Epidemiology, treatment and outcome of patients after severe traumatic brain injury in European regions with different economic status

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Background: We hypothesized that the economic status of a region might influence quality of care and outcome of patients with severe brain trauma. Methods: Between January 2001 and December 2005, 13 centres enrolled patients with severe brain trauma. Data on accident, treatment and outcomes were collected prospectively. The regions were classified as ‘high income’ (Austria, five centres), ‘upper middle income’ (UMI) (Croatia, Slovakia, six centres) or ‘lower middle income’ (LMI) (Bosnia, Macedonia, two centres). Data on epidemiology, treatment and outcomes were compared according to this classification. Quality of care was assessed using a new scoring system. Results: A total of 1172 data sets were analysed. Patients from the wealthier regions were significantly older. Low-level falls and traffic accidents contributed to more than two-thirds of all cases. Violence-related trauma was significantly more frequent in ‘middle income’ regions. Treatment quality was significantly different; treatment according to guidelines for brain trauma management was provided most frequently for patients from high-income regions. Compared with expected mortality rates, mortality was 6.5% lower in the ‘high-income’ centres, 2.4% lower in the ‘UMI’ centres and 13% higher in the ‘LMI’ centres. Advanced age, poor neurological status, high trauma severity and poor quality of care were associated with significantly lower odds for survival. Conclusions: The association between the economic status and outcome of severe traumatic brain injuries was due to the quality of care. Successful implementation of guidelines for brain trauma management requires a well-funded health care system.

Keywords: gross domestic product, guidelines, traumatic brain injury—epidemiology, traumatic brain injury—treatment, traumatic brain injury—outcome

Introduction

Traumatic brain injuries (TBI) represent a serious public health problem in all countries of Europe. It has been estimated that in the European Union, TBI accounts for 1 million hospital admissions per year.1 Tagliaferri et al.2 reported that TBI accounted for the majority of trauma deaths in Europe. According to their analysis of 26 studies, the aggregated (i.e. fatal plus hospitalized) incidence rate is 235 cases/100,000 people/year, the average mortality is 15/100,000 people/year, the case fatality rate is 2.7% and the ratio of mild to moderate to severe TBI is 22:1.5:13; this equals about 10 cases of severe TBI/100,000 people/year. In a previous paper,1 we reported that this ratio was 14.5:2:1 in an Austrian hospital and we estimated that the incidence rate (hospital admissions) of cases with severe TBI was 16/100,000 people/year in Austria.

Over the last 10 years, the International Neurotrauma Research Organization (based in Vienna, Austria) has coordinated projects in various European countries. The project ‘Reducing mortality and long-term disability of TBI victims through research into treatment procedures used in Bosnia-Herzegovina, Macedonia and Croatia’ addressed issues of TBI guidelines implementation, evaluation of results and subsequent development of national policies in these countries. Another large project (‘Effects of the use of guidelines for the treatment of patients with severe TBI’) was carried out in Austria and the results have recently been published.3–8 Some smaller projects included centres from Slovakia. For all these projects, a similar database was used to collect the required data. The centres at which this data were collected are located in regions of varying economic status: Austria is a ‘high-income’ (HI) country, Slovakia and Croatia are ‘upper middle income’ (UMI) countries and Bosnia-Herzegovina (Bosnia) and the Former Yugoslav Republic of Macedonia (Macedonia) are ‘lower middle income’ (LMI) countries. Thus, these projects afforded us the unique opportunity of comparing data on epidemiology, treatment and outcomes in European regions of varying economic status.

The aim of this paper is to compare hospital-based epidemiology, treatment and outcomes of patients with severe TBI from centres located in European countries of varying economic status and to describe factors that may have contributed to these results. Our hypothesis was that the economic status would influence the quality of the health care system and that this would result in outcome differences.

Methods

The data for this study were collected in 13 centres located in Austria, Bosnia, Croatia, Macedonia and Slovakia. All centres were of tertiary care level; they included six University Departments of Neurosurgery (Graz, Osijek, Rijeka, Sarajevo, Skopje and Zagreb), five large City Hospitals (Banska Bystrica, Klagenfurt, Martin, Michalovce and Salzburg), one Centre for
Neurosurgery and Neurology (Linz) and one free-standing Trauma Centre (Vienna).

