In the United States, 1.4 million traumatic brain injuries (TBI) occur every year resulting in 235,000 hospitalizations and 50,000 deaths. There are currently 5.3 million Americans living with TBI-related disability. Fortunately, intensive care unit (ICU) management of TBIs has improved. Implementation of national guidelines has resulted in increased survival, decreased costs and length of stay, and improved favorable outcomes following TBI.

Increased intracranial pressure (ICP) above 20 mmHg is a strong predictor of poor outcome following TBI. As such, ICP monitors have become integral in the ICU management of these patients.1,2,3

ABSTRACT: Purpose: To determine our institutional adherence to the Brain Trauma Foundation guidelines with respect to intracranial pressure (ICP) monitoring, and examine the relationship between external ventricular drain (EVD) use and mortality. Materials & Methods: Retrospective cohort study of 171 patients with severe traumatic brain injury (TBI). Propensity score adjusted logistic regression was used to model the association between EVD use and mortality. Results: EVDs were inserted in 98 of 171 patients. Of the 73 patients without an EVD, 63 (86%) would have qualified for ICP monitoring under the current guidelines. EVDs were in situ for a median of 8 days (SD 6). In adjusted analyses, EVD use was associated with hospital mortality (OR 2.8, 95% CI: 1.1 – 7.1, p=0.04) and 28-day mortality (OR 2.1, 95% CI: 0.80 – 5.6, p=0.13). We observed significant modification of the association between EVD and 28-day mortality by GCS within 12 hours (p-interaction = 0.04), indicating strong association only among those patients with GCS score of at least 6 (OR 5.0, 95% CI: 1.5 – 16.7, p<0.01).

Conclusions: The association of EVD with 28-day mortality was only apparent among patients with GCS score of ≥ 6. Further research is warranted to further refine which patients may benefit from ICP monitoring.

RÉSUMÉ: Drain ventriculaire externe et mortalité chez les patients atteints de lésion cérébrale traumatique sévère. Objectif : Cette étude visait à déterminer la fidélité de notre institution aux lignes directrices de la Brain Trauma Foundation concernant la surveillance de la pression intracrânienne (PIC) et à examiner la relation entre l’utilisation d’un drain ventriculaire externe (DVE) et la mortalité. Matériaux et méthodes : Il s’agit d’une étude rétrospective portant sur une cohorte de 171 patients atteints de lésion cérébrale traumatique (LCT). Nous avons utilisé une analyse de régression logistique ajustée pour l’indice de tendance pour modéliser l’association entre l’utilisation d’un DVE et la mortalité. Résultats : Un DVE a été mis en place chez 98 des 171 patients. Parmi les 73 patients qui n’ont pas reçu de DVE, 63 patients (86%) auraient dû en recevoir un selon les lignes directrices actuelles. La médiane du temps pendant lequel le DVE a été laissé en place était de 8 jours (écart type de 6 jours). Les analyses ajustées ont montré que l’utilisation d’un DVE était associée à la mortalité hospitalière (RC 2.8; IC à 95% de 1.1 à 7.1; p = 0.04) et à la mortalité au cours des 28 premiers jours (RC 2.1; IC à 95% de 0.80 à 5.6; p = 0.13). Nous avons observé que l’association entre le DVE et la mortalité au cours des 28 premiers jours était modifiée significativement par le score à l’échelle de coma de Glasgow (SCG) dans les 12 premières heures (p-interaction = 0.04), ce qui indique une association importante seulement chez les patients dont le SCG était d’au moins 6 (RC 5.0; IC à 95% de 1.5 à 16.7; p < 0.01). Conclusions : L’association entre le DVE et la mortalité au cours des 28 premiers jours n’était évidente que chez les patients dont le SCG était de 6 ou plus. Il faudra effectuer d’autres recherches pour mieux définir quels patients sont susceptibles de bénéficier de la surveillance de la PIC.


