Clinical Research

Trends in epidemiological and clinical characteristics in severe traumatic brain injury: Analysis of the past 25 years of a single centre data base

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ABSTRACT

Objective: To describe the demographic and clinical profiles of a cohort of environmentally representative severe traumatic brain injury (TBI) cases collected for the past 25 years and to analyse the changes that occurred by dividing the analysis period into 3 equal time periods. Material and methods: This was an observational cohort study of consecutive adult patients (>14 years of age) with severe closed TBI (Glasgow Coma Scale score [GCS] ≤ 8) who were admitted during the first 48 h after injury to the 12 de Octubre hospital from 1987 to 2012. The most relevant epidemiological and clinical variables reported in the literature were defined and compared in 3 equal time periods (1987–1995, 1996–2004 and 2005–2014).

Results: There was a 13% reduction in the frequency of severe TBI from the first to the last time period. An increase in the mean age from 35 to 43 years was observed, whereas the frequency of severe TBI according to sex remained approximately the same during the last decades of life. A distinct change was observed in the injury mechanism; traffic accidents decreased from 76% to 55%, particularly those involving 4-wheeled vehicles. However, falls increased significantly, especially in older women, and contusion and subdural haematoma were the most frequent structural injuries. Motor scores could not be reliably assessed for the last time period because of early intubation and sedative drug use.

Conclusions: TBI epidemiology in Western countries has changed. This trend was also observed in our environment as an increase in mean age, which reflected the increase in falls among elderly patients.

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Palabras clave:
Traumatismo craneal grave
Epidemiología
Mecanismo
GCS

Objetivo: Describir el perfil demográfico y clínico de una cohorte de TCE grave recogida en los últimos 25 años, representativa de nuestro medio y analizar los cambios que han sucedido a lo largo de estos años, dividiéndolos en tres periodos de tiempo iguales.


Resultados: Existe una reducción de la frecuencia de TCE grave de un 13% entre el primer y último periodo de tiempo. Se aprecia un aumento de la edad media de 35 a 43 años, la frecuencia de TCE grave por sexo se iguala en las últimas décadas de la vida. Se aprecia un cambio en el mecanismo del trauma, el accidente de tráfico ha disminuido un 76% a un 55%, sobre todo se ha reducido el accidente en vehículo-4 ruedas. Sin embargo, han aumentado notablemente las caídas, especialmente en mujeres de mayor edad, siendo la lesión estructural más frecuente la contusión y el hemATOMA subdural. En el último periodo de tiempo no se pudo determinar con fiabilidad la puntuación motora, debido a la intubación precoz y el uso de drogas sedantes.

Conclusiones: La epidemiología del TCE ha cambiado en los países occidentales, esta tendencia también se observa en nuestro medio, con un aumento de la edad media que refleja el aumento de caídas en la población de pacientes de edad avanzada.

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Introduction

The incidence of traumatic brain injury (TBI) is highly variable among published series. This variability is due to variability in the definition of TBI, which complicates comparisons of different series. Nevertheless, TBI is a major social and economic problem in the Western world, particularly in young patients, and is gaining considerable importance in emerging countries, given the high incidence of traffic accidents.

In the USA, 1.7 million people/year sustained TBIs during the period from 2002 to 2006; although 81% of these patients were treated and discharged from emergency units, 275,000 (16%) were hospitalised and 52,000 (3%) died. These data represent an overall incidence of 576 cases per 100,000 people/year, a rate that was somewhat lower than that reported in a recent study from New Zealand of 790 cases per 100,000 people/year. The cost estimate of TBIs in the USA in 2010 was US$ 76.5 billion (US$ 11.5 billion in direct costs and US$ 64.8 billion in indirect costs such as lost work time).

Tagliaferri et al. conducted a review of the incidence of TBI in several European countries in the last 20 years and found that the average annual incidence varied between 150 and 300/100,000 people, depending on the definition of TBI and the population included (paediatric population, admission to the hospital or emergency unit). The average annual mortality was approximately 15/100,000 people. A study conducted in Scotland found that the incidence of TBI-related disability in patients admitted to hospitals ranged from 100 to 150/100,000 people, a figure higher than the previously published rates.