The data were collected between January 2001 and June 2005 but none of the centres provided data on patients for more than 3 years. This reflects the fact that the centres collected data for different projects. Patients were included if they had ‘severe TBI’ according to the criteria defined by the US National Traumatic Coma Database9 such as a Glasgow Coma Scale (GCS) score of 8 or less following resuscitation or a GCS score deteriorating to 8 or less within 48 h of injury. Only patients who survived at least until admission to the intensive care unit (ICU) were enrolled into this study.

Each patient was examined by a physician immediately after admission to the study centre and a computed tomography scan was done as soon as possible thereafter. The patients then underwent appropriate surgery and/or were admitted to the ICU. Surgical care was provided by neurosurgeons alone (seven centres) or by trauma surgeons (six centres), who had the option of consulting neurosurgeons for more difficult cases. Intensive care was provided by anaesthetists alone (nine centres) or in cooperation with neurosurgeons (four centres). The whole treatment process in each centre was supposed to be based on the guidelines for the management of patients with severe TBI published by the Brain Trauma Foundation10 and was introduced at the start of the projects in each centre.

Data collection was done using the International Traumatic Coma Project database.4,11 This database allowed for data collection over the Internet; it recorded basic demographic data of the patient, cause and location of trauma, pre-hospital status and treatment, mechanism and severity of trauma, results of computed tomography scans, results of lab testing and data on surgical procedures and outcomes. Information on status and treatment was recorded in detail for the first 10 days. In addition, data on duration of various treatments, on complications, and on outcome were collected on discharge from the ICU. Information on status and location was recorded at 3, 6 and 12 months after injury. In most centres, data were collected by a local researcher. In the Austrian centres, data were extracted from the prospectively collected records by a single researcher who visited the centres at regular intervals. Personal data protection was observed and the identifiers were kept separately from the data.

According to the per capita gross domestic product (GDP) of each country as reported by the WHO in 2007, the five Austrian centres were classified as ‘HI’ (GDP = 37213 USD), the six centres from Croatia and Slovakia were classified as ‘UMI’ (GDP 7724 and 8803 USD, respectively) and the two centres from Bosnia and Macedonia were classified as ‘LMI’ (GDP 2183 and 2637 USD, respectively). The relevant data on epidemiology, resources, treatment procedures and outcomes. The pooled data from these three groups of centres were then analysed for differences in epidemiology, resources, treatment procedures and outcomes.

The Trauma and Injury Severity Score method (TRISS)12 was used to estimate expected mortality rates. ‘Favourable outcome’ was defined as a Glasgow Outcome Score of 5 or 4; ‘unfavourable outcome’ was defined as a Glasgow Outcome score of 3 or less.

To assess quality of care, a scoring system was created. Treatment procedures (those recommended by the guidelines for the management of patients with severe TBI are marked as ‘ guideline’) and systems factors were scored as follows:

- **Pre-hospital treatment**
  - Airway management (guideline): not indicated = 0; endotracheal intubation = +5; other airway management = +3; no airway management = −5
  - Direct transfer to study centre (guideline): yes = +3; no = −3
  - Helicopter transfer: yes = +2; no = 0

- **Hospital treatment (first 48 h)**
  - Interval admission—CT scan: <60 min = +3; >60 min = −3
  - Intracranial pressure monitoring (guideline): used = +3; not used = −3
  - Ventilation: arterial pCO2 between 32 mmHg and 40 mmHg (guideline): yes = +3; no = −3
  - Body temperature below 38.5°C: yes = +3; no = −3
  - Steroids used (guideline): yes = −5; no = +5

- **System factors**
  - Number of nurses per ICU bed: <2 = +1; 2–3 = +2; >3 = +3
  - Percentage of ICU patients with methicillin-resistant *Staphylococcus aureus* infections: <2% = +3; 2–5% = +2; 5.1–10% = +1; >10% = 0

The scores for pre-hospital and hospital treatment were calculated for each patient and the system scores were calculated for each centre. The mean values for these three scores were then calculated for each of the regions.

Statistical analysis was performed with the open source statistical package R.13 Analysis of variance (for comparisons of means), Chi-square tests (3 × n tables for comparisons of proportions) and Fisher’s tests (for comparisons of proportions) were used as appropriate. A logistic regression was done to identify factors influencing outcomes; for these, ‘survival’ was coded as ‘1’ and ‘death’ as ‘0’. A *P*-value of <0.05 was considered statistically significant.

