1. Introduction

Traumatic cerebrospinal fluid (CSF) leakage occurs in 2% of patients with traumatic brain injury (TBI), and 12–20% of those with basilar skull fractures.\(^1\)–\(^3\) Fractures relating to the frontal or ethmoidal sinuses and longitudinal temporal areas are most commonly associated with CSF leakage.\(^1\) A high incidence of post-traumatic CSF leakage occurs after patients experience blunt head trauma.\(^4\) The interaction of forces with regard to the different aspects of impact causes injury in different components of the brain. Brain surface contact with forces of acceleration or deceleration causes primary brain damage. Skull fracture, CSF leakage and intracranial hemorrhage (ICH) are categorized as the types of brain damage that are due to contact forces.\(^5\) The cause–effect relations are still unknown.

Traumatic ICH is a major cause of preventable death after head injury.\(^6\) It is the result of direct parenchymal damage to brain tissue during the contact of the external impact. Early detection of hematomas can improve outcomes. Therefore, neurosurgeons need to predict which patients are likely to develop hematoma and to detect this complication before the brain becomes irreversibly damaged.\(^6\)–\(^9\)

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**Background/Purpose:** The aim of the present study was to review the clinical manifestations, risk factors and outcome in traumatic brain injury (TBI) patients with post-traumatic cerebrospinal fluid (CSF) leakage.

**Methods:** We reviewed the medical records of 1,323 patients who were identified with CSF leakage that occurred after head trauma.

**Results:** Patients complicated with CSF leakage manifested a more rigorous clinical course and poorer outcome compared to patients with other TBI features: in mild head injury, patients with brain injury complicated with CSF leakage alone had a 24.5% risk ratio for developing intracranial hemorrhage, and the presence of post-traumatic CSF leakage with or without skull fracture resulted in a higher percentage of fatality.

**Conclusion:** Post-traumatic CSF leakage amongst head injury patients has serious complications in nonfatal TBI cases, and indicates a risk of developing post-traumatic intracranial hemorrhage as the patients' final outcome.
Patients with post-traumatic ICH commonly have a history of skull fracture and impaired level of consciousness. Whether or not patients with CSF leakage are at greater risk of developing fatal and nonfatal complications of TBI remains unknown. Previous publications on post-traumatic CSF leakage often described the diagnoses and management of the disease. Many studies are limited because of their small sizes, which do not reflect the actual clinical data. Therefore, we started a project to investigate nonfatal confounding factors. We also wanted to clarify the interconnection among the variables of TBI severity, progression of the insult to the development of CSF leakage, post-traumatic ICH, and final neurological outcome.

2. Methods

2.1. Patients

We reviewed the medical and radiological study records of 1,323 patients who were identified to have CSF leakage after head trauma between 1993 and 2002. Data were collected from a population-based study of 79,772 TBI cases admitted to neurosurgical units at 56 regional hospitals in Taiwan. We reviewed information on patients’ demographics, mechanisms of injury, clinical presentations, sources of CSF leakage, results of computed tomography (CT), timing of surgery and outcome of the insult.

2.2. Degrees of severity

We used the Glasgow Coma Scale (GCS) to determine the degree of TBI severity, which was classified into three categories (mild, moderate, severe) as shown in Table 1.

To classify TBI outcome at the time of hospital discharge, the Glasgow Outcome Scale was used, where a score of 1 indicates death, a score of 2 indicates a persistent vegetative state, a score of 3 indicates severe disability, a score of 4 indicates moderate disability, and a score of 5 indicates good recovery.

The definitions and case ascertainment procedures used in this series were standardized in Taiwan. The definition of a skull fracture was stated as radiological findings of either linear fracture of the skull vault or various forms of basilar skull fractures. All the skull fractures and ICH were identified with brain X-ray and CT. We identified the presence of intracranial hematomas according to the radiologists’ and surgeons’ reports for case ascertainment.

2.3. Statistical analysis

The initial clinical characteristics and the frequency of development of post-traumatic ICH in different degrees of TBI severity were compared. Categorical variables were expressed as rates. Using SPSS version 11.5 (SPSS Inc., Chicago, IL, USA) for Windows, we used Pearson’s χ² test to obtain the p value. The differences were significant if p < 0.05. Logistic regression analysis was used to predict the post-traumatic evolution of ICH based on clinical variables thought to have probable prognostic value according to previous studies. We used odds ratios and their 95% confidence intervals to represent the relative risks of skull fracture, post-traumatic amnesia and CSF leakage in the development of ICH. The final neurological outcomes in the mildly head-injured patients who featured different clinical characteristics were included in this study.

3. Results

3.1. Demographic data

We analyzed the age and sex distribution of the 1,323 TBI patients with CSF leakage during the period 1993–2002. Of the 1,323 patients, 897 (67.8%) were males and 426 (32.2%) were females. The mean age was 36.99 years. Women were younger than men (mean age of men, 37.60 years; mean age of women, 35.47 years). There were 322 (24.3%) patients between the ages of 20 and 29 years. CSF otorrhea was the most common presentation of post-traumatic CSF leakage: 843 patients had CSF otorrhea while 480 had CSF rhinorrhea.

