ORIGINAL PAPER



Severe traumatic brain injury (TBI) – a seven-year comparative study in a Department of Forensic Medicine

RĂZVAN ŞTEFAN ŢOLESCU¹⁾, MARIAN VALENTIN ZORILĂ²⁾, MIRCEA-SEBASTIAN ŞERBĂNESCU³⁾, KAMAL CONSTANTIN KAMAL⁴⁾, GEORGE LUCIAN ZORILĂ⁵⁾, ILIE DUMITRU⁶⁾, CHAROULA FLOROU⁷⁾, LAURENŢIU MOGOANTĂ⁸⁾, ION ALEXANDRU VĂDUVA¹⁾, LILIANA STANCA²⁾, ROXANA EUGENIA ZĂVOI²⁾

¹⁾PhD Student, Department of Histology, University of Medicine and Pharmacy of Craiova, Romania

²⁾Department of Forensic Medicine, University of Medicine and Pharmacy of Craiova, Romania

³⁾Department of Medical Informatics and Biostatistics, University of Medicine and Pharmacy of Craiova, Romania

⁴⁾Department of Family Medicine, University of Medicine and Pharmacy of Craiova, Romania

⁵⁾Department of Obstetrics and Gynecology, University of Medicine and Pharmacy of Craiova, Romania

⁶⁾Department of Road Vehicles, Transportation and Industrial Engineering, Faculty of Mechanics, University of Craiova, Romania

⁷⁾Department of Forensic Pathology, Faculty of Medicine, University of Thessaly, Greece

⁸⁾Department of Histology, University of Medicine and Pharmacy of Craiova, Romania

Abstract

Deaths caused by traumatic brain injury (TBI) increase in incidence every year worldwidely, mainly in developing countries. Thus, World Health Organization (WHO) estimates that in 2020, TBI will become the third main cause of death. In our study, we evaluated the deaths caused by TBI recorded within the Institute of Forensic Medicine of Craiova, Romania, between 2011 and 2017. Therefore, according to age, the cases were divided into two groups: people aged 0-18 years old (including 18 years old) and people aged over 18 years old (a total of 1005 cases, of which 971 were adults and 34 included in the age group 0-18 years old). In both groups, most patients were males from the rural area. In adults, falling was the main legal entity of the cases, followed by car accidents (which were the most common in children). In both groups, in car accidents, most of them were pedestrians and car occupants. Various aggressions (human, animal, self-injury) were found in 94 (9.68%) of the adult cases and in four (11.76%) cases of children. Another parameter under study was the blood alcohol concentration, being observed that most of the subjects with positive blood alcohol content died from car accidents. By evaluating the Glasgow Coma Scale (GCS) score as a prognostic factor, most of the subjects presented third and fourth degree coma at admission; still, 5.14% of the adult patients who deceased had GCS score 15 at admission, death occurring probably by developing some intracranial hematomas in time. Regarding the morphology of the lesions, most patients presented various forms of cranial fractures, 185 (19.05%) adults in association with extradural hemorrhages/hematomas, but also there were four cases with extradural hematomas without any cranial fractures. In children, there was highlighted a single case of extradural hemorrhage under the fracture line. Seventy-eight percent of the adults and 44.12% of children presented subdural hematomas associated with other meningo-cerebral lesions. Also, 83.63% of the adults and 97% of children presented brain contusions. In both groups, brain laceration was observed in approximately 50% of the cases.

Keywords: traumatic brain injury, mortality, mechanical forces, road traffic accidents, falls, violence.

Introduction

Traumatic brain injury (TBI) represents one of the main causes of morbidity, mortality and disability, all over the world. It is estimated that worldwidely, every year, between 50 and 74 million people, of all ages, suffer a TBI [1, 2]. In the last decades, the TBI incidence continued to grow in almost all the countries of the world. Only in USA there are recorded about 2.5 million TBIs every year, thus costing the American healthcare system approximately 76.5 billion dollars [3, 4]. Also, in USA, TBIs are responsible for about 50 000 deaths every year [5, 6]. Based on some estimations of the *World Health Organization* (WHO), TBI will become the third main cause of death and disability until 2020 [7, 8].

TBIs are caused by direct traumas on the head that cause neuronal lesions or dysfunctions. These are caused most often by falling from various heights, motorcar accidents, sports accidents, human or animal aggressions [9–14]. These mechanical forces vary in intensity and action mechanism, thus causing various lesions of the brain. Generally, TBIs are classified as mild, moderate or severe forms [15, 16].

The patients that survive after TBI frequently present minor or severe disabilities, manifested by cognitive, motor or emotional deficiencies, with an impact on the patient's life quality, and also on the patient's family and society [17, 18]. According to some studies, in 2005, in USA, there were about 3.17 million people (approximately 1.1% of the population), who presented complications or disabilities following TBI, manifested through various neurological and psychological diseases [19, 20].

The incidence and occurring mechanisms of TBI vary from one geographical area to another and even from one country to another. Also, the causes leading to TBI vary a lot according to the age of exposed persons: if in persons aged less than 14 years old, the main cause of TBI is represented by falling from various heights, in teenagers and adult persons, the main cause of TBI is represented by car accidents [21–23].

Aim

In our study, we evaluated the deaths caused by TBIs investigated in a Department of Forensic Medicine in Romania – the Institute of Forensic Medicine of Craiova –, over a period of seven years, both in the adult population and in the under-aged people (0–18 years old).

A Materials and Methods

Our study is a retrospective one, analyzing all the deaths caused by TBIs occurring in adults and children, between January 1, 2011–December 31, 2017, diagnosed within the Institute of Forensic Medicine of Craiova. The analyzed data were extracted from the forensic reports on corpses performed by the forensic doctors in the abovementioned period, as well as from the results of the complementary investigations required during autopsies (histopathological and toxicological ones). Other data were extracted from the general clinical observation sheets in various Clinics and Hospitals, especially in the Emergency County Hospital of Craiova, where there was admitted an important number of TBI patients, right after the TBI occurrence or shortly after; also, some data were taken from the emergency medical records performed by the doctors within the Emergency Department (ED) of the above-mentioned Hospital (for the cases that arrived here and deceased), as well as from the investigation records performed by the criminal investigation officers at site.