In Spain, there have been few epidemiological studies of TBI. In a study conducted in Cantabria, Vázquez-Barquero et al. found a TBI incidence of 91/100,000 people, of which 60% of the cases resulted from traffic accidents; the age-adjusted mortality was 19.7/100,000 people. Pérez et al. in a national study based on the Conjunto Mínimo Básico de Datos (CMDB) of patients discharged from hospitals between 2000 and 2009, reported a TBI incidence of 472.6/million people. The TBI incidence was significantly reduced during this period because of a decrease in traffic accidents; however, the incidence rates of other causes of TBI increased dramatically, particularly in the population over 65 years of age.

This trend towards changes in the causes of TBI can be observed in all Western countries and is due to a decrease in traffic accidents and concomitant increase in falls in an increasingly ageing population, consequently leading to an increase in the mean age of the affected population. Today, falls in populations older than 75 years of age comprise the most common cause of TBI in countries with high standards of living. The high level of associated comorbidity and frequent use of anticoagulants in this population might negatively influence the outcomes of these patients.

To date, no drug trials have shown significant reductions in severe TBI-related mortality. The high costs of these studies and the selection of the included population, which
limit the applicability of such studies, have determined the change in orientation that has been recently associated to TBI research.\textsuperscript{13,14} Therefore, it has become increasingly more important to perform multinational prospective observational studies based on common data in order to better describe TBIs and define the best clinical care for these patients. To this end, an American study is currently underway (Track-TBI\textsuperscript{a}), and another study will soon be implemented in Europe (www.center-tbi.eu).

Our hospital, which harbours an exclusive intensive care unit (ICU) for trauma patients, has a long record of experience in the management of TBI patients. The results of our study have been partially described in other previous studies.\textsuperscript{15-17} This is the first study in a series in which we will describe the epidemiological and clinical data, radiological findings, surgical management and final outcomes of patients with severe TBI and how these variables have changed over the last 25 years.

**Objective**

To describe the demographic and clinical profiles of a cohort of environmentally representative severe TBI cases collected during the past 25 years in order to analyse the changes that occurred during this period, which was divided into 3 equal time periods. In addition, we will verify whether variations similar to those observed in neighbouring countries also exist in our country’s TBI pattern.

**Materials and methods**

**Location**

The 12 de Octubre Hospital serves a population of nearly 600,000 people in the southern Community of Madrid. The hospital includes an ICU that specialises in the treatment of multiple traumas and a heliport that serves as a reference for the rest of the autonomous community and, occasionally, neighbouring communities. Accident site attendance is provided by a team supporting medical and non-medical staff (Servicio de Urgencias Médicas de Madrid, SUMMA) who are specialists in the outpatient care of trauma patients.

All patients who present with severe TBI at admission or after clinical deterioration were admitted to the ICU of the 12 de Octubre Hospital.

**Study population**

(1) **Inclusion criteria:** For this study, data were collected from patients who had been consecutively enrolled at the 12 de Octubre Hospital after suffering a severe TBI (STBI) from January 1, 1987 to December 31, 2012 and who fulfilled the following criteria:

- Age \(\geq\)15 years.
- Glasgow Coma Scale score (GCS) \(<8\) after nonsurgical resuscitation at admission or GCS deterioration within 48 h; this criterion determined the existence of 2 populations:
  - (a) Patients who presented with consistent scores \(<8\) and (b) those who were conscious at the accident scene or hospital admission but later experienced clinical deterioration within a 48-h period.
- Admission to the hospital and performance of a cranial computed tomography (CT) scan within 48 h of the injury.

(2) **Exclusion criteria**

- Admission or CT scan performed \(<48\) h after the injury.
- Age \(<15\) years (paediatric population).
- Penetrating gunshot wounds.
- Death prior to performing the CT scan.
- Intubated patients or those with a low level of awareness who improved to the point of responding to orders after sedation withdrawal or after the effect of intoxication waned. The CT scans of these patients were normal or featured only small lesions without mass effects. None of these patients required monitoring or surgery and all were discharged from the hospital after a few days with good neurological conditions.