3.2. Various mechanisms of TBI causing CSF leakage

This study showed that motor vehicle accidents were the most frequent mechanism of TBI to cause CSF leakage (77%). When patients were grouped according to sex, motor vehicle accidents remained the most frequent cause of post-traumatic CSF leakage in both groups. Falls led assaults as the second most frequent cause of post-traumatic CSF leakage in both sexes (Figure 1). Motorcycles were the major type of transportation seen at the site of accident in both sexes (men, 75.2%; women, 73.6%).

<table>
<thead>
<tr>
<th>TBI severity</th>
<th>GCS score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Between 13 and 15</td>
</tr>
<tr>
<td>Moderate</td>
<td>Between 9 and 12, or if computed tomography reveals intracranial hemorrhage, or if craniotomy was necessary at a GCS between 13 and 15</td>
</tr>
<tr>
<td>Severe</td>
<td>≤8</td>
</tr>
</tbody>
</table>
3.3. Risk of developing ICH in head-injured patients complicated with CSF leakage

Tables 2–4 summarize the risk of developing intracranial hematomas in head-injured patients complicated with CSF leakage at different levels of severity of head injury. Statistics show that a higher percentage of patients who suffer from post-traumatic amnesia, skull fracture and CSF leakage experience an associated ICH after minor TBI (GCS score, 13–15) compared to patients who do not suffer these things. In this group, patients with CSF leakage alone had a risk of 24.5%, i.e., they were 2.55 times more likely than those without CSF leakage to develop post-traumatic ICH. We also noted that patients with a combination of skull fracture, post-traumatic amnesia and CSF leakage were

<table>
<thead>
<tr>
<th>PTA/SF/CSF leakage</th>
<th>Patients, n</th>
<th>Patients with post-traumatic ICH, n (%)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>– / – / –</td>
<td>56,340</td>
<td>7630 (13.5)</td>
<td>1</td>
</tr>
<tr>
<td>+ / + / +</td>
<td>7</td>
<td>5 (41.7)</td>
<td>27.48* (14.8–50.9)</td>
</tr>
<tr>
<td>+ / – / –</td>
<td>3932</td>
<td>1444 (36.7)</td>
<td>7.24* (6.9–7.59)</td>
</tr>
<tr>
<td>– / + / –</td>
<td>4863</td>
<td>2183 (44.9)</td>
<td>5.90* (5.59–6.22)</td>
</tr>
<tr>
<td>– / – / +</td>
<td>106</td>
<td>26 (24.5)</td>
<td>2.55* (1.8–3.63)</td>
</tr>
<tr>
<td>+ / + / –</td>
<td>766</td>
<td>532 (69.5)</td>
<td>26.36* (23.86–29.12)</td>
</tr>
<tr>
<td>+ / + / +</td>
<td>6</td>
<td>2 (33.3)</td>
<td>14.10* (7.03–28.3)</td>
</tr>
<tr>
<td>– / + / +</td>
<td>81</td>
<td>32 (39.5)</td>
<td>5.81* (4.098–8.25)</td>
</tr>
</tbody>
</table>

*p < 0.001 vs. its corresponding control, χ² test. OR = odds ratio; CI = confidence interval.

<table>
<thead>
<tr>
<th>SF/CSF leakage</th>
<th>Patients, n</th>
<th>Patients with post-traumatic ICH, n (%)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>– / –</td>
<td>5618</td>
<td>3094 (55.1)</td>
<td>1</td>
</tr>
<tr>
<td>+ / +</td>
<td>21</td>
<td>15 (71.4)</td>
<td>2.039* (0.790–5.264)</td>
</tr>
<tr>
<td>– / +</td>
<td>20</td>
<td>11 (55.0)</td>
<td>0.997 (0.413–2.410)</td>
</tr>
<tr>
<td>+ / –</td>
<td>1716</td>
<td>1292 (75.3)</td>
<td>2.486* (2.201–2.807)</td>
</tr>
</tbody>
</table>

*p < 0.001 vs. its corresponding control, χ² test. OR = odds ratio; CI = confidence interval.

<table>
<thead>
<tr>
<th>SF/CSF leakage</th>
<th>Patients, n</th>
<th>Patients with post-traumatic ICH, n (%)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>– / –</td>
<td>4560</td>
<td>3591 (78.8)</td>
<td>1</td>
</tr>
<tr>
<td>+ / +</td>
<td>81</td>
<td>73 (90.1)</td>
<td>2.462* (1.183–5.127)</td>
</tr>
<tr>
<td>– / +</td>
<td>43</td>
<td>32 (74.4)</td>
<td>0.785 (0.394–1.563)</td>
</tr>
<tr>
<td>+ / –</td>
<td>2119</td>
<td>1873 (88.4)</td>
<td>2.055* (1.767–2.389)</td>
</tr>
</tbody>
</table>

*p < 0.001 vs. its corresponding control, χ² test. OR = odds ratio; CI = confidence interval.
27.48 times more likely to develop post-traumatic ICH compared to patients without this combination. In moderately and severely head-injured patients, the presence of post-traumatic CSF leakage does not increase the risk of developing post-traumatic ICH. The results are statistically significant for each evaluation ($p < 0.05$)

Not all TBI cases complicated with CSF leakage and post-traumatic ICH were attributed to brain contusions. Contusive lesions were detected in only 282 (44.3%) patients with post-traumatic ICH. Generalized brain edema was found in 245 (38.5%) patients with ICH.