**Results**

A total of 1172 data sets was available for analysis; 406 (34.6%) from ‘HI’, 337 (28.8%) from ‘UMI’ and 439 (36.6%) from ‘LMI’ centres. Data quality was quite good. Key data like age or gender were not recorded in five cases only, data on long-term outcome were missing in 69 cases (5.9%), TRISS data were missing in 53 patients (4.5%). The proportion of missing data on status (e.g. blood pressure, GCS) or treatment (e.g. intracranial pressure monitoring, ventilation) was <5%.

An overview of epidemiology, trauma mechanisms and trauma severity is given in table 1. There was a significant difference in the male:female ratio (more female patients in the ‘HI’ centres) and the patients from the ‘HI’ and ‘UMI’ centres were significantly older. Occupation of the patients was significantly different between the three regions. The ‘HI’ centres enrolled fewer students and more retired people. Trauma mechanisms were also significantly different between the regions. Low-level falls and traffic accidents were the most frequently reported mechanisms of trauma, contributing to more than two-third of all cases in each of the groups. Violence (both blunt and penetrating) was a significantly more frequent cause of TBI in the ‘UMI’ and ‘LMI’ economies. The patients from the ‘LMI’ centres had a higher GCS and the lowest expected mortality.

Treatment data are given in table 2. With regard to pre-hospital treatment, endotracheal intubation was done most frequently in ‘HI’ cases. The infused volume was significantly larger in ‘LMI’ centres. Pre-hospital management was provided by emergency physicians rather than paramedics in most of the ‘HI’ and ‘UMI’ cases and in only half of the ‘LMI’ cases. The rate of patients transported by helicopter decreased significantly with decreasing wealth. With regard to hospital treatment, ‘HI’ centres received most of their patients directly from the scene of accident, whereas the other centres had a
significantly higher rate of secondary transfers. Immediate neurosurgical treatment was less frequently done in ‘LMI’ cases. Steroids were used almost exclusively by ‘LMI’ centres. Patients from ‘HI’ centres had more brain scans, more days of deep sedation, ventilation and intensive care and had a higher rate of intracranial pressure monitoring.

With regard to quality of care, the number of available nurses per intensive care bed decreased significantly \( (P < 0.0001) \) with decreasing wealth (3.4 vs. 1.8 vs. 0.9/bed, respectively). Also, the ‘LMI’ centres reported that they frequently had no funding to buy intracranial pressure monitoring catheters, although the necessary monitors were available. Rates of infections with methicillin-resistant \( S. \ aureus \) increased significantly \( (P < 0.0001) \) with decreasing wealth (0.6 vs. 9.0 vs. 27.0% of all intensive care patients, respectively). The three quality scores (table 2) were significantly different between the groups and decreased with decreasing wealth.

Outcomes are shown in table 3. Mortality rates at the ICU increased significantly with decreasing wealth. Compared with the expected mortality rates (table 1), mortality was 6.5% lower than expected in the ‘HI’ centres, 2.4% lower than...
**Table 3 Outcomes**

<table>
<thead>
<tr>
<th>Economy</th>
<th>HI</th>
<th>n</th>
<th>UMI</th>
<th>n</th>
<th>LMI</th>
<th>n</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU mortality (%)</td>
<td>31 (26–35)</td>
<td>124</td>
<td>38 (33–44)</td>
<td>129</td>
<td>46 (41–51)</td>
<td>197</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lung infection (%)</td>
<td>8 (6–11)</td>
<td>32</td>
<td>23 (18–27)</td>
<td>76</td>
<td>14 (11–17)</td>
<td>59</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sepsis (%)</td>
<td>4 (2–6)</td>
<td>14</td>
<td>17 (13–21)</td>
<td>56</td>
<td>8 (6–11)</td>
<td>33</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>GCS at ICU discharge</td>
<td>10.7 (10.2–11.2)</td>
<td>290</td>
<td>9.1 (8.5–9.7)</td>
<td>224</td>
<td>9.6 (9–10.2)</td>
<td>348</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>90-day mortality (%)</td>
<td>42 (37–47)</td>
<td>170</td>
<td>48 (43–54)</td>
<td>162</td>
<td>55 (50–59)</td>
<td>234</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Favourable outcome (%)</td>
<td>34 (29–39)</td>
<td>138</td>
<td>28 (23–33)</td>
<td>93</td>
<td>34 (30–39)</td>
<td>146</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are presented as mean values or percentages (95% confidence intervals in parenthesis)

HI = high income; UMI = upper middle income; LMI = lower middle income; NS = not significant

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**Table 4 Factors related to intensive care unit survival (coded as ‘1’)**