Medical treatment was performed in the multiple trauma specialty ICU at our hospital and we did not intend to analyse this treatment. The patients were treated equally according to internationally accepted guidelines.\textsuperscript{18}

(3) The enrolled patients were classified into the following 3 equal time periods in a conventional manner: (a) 1987–1995, (b) 1996–2004 and (c) 2005–2012; the data from these 3 periods were compared.

**Data collection and definitions**

Data were collected at admission by medical personnel of the ICU or the Neurosurgery Department. The collected variables included those that have usually been described in the literature as demonstrating greater prognostic power.\textsuperscript{7}

(1) **Demographic variables and trauma characteristics:**

- Age: In years; as a continuous variable and in groups of 5 years.
- Sex: Male and female
- Mechanism of injury:
  - (a) Traffic accidents
    - Vehicle occupant
    - Pedestrian
    - Motorcycle rider
    - Bicycle rider
  - (b) Fall
    - Own height
    - Precipitated
  - (c) Direct Hit on the Head (by a moving or stationary object): Aggression, sports and work, among others.
  - (d) Other: Crush, Blast, or not determined.

To ensure greater consistency in the statistical analysis, the mechanism was also classified into 3 groups, traffic accident, fall and impact/other.

(2) **Clinical characteristics of the patient**

- GCS at the accident site (eye, verbal, motor): Patients were intubated if they exhibited a GCS \(<8\) or for any other cause as determined by the Outpatient Care physicians. The best score was determined using the extremity with the best response after Outpatient Care stabilisation.
- GCS upon admission to the hospital (eye, verbal, motor) after nonsurgical resuscitation. If patients were under the influence of sedative medication, which hampered clinical assessments, the best motor response was considered for the analysis after performing a sedation window if possible. When a reliable motor score could not be obtained because of the effects of drugs, a different known category (non-assessable) was assigned and included independently of the other analytical categories.

- Pupillary reactivity: The first observation after nonsurgical resuscitation was considered and classified as (a) both reactive pupils; (b) one non-reactive pupil; (c) none pupil reacting; (d) non-assessable (e.g., glass eye, facial trauma).

- Deterioration in the first 48 h: (a) a clinical decrease of at least 2 points on the GCS; (b) a change in the pupillary response; (c) a change in the CT category due to the appearance of new lesions or the growth of existing ones following the initial CT scan; (d) increased intracranial pressure; (e) systemic or other impairments attributable to systemic trauma and (f) sedation during transfer.

- Secondary Insults during the Early Hours after Trauma:
  - Shock (systolic blood pressure (SBP) < 90 mm Hg or clinically suspected incident such as cardiac arrest)
  - Hypoxia (partial oxygen pressure (pO2) ≤ 60, haemoglobin oxygen saturation (SaO2) < 90% or partial oxygen pressure in the arterial blood (PaO2) < 8 kPa, or clinically suspected)

(3) Structural damage (CT): Although we will not discuss in depth the changes that occurred according to the CT images of the study patients, we include this variable because we will relate it to the different mechanisms of TBI. All patients underwent CT scans within 48 h. We chose the first CT scan performed upon admission and classified this scan according to the mass lesion type combined with the following: (a) Contusion, (b) contusion and epidural, (c) contusion and subdural, (d) contusion, epidural and subdural, (e) epidural, (f) epidural and subdural, and (g) subdural. Furthermore, we classified the presence or absence of subarachnoid haemorrhage (SAH) and intraventricular haemorrhage (IVH).

Continuous variables are presented as mean ± SD and categorical variables as absolute and relative frequencies. The statistical significance of the comparison of proportions was determined using chi-square or Fisher exact test from contingency tables. The Cochran–Mantel–Haenszel test was used for ordinal variables, e.g, stratified age or time periods. Comparisons of the distributions of continuous measurements, age or admission time, were made using the analysis of variance (ANOVA), with adjusted p-value for multiple testing (Bonferroni method). All data analysis was generated using SPSS, version 16.0 (SPSS, Inc., Chicago, IL, USA).

