

Underestimated Traumatic Brain Injury in Multiple Injured Patients; Is the Glasgow Coma Scale a Reliable Tool?

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Received date: March 16, 2017; Accepted date: April 12, 2017; Published date: April 20, 2017

Citation: Mica L, Jensen KO, Keller C, Wirth SH, Simmen H, et al. (2017) Underestimated Traumatic Brain Injury in Multiple Injured Patients, is the Glasgow Coma Scale a Reliable Tool? Trauma Acute Care 2: 42.

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Abstract

Background: Traumatic brain injuries are common in multiple injured patients. Here, the impact of traumatic brain injuries according age and mortality and predictive value was investigated.

Methods: Totally 2952 patients were included into this sample. The inclusion criteria were age ≥ 16 years and an injury severity score >16 . The patient sample was divided into 8 groups according to the age decades. Data were analyzed using IBM SPSS® for Windows version 22.0; analysis of variance was used for continuous normally distributed data and χ^2 test was used for categorical data. The predictive quality for death of the different injuries was analyzed using receiver operating characteristic curves and is given as area under the curve (AUC). Independent predictivity was analyzed by binary logistic regression. Data were considered significant if $p < 0.05$. Data are presented as the mean \pm standard deviation.

Results: The analysis revealed a discrepancy in the predictive quality of GCS (AUC: 0.223, $p < 0.001$) and the abbreviated injury score (AIS) for the head (AUC: 0.764, $p < 0.001$). The highest predictive quality of the AIS head for death was shown in the decade of 36-45 years (AUC: 0.832, $p < 0.001$). The traumatic brain injury revealed as an independent predictor of death ($p < 0.001$). The mortality rate was increasing according to the age significantly within the decades ($p < 0.001$).

Conclusion: Even if the initial GCS indicates an intermediate traumatic brain injury, attention should be given to aggravating dynamics of the traumatic brain injury.

Level of evidence: Retrospective cohort study: Level II.

Keywords: Cranio-cerebral trauma; Glasgow coma scale; Age; Multiple injuries

Abbreviations:

AIS: Abbreviated Injury Severity Score; ANOVA: Analysis of Variance; APACHE II: Acute Physiology and Chronic Health Evaluation; ATLS: Advanced Trauma Life Support; AUC: Area under the Curve; CT: Computed Tomography; GCS: Glasgow Coma Scale; IBM: International Business Machines Corporation; ISS: Injury Severity Score; NISS: New Injury Severity Score; ROC: Receiver Operating Curve; SAPS: Simplified Acute Physiology Score; SPSS: Statistical Package for the Social Sciences; TBI: Traumatic Brain Injury; TRISS: The Trauma Score-Injury Severity Score; HKT: Hematocrit; PT: Prothrombin Time.

Introduction

Multiple trauma is the main cause for early death in the productive young adult. Mostly dangerous activities and dangerous behaviour lead to the multiple injury pattern very often associated with early death. Traumatic brain-scall injuries isolated or in combination with multiple injuries have a high incidence overall the world. The World Health Organisation estimates 150 to 300 new cases in 100,000 inhabitants per year [1]. The average lethality of thaumatic brain-scall injuries in being estimated 1-6.2% all over the world [1]. The range of complication after traumatic brain injuries is wide: seizures, sleep disorders, recurrent nausea and vomiting, impaired speech, ataxia, agitation, depression, anxiety, aggression, and restlessness may occur and severely handicap the patient [2]. The initial treatment according to Advanced Trauma Life Support (ATLS) might distort the dynamics of the Glasgow Coma Scale (GCS) due to airway management or oro-facial trauma and may fail to assess the cranio-cerebral injury correctly [3]. The treatment of multiple injured patients with traumatic brain injuries is expensive and time consuming. A good and clear management does not provide any guarantee for success and the patients suffer very often residual neurologic deficits. These deficits complicate the reintegration into the society and the return to the initial employment. Anticipating the posttraumatic

dynamics of the traumatic brain injury the thesis was elaborated to identify the main killer according to the life span decade and to analyze the dominating injury pattern in the setting of multiple trauma especially the role of traumatic brain injury.

Methods

Definition

Traumatic brain injury (TBI) is an acquired injury to the brain that occurs from sudden trauma to the head [2].