In order to perform the study, the data obtained from these medical and forensic records were introduced into Excel sheets, for a subsequent statistical processing. There were performed charts showing the main characteristics of the TBI patients; also, in our study we used macroscopic images performed during forensic autopsies within the Institute of Forensic Medicine of Craiova on deceased persons due to TBIs.

The extracted data regarding death cases caused by TBI were divided into two large groups: a group of adults and a group of children and teenagers (aged 0–18 years old), mainly studying the comparative elements between the two groups. We mention the fact that the study was performed after the previous approval of the management of the Institute of Forensic Medicine of Craiova, also being respected the measures for keeping the confidentiality and protection of personal data, according to present laws.

Results

Within the Institute of Forensic Medicine of Craiova, between January 1, 2011–December 31, 2017, there was performed a number of 4626 forensic autopsies under the circumstance of violent death or suspicion of violent death; after the autopsies, there was established that during this period the number of violent deaths was 2924, representing 63.2% of the total of deaths, the rest of 1702 (36.8%) cases being non-violent deaths. In the seven years under study, the number of violent deaths varied between 385 and 460, the mean value of violent deaths being 417/year (Figure 1). Of the violent deaths, the ones caused by TBI were 1005, of which 34 (3.38%) deaths occurred in children and 971 (96.62%) deaths occurred in adults (Figure 2).

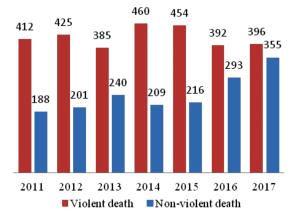


Figure 1 – Distribution of violent and non-violent deaths within the Institute of Forensic Medicine of Craiova, Romania, between 2011 and 2017.

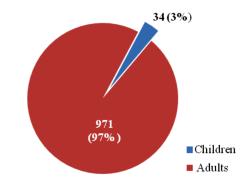


Figure 2 – Distribution of deaths on the two age groups under study.

Regarding the gender distribution of TBI deaths in adults, we observed that of 971 cases, 765 (78.78%) were males and only 206 (21.22%) were females. In children, the situation was similar, in that out of the 34 deaths by TBI, 26 (76.47%) were males and eight (23.53%) deaths were females (Figure 3).

Studying the death distribution according to the social environment, in adults, 627 (64.37%) persons were from the rural area, while 344 (35.43%) were from the urban area; in children, 20 (58.82%) cases were from the rural area and 14 (41.18%) cases were from the urban area (Figure 4).

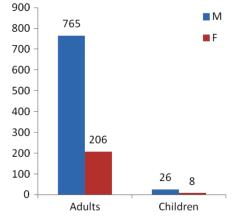


Figure 3 – Distribution of violent deaths according to gender.

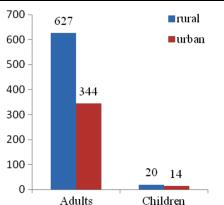


Figure 4 – Distribution of deaths according to the social environment.

Regarding the legal framing, an important percentage of the cases, both in adults and children, was the prerogative of car accidents. Therefore, in the adult persons, of the total number of 971 deaths, 307 (31.61%) were caused by car accidents. Of these, the pedestrians were the most affected, the number of deaths caused by car accidents involving pedestrians being 118, representing 12.15% of the total of violent deaths in adults, namely 38.45% of car accidents. The occupants of the cars (drivers and passengers) totalized a number of 84 deaths, representing 8.65% of the deaths by TBI in adults, namely 27.36% of car accidents. Also, 62 deaths, representing 6.38% of the deaths by TBI or 20.19% of car accidents, were recorded in bikers; 22 representing 2.26% of the deaths by TBI in adults and 7.16% of car accidents were recorded as a result of car accidents with victims occupying animal-tracting vehicles, while 21 cases of violent deaths, representing 2.16% of TBI deaths in adults and 6.68% of car accidents resulted in the drivers of other types of vehicles (motorcycles, mopeds) (Figures 5 and 6).

In children, of the total number of 34 deaths, 26 (76.47%) were due to car accidents. Of these, 16 cases, representing 47.06% of the total deaths in children, involved pedestrians; eight (23.53%) cases were represented by children present in a car at the impact moment, while two (5.88%) teenagers were injured driving a moped.

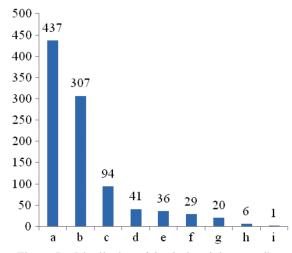


Figure 5 – Distribution of deaths in adults according to the legal framing. a: Fallings; b: Car accidents; c: Aggressions; d: Various accidents; e: Non-legal framing after autopsy, f: Fallings from height; g: Train accidents; h: Work accidents; i: Airplane accident.

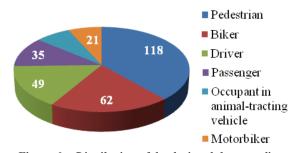


Figure 6 – Distribution of deaths in adults according to the type of traffic accident.

Another mechanism of violent death was the one by falling, a mechanism that affected especially the elderly. In adults, the number of deceased persons by falling was 437 (the most significant number in our statistics regarding the legal frame), representing 45% of the total of TBI deaths, thus exceeding the deaths caused by car accidents. In children, there was recorded only one case of death caused by falling (out of bed).

Other violent deaths by TBI were represented by aggressions (human, animal or self-injuries). In adults, 94 persons (9.68% of the total of deaths) were victims of aggressions: 80 (8.23%) individuals deceased because of human aggressions; nine individuals (0.92% of TBI deaths) died because of animal aggression, while five deceased due to self-injuries (0.51% of the deaths).

In children, three (8.82%) cases suffered lesions because of animal aggressions and only one child (3%) was recorded as a death caused by human aggression. Also, in children, there were recorded two deaths because of the fall of blunt bodies on the head (a television and a tree branch, respectively) and a death caused by a train accident (Figure 7).

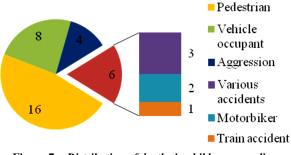


Figure 7 – Distribution of deaths in children according to the legal framing.