**Results**

A total of 1830 patients met the study criteria; Fig. 1 shows the annual breakdown. Regarding the individual periods, 746 patients (40.8%) were admitted from 1987 to 1995, 587 (32.1%) from 1996 to 2004 and 497 (27.2%) from 2005 to 2012, yielding a 13% decrease in admissions between the first and last time periods.

**Demographic data and mechanism of injury**

The mean age (Table 1) increased significantly over the 3 time periods from 35 years in the first period to 43.5 years in the last period (p-value < 0.001), and all differences between the groups were significant (adjusted p-value < 0.001). The overall mean age was 38.4 years. The delay between trauma and admission was significantly reduced throughout the study. In the first period, it was 3.4 h and approximately 50% of the cases transferred from other centres. In the last period, this delay was reduced to 1.5 h because of a substantial improvement in prehospital care as well as increased assisted airlifting and ground transfer directly from the accident scene (85%; adjusted p-value < 0.001).

The proportion of male patients remained stable at all 3 time periods (p-value = 0.54), representing approximately 80% of all TBI cases (Table 2).

Fig. 2 shows the relationship between age and sex (p-value < 0.001). As we can see, the percentage of women approached that of men with advancing age and became equal at and after 70 years of age. Fig. 3 shows the population pyramid, from which we can appreciate the increased incidence of TBI in women over 70 years of age.

Fig. 4 shows a population pyramid in which age and sex were related with the trauma mechanism. As shown in the pyramid, the incidence rates of TBI secondary to vehicle accidents and hits were similar between the sexes. A higher incidence of accidents caused by 2-wheeled vehicles (motorcycles and bicycles) was observed in males; such accidents had a very low or no impact on women over 45 years of age. In the group affected by falls, a higher incidence was observed in women over 70 years of age. The incidence of precipitation was higher in women between 21 and 35 years of age. The
impact incidence peaked in women between 41 and 45 years of age.

As shown in Fig. 5, there was a significant reduction in traffic accidents (all causes); although traffic accidents accounted for approximately 75% of TBI cases between 1987 and 1995, in the last period this incidence decreased to 55% (p-value < 0.001). Between the same periods, the incidence of falls doubled from 19% to 37%. When the causes of traffic accidents were analysed (Fig. 6), a 50% reduction was observed in the incidence of TBI in 4-wheeled vehicle occupants; the proportions of the other causes of accidents (pedestrian, bicycle, motorcycle) remained consistent.

Table 1 shows the relationship between the trauma mechanisms, which were clustered as traffic accidents, falls and impacts, and the types of radiological injury revealed during the initial CT scan. Diffuse lesions were more frequently observed with traffic accidents, subdural trauma and the presence of SAH were more prominent with falls and epidural haematoma and the association between contusion and subdural haematoma were the most common injuries associated with impacts.

**Clinical features**

Table 2 shows the variations in pupil reactivity among the patients enrolled during the 3 periods. The proportion of reactive pupils remained relatively constant, with a higher incidence of single nonreactive pupils in the first period and a higher incidence of both nonreactive pupils in the last period.

The most relevant finding associated with the motor score was the progressive difficulty in assessing motor responses due to the use of sedative and paralytic drugs; therefore, this variable could not be properly evaluated in nearly 50% of the patients during the last time period.

Approximately 50% of the patients suffered some type of deterioration. We did not consider 89 cases that experienced deterioration after 48 h consequent to various causes such as sepsis, multiple organ failure, infection or other causes related to multiple trauma. In Table 3, we compared the time at which deterioration occurred within the first 48 h during the 3 time periods. Deterioration occurred earlier (p=0.000) in the last 2 groups, in which deterioration manifested during the first 6 h in approximately 1/3 of the cases.