<table>
<thead>
<tr>
<th>Factors related to intensive care unit survival</th>
<th>Odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1: adjusted for age, GCS and ISS (R² = 0.128)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UMI center</td>
<td>0.70 (0.51–0.96)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LMI center</td>
<td>0.51 (0.38–0.68)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Model 2: adjusted for age, GCS and ISS (R² = 0.457)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UMI center</td>
<td>0.75 (0.51–1.10)</td>
<td>NS</td>
</tr>
<tr>
<td>LMI center</td>
<td>0.16 (0.11–0.22)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age</td>
<td>0.96 (0.96–0.97)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>First GCS</td>
<td>1.44 (1.34–1.54)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ISS</td>
<td>0.95 (0.93–0.96)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Model 3: adjusted for age, GCS, ISS and quality score (R² = 0.469)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UMI center</td>
<td>1.23 (0.66–2.24)</td>
<td>NS</td>
</tr>
<tr>
<td>LMI center</td>
<td>0.49 (0.23–1.08)</td>
<td>NS</td>
</tr>
<tr>
<td>Age</td>
<td>0.96 (0.95–0.97)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>First GCS</td>
<td>1.46 (1.35–1.57)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ISS</td>
<td>0.94 (0.93–0.96)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Quality score (Prehospital)</td>
<td>0.99 (0.95–1.03)</td>
<td>NS</td>
</tr>
<tr>
<td>Quality score (Hospital)</td>
<td>1.04 (1.01–1.06)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Quality score (System)</td>
<td>1.20 (1.03–1.41)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

HI = high income; UMI = upper middle income; LMI = lower middle income; ISS = Injury Severity Score; NS = not significant

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Discussion

To the best of our knowledge, this is the first study that has compared hospital-based epidemiology, treatment and outcomes of patients with severe TBI in European regions of varying economic status. Hukkelhoven et al.14 used data from the tirilazad trials to compare data from some European regions. They found differences in epidemiology, clinical status and computed tomography findings but outcomes (i.e. mortality and rates of favourable outcome), although significantly worse than those in North America, were not different within European regions. The main reason for this lack of outcome differences might be the fact that all centres were from ‘HI’ regions. Our study shows a strong association between the economic status of a region and the outcome after severe TBI. Some of the possible reasons for this are discussed below.

The management of patients with severe TBI has several important elements: adequate pre-hospital care, rapid transport to a specialized centre, complex in-hospital care and rehabilitation. Our study demonstrates that the economic status of a region may influence all of these elements. In addition, there may be other factors (e.g. a higher level of violence, bad roads or lack of work safety regulations) that may lead to a higher incidence of TBI. Hyder et al.1 stated that ‘...middle income countries face a higher preponderance of risk factors for cases of TBI and have inadequately prepared health systems to address the associated health outcomes’. This is at least partly true for the regions included in our study.

We found that the rate of violence-related TBI (i.e. assault and gunshot) increased significantly with decreasing wealth. The rate of traffic-related TBI also increased with decreasing wealth, despite the fact that the ratio of cars/1000 people is approximately 500:250:140 for the three regions studied. However, it has to be noted that the epidemiological data of our study are based on admissions to tertiary care centres.

In the ‘UMI’ and ‘LMI’ centres, <60% of the patients were provided most frequently in the ‘HI’ centres and was provided least frequently in the ‘LMI’ centres. The ‘LMI’ patients also received airway management and fluid resuscitation quite frequently but the amount of fluid given was significantly higher. Quality of care after TBI is associated with the economic status of a region: less wealthy regions are not able to provide comprehensive care. The ‘LMI’ centres, some ‘triage effects’ are obvious: mean age was significantly lower in cases (i.e. older patients and patients with a low GCS) were admitted less frequently than in the ‘HI’ and ‘UMI’ centres.

Factors that were related to intensive care survival according to the logistic regression models are listed in table 4. Odds ratios for ICU survival were significantly lower in ‘UMI’ and ‘LMI’ centres (Model 1). After adjustment for age, neurological status (first GCS) and trauma severity (Injury Severity Score), there was still a ‘centre effect’: compared with the ‘HI’ centres, ‘UMI’ centres and ‘LMI’ centres had significantly worse outcomes (i.e. surgical evacuation of haematomas, monitoring of intracranial pressure, sedation and ventilation) was again provided most frequently in the ‘HI’ centres and was provided least frequently by ‘LMI’ centres.