Another parameter studied was the blood alcohol content. Blood samples were taken for alcohol determination in 355 (36.56%) adult cases. In nine cases (2.54%) of the cases where blood alcohol content was found), most of them occurring in car accidents, we observed very high blood alcohol level over 2.5 g‰. A blood alcohol content between 1.5-2.5 g‰ was found in 34 cases (9.57% of the cases where blood was taken for establishing the alcohol content), of which 19 cases of car accidents, four cases of fallings and four cases of human aggressions; within the values of blood alcohol 0.5-1.5 g‰, there were recorded 57 (16.05%) cases, of which 31 cases of car accidents and 13 fallings; positive blood alcohol content less than 0.5 g‰ were found in 29 cases (8.16% of the 355 cases), of which 13 car accidents, seven fallings and five human aggressions. In 226 cases (63.66% of the

adults where there was taken blood for alcohol content) presented negative toxicological tests for blood alcohol. In three cases of children and teenagers, there were observed a positive blood alcohol content (less than 0.5 g‰) in two cases of car accidents: pedestrians and an 11-year-old girl, victim of a human aggression with blunt object and a stabbing-cutting object (knife).

The Glasgow Coma Scale (GCS) score was recorded in the medical documents of 629 (64.77%) adults, namely in 20 (58.82%) children of the admitted patients. Studying the value of the GCS score at admission, in adults, we observed that 172 patients presented fourth degree coma (27.34% of the cases where the GCS score was recorded), 171 (27.19%) patients presented third degree coma, 124 (19.71%) patients second and first degree coma (GCS score 6–8), 128 (20.35%) patients presented altered



Figure 8 – Comminuted fracture of the vault with intrusive fragments localized at impact area (3-year-old girl, car accident).

TBIs also caused lesions of the meningo-cerebral vessels, which manifested through various types of hemorrhages. Thus, hemorrhages/hematomas in the extradural space were found in 189 (19.46%) adults. The correlation of skull fractures with extradural hemorrhages in adults showed that 185 cases (19.05% of adults) presented extradural hemorrhages/hematomas occurring in the fracture foci, but there were also four (0.41%) cases where there were observed extradural hemorrhages with no skull fracture (Figures 10 and 11).

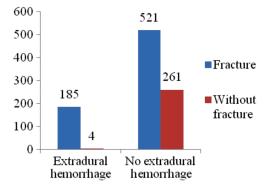


Figure 10 – Report of extradural hemorrhage/hematoma on cranial fracture in adults.

In a single case of a child, there was highlighted an extradural hemorrhage under the fracture line; in the other cases of children diagnosed with skull fracture, there were consciousness (GCS score 9–14), and 34 (5.41%) patients presented preserved consciousness (GCS score 15).

Of the children where there was recorded the GCS score at admission, 17 (85% of the cases with a recorded GCS score at admission) presented profound coma with GCS score 3, while three children presented third degree coma (15% of children). In the other 14 deaths recorded in children, there could not be established the GCS score.

Studying the morphology of injuries, 706 (72.7%) adult persons and 27 (79.41%) children presented various forms of skull fractures, showing a high intensity of the impact. Of these, 600 (84.98%) of the total patients with skull fractures presented fractures of the vault and base; in 93 (13.17%) cases, there were found single vault fractures, without irradiation to the skull base, and 13 (1.84%) cases presented isolated fractures of skull base (Figures 8 and 9).



Figure 9 – Comminuted skull fracture with detachment of bone esquillae and effraction of brain matter in the exit orifice (21-year-old male, suicide by shooting).

not highlighted any extradural hemorrhages, an aspect that can be explained by a high adherence of the dura mater on the endocranium in children.

Regarding the subdural hemorrhages and hematomas, in the group of adults, they were present in 758 cases (78% of the total of studied cases); in 150 (15.45%) cases, subdural hemorrhages were associated with extradural hemorrhages. Regarding the clinical forms of subdural hematomas in adults, 354 (46.7%) cases presented acute forms, with a survival period less than three days; 332 (43.8%) cases presented subacute forms, with a survival period of 3–15 days and 72 (9.5%) cases were chronic forms, with a survival period more than 15 days (Figures 12 and 13).

In children, we found 15 cases (44.12% of deaths) of subdural hemorrhages/hematomas; six (17.65%) cases presented acute forms, while nine (26.47%) cases presented subacute forms.

Leptomeningeal hemorrhages highlighted during autopsy, either diffuse or localized, were present in 928 (95.57%) adults and in 33 (97%) children, most often in association with other meningo-cerebral injuries (Figures 14 and 15).

Regarding brain contusions, they were observed during autopsies and confirmed pathologically in 812 (83.63%) adults, of which 341 (42%) dead persons presented contusions in the cerebral trunk. Of the persons with brain contusions localized in the cerebral trunk, 233 cases arrived to the ED or they were admitted to Hospital, persons in whose medical records there was also recorded the GCS score. Thus, of the patients with brain contusions localized in the cerebral trunk, 85 (10.46%) presented profound coma, 78 (9.6%) patients presented third degree coma, 34 (4.18%) second and superficial coma, and a number of 36 (4.43%) patients presented a preserved or slightly altered consciousness (GCS score >8) (Figures 16 and 17).

In children and teenagers, 33 (97%) dead persons presented brain contusions, of which 16 (47%) with a localization in the cerebral trunk.

Post-traumatic parenchymatous hematomas in the contusive foci were highlighted in 126 (12.97%) adults and in a single child (Figure 18).

Brain laceration was diagnosed in 493 adults and 17 children (approximately 50% of the deceased), mainly found with severe TBIs (Figure 19).



Figure 11 – Extradural hematoma with typical localization in the Gerard-Marchand space (57-year-old male, falling).



Figure 12 – Subacute subdural hematoma after four days of survival (70-year-old male, falling).



Figure 13 – Chronic subdural hematoma after a survival period of 22 days (84-year-old male, falling).

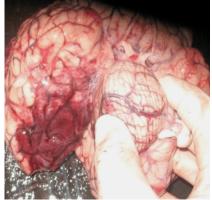


Figure 14 – Localized leptomeningeal hemorrhage (51-year-old male, car accident).



Figure 15 – Diffuse leptomeningeal hemorrhage "in the canvas" (3-year-old boy, car accident).

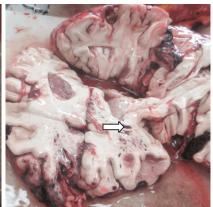


Figure 16 – Cortical and subcortical brain contusions: Pitres section (52-year-old male, car accident).