During the first 6 h after TBI (Fig. 8), clinical (clinical and pupillary) impairments were the most common, accounting for 80% of all deterioration during this period; these
Impairments decreased in frequency during subsequent periods, in which radiological deterioration and elevated intracranial pressure (ICP) were more common. In Fig. 9, the frequencies of the deterioration causes are shown for the 3 time periods; reductions in radiological damage and elevated ICP were observed in the later 2 periods along with increased systemic trauma-related deterioration.

At the accident site, 1386 (75.7%) patients had a GCS ≤ 8 and 435 (23.8%) had a GCS > 8 (the GCS was untestable in 9 patients). Upon admission, 1663 (91%) had a GCS ≤ 8 and 166 (9%) had a GCS > 8. After 6 h, 1723 (94%) patients had a GCS ≤ 8 and 107 (6%) had a GCS > 8. The latter group’s scores deteriorated to ≤ 8 at 48 h after TBI.

**Secondary insults**

In Table 4, we can appreciate the significant reduction in the incidence of hypoxia across the 3 time periods.
Fig. 7 – Relationship between the injury mechanism and structural lesion type on CT.

Fig. 8 – Cause and time of deterioration.

Fig. 9 – Time profile of deterioration.
Table 3 – Time of deterioration-48 h in the 3 time periods (89 patients with deterioration after 48 h not included).

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Non deterioration</td>
<td>335 (48.1)</td>
<td>313 (56.0)</td>
<td>251 (51.6)</td>
<td>899 (51.6)</td>
</tr>
<tr>
<td>Deterioration ≤6 h</td>
<td>162 (23.3)</td>
<td>170 (30.4)</td>
<td>184 (37.9)</td>
<td>516 (29.6)</td>
</tr>
<tr>
<td>Deterioration 6–12 h</td>
<td>53 (7.6)</td>
<td>42 (7.5)</td>
<td>28 (5.8)</td>
<td>123 (7.1)</td>
</tr>
<tr>
<td>Deterioration 12–24 h</td>
<td>66 (9.5)</td>
<td>22 (3.9)</td>
<td>12 (2.5)</td>
<td>100 (5.7)</td>
</tr>
<tr>
<td>Deterioration 24–48 h</td>
<td>80 (10.7)</td>
<td>12 (2.1)</td>
<td>11 (2.3)</td>
<td>103 (5.9)</td>
</tr>
<tr>
<td>Total</td>
<td>696 (100)</td>
<td>559 (100)</td>
<td>486 (100)</td>
<td>1741 (100)</td>
</tr>
</tbody>
</table>

Mean deterioration, 1987–1995: 15.0 h.
Mean deterioration, 1996–2004: 6.0 h
Mean deterioration, 2004–2012: 5.4 h
ANOVA with continuous variable (time of deterioration): 0.000. The difference between the first and the other 2 groups was significant (adjusted p-value: 0.000).

Table 4 – Secondary insults during the 3 time periods.

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>Hypoxia</td>
<td>245 (32.8)</td>
<td>133 (22.7)</td>
<td>121 (24.3)</td>
<td>499 (27.3)</td>
<td>0.000</td>
</tr>
<tr>
<td>Shock</td>
<td>275 (36.9)</td>
<td>245 (41.7)</td>
<td>193 (38.8)</td>
<td>713 (39.0)</td>
<td>NS</td>
</tr>
</tbody>
</table>

(p-value < 0.001). The incidence of shock remained at approximately 39% across the 3 periods (p-value = 0.37). Shock was found to correlate with the TBI mechanism and occurred more frequently in patients who suffered from road traffic accidents (43%) (p-value < 0.001).

Discussion

In this first study of a cohort of patients with TBI from the 12 de Octubre Hospital, in which we analysed changes in the epidemiological and clinical features over the last 25 years, we confirmed that during the observed time period there was a trend towards a decreased incidence of TBI consequent to traffic accidents (particularly cases involving 4-wheeled vehicle occupants), although a remarkable increase was observed in the incidence of TBI consequent to falling among older individuals, especially women. This change in the mechanism of injury led to an increase in the mean age of the TBI population.