With regard to pre-hospital treatment, management according to the guidelines (i.e. endotracheal intubation, fluid resuscitation and rapid transport to an appropriate centre,) was done most frequently in ‘HI’ centres. The ‘LMI’ patients also received airway management and fluid resuscitation quite frequently but the amount of fluid given was significantly higher. This was most probably due to longer transportation times; unfortunately, we have no reliable data on the time of accident in cases of secondary transfer and thus cannot calculate pre-hospital times. The highest rates of patients without airway management or fluid resuscitation were found in the ‘UMI’ centres; the reasons for this are unclear. With regard to hospital treatment, management according to the guidelines (i.e. surgical evacuation of haematomas, monitoring of intracranial pressure, sedation and ventilation) was again provided most frequently in the ‘HI’ centres and was provided least frequently by ‘LMI’ centres.
With regard to hospital mortality, our results (90-day mortality 42–55%) are comparable to those reported in other observational studies. Lower rates (30 and 34%, respectively) were reported by French and British groups. Rates comparable to those from the ‘LMI’ centres were published by a German and another French group. Much lower mortality rates have been reported from clinical trials. Mortality rates in the tirilazad trial were 26% (treatment) and 25% (placebo) but in this trial, 15% of the patients had moderate TBI only and patients with GCS scores of 3 were excluded. The lowest mortality rate (17%) published so far was seen in the dexanabinol trial. But again, the ‘worst cases’ excluded. The lowest mortality rate (17%) published so far was seen in the dexanabinol trial.20 But again, the ‘worst cases’ (GCS = 3 or age > 65 years) were excluded in this trial. There is no doubt that mortality from TBI has been decreasing in recent years; the low rates found in reports of clinical trials, however, have to be interpreted with caution. If all patients aged >65 years and all patients with a GCS of 3 (n = 498 cases) were excluded from our study, the 90-day mortality would decrease to 20.6% (‘HI’ centres), 21.4% (‘UMI’ centres) and 30.1% (‘LMI’ centres). Contrary to previous studies that reported significantly better outcomes either for males or for postmenopausal females, we found no influence of gender upon mortality.

Cases from ‘LMI’ centres had a significantly higher mortality. In part, this might be explained by the more frequent use of steroids. The results of the ‘CRASH’ trial, which was published towards the end of data collection for this study, showed that the use of steroids was associated with an increase in mortality (odds ratio 1.18, 95% confidence interval 1.09–1.27). But other factors may have been important, too. All ‘middle income’ centres had a shortage of intensive care nurses and this may have contributed to the high rates of lung infection and sepsis, which increased mortality rates. Longer transportation times, lower rates of intracranial pressure monitoring and shorter duration of intensive care may also have played a role. We have not been able to show that individual treatment or system factors (e.g. endotracheal intubation, intracranial pressure monitoring or number of nurses) are associated with poor outcomes. There were, however, significant differences in the quality of care scores, which summarize many of these individual treatment factors. Our results demonstrate that age, neurological status, trauma severity and overall quality of care are the most important factors that determine outcomes after severe TBI.

The process of care was supposed to be based on the guidelines for TBI management that had been introduced at the start of the projects in all centres. The adherence to the guidelines was closest in the treatment of patients at ‘HI’ centres, followed by that of the ‘UMI’ and the ‘LMI’ patients. Thus, guideline compliance seems to be associated with better outcomes. A comparable result was found in an earlier study by Fakhry et al. However, guideline compliance is nearly impossible in regions that lack the means to provide efficient pre-hospital care, rapid transport and high-level hospital care.

In conclusion, our study demonstrates a significant association between the economic status of a region and the outcome of patients with severe TBI. This is due to the overall quality of care. Epidemiological factors (higher rates of violence-related TBI), treatment factors (e.g. rates of pre-hospital intubations, direct transfers and intracranial pressure monitoring) and lack of resources (e.g. intensive care nurses, equipment to monitor intracranial pressure) may have contributed to this result. Successful implementation of the guidelines for TBI management requires a well-funded health care system.

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Conflicts of interest: None declared.

Key points

- Outcome after traumatic brain injury depends on age, neurological status, trauma severity and quality of care.
- Quality of care depends on the economic status of a region; high-income regions provide better quality of care.
- Adherence to the guidelines for traumatic brain injury management was more frequently observed in high-income regions and this was associated with better outcomes.
- Successful implementation of the guidelines for traumatic brain injury management requires a well-funded health care system.

References


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