Patient sample

In this retrospective cohort study, we included 2952 patients with multiple trauma admitted to the trauma bay of the University Hospital of Zürich (Switzerland) acquired from the

year 2000 to 2014. The inclusion criteria were an injury severity score (ISS) >16 points, age \geq 16 years, and admission within at least 24 h of incurring the multiple trauma. The patient sample was subdivided into eight groups according to life span decades (Table 1).

Diagnostic protocol

Unstable patients underwent resuscitative procedures according to the ATLS guidelines of the American College of Surgeons. Hemodynamically stable patients received diagnoses according to clinical findings or whole-body computed tomography (CT) in uncertain situations. Hemodynamically unstable patients received focus-oriented diagnostics with immediate problem solving according to the ATLS and Definitive Surgical Trauma Care guidelines [3].

Table 1: Characteristics of the patient sample at admission.

Group (a)	16-25	26-35	36-45	46-55	56-65	66-75	76-85	>85	p-value
Age (a)	20.5 \pm 2.7	30.3 \pm 2.8	40.6 \pm 2.8	50.5 \pm 2.9	60.4 \pm 2.8	70.2 \pm 2.9	80.0 \pm 2.7	88.3 \pm 2.3	<0.00*
Sex (male/female)	484/126	405/115	396/123	316/116	270/77	179/91	95/108	26/25	<0.00†
GCS accident	9.1 \pm 4.9	10.3 \pm 4.9	10.5 \pm 4.8	10.1 \pm 5.0	9.8 \pm 4.9	9.9 \pm 4.9	9.5 \pm 4.7	10.4 \pm 4.3	<0.00*
GCS admission	7.7 \pm 5.4	9.0 \pm 5.5	9.4 \pm 5.5	9.0 \pm 5.5	8.6 \pm 5.5	8.5 \pm 5.5	8.0 \pm 5.3	8.7 \pm 5.2	<0.00*
Lactate (mmol/L)	3.2 \pm 2.5	3.0 \pm 2.5	3.3 \pm 3.0	3.1 \pm 2.6	2.8 \pm 2.2	2.8 \pm 2.5	2.9 \pm 2.5	3.0 \pm 2.9	0.329*
Base Excess (mmol/L)	-4.3 \pm 5.1	-3.7 \pm 5.1	-4.3 \pm 6.0	-4.0 \pm 5.5	-3.2 \pm 4.6	-3.3 \pm 5.9	-3.1 \pm 5.4	-4.4 \pm 8.0	0.052*
HKT (%)	33.4 \pm 8.9	33.7 \pm 8.6	33.7 \pm 8.5	33.2 \pm 8.5	33.6 \pm 8.0	33.8 \pm 8.2	32.5 \pm 8.3	32.2 \pm 8.7	0.757*
PT (%)	74.6 \pm 21.5	79.4 \pm 22.1	82.2 \pm 19.5	82.3 \pm 20.7	80.5 \pm 22.8	80.5 \pm 22.5	70.1 \pm 27.6	67.0 \pm 25.0	<0.001*
Platelets (x10 ³ / μ L)	740 \pm 120	214 \pm 87	212 \pm 86	203 \pm 79	199 \pm 80	204 \pm 92	219 \pm 206	212 \pm 130	0.890*
APACHE II	14.6 \pm 8.5	12.9 \pm 9.0	12.8 \pm 8.6	14.6 \pm 8.6	16.1 \pm 8.9	17.9 \pm 8.7	19.7 \pm 8.0	18.4 \pm 8.0	<0.00*
SAPS II	24.0 \pm 15.6	21.1 \pm 16.2	23.1 \pm 14.0	27.8 \pm 15.3	32.0 \pm 15.8	34.0 \pm 15.1	40.3 \pm 15.0	37.2 \pm 14.8	<0.00*
TRISS	0.705 \pm 0.294	0.758 \pm 0.274	0.777 \pm 0.264	0.764 \pm 0.279	0.783 \pm 0.257	0.761 \pm 0.28	0.741 \pm 0.283	0.723 \pm 0.309	<0.00*
ISS	29.9 \pm 14.4	28.9 \pm 13.4	28.5 \pm 13.5	28.1 \pm 14.1	27.7 \pm 13.8	27.2 \pm 14.8	28.7 \pm 16.9	30.9 \pm 19.2	0.046*
NISS	39.7 \pm 17.4	37.2 \pm 16.3	37.8 \pm 16.0	37.1 \pm 17.0	38.6 \pm 16.2	37.9 \pm 18.0	38.8 \pm 18.0	43.3 \pm 19.9	0.072*

Data are given as mean \pm SD, Kolmogorov Smirnov $p > 0.05$ for all groups. *ANOVA, † χ^2 , significant if $p < 0.05$.