Figure 17 – Severe brain contusions localized in the cerebral trunk (50-year-old male, falling from height).

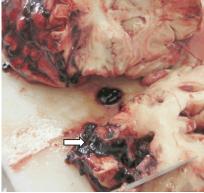


Figure 18 – Intraparenchymatous hematoma developed in the contusion foci with effraction in the subdural space (66-year-old male, falling).



Figure 19 – Massive brain laceration, transfixiant wound of the head (31-year-old male, suicide by shooting).

Discussions

TBI represents a major health problem worldwidely, with an incidence of about 100–600/100 000 inhabitants and a mortality rate for severe TBI of about 20–50% in developed countries and up to 90% in other countries [24, 25]. It is estimated that every year, only in the USA die approximately 52 000 persons due to TBIs [26]. The annual incidence of TBI is estimated to 50 million cases all over the world. Also, it is considered that approximately half of the planet's individuals will suffer a TBI during their lifetime [26, 27].

TBI represents a major problem for victims, families and community, because even a minor TBI may lead to the onset of a disability for life, with very high medical and social expenses. The total lifetime expenses in patients with moderate and severe TBIs were estimated to 8.6 billion dollars in 2008 in Australia [28] and to 60 billion dollars in 2000, in USA [29]. Other studies showed that every year TBIs cost the global economy approximately 400 billion USA dollars, representing 0.5% of the worldwide total income [26, 27], while 60% of the patients with severe TBIs either die or remain with at least one severe permanent disability, thus requiring high social costs, sometimes becoming socially dependent.

In the European Union (EU), there is estimated that, every year, over a million people are admitted to hospital with a moderate or severe TBI, which makes TBI one of the major causes of morbidity and mortality in EU [3, 30, 31]. Systematic epidemiological studies showed that in EU there live over 7.7 million people with disabilities caused by a TBI [31].

In order to understand the severity of the brain lesions caused by TBIs, we should mention that, besides the primary lesions resulted by the mechanical forces applied on the skull at the trauma moment, there also appear secondary lesions, which represent a cascade of biochemical and molecular changes induced by the TBI. These imply the onset of the oxidative stress, the accumulation of reactive oxygen species, the increase of excitotoxicity of the excessive glutamate, the triggering of some neuroinflammatory local processes, process causing mitochondrial dysfunctions at a neuronal and glial level, local ischemia, cerebral edema, etc., having as the final result the neuronal cell death [32-36]. Therefore, the persons with severe and moderate TBIs are considered major emergencies, which require a complex treatment and a careful monitoring during a large period of time, as a TBI is produced in seconds or milliseconds, whereas the biological consequences may last for a lifetime [37].

In our study, within the Institute of Forensic Medicine of Craiova, we analyzed the deaths caused by TBIs over a period of seven years. Our study proved that TBI is a pathology found from the newborn to the elderly, but most (97%) of the deaths by TBI occurred in adult persons (over 18 years old).

Most of the studies approaching TBI showed that this pathology is found in all people, all ethnic groups and all ages [2]. In USA, the age of patients is closely related to the TBI incidence. Thus, children aged between 0 and 4 years old, teenagers aged between 15 and 19 years old and adults aged over 65 years old, are among the most

susceptible to be affected by a TBI. Post-traumatic hospitalization and death are more frequent in the adults aged over 75 years old, which suggests that the age at injury time represents a risk factor as far as an immediate or long-term recovery is concerned [37].

Although the percentage of deaths in children was quite low (3%) in our study, it should be proven that TBIs in children are quite frequent, but have various intensities and only a relatively low percentage of severe TBIs result in death. Similar data have been also highlighted by the studies performed by American Centers for Disease Prevention and Control regarding pediatric TBI, showing that approximately 475 000 children aged between 0–14 years old undergo a TBI every year, of which up to 90% are the ones with mild lesions that go back home, 37 000 are hospitalized and 2685 die because of the injuries. The annual rate of mortality caused by the TBIs in children younger than 4 years old was 5 to 100 000 inhabitants [38]. Although a relatively small number of children die by TBI, there are studies showing that a TBI during childhood may have negative effects on the child's development, the child being prone to develop cognitive, behavioral or emotional deficiencies, even at an adult age [39-41].

Regarding the gender of the deceased persons because of a TBI, in our study, we observed that males represented more than 3/4 of violent deaths by TBI, both in children and in adults. Similar data were also reported by Majdan et al. (2016), who showed that in 2012 in the 25 EU countries and Turkey there were recorded 33 415 deaths caused by a TBI, of which 22 886 (68%) were males [42]. Most deaths were recorded in people aged over 65 years old [42]. Another study, performed in Norway, showed that severe TBIs occurred in a higher number in men than in women, in all age groups, while the number of deaths was higher in the elderly [43]. Similar data regarding severe TBIs and mortality according to gender were also displayed by other studies from Europe, Asia or America [11, 21, 44, 45]. We consider that these differences related to gender are due to the fact that men are more involved in economical activities, consume more alcohol, drive more often; also, we consider that deaths by TBI are more numerous in the elderly due to a co-existence of other comorbidities that affect the balance, alter attention, work capacity or reason.

Another particular aspect of our study was the distribution of TBI deaths as violent according to the social environment. We observed that about 2/3 of deaths by TBI, both in adults and in children, were recorded in the rural area. This aspect may be due to the medical healthcare system that does not provide a rapid access for the patients in the rural areas to specialized medical services, namely to ED, intensive care unit (ICU), neurology or brain surgery.

The analysis or "legal framing" in our study showed that most deaths were caused by fallings from various heights (48%), followed by car accidents (about 33%). Our data are in accordance with the results of other studies highlighting that the first causes of violent death are fallings and car accidents [26, 46–50].

Another factor involved in the etiopathogeny of violent deaths by TBI is alcohol intake. In our study,

38.87% of deceased persons by a TBI, in whom there could be established the blood alcohol content, had consumed alcohol before the traumatic event. This risk factor contributed to the mechanism that led to their death, such as: traffic accidents, fallings, human aggressions, etc. Numerous studies showed that alcohol is a major risk factor in the onset of TBI and violent deaths, in a high percentage (30–50%) [49–53]. Posti *et al.* (2019) showed that in Finland the reduction of alcohol intake with 1.2% every year was accompanied by the decrease of severe TBI by approximately 4.3% in men and by 2.4% in women [54].

