to overall survival following ICP monitoring.[1,6–10] The existing doubt in efficacy has even been acknowledged in recent editions of guidelines for severe TBI management.[1] The largest randomized control trial did not reveal any survival benefit in patients subjected to ICP monitoring, and the authors concluded that ICP monitor-guided therapy was not superior to care based on the imaging and clinical examination only.[9] That study has been criticized for being conducted in countries where prehospital services and hospital conditions are not comparable to the conditions in the US and many European countries. In a prospective observational study, including 14 trauma centers from the Los Angeles regional trauma system, no correlation between BTF guidelines compliance rates with ICP monitoring and mortality could be detected.[17] Nonetheless, there are studies that have shown improvements in survival when ICP monitoring is adopted in patients with severe TBI. Talving et al. demonstrated a 69% mortality reduction when patients were subjected to ICP monitoring.[7] Alali et al. carried out an analysis of the TQIP database for the years of 2009–2011 and found that there was a survival benefit for the use of ICP monitoring in 1874 patients (17.6% of the total study population).[10] In contrast, Aiolfi et al. detected a trend toward increased mortality (OR: 1.12; 95% CI: 0.983–1.275, P = 0.088) when analyzing 1519 ICP-monitored patients (11.5% of the study population) recruited from the TQIP database.[18] Both of these studies included the same type of patient population with an intracranial AIS ≥3 and AIS of <2 for all other body regions. A 7-year period analysis of the National Trauma Databank done by Shafi et al. revealed a 45% risk reduction in survival (adjusted OR: 0.55, 95% CI: 0.39–0.76, P < 0.001).[10] The current study showed a 60% increased risk for mortality (OR: 1.6, 95% CI: 1.1–2.5, P = 0.038) in a matched population of isolated severe TBI patients.

In addition, there was an association between ICP monitoring and systemic complications in the current study. There was a significant increase in the incidence of DVT in patients with ICP monitoring (OR: 7.8%, 95% CI: 5.7–10.3 vs. OR: 3.1%, 95% CI: 1.9–4.9, P = 0.001) despite the fact that a larger proportion of this subgroup was treated with venous thromboembolism (VTE) prophylaxis in comparison to matched controls (54.1% vs. 42.5%, P < 0.001). The timing for VTE prophylaxis initiation, however, occurred later in the ICP-monitored cohort (at 140 [SD 7.1] min vs. 112 [SD 9.2] min, P = 0.043). Furthermore, a trend toward increased incidence of ARDS and sepsis could be noticed in the ICP-monitored group. Similarly, Aiolfi et al. also reported significantly higher overall complication rates including, but not limited to, DVT, ARDS, and sepsis in patients with a severe TBI who had been ICP monitored.[18] One explanation for these findings could be the longer ICU LOS with more aggressive intervention and delay in early mobilization for patients subjected to ICP monitoring. In a retrospective analysis from the Netherlands, Cremer et al. concluded that patients managed with ICP monitoring had prolonged mechanical ventilation and increased levels of therapy intensity, without evidence of improved outcome.[11] Haddad et al. also found a significant increase in mechanical ventilation duration, need for tracheostomy, and ICU LOS for ICP-monitored TBI patients.[19] Such aspects should be entered into cost–benefit analysis for ICP monitoring. In contrast to previous studies, the current study design limited inclusion to patients with an isolated severe TBI. In preceding studies utilizing the TQIP databank, and even in the prospective observational study carried out by Talving et al., the authors did not account for extracranial injuries,[7,8] which could have an impact on the overall outcome.[2,3,20]
Our definition of isolated TBI generates a more homogenous study population with fewer confounders that could affect the main outcome.

Furthermore, by propensity score matching for variables recommended for ICP monitoring and known factors influencing outcome after severe TBI, the homogeneity of the study population is strengthened even further. Despite these factors, our study does carry limitations. The retrospective use of a database does not allow for matching of all potentially confounding variables. We cannot report the reason for the decision to omit ICP monitoring. Further, our study design prevents us from determining the specific cause of increased mortality in the ICP-monitored cohort, which is also lacking in the previous studies on the subject. No data on the ICP levels and the timing of intervention based on those values were available for comparison between the groups. The specific cause of death is of paramount importance for elucidating the relationship of ICP monitoring and mortality and should be investigated in prospective studies. Finally, due to database limitations, we are unable to analyze neurological functional outcome that should also be considered as an equally important outcome measure after TBI.

CONCLUSION

Less than a fifth of the patients with an isolated severe TBI were subjected to ICP monitoring. In a propensity score-matched cohort of 1154 patients with an isolated severe TBI, the use of ICP monitoring was associated with a significant risk increase in mortality as well as longer ICU and total hospital LOS. Consequently, future studies need to establish in which type of brain injury patients benefit from ICP monitoring.

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Conflicts of interest

There are no conflicts of interest.

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