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patients and are currently a level II recommendation (moderate
degree of clinical certainty) from the Brain Trauma Foundation
(BTF).9 Despite these recommendations, there remains
significant variability in practice of ICP monitoring. A survey of
Canadian Neurosurgeons showed that although the majority use
ICP monitoring in their patients, only 20.4% have a high level of
confidence that routine monitoring improves outcomes in severe
TBI. Nearly 80% felt that a prospective trial evaluating ICP
monitoring is warranted.10 Furthermore, a recent study
demonstrated that although ICP monitoring was underutilized as
per the BTF guidelines, it was associated with worsening of
survival compared to the group who did not receive ICP
monitoring.11 The literature is further complicated by various
types of ICP monitors used clinically. With the unreliaibility of
subarachnoid and extradural locations, intra-parenchymal
monitors and external ventricular drains (EVDs) are currently
the most widely used. EVDs have the added benefit of draining
cerebrospinal fluid, thus functioning as both monitor and therapy
for elevated ICP.

Thus, the goals of this study are twofold: (1) to examine the
adherence to BTF guidelines within our institution, a Canadian
tertiary academic ICU and (2) examine the relationship between
EVD use on 28-day and hospital mortality.

METHODS

Patient Inclusion & Data Collection

A retrospective cohort was constructed using the ICU
database of all patients admitted to the ICU at Vancouver
General Hospital with a severe TBI (Glasgow Coma Scale
(GCS) <=8) between May 2000 and March 2006. Vancouver
General Hospital is a 550 bed, tertiary care hospital affiliated
with the University of British Columbia. The ICU is a closed, 27-
bed, mixed medical-surgical unit, which operates with a 1:1
nurse to patient ratio, with resident and fellow staff in
attendance. We excluded patients who were obeying commands
within 12 hours, indicating a non-severe TBI. We further
excluded those who died within 12 hours of ICU admission, as
these patients were likely to succumb irrespective of EVD status.
None of these patients died from complications related to EVD
insertion. Patients were also excluded if they had a concomitant
high cervical spine injury or obvious non-traumatic causes of
their decreased level of consciousness (e.g. aneurysmal
subarachnoid hemorrhage) identified during the chart review.
All charts were reviewed and data collected using standardized
forms. Data acquired included information on the type of injury,
ICU management and monitoring information. Type and severity
of injury was characterized by: best GCS in 12 hours,
mechanism and type of TBI (diffuse axonal injury, parenchymal
contusions, extra-axial collections, basal skull or calvarial
fractures), surgical procedures performed and features
suggestive increased ICP on CT scan on from radiology reports
(mixed density lesion > 25mm, midline shift > 5mm, cisternal
compression) and baseline vital signs. Traumatic brain injury
management included use of bolus mannitol in ER (dose 1g/kg),
cooling (target temperature and duration of therapy) and use of
neuromuscular blockers. Monitoring data acquired included use
of EVD, ICP measurements (if EVD present), use and values of
jugular venous oximetry, and daily GCS. Demographic and
outcome information, including 28-day and hospital mortality,
were obtained from the ICU database. In addition, the ICU
database contained the Acute Physiology and Chronic Health
Evaluation (APACHE) II score, baseline admission laboratory
values and vital signs for the first 24 hours.

Traumatic Brain Injury Management

Care of patients suffering TBI at our institution has been
protocolized since 1995. All patients are maintained with: head
of bed elevated above 30 degrees with their neck in a neutral
position, mean arterial pressure >=70 mmHg (ensure adequate
intravascular volume replacement with normal saline, and using
norepinephrine infusion if required) and PaO2 >= 70 mmHg. If
ICP increases > 20 mmHg for greater than five minutes without
stimulation, the EVD is opened to 26 cm H2O and cerebrospinal
fluid is drained. Opened EVDs are closed every hour to measure
ICP. Cerebral oxygen extraction ratio is maintained < 40% by
ensuring adequate cerebral perfusion pressure, sedation and
paralysis (if required), and careful titration of arterial CO2
tension to modify cerebral blood flow. In addition, hyperthermia
is avoided by using acetaminophen 650 mg every four hours and
cooling blankets if required to keep the core temperature < 38
degrees. More aggressive cooling measures may be instituted on
an individual basis to maintain ICP < 20 mmHg if the above
maneuvers are insufficient.