The evaluation of the severity of brain lesions according to the GCS score in our study could be performed only in the cases where the patient preserved his vital functions and came to the ED. Of the 1005 individuals deceased after a TBI, the GCS score was performed on 649 (64.58%) of the patients (adults and children); of these, 363 (56%) presented third or fourth degree coma, with very low values of GCS score and died in the immediate days following the trauma. Still, there should be observed that even though 128 patients presented altered consciousness (GCS score 9–14), while 34 patients presented a preserved conscious state (GCS is not a clear prognosis indicator.

GCS is an instrument of neurological evaluation intensely used in classifying brain lesions, especially in the acute stage of the lesions: the lower the GCS score, the more intense the brain lesions are [55]. Still, the patients over 65 years old had a poorer progress, regardless of the nature of the traumatic injury or GCS score at hospital admission, due to the cerebral changes related to age and some comorbidities [56, 57]. Due to these reasons, numerous studies considered that old age represents an important risk factor in TBIs [58–61].

The morphological study of the brain performed during the necropsy examination showed the presence of complex lesions in all cases, starting from lesions of the skull, vascular lesions (diffuse meningeal hemorrhages, extradural, subdural, intracerebral hematomas), associated with lacerations of cerebral matter or diffuse parenchymatous lesions.

We are convinced that to the macroscopic lesions there were added other microscopic ones that finally led to the death of the injured person.

Conclusions

In the Institute of Forensic Medicine of Craiova, there were recorded 1005 deaths by TBI between 2011 and 2017 (971 cases in adults and 34 cases in individuals aged 0-18 years old). In both groups, the majority were males from the rural area. Most cases in adults were caused by fallings – 437 (45% of the violent deaths due to TBI), followed by car accidents – 307 (31.61%) cases. In children, 26 (76.47%) cases were the result of car accidents, with only one case of falling. Because of human aggressions, there were recorded 80 (8.23%) cases in adults and one (3%) case of death in children. Most positive blood alcohol contents found in the adult group were the result of car accidents, followed by fallings, an aspect also found in the group of children (two cases of car accidents). Of the patients with a recorded GCS score at admission, a high

number of adults presented third and fourth degree comas at admission (343 cases, representing 54.53%) but there were also 34 (5.41%) cases of deaths who presented a preserved conscious state at admission (GCS score 15). In children, all the patients presented third and fourth degree comas at admission. In both groups, most of the patients presented cranial fractures, namely 706 adults and 27 under-aged individuals. Of the adult patients with cranial fracture, 185 presented extradural hemorrhages/ hematomas under the fracture line, but there were also four cases of extradural hemorrhages in the absence of cranial fracture. In children, there was found a single case of extradural hemorrhage below the fracture (high adherence of dura mater in children). Seventy-eight percent of the adult patients presented subdural hemorrhages/ hematomas, most of them (90.5%) acute and subacute forms. The 15 subdural hematomas found in children were also acute and subacute forms. Most patients presented brain contusions, of which an important percentage with localization in the cerebral trunk. Also, in 126 (12.97%) cases of adults and one case of a child, the necropsy examination highlighted the presence of intra-parenchymatous hematomas in the contusion foci. In approximately 50% of deaths by TBI, there were recorded brain lacerations.

Conflict of interests

The authors declare that they have no conflict of interests.

Authors' contribution

Răzvan Ștefan Țolescu & Marian Valentin Zorilă have contributed equally to this paper.

References

- [1] Maas AIR, Menon DK, Adelson PD, Andelic N, Bell MJ, Belli A, Bragge P, Brazinova A, Büki A, Chesnut RM, Citerio G, Coburn M, Cooper DJ, Crowder AT, Czeiter E, Czosnyka M, Diaz-Arrastia R, Dreier JP, Duhaime AC, Ercole A, van Essen TA, Feigin VL, Gao G, Giacino J, Gonzalez-Lara LE, Gruen RL, Gupta D, Hartings JA, Hill S, Jiang JY, Ketharanathan N, Kompanje EJO, Lanyon L, Laureys S, Lecky F, Levin H, Lingsma HF, Maegele M, Majdan M, Manley G, Marsteller J, Mascia L, McFadyen C, Mondello S, Newcombe V, Palotie A, Parizel PM, Peul W, Piercy J, Polinder S, Puybasset L, Rasmussen TE, Rossaint R, Smielewski P, Söderberg J, Stanworth SJ, Stein MB, von Steinbüchel N, Stewart W, Steyerberg EW, Stocchetti N, Synnot A, Te Ao B, Tenovuo O, Theadom A, Tibboel D, Videtta W, Wang KKW, Williams WH, Wilson L, Yaffe K; InTBIR Participants and Investigators. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. Lancet Neurol, 2017, . 16(12):987–1048. https://doi.org/10.1016/S1474-4422(17)30 371-X PMID: 29122524
- [2] Dewan MC, Rattani A, Gupta S, Baticulon RE, Hung YC, Punchak M, Agrawal A, Adeleye AO, Shrime MG, Rubiano AM, Rosenfeld JV, Park KB. Estimating the global incidence of traumatic brain injury. J Neurosurg, 2019, 130(4):1080–1097. https://doi.org/10.3171/2017.10.JNS17352 PMID: 29701556
- [3] Hyder AA, Wunderlich CA, Puvanachandra P, Gururaj G, Kobusingye OC. The impact of traumatic brain injuries: a global perspective. NeuroRehabilitation, 2007, 22(5):341–353. https:// doi.org/10.3233/NRE-2007-22502 PMID: 18162698
- [4] Coronado VG, McGuire LC, Sarmiento K, Bell J, Lionbarger MR, Jones CD, Geller AI, Khoury N, Xu L. Trends in traumatic brain injury in the U.S. and the public health response: 1995– 2009. J Safety Res, 2012, 43(4):299–307. https://doi.org/10. 1016/j.jsr.2012.08.011 PMID: 23127680
- [5] Langlois JA, Rutland-Brown W, Wald MM. The epidemiology and impact of traumatic brain injury: a brief overview. J Head Trauma Rehabil, 2006, 21(5):375–378. https://doi.org/10.10 97/00001199-200609000-00001 PMID: 16983222