### 3.4. Relationship between CSF leakage, skull fracture and Glasgow Outcome Scale

Figure 2 shows the relationship between CSF leakage, skull fracture and Glasgow Outcome Scale scores. There was a higher percentage of Glasgow Outcome Scale score 1 (death) in mildly head-injured patients who had CSF leakage with or without skull fracture at the time of admission compared to other study groups within the study population.

### 3.5. Illustrative case

A 60-year-old male was seen in our emergency room with closed head injury. He was alert on admission. The initial brain CT showed marked frontal contusion and pneumocephalus 4 hours post-trauma. CSF rhinorrhea was noted 12 hours after the incident. Neurological worsening was seen on the second day, with CT showing newly developed ICH (Figure 3). The patient was eventually discharged in a stable condition with his post-traumatic CSF leakage resolved.

### 4. Discussion

In our previous study, we collected more than 50,000 cases of TBI patients in the 6 years from 1996 to 2002 to establish a regional databank of patients with post-traumatic CSF leakage, with its major source being victims of traffic-related accidents. Motorcycle traffic injuries, in particular, accounted for 65% of affected cases. Motorcycle accidents were, therefore, not only the most important cause of TBI in Taiwan, but also occurred with the highest incidence in young adults with post-traumatic CSF leakage.

The actual levels of risk were calculated by assuming that our series included all cases of post-traumatic hemorrhage, surgically significant or nonsurgically significant, that occurred in this region from year 1993 to 2002. Our data reflected the actual percentage risk of developing post-traumatic hemorrhage after complicated TBI. Patients with lesions seen on CT were largely managed conservatively, and only one sixth of them received surgical treatment due to expanding ICH. Head-injured patients with traumatic CSF leakage are difficult for clinicians to manage. The severity of head injury has little correlation with formation of CSF leakage. CSF leakage may occur in patients who suffer no loss of consciousness or acute neurological worsening. In this study, we examined various clinical presentations to come out with some guidelines to treat patients with post-traumatic CSF leakage. The association between CSF leakage and post-traumatic ICH is clinically significant. In our previous study that evaluated head-injured patients’ risk of developing surgically significant intracranial hematomas, we concluded that skull
fracture and impaired consciousness are two risk factors.10 The presence of both risk factors greatly increases the risk of post-traumatic intracranial hematoma.10,11 In this study, we added the feature of post-traumatic CSF leakage to establish various risks of developing post-traumatic ICH, especially in mildly head-injured patients (GCS score, 13–15). The presence of CSF leakage with or without radiological findings of skull fracture increased the risk of developing post-traumatic hemorrhage. We tentatively speculate that during the course of impact to the mildly-injured brain, the breakage of the continuity of the dura mater that results in CSF leakage means that primary damage to the nervous system has already taken place after the contact of the external force. Further brain damage caused by hematoma may occur following the initial impact. It is well documented that CSF leakage produces a decrease in intracranial pressure and an increase in cerebral perfusion pressure that is sufficient to enhance the blood leakage from a subclinical, not radiologically detected, small brain contusion up to larger contusions and secondary hemorrhages. The results of our study further stress the relationship between intracranial pressure and cerebral perfusion pressure in promoting such an effect.19

When the level of consciousness is markedly impaired (GCS score, <12), patients are likely to have primary damage to the brain parenchyma.20 In these moderately or severely head-injured patients, data evaluation shows that CSF leakage is not as influential as in mild cases in determining the risk of developing post-traumatic ICH.

The findings of this study show that the presence of post-traumatic CSF leakage with or without skull fracture increased the risk of death in mildly head-injured patients, and that patients with skull fracture and post-traumatic CSF leakage were at higher risk of death. Based on these findings, we suggest that death may be due to unresolved complications caused by CSF leakage.

Traditional criteria stress worsening consciousness as the classical clinical feature of hematoma, but the actual objective is to identify patients at risk before consciousness deteriorates. To determine which mildly head-injured patients need admission to hospital for observation, an immediate CT scan should be performed without waiting for signs of consciousness deterioration. Our study results provide an alternative basis for evolving policies to manage mildly head-injured patients. Head-injured patients with CSF leakage without skull fracture have an intermediate level of risk for intracranial hematoma and are oriented at the time of examination. Clearly, these patients deserve further clinical investigation.

Based on our results, we conclude that the presence of the trio of skull fracture, impaired consciousness and CSF leakage indicates poor clinical outcome. The presence of this trio increases the risk of developing post-traumatic hemorrhage, and some head-injured patients with CSF leakage and skull fracture will have unfavorable neurologic outcome, possibly due to severe damage to the brain parenchyma. Therefore, it is worthwhile to pay more attention to any sign of direct brain damage when a TBI patient shows signs of both CSF leakage and skull fracture, regardless of their level of consciousness.

Acknowledgments

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References