Statistical Analysis

All analyses were performed with Stata 10.0 (StataCorp.
2007. Stata Statistical Software: Release 10. College Station,
TX: StataCorp LP). Univariate analyses utilizing Fisher’s exact
testing for categorical data and independent t-tests for
continuous data were used where appropriate. Wilcoxon rank-
sum tests were used for ordinal data, and non-normally
distributed continuous data. All tests were two-sided and a p-
value < 0.05 was considered statistically significant.

Propensity Score & Logistic Regression Model

We used a multivariable logistic regression model to estimate
the propensity of having an EVD inserted based on a large
number of relevant covariates. Linearity in the log odds of
continuous covariates was assessed visually, and by using
likelihood ratio testing when constructing the propensity score.
Covariates in the propensity score were selected based on their
predictive ability to estimate insertion of an EVD (p < 0.2) and
included: age, APACHE II score, increased ICP on computerized
tomography scanning, administration of mannitol in the
emergency room, year of admission, subdural hematoma, diffuse
axonal injury, craniootomy performed, systolic blood pressure <
90 mmHg and arterial oxygen tension < 70 mmHg. Including
these variables in the propensity score eliminates associations of
all of the included variables with EVD insertion, and thus
confounding by these covariates. The final c-statistic of the
propensity score was 0.79.

We evaluated the association between EVD and 28-day and
in-hospital mortality by using logistic regression models. These
models included presence of EVD, GCS and the propensity
score. We also assessed for effect measure modification of EVD
on mortality by level of GCS by introducing an interaction term
into the model. We used the Likelihood ratio test to assess the significance of the interaction in the final model.

The protocol was approved by Clinical Research Ethics Board at the University of British Columbia and Vancouver General Hospital.

**RESULTS**

Reviewed and included in the analysis were 273 charts and 171 patients. (Figure 1). The baseline characteristics are presented in Table 1. External ventricular drains were inserted in 98 patients. Patients in whom EVDs were inserted were younger, had lower best GCS within 12 hours, receive mannitol more frequently, were more likely to have a subdural hematoma or features suggestive of increased ICP on initial CT scan of the head, and undergo a craniotomy. Based on the current BTF guidelines for use of ICP monitors (GCS <=8 with an abnormality on CT scan), 63 of 73 patients in the non-EVD group would have qualified for ICP monitoring.

Outcomes by EVD status are presented in Table 2. Hypothermia and jugular mixed venous oximetry were used more frequently in patients with EVDs. Patients with EVDs spent more time being mechanically ventilated and had a longer stay in the ICU. Patients with EVDs tended to have higher 28-day mortality (23% vs. 12%, p=0.07) and hospital mortality (29% vs. 12%, p < 0.01). The EVDs remained in situ for a median of eight days (SD six days).

In adjusted analyses, EVD use was associated with hospital mortality (OR 2.76, 95% CI: 1.07, 7.08, p=0.04) and 28-day mortality (OR 2.12, 95% CI: 0.80, 5.62, p=0.13), although the latter did not reach significance. Subgroup analysis demonstrated significant effect measure modification of EVD on mortality by level of GCS (Figure 2) in a propensity score-adjusted model (p interaction =0.04). In other words, the risk of EVD on mortality differed by levels of GCS in the first 12 hours. In patients without an EVD, the probability of 28-day mortality decreased with increasing GCS. However, in patients with an EVD, the probability of 28-day mortality did not appear to change much with increasing GCS. As part of an exploratory analysis to quantify the differential effect of EVD on mortality, GCS was dichotomized to less than 6 versus 6 or greater based on the intersection of the probability distribution curves in Figure 2. The adjusted results are presented in Table 3. Test of interaction was repeated using the dichotomized GCS score and remained significant (p=0.01 for 28-day mortality and p=0.03 for hospital mortality). When GCS was less than 6, use of EVDs were not