- [6] Stocchetti N, Maas AIR. Traumatic intracranial hypertension. N Engl J Med, 2014, 371(10):972. https://doi.org/10.1056/ NEJMra1208708 PMID: 24869722
- [7] Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. Lancet, 1997, 349(9064):1498–1504. https://doi.org/10.1016/ S0140-6736(96)07492-2 PMID: 9167458
- [8] Zhao J, Xu C, Cao H, Zhang L, Wang X, Chen S. Identification of target genes in neuroinflammation and neurodegeneration after traumatic brain injury in rats. PeerJ, 2019, 7:e8324. https://doi.org/10.7717/peerj.8324 PMID: 31875163 PMCID: PMC6925952
- [9] Masson F, Thicoipe M, Aye P, Mokni T, Senjean P, Schmitt V, Dessalles PH, Cazaugade M, Labadens P; Aquitaine Group for Severe Brain Injuries Study. Epidemiology of severe brain injuries: a prospective population-based study. J Trauma, 2001, 51(3):481–489. https://doi.org/10.1097/00005373-20010900 0-00010 PMID: 11535895
- [10] Walder B, Haller G, Rebetez MM, Delhumeau C, Bottequin E, Schoettker P, Ravussin P, Brodmann Maeder M, Stover JF, Zürcher M, Haller A, Wäckelin A, Haberthür C, Fandino J, Haller CS, Osterwalder J. Severe traumatic brain injury in a high-income country: an epidemiological study. J Neurotrauma, 2013, 30(23):1934–1942. https://doi.org/10.1089/neu.2013. 2955 PMID: 23822874
- [11] Mauritz W, Brazinova A, Majdan M, Leitgeb J. Epidemiology of traumatic brain injury in Austria. Wien Klin Wochenschr, 2014, 126(1–2):42–52. https://doi.org/10.1007/s00508-013-0456-6 PMID: 24249325 PMCID: PMC3904034
- [12] Hutchison MG, Lawrence DW, Cusimano MD, Schweizer TA. Head trauma in mixed martial arts. Am J Sports Med, 2014, 42(6):1352–1358. https://doi.org/10.1177/0363546514526151 PMID: 24658345
- [13] Song SY, Lee SK, Eom KS; KNTDB Investigators. Analysis of mortality and epidemiology in 2617 cases of traumatic brain injury: Korean Neuro-Trauma Data Bank System 2010–2014. J Korean Neurosurg Soc, 2016, 59(5):485–491. https://doi.org/ 10.3340/jkns.2016.59.5.485 PMID: 27651867 PMCID: PMC 5028609
- [14] Chen M, Soosaipillai A, Fraser DD, Diamandis EP. Discovery of novel plasma biomarker ratios to discriminate traumatic brain injury. F1000Res, 2019, 8:1695. https://doi.org/10.12 688/f1000research.20445.1 PMID: 32047603 PMCID: PMC 6979479
- [15] Signoretti S, Lazzarino G, Tavazzi B, Vagnozzi R. The pathophysiology of concussion. PM R, 2011, 3(10 Suppl 2):S359–S368. https://doi.org/10.1016/j.pmrj.2011.07.018 PMID: 22035678
- [16] Mckee AC, Daneshvar DH. The neuropathology of traumatic brain injury. Handb Clin Neurol, 2015, 127:45–66. https:// doi.org/10.1016/B978-0-444-52892-6.00004-0 PMID: 25702209 PMCID: PMC4694720
- [17] Ritter AC, Wagner AK, Fabio A, Pugh MJ, Walker WC, Szaflarski JP, Zafonte RD, Brown AW, Hammond FM, Bushnik T, Johnson-Greene D, Shea T, Krellman JW, Rosenthal JA, Dreer LE. Incidence and risk factors of posttraumatic seizures following traumatic brain injury: a Traumatic Brain Injury Model Systems Study. Epilepsia, 2016, 57(12):1968–1977. https:// doi.org/10.1111/epi.13582 PMID: 27739577
- [18] Puntambekar SS, Saber M, Lamb BT, Kokiko-Cochran ON. Cellular players that shape evolving pathology and neurodegeneration following traumatic brain injury. Brain Behav Immun, 2018, 71:9–17. https://doi.org/10.1016/j.bbi.2018.03. 033 PMID: 29601944
- [19] Zaloshnja E, Miller T, Langlois JA, Selassie AW. Prevalence of long-term disability from traumatic brain injury in the civilian population of the United States, 2005. J Head Trauma Rehabil, 2008, 23(6):394–400. https://doi.org/10.1097/01.HTR.00003 41435.52004.ac PMID: 19033832
- [20] Ng SY, Lee AYW. Traumatic brain injuries: pathophysiology and potential therapeutic targets. Front Cell Neurosci, 2019, 13:528. https://doi.org/10.3389/fncel.2019.00528 PMID: 31827423 PMCID: PMC6890857
- [21] Coronado VG, Xu L, Basavaraju SV, McGuire LC, Wald MM, Faul MD, Guzman BR, Hemphill JD; Centers for Disease Control and Prevention (CDC). Surveillance for traumatic brain injuryrelated deaths – United States, 1997–2007. MMWR Surveill Summ, 2011, 60(5):1–32. PMID: 21544045