Time of admission

The time of entry at our hospital was significantly reduced from 3.4 h to 1.5 h. Moreover, the quality of the transfer improved, and such procedures are currently handled by trained medical personnel and supported by ambulances, helicopters and an ICU, thus reducing transfers from other hospitals from 45% to 10% and yielding better and faster patient transportation. Although we do not have accurate data, very few patients with severe TBI were treated at primary hospitals without ICUs specialised in the management of TBI.

Age, sex and TBI mechanism

This trend towards reducing injuries from traffic accidents has been observed in western countries,3–5,12,20–22 consequent to the implementation of regulatory laws targeting road traffic. In emerging countries with lower economic levels, there remain high proportions of young patients with TBI secondary to traffic accidents.12,23 In our series, the mean ages of patients affected by car and motorcycle accidents were 32 and 28 years, respectively. In recent decades, there has been an increase in the mean age of the patients with TBI. Specifically, the mean age in the traumatic coma data bank (TCDB) was 25 years but was reported as approximately 45–48 years in more recent studies,20,22 an age similar to the 43.5 years observed in the last period of our study (2005–2012). This change could be explained by the reduced incidence of traffic accident-induced TBI and the proportional increase in TBI among more elderly patients rather than in populations with increased life expectancies. In our series, the mean age of patients who experienced falls was 60.3 years, a significantly different value (p = 0.000) from that of groups affected by other causes of TBI. This older age group has a high mortality rate due to associated comorbidities or the increased susceptibility of the aged brain to evolve poorly.24

In all series,20,22,26 the frequencies of TBI in males ranged from 70% to 80%; however this frequency shifted to become nearly equal to that of women in later decades, perhaps because of the greater longevity of women.

As shown in Fig. 7, there appears to be a clear relationship between the mechanism of injury and type of structural lesion observed on CT. Accordingly, we observed that associations occurred more frequently between mass-type lesions and direct trauma or falls (contusions, subdural haematoma) and between diffuse lesions (IVH and absence of mass lesions) and traffic accidents.

In Spain, there have been few epidemiological studies on TBI17,10 but if we compare the most recent results10 with those of older data bases,3,16,26 these tendencies towards changes can be observed, including an increase in the mean age (in our series, this variable increased from 35 to 43 years). Although traffic accidents still comprise the most common cause of TBI, the frequency of such incidents has decreased markedly; however, the incidence of falls has increased dramatically. In our series, the incidence of falls doubled in frequency and in a report by Pérez et al.,10 the increase in this category was 87%.
This nationwide reduction in traffic accidents can be validated according to the data published by the Dirección General de Tráfico, DGT,11 which reported a continued decline in traffic accident victims between 2004 and 2011.

**Classification of TBI severity and deterioration**

TBI investigations have changed in recent years following the publication of IMPACT and CRASH.23,27 In pharmacological studies, strict inclusion criteria were imposed to reduce the heterogeneity of TBI. This strict criteria-based case selection entailed a substantial reduction in patient recruitment that conditioned the final evolution.18 Furthermore, a decrease in heterogeneity was not achieved because significant imbalances were observed between the populations. For this reason, this concept is currently changing and it is considered preferable to conduct studies with extremely broad inclusion criteria.14 In the near future, a prospective observational study without restricted inclusion criteria will be performed in 80 European centres, featuring the uniform collection of variables to better characterise the TBI population and comparative studies between centres (http://www.center-tbi.eu/). These studies are expected to define the best effective clinical care that could provide clinical evidence and treatment guidelines.13

In Table 5, we compare our results of the last period of time (2005–2012) with those of a series of recently published observational studies as well as the older IMPACT data corresponding to this type of study (TCDB, EBIC and UK4).29 In these studies, an increase in the mean age and the frequency of falls were observed relative to the findings of previous studies. In our series, there was a higher incidence of hypotension (38.8%) and, in 50% of the patients, adequate motor scores could not be obtained upon admission because of prior intubation. In the Prospective Observational Cohort Neurotrauma (POCON) study,20 74% of the patients had no motor responses upon admission and 32% had no pupillary responses, perhaps consequent to prehospital treatment.