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**Table 1: Baseline patient characteristics by EVD status**

<table>
<thead>
<tr>
<th></th>
<th>EVD Inserted (n=98)</th>
<th>No EVD (n=73)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y (SD)</td>
<td>35 (15.4)</td>
<td>42 (18.0)**</td>
<td></td>
</tr>
<tr>
<td>Female gender, n(%)</td>
<td>21 (21.4)</td>
<td>18 (24.7)</td>
<td></td>
</tr>
<tr>
<td>Mean APACHE II (SD)</td>
<td>23.5 (4.5)</td>
<td>23.4 (5.0)</td>
<td></td>
</tr>
<tr>
<td>SBP &lt;90 mmHg, n(%)</td>
<td>20 (20.4)</td>
<td>12 (16.4)</td>
<td></td>
</tr>
<tr>
<td>PaO2c &lt;70 mmHg, n(%)</td>
<td>10 (10.2)</td>
<td>5 (6.8)</td>
<td></td>
</tr>
<tr>
<td>Best GCS½ in 12 hours (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GCS &lt; 6, n(%)</td>
<td>42 (42.9)</td>
<td>10 (13.7)**</td>
<td></td>
</tr>
<tr>
<td>GCS 6-8, n(%)</td>
<td>51 (52.0)</td>
<td>53 (72.6)**</td>
<td></td>
</tr>
<tr>
<td>GCS 9-12, n(%)</td>
<td>5 (5.1)</td>
<td>10 (13.7)**</td>
<td></td>
</tr>
<tr>
<td>Mannitol, n(%)</td>
<td>61 (62.2)</td>
<td>24 (32.9)**</td>
<td></td>
</tr>
<tr>
<td>CT Head, n(%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traumatic SAHi</td>
<td>49 (50.0)</td>
<td>42 (57.5)</td>
<td></td>
</tr>
<tr>
<td>DAIi</td>
<td>33 (33.7)</td>
<td>19 (26.0)</td>
<td></td>
</tr>
<tr>
<td>Subdural hematoma</td>
<td>46 (46.9)</td>
<td>20 (27.4)**</td>
<td></td>
</tr>
<tr>
<td>Features of Increased ICPh</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal Skull Fracture</td>
<td>23 (23.5)</td>
<td>19 (26.0)</td>
<td></td>
</tr>
<tr>
<td>Craniotomy performed, n(%)</td>
<td>44 (44.9)</td>
<td>21 (28.8)*</td>
<td></td>
</tr>
</tbody>
</table>

*standard deviation; bAcute Physiology and Chronic Health Evaluation; c systolic blood pressure in mmHg; d arterial partial pressure of oxygen in mmHg; eGlasgow Coma Scale; fsubarachnoid hemorrhage; gdiffuse axonal injury; hintracranial pressure; * p-value <0.05; ** p-value <0.01

**Table 2: ICU management and outcomes by EVD status**

<table>
<thead>
<tr>
<th></th>
<th>EVD Inserted (n=98)</th>
<th>No EVD (n=73)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic hypothermia &lt; 35°C, n(%)</td>
<td>32 (32.7)</td>
<td>0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Therapeutic hypothermia &lt; 38°C, n(%)</td>
<td>52 (53.1)</td>
<td>6 (8.2)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Jugular bulb inserted, n(%)</td>
<td>78 (79.6)</td>
<td>2 (2.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Median days of EVDii (SD)</td>
<td>8 (8.2)</td>
<td>0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Median days of MVii (SD)</td>
<td>12.2 (11)</td>
<td>5.2 (7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Median ICU days (SD)</td>
<td>14 (11)</td>
<td>6 (8)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>28-day Mortality, n(%)</td>
<td>22 (22.4)</td>
<td>9 (12.3)</td>
<td>0.07</td>
</tr>
<tr>
<td>Hospital Mortality, n(%)</td>
<td>28 (28.6)</td>
<td>9 (12.3)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