- [22] Wang D, Zhao W, Wheeler K, Yang G, Xiang H. Unintentional fall injuries among US children: a study based on the National Emergency Department Sample. Int J Inj Contr Saf Promot, 2013, 20(1):27–35. https://doi.org/10.1080/17457300.2012. 656316 PMID: 22308963
- [23] Taylor CA, Bell JM, Breiding MJ, Xu L. Traumatic brain injuryrelated emergency department visits, hospitalizations, and deaths – United States, 2007 and 2013. MMWR Surveill Summ, 2017, 66(9):1–16. https://doi.org/10.15585/mmwr.ss6609a1 PMID: 28301451 PMCID: PMC5829835
- [24] Park E, Bell JD, Baker AJ. Traumatic brain injury: can the consequences be stopped? CMAJ, 2008, 178(9):1163–1170. https://doi.org/10.1503/cmaj.080282 PMID: 18427091 PMCID: PMC2292762
- [25] Risdall JE, Menon DK. Traumatic brain injury. Philos Trans R Soc Lond B Biol Sci, 2011, 366(1562):241–250. https://doi. org/10.1098/rstb.2010.0230 PMID: 21149359 PMCID: PMC 3013429
- [26] Faul M, Xu L, Wald MM, Coronado VG. Traumatic brain injury in the United States: emergency department visits, hospitalizations and deaths 2002–2006. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Injury Prevention and Control, Division of Injury Response, Atlanta, GA, USA, March 2010, https://www.cdc.gov/traumaticbraininjury/pdf/blue_book.pdf.
- [27] Khellaf A, Khan DZ, Helmy A. Recent advances in traumatic brain injury. J Neurol, 2019, 266(11):2878–2889. https://doi. org/10.1007/s00415-019-09541-4 PMID: 31563989 PMCID: PMC6803592
- [28] Collie A, Keating C, Pezzullo L, Gabbe B, Cooper J, Brown D, Olver J, McCartin F, Trethewey P. Brain and spinal cord injury in Australia – economic cost and burden of disease. IP Safety 2010 Abstracts, Inj Prev, 2010, 16(Suppl 1):A25– A26. https://doi.org/10.1136/ip.2010.029215.92
- [29] Corso P, Finkelstein E, Miller T, Fiebelkorn I, Zaloshnja E. Incidence and lifetime costs of injuries in the United States. Inj Prev, 2006, 12(4):212–218. https://doi.org/10.1136/ip.2005. 010983 PMID: 16887941 PMCID: PMC2586784
- [30] Tagliaferri F, Compagnone C, Korsic M, Servadei F, Kraus J. A systematic review of brain injury epidemiology in Europe. Acta Neurochir (Wien), 2006, 148(3):255–268; discussion 268. https://doi.org/10.1007/s00701-005-0651-y PMID: 16311842
- [31] Angeloni C, Prata C, Dalla Sega FV, Piperno R, Hrelia S. Traumatic brain injury and NADPH oxidase: a deep relationship. Oxid Med Cell Longev, 2015, 2015:370312. https://doi.org/10. 1155/2015/370312 PMID: 25918580 PMCID: PMC4397034
- [32] Morganti-Kossmann MC, Satgunaseelan L, Bye N, Kossmann T. Modulation of immune response by head injury. Injury, 2007, 38(12):1392–1400. https://doi.org/10.1016/j.injury.2007.10.005 PMID: 18048036
- [33] Saatman KE, Duhaime AC, Bullock R, Maas AI, Valadka A, Manley GT; Workshop Scientific Team and Advisory Panel Members. Classification of traumatic brain injury for targeted therapies. J Neurotrauma, 2008, 25(7):719–738. https://doi. org/10.1089/neu.2008.0586 PMID: 18627252 PMCID: PMC 2721779
- [34] Donkin JJ, Vink R. Mechanisms of cerebral edema in traumatic brain injury: therapeutic developments. Curr Opin Neurol, 2010, 23(3):293–299. https://doi.org/10.1097/WCO.0b013e3 28337f451 PMID: 20168229
- [35] Motori E, Puyal J, Toni N, Ghanem A, Angeloni C, Malaguti M, Cantelli-Forti G, Berninger B, Conzelmann KK, Götz M, Winklhofer KF, Hrelia S, Bergami M. Inflammation-induced alteration of astrocyte mitochondrial dynamics requires autophagy for mitochondrial network maintenance. Cell Metab, 2013, 18(6):844–859. https://doi.org/10.1016/j.cmet.2013.11. 005 PMID: 24315370
- [36] Beitchman JA, Griffiths DR, Hur Y, Ogle SB, Bromberg CE, Morrison HW, Lifshitz J, Adelson PD, Thomas TC. Experimental traumatic brain injury induces chronic glutamatergic dysfunction in amygdala circuitry known to regulate anxietylike behavior. Front Neurosci, 2020, 13:1434. https://doi.org/ 10.3389/fnins.2019.01434 PMID: 32038140 PMCID: PMC 6985437
- [37] Kokiko-Cochran ON, Godbout JP. The inflammatory continuum of traumatic brain injury and Alzheimer's disease. Front Immunol, 2018, 9:672. https://doi.org/10.3389/fimmu.2018.00672 PMID: 29686672 PMCID: PMC5900037

- [38] Araki T, Yokota H, Morita A. Pediatric traumatic brain injury: characteristic features, diagnosis, and management. Neurol Med Chir (Tokyo), 2017, 57(2):82–93. https://doi.org/10.2176/ nmc.ra.2016-0191 PMID: 28111406 PMCID: PMC5341344
- [39] Anderson V, Brown S, Newitt H, Hoile H. Educational, vocational, psychosocial, and quality-of-life outcomes for adult survivors of childhood traumatic brain injury. J Head Trauma Rehabil, 2009, 24(5):303–312. https://doi.org/10.1097/HTR.0b013e3 181ada830 PMID: 19858964
- [40] Yeates KO, Gerhardt CA, Bigler ED, Abildskov T, Dennis M, Rubin KH, Stancin T, Taylor HG, Vannatta K. Peer relationships of children with traumatic brain injury. J Int Neuropsychol Soc, 2013, 19(5):518–527. https://doi.org/10.1017/S13556177120 01531 PMID: 23340166
- [41] Scholten AC, Haagsma JA, Cnossen MC, Olff M, van Beeck EF, Polinder S. Prevalence of and risk factors for anxiety and depressive disorders after traumatic brain injury: a systematic review. J Neurotrauma, 2016, 33(22):1969–1994. https://doi.org/ 10.1089/neu.2015.4252 PMID: 26729611
- [42] Majdan M, Plancikova D, Brazinova A, Rusnak M, Nieboer D, Feigin V, Maas A. Epidemiology of traumatic brain injuries in Europe: a cross-sectional analysis. Lancet Public Health, 2016, 1(2):e76–e83. https://doi.org/10.1016/S2468-2667(16) 30017-2 PMID: 29253420
- [43] Andelic N, Anke A, Skandsen T, Sigurdardottir S, Sandhaug M, Ader T, Roe C. Incidence of hospital-admitted severe traumatic brain injury and in-hospital fatality in Norway: a national cohort study. Neuroepidemiology, 2012, 38(4):259–267. https://doi. org/10.1159/000338032 PMID: 22678449
- [44] Masson F, Thicoipe M, Mokni T, Aye P, Erny P, Dabadie P; Aquitaine Group for Severe Brain Injury Study. Epidemiology of traumatic comas: a prospective population-based study. Brain Inj, 2003, 17(4):279–293. https://doi.org/10.1080/0269 905021000030805 PMID: 12637181
- [45] Wu X, Hu J, Zhuo L, Fu C, Hui G, Wang Y, Yang W, Teng L, Lu S, Xu G. Epidemiology of traumatic brain injury in eastern China, 2004: a prospective large case study. J Trauma, 2008, 64(5):1313–1319. https://doi.org/10.1097/TA.0b013e318165c 803 PMID: 18469656
- [46] Carron SF, Alwis DS, Rajan R. Traumatic brain injury and neuronal functionality changes in sensory cortex. Front Syst Neurosci, 2016, 10:47. https://doi.org/10.3389/fnsys.2016.0 0047 PMID: 27313514 PMCID: PMC4889613
- [47] Vella MA, Crandall ML, Patel MB. Acute management of traumatic brain injury. Surg Clin North Am, 2017, 97(5):1015–1030. https://doi.org/10.1016/j.suc.2017.06.003 PMID: 28958355 PMCID: PMC5747306
- [48] Brazinova A, Rehorcikova V, Taylor MS, Buckova V, Majdan M, Psota M, Peeters W, Feigin V, Theadom A, Holkovic L, Synnot A. Epidemiology of traumatic brain injury in Europe: a living systematic review. J Neurotrauma, 2018, Dec 19. https:// doi.org/10.1089/neu.2015.4126 PMID: 26537996
- [49] Florou C, Zorilă AL, Zorilă MV, Marinescu MA, Andrei CM, Păvăloiu RM, Mogoantă L, Zăvoi RE. Clinico-statistical and morphological aspects of severe traumatic brain injuries. Rom J Morphol Embryol, 2016, 57(2):391–400. PMID: 27516010
- [50] Zorilă AL, Zorilă MV, Marinaş MC, Ţolescu RŞ, Zorilă GL, Florou C, Neamţu MC, Knieling A, Busuioc CJ. Evaluation of