We face the fundamental problem of lacking a TBI classification based on minimally variable criteria such as a biochemical determination of coronary ischaemia. There is growing interest in developing a pathophysiological classification for TBI but, to date, the GCS is used to classify patients. In modern systems of care for patients with STBI, intubation has become more frequent at the accident site and thus clinical assessments can pose serious problems. Balestrieri et al.13 reported a loss of predictive ability of the GCS beginning 1997 as a result of the increased use aggressive prehospital treatment measures. Moreover, there are no standard criteria for performing the GCS. In cases of STBI, the motor component has been found to maintain the highest predictive power, and thus there is a trend to replace the total GCS with the motor score. Clinical assessments require patient stabilisation without the effects of sedative medication, although

### Table 5 – Comparison of epidemiological, clinical and CT data from several observational studies of TBI.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Categories</th>
<th>IMPACT OBS</th>
<th>Andriessen</th>
<th>Austria</th>
<th>Miburgh</th>
<th>12 de Octubre</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(Lingsma)</td>
<td>(POCON)</td>
<td>(N = 492)</td>
<td>(N = 363)</td>
<td>(N = 497)</td>
</tr>
<tr>
<td>Hospital admission</td>
<td>24–72</td>
<td>72 h</td>
<td>48</td>
<td>NR</td>
<td>48 h</td>
<td>43.5</td>
</tr>
<tr>
<td>Age</td>
<td>Mean</td>
<td>32</td>
<td>46</td>
<td>48</td>
<td>39</td>
<td>43.5</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>75</td>
<td>70.0</td>
<td>72.0</td>
<td>74.0</td>
<td>77.3</td>
</tr>
<tr>
<td>Traffic</td>
<td>75.0 (TCDB)</td>
<td>51.0</td>
<td>44.0</td>
<td>59.5</td>
<td>55.5</td>
<td></td>
</tr>
<tr>
<td>Falls</td>
<td>16.0</td>
<td>37.0</td>
<td>41.0</td>
<td>24.2</td>
<td>37.0</td>
<td></td>
</tr>
<tr>
<td>Impact (assault, sport, etc.)</td>
<td>–</td>
<td>7.0</td>
<td>7.0</td>
<td>14.1</td>
<td>7.2</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>–</td>
<td>4.0</td>
<td>9.0</td>
<td>2.2</td>
<td>0.2</td>
<td></td>
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<tr>
<td>Motor score on admission</td>
<td>Nothing</td>
<td>29.0</td>
<td>74.0</td>
<td>13.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extension</td>
<td>18.0</td>
<td>2.0</td>
<td>4.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal flexion</td>
<td>12.0</td>
<td>4.0</td>
<td>GCS3–5 = 51%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal flexion</td>
<td>7.0</td>
<td>11.0</td>
<td>GCS ≥ 6 = 49%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Locate/Obey</td>
<td>17.0</td>
<td>8.0</td>
<td>Mean GCS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non assessable</td>
<td>17.0</td>
<td>0.0</td>
<td>(IQR) 4 (3–6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non assessable/unknown</td>
<td>–</td>
<td>0.0</td>
<td>49.9</td>
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<tr>
<td>Hypotension</td>
<td>Both reactive</td>
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<td>54.0</td>
<td>NR</td>
<td></td>
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<tr>
<td>One reactive</td>
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<td>8.0</td>
<td>NR</td>
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<tr>
<td>Both nonreactive</td>
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<td>32.0</td>
<td>62.8</td>
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<tr>
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<td>26.0</td>
<td>31.7</td>
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<tr>
<td>Yes</td>
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<tr>
<td>% in prehospital.</td>
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</table>

### Notes

a = 11 (2%): Gunshot.

b = 4 (1%): Gunshot.
c = 3 (0.8%): Gunshot.
d = % in prehospital.
this is not always possible. It is believed that the best GCS obtained after resuscitation should be used but in one study, the post-resuscitation motor score could only be properly evaluated in 62% of cases included. There remains no general consensus on the best method of GCS determination in intubated patients under the influence of sedative medication; further studies are required to clarify this point. The IMPACT study recommended that the GCS be obtained at the time of enrolment. The use of a GCS obtained during the prehospital stage or at an intermediate hospital is not recommended because such scores have lost their prognostic values.