*external ventricular drain; bstandard deviation; cmechanical ventilation
associated with 28-day mortality (OR 0.47, 95% CI: 0.11 – 2.1, p=0.32) or hospital mortality (OR 0.76, 95% CI: 0.18 – 3.2, p=0.71). However, when GCS was 6 or greater, EVDs were associated with an increased risk of 28-day mortality (OR 5.0, 95% CI: 1.5 – 16.7, p<0.01) and hospital mortality (OR 5.6, 95% CI: 1.7 – 18.4, p<0.01).

**DISCUSSION**

In our study, EVD use was associated with a longer ICU length of stay and days of mechanical ventilation in patients with severe traumatic brain injuries admitted to the ICU. Propensity score-adjusted, multivariable regression modeling demonstrated that EVD use was associated with increased risk of hospital mortality (p=0.04) and 28-day mortality (p=0.13). However, this association was entirely driven by a substantially increased risk among patients with a GCS score of at least 6.

A recent retrospective study showed decreased survival associated with ICP monitoring; however, only 46% of the ICP monitors in their cohort were ventriculostomies. As such, one of the main benefits of EVDs, drainage of CSF to treat intracranial hypertension, was not present in the majority of their cohort. Furthermore, the authors did not examine for effect modification of ICP monitoring by admission GCS. It’s not surprising that the association of EVDs on mortality may depend on GCS. As patients with higher GCSs will tend to have less severe TBIs, the potential benefit to ICP monitoring may decrease. As expected, patients in our study with EVDs had more interventions aimed at reducing ICP, including sedation and neuromuscular blockade, which themselves increase morbidity in critically ill patients. Our results are in keeping with a recent observational study by Cremer and colleagues which demonstrated that compared to patients without ICP monitoring, those with ICP / CPP targeted therapy had longer duration of mechanical ventilation, and increased intensity of therapy as defined by increased use of sedatives, mannitol, vasopressors and barbiturates. Thus, patients with less severe brain injuries would expect to benefit less from ICP monitoring, yet still be subjected to the therapies used to reduce ICP.

Another consideration is the duration of ICP monitoring. As patients improve and their ICPs normalize, the potential benefit of an EVD would diminish. The median length of EVD use in our cohort was eight days, with 44% of EVDs being in situ for ten or more days. A recent study of patients with severe TBIs by Stocchetti demonstrated a peak ICP in 80% of cases by Day 5, and 99% by Day 10. Thus, very few patients would benefit from ICP monitoring for greater than ten days. After Day 6, the mean ICPs in our cohort were less than 16 mmHg, regardless if the EVD was removed that day or not. As such, the use of EVDs in less severely ill patients, or for a protracted period of time, may suffer the same limitations as the pulmonary artery catheter, which themselves have failed to improve outcomes in all but the most severely ill patients.

**Figure 2:** Probability of 28-day mortality versus admission GCS by EVD status. Solid line represents patients with an EVD while the dashed line represents patients without an EVD. Subgroup test of interaction p-value is 0.04 indicating that there that the probability of mortality between those with and EVD and those without, differs by their admission GCS.