brain injuries in children deceased due to head trauma. Rom J Morphol Embryol, 2017, 58(4):1417–1428. PMID: 29556636

- [51] Shahin H, Gopinath SP, Robertson CS. Influence of alcohol on early Glasgow Coma Scale in head-injured patients. J Trauma, 2010, 69(5):1176–1181; discussion 1181. https://doi.org/10. 1097/TA.0b013e3181edbd47 PMID: 21068620 PMCID: PMC 3485579
- [52] Scheenen ME, de Koning ME, van der Horn HJ, Roks G, Yilmaz T, van der Naalt J, Spikman JM. Acute alcohol intoxication in patients with mild traumatic brain injury: characteristics, recovery, and outcome. J Neurotrauma, 2016, 33(4):339–345. https://doi.org/10.1089/neu.2015.3926 PMID: 26230219
- [53] Grzelczak AC, Ceccon A, Guetter CR, Pimentel SK. Evaluation of traumatic brain injury patients with signs of alcohol intoxication. Rev Col Bras Cir, 2019, 46(5):e20192272. https://doi.org/10. 1590/0100-6991e-20192272 PMID: 31778395
- [54] Posti JP, Sankinen M, Sipilä JOT, Ruuskanen JO, Rinne J, Rautava P, Kytö V. Fatal traumatic brain injuries during 13 years of successive alcohol tax increases in Finland – a nationwide population-based registry study. Sci Rep, 2019, 9(1):5419. https://doi.org/10.1038/s41598-019-41913-8 PMID: 30931989 PMCID: PMC6443785
- [55] Fenn NE 3rd, Sierra CM. Hyperosmolar therapy for severe traumatic brain injury in pediatrics: a review of the literature. J Pediatr Pharmacol Ther, 2019, 24(6):465–472. https://doi. org/10.5863/1551-6776-24.6.465 PMID: 31719807 PMCID: PMC6836706
- [56] Liew TYS, Ng JX, Jayne CHZ, Ragupathi T, Teo CKA, Yeo TT. Changing demographic profiles of patients. with traumatic brain injury: an aging concern. Front Surg, 2019, 6:37. https:// doi.org/10.3389/fsurg.2019.00037 PMID: 31334245 PMCID: PMC6618294
- [57] Kehoe A, Smith JE, Bouamra O, Edwards A, Yates D, Lecky F. Older patients with traumatic brain injury present with a higher GCS score than younger patients for a given severity of injury. Emerg Med J, 2016, 33(6):381–385. https://doi.org/10.1136/ emermed-2015-205180 PMID: 26825613
- [58] Monsef Kasmaei V, Asadi P, Zohrevandi B, Raouf MT. An epidemiologic study of traumatic brain injuries in emergency department. Emerg (Tehran), 2015, 3(4):141–145. PMID: 26495403 PMCID: PMC4608347
- [59] Johnson VE, Stewart W. Traumatic brain injury: age at injury influences dementia risk after TBI. Nat Rev Neurol, 2015, 11(3): 128–130. https://doi.org/10.1038/nrneurol.2014.241 PMID: 25534914
- [60] Lueckel SN, Teno JM, Stephen AH, Benoit E, Kheirbek T, Adams CA Jr, Cioffi WG, Thomas KS. Population of patients with traumatic brain injury in skilled nursing facilities: a decade of change. J Head Trauma Rehabil, 2019, 34(1):E39–E45. https:// doi.org/10.1097/HTR.00000000000393 PMID: 29863612 PMCID: PMC6274633
- [61] Ruge T, Carlsson AC, Hellstrom M, Wihlborg P, Undén J. Is medical urgency of elderly patients with traumatic brain injury underestimated by emergency department triage? Ups J Med Sci, 2020, 125(1):58–63. https://doi.org/10.1080/03009 734.2019.1706674 PMID: 31986958 PMCID: PMC7054978

Corresponding authors

Mircea-Sebastian Şerbănescu, Lecturer, MD, PhD, Department of Medical Informatics and Biostatistics, University of Medicine and Pharmacy of Craiova, 2 Petru Rareş Street, 200349 Craiova, Dolj County, Romania; Phone +40745–766 610, e-mail: mircea_serbanescu@yahoo.com

George Lucian Zorilă, University Assistant, MD, PhD, Department of Obstetrics and Gynecology, University of Medicine and Pharmacy of Craiova, 2 Petru Rareş Street, 200349 Craiova, Dolj County, Romania; Phone +40741–236 305, e-mail: zorilalucian@gmail.com