Scoring systems

The overall physiological impairment was evaluated from the acute physiology and chronic health evaluation (APACHE II) score of the patient at admission [4]. The ISS and the new injury severity scale (NISS) were used to define the severity of trauma [5,6]. The abbreviated injury scale (AIS; 2005 version) was used to describe injuries in specific anatomical regions. The Trauma

Score - Injury Severity Score (TRISS) was used to analyse the probability of death in the patient sample at admission [7]. The Simplified Acute Physiology Score (SAPS II) was calculated according to Le Gall at admission [8].

Laboratory parameters

Blood lactate levels, pH, and hematocrits were measured at intervals using a blood gas analyzer (ABL800 Flex, Radiometer, Thalwil, Switzerland). The prothrombin time was measured using a standardized method [9].

Statistical analysis

Data are presented as the mean \pm standard deviation for continuous variables and as percentages for categorical variables. Two-tailed Kolmogorov–Smirnov test was used for normality testing, and if $p > 0.05$, the data were considered to be normally distributed. The data for the groups were compared

using a χ^2 test and Kruskal–Wallis test for categorical data and one-way analysis of variance (ANOVA) for continuous data. If a Kolmogorov–Smirnov test showed $p < 0.05$, Mann–Whitney U test was used for continuous data. Results were considered significant if $p < 0.05$. The predictive quality of the different injuries was reported as the area under (AUC) the receiver operator characteristic curve (ROC). Independent predictivity was analyzed using binary logistic regression. The goodness of fit for the binary logistic regression was analyzed by the Hosmer–Lemeshow test and considered as good if $p > 0.05$. Data were analyzed using IBM SPSS® Statistics for Windows software (version 22.0; IBM Corp., Armonk, NY, USA).

Table 2: Injury pattern according to each decade of life.

Group (a)	AIS Head	AIS Face	AIS Thorax	AIS Abdomen	AIS Spine	AIS Extr.	AIS Pelvis	AIS Skin
16-25	3.0 \pm 1.9	0.6 \pm 1.1	1.7 \pm 1.7	1.3 \pm 1.9	0.8 \pm 1.4	1.5 \pm 1.5	0.6 \pm 1.2	0.5 \pm 0.8
26-35	2.6 \pm 2.0	0.6 \pm 1.1	1.8 \pm 1.7	1.3 \pm 1.9	0.9 \pm 1.4	1.6 \pm 1.5	0.7 \pm 1.3	0.6 \pm 0.9
36-45	2.7 \pm 2.0	0.6 \pm 1.1	1.7 \pm 1.7	1.2 \pm 1.8	0.9 \pm 1.5	1.4 \pm 1.5	0.6 \pm 1.2	0.4 \pm 0.8
46-55	2.6 \pm 2.0	0.6 \pm 1.1	1.8 \pm 1.7	1.0 \pm 1.7	0.9 \pm 1.4	1.4 \pm 1.4	0.5 \pm 1.2	0.4 \pm 0.8
56-65	2.9 \pm 2.0	0.5 \pm 1.0	1.6 \pm 1.7	0.9 \pm 1.6	0.7 \pm 1.3	1.4 \pm 1.5	0.5 \pm 1.2	0.5 \pm 0.8
66-75	3.2 \pm 1.9	0.5 \pm 0.9	1.5 \pm 1.7	0.6 \pm 1.3	0.7 \pm 1.3	1.0 \pm 1.3	0.5 \pm 1.1	0.4 \pm 0.6
76-85	3.3 \pm 1.9	0.4 \pm 0.9	1.4 \pm 1.7	0.6 \pm 1.4	0.6 \pm 1.2	1.1 \pm 1.4	0.5 \pm 1.1	0.5 \pm 0.8
>85	3.6 \pm 1.9	0.4 \pm 0.9	1.1 \pm 1.6	0.5 \pm 1.3	0.7 \pm 1.4	0.8 \pm 1.3	0.7 \pm 1.3	0.6 \pm 0.8
p-value	<0.001	0.103	0.004	<0.001	0.422	<0.001	0.537	0.020

Given is the mean AIS \pm SD. $p > 0.05$ for Kolmogorov Smirnov for all data, ANOVA significant if $p < 0.05$

Results

Patient sample

Over all the groups a double peaked situation has been observed; an increase or decrease of the parameters at very young ages and again an increase or decrease of the parameters at older ages (Table 1). Interestingly the GCS score was decreasing in the older groups and increased in the age group >85 years (Table 1). As expected the APACHE II score was certainly increasing according the age group as a function of medical history and age (Table 1).