**Table 3:** Propensity score-adjusted multivariable model of EVD status on mortality by level of GCS

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ORa</th>
<th>seb</th>
<th>95% CIc</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>28-day Mortality†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>2.1</td>
<td>1.1</td>
<td>0.80, 5.6</td>
<td>0.13</td>
</tr>
<tr>
<td>GCS &lt; 6</td>
<td>0.47</td>
<td>0.36</td>
<td>0.11, 2.1</td>
<td>0.32</td>
</tr>
<tr>
<td>GCS &gt;= 6</td>
<td>5.0</td>
<td>3.1</td>
<td>1.5, 16.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hospital Mortality‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>2.8</td>
<td>1.3</td>
<td>1.1, 7.1</td>
<td>0.04</td>
</tr>
<tr>
<td>GCS &lt; 6</td>
<td>0.76</td>
<td>0.56</td>
<td>0.18, 3.2</td>
<td>0.71</td>
</tr>
<tr>
<td>GCS &gt;= 6</td>
<td>5.6</td>
<td>3.4</td>
<td>1.7, 18.4</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

*aOR= odds ratio adjusted for age, APACHE, increased ICP on CT, mannitol, year of admission, craniotomy, subdural hematoma, diffuse axonal injury, systolic blood pressure < 90 mmHg and arterial oxygen tension < 70 mmHg; bstandard error; c95% confidence intervals; †p= 0.01, ‡p=0.03 for interaction
Much like the pulmonary artery catheter, use of EVDs is subject to strong confounding by indication. In spite of well-recognized guidelines, physicians will utilize ICP monitoring based on clinical judgment. As such, determining an unbiased estimate of the association of EVD with mortality is difficult, even if information on important confounders is available. We have made efforts to reduce confounding by restricting our cohort to have more comparable EVD and non-EVD groups. However, confounding by indication may still be present in our data, as patients receiving EVDs were younger, with a lower GCS, and more likely to have features of increased ICP on admission CT scan. This type of confounding was also observed in a recent cohort study from Austria, where ICP monitors were more likely to be inserted in younger patients, females and those with isolated TBIs.\(^{19}\) In their study, patients with higher severity of illness, as measured by the Abbreviated Injury Scale of the head, were more likely to receive ICP monitoring. Increased intracranial pressure monitors were not associated with mortality, although they did not present outcomes by level of GCS, nor examine for interaction effects of ICP monitors by level of the Abbreviated Injury Scale or GCS. As with all observational data, unmeasured or residual confounding remains an alternative explanation for our findings. Additionally, in only considering mortality, we are not able to determine potential functional outcomes associated with EVD use in our population. Finally, generalizability is limited to ICUs with similar patient profiles and practice patterns as our own.

Strengths of our study include detailed clinical information from the chart using standardized data collection forms, uniform ICP monitor type, and use of propensity score-adjusted logistic regression modeling for control of confounding. Using this approach, we were able to control for a wide range of potential confounders. Propensity score adjusted models are less biased, more robust, and have greater power than traditional logistic regression when there are few outcome events.\(^{20,21}\)

Within the strict guidelines of the BTF, EVDs were underutilized in our cohort. However, this may simply reflect the baseline differences between groups as mentioned previously. As such, it may be that clinicians are appropriately triaging the use of EVDs to those patients who are more severely ill. Although EVDs were associated with an increased 28-day and hospital mortality, this was only apparent in the subgroup of patients who had a better neurologic status in the first 12 hours (GCS \(>6\)). Thus, further study to identify patients who may benefit from EVD use is warranted. In the meantime, given the association between intracranial hypertension and poor outcomes,\(^ {6,7,22}\) coupled with evidence demonstrating a high risk of intracranial hypertension with GCS \(\leq 8\) and an abnormal CT head,\(^3\) it is difficult to recommend more restricted use of EVDs. However, clinicians should consider removing EVDs soon after the ICP begins to abate, and the patient can be followed clinically.

In conclusion, we have demonstrated that EVD use was associated with increased mortality; however, this was driven entirely by those patients with a best GCS \(\geq 6\). Further research is warranted to further refine which patients may benefit from ICP monitoring.

**DISCLOSURES**

Dr. Kurth has received within the last two years investigator-initiated research funding from the National Institutes of Health and Merck. Further, he is a consultant to i3 Drug Safety and World Health Information Science Consultants, LLC; he received honoraria from Genzyme, Merck, and Pfizer for educational lectures.

**REFERENCES**