We independently rated the motor responses obtained under sedation and proved that there was a significant increase in the frequency of this variable. Similarly, this problem has not been solved in other recent studies. A Dutch study (POCON) found that 70% of patients had a motor score of 1, possibly indicating that many sedated patients with no responses were assigned a score of 1. In the IMPACT study, a worse OR was observed in the final outcomes of patients with M2 vs. M1 scores, indicating that the M1 population includes a mixture of sedated patients with different motor responses. The same problem arises when assessing pupillary responses that might have been altered by deep sedation/relaxation.

Another problem associated with patient classification is related to the time at which the classification is made. Indeed, TBI is a dynamic disease and time fluctuations can induce variability in TBI classification. In our study, we defined an inclusion window of 48 h although this option was very variable. In the IMPACT study, the inclusion windows ranged from a few hours in pharmacological studies to 72 h in an observational study.

Another fact that supported the variable nature of STBI was that approximately 50% of our patients experienced some type of deterioration (e.g., clinical, radiological, systemic) during the first 48 h after trauma, and no significant differences were observed between the 3 time periods. By analysing these changes with respect to the time periods, we found that clinical deterioration was similar across the 3 groups (approximately 30%) although the incidence of radiological worsening decreased in the last period whereas deterioration associated with systemic associated trauma increased. Notably, deterioration occurred significantly earlier in the last 2 time groups (5–6 h) and the most frequent cause of early deterioration was clinical deterioration (clinical and pupillary).

**Mechanism and associated brain injury**

The mechanism of injury is highly clinically relevant because it affects the type of intracranial lesion depending on whether direct skull contact or acceleration occurred, although in most cases the different types of damage and lesions (focal and mass) are associated. However, in direct cranial impacts due to assault, sports or work, a higher frequency of focal lesions (contusions, haematomas, brain lacerations) leading to the formation of extra or intracranial haematomas was observed. Falls are associated with older age and usually induce intracranial or subdural haematomas. Traffic accidents are associated with a higher frequency of diffuse lesions that are usually caused by a sudden movement of the head (petechiae). This pattern of lesions has been described previously.

**Secondary insults**

After the initial TBI, the brain is vulnerable to secondary damage that can be increased by secondary insults, particularly hypotension and hypoxia. Shock occurred more frequently in our series than in other recently published series, perhaps because of the higher incidence of multiple traumas secondary to traffic accidents. In our series, the incidence of shock was similar across the 3 analysed time periods and reached a level of approximately 39%. Furthermore, 43% of patients with traffic accident-induced TBI had hypotension. However, the incidence of hypoxia has decreased significantly from 1995 to the present, thus indicating improvements in prehospital care. The combination of shock and hypotension was observed in 346 (18.9%) patients. The association between these secondary insults is known to significantly worsen the final outcome.

**Limitations**

Similar to the EBIC study, our series was an observational study with no external auditing process, which might cast doubt upon the data quality. However, the data credibility was based on the low absence of uncollected acute-phase variables and the consistent results, as proven through an internal validation process.

**Conclusions**

In the last 25 years, there has been a trend towards changes in the characteristics of patients with severe TBI. Throughout this period, the conditions for patient transport have significantly improved, leading to a reduced incidence of hypoxia. An increase in the mean patient age and a major increase in failing as the mechanism of injury were observed, particularly in older women; however, traffic accidents remain the most common cause in our overall environment, despite that the incidence of car accidents decreased dramatically during the study period. The performance of clinical assessments upon admission has been complicated by the use of sedative drugs; however, there is a current lack of a universally accepted consensus regarding the determination of such scores.

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**Conflicts of interest**

The authors declare no conflicts of interest.
REFERENCES