Injury pattern

The analysis of the different AIS scores in the different anatomical regions revealed mostly significant decrease as a function of the age and if not significant a tendency to decrease was found (Table 2). However, the AIS for the head revealed opposite dynamics of the severity. The analysis revealed significantly increasing AIS for the head as a function of the age (Table 2).

Table 3: Shown is the AUC of ROC for each injured anatomical region according to the death in each age group.

Group (a)	AIS Head	AIS Face	AIS Thorax	AIS Abdomen	AIS Spine	AIS Extr.	AIS Pelvis	AIS Skin
Total	0.764/ <0.001	0.467/0.006	0.474/0.028	0.477/0.054	0.448/ <0.001	0.399/<0.001	0.495/0.705	0.451/<0.001
16-25	0.764/ <0.001	0.468/0.007	0.474/0.032	0.477/0.057	0.448/ <0.001	0.400/<0.001	0.496/0.737	0.450/<0.001
26-35	0.786/ <0.001	0.531/0.359	0.510/0.764	0.479/0.529	0.428/0.032	0.419/0.015	0.499/0.988	0.485/0.649
36-45	0.832/ <0.001	0.450/0.097	0.432/0.024	0.417/0.006	0.437/0.037	0.353/<0.001	0.470/0.320	0.456/0.146

46-55	0.744/ <0.001	0.469/0.354	0.481/0.567	0.527/0.430	0.452/0.150	0.402/0.004	0.488/0.717	0.440/0.072
56-65	0.780/ <0.001	0.481/0.586	0.472/0.420	0.469/0.356	0.438/0.069	0.390/0.001	0.494/0.866	0.429/0.037
66-75	0.699/ <0.001	0.427/0.044	0.510/0.774	0.516/0.667	0.480/0.580	0.493/0.838	0.509/0.804	0.449/0.156
76-85	0.757/ <0.001	0.469/0.448	0.446/0.196	0.539/0.343	0.418/0.050	0.374/0.002	0.510/0.818	0.407/0.025
>85	0.719/0.017	0.587/0.347	0.621/0.188	0.513/0.886	0.563/0.493	0.508/0.929	0.561/0.507	0.439/0.507
Data are given as AUC/p-value								

Predictive quality

To test the predictive quality of each AIS for the death of the patients ROCs were performed with the according p-values (Table 3). The reason why the highest AUC (0.832) was reached at the age of 36-45 years (Table 3) together with a lower AIS of

2.7 ± 2.0 (Table 2) remains unclear. The analysis showed the traumatic brain injury measured by AIS as the killer number one in multiple trauma conditions compared to the GCS. Here, the AUC was poor (Table 4).

Table 4: Shown is the AUC of ROC for GCS on trauma side and GCS at admission according to the death in each age group.

Group (a)	GCS accident	GCS admission
Total	0.223/<0.001	0.247/<0.001
16-25	0.198/<0.001	0.252/<0.001
26-35	0.201/<0.001	0.246/<0.001
36-45	0.134/<0.001	0.174/<0.001
46-55	0.188/<0.001	0.214/<0.001
56-65	0.228/<0.001	0.233/<0.001
66-75	0.288/<0.001	0.266/<0.001
76-85	0.267/<0.001	0.253/<0.001
>85	0.344/0.099	0.365/0.092
Data are given as AUC/p-value		

Independent predictors

The binary logistic regression of the patient sample and death as outcome parameter showed a clear picture over all age groups for AIS head. For almost all age groups the AIS head was an independent predictor of death with high odd's ratios

reaching the maximum in the 36-45 years group (odds: 2.525) (Table 5). The test of goodness of fit by the Hosmer-Lemeshow test showed a balanced distribution a goodness of fit except the age group 66-75 years and in the total analysis of the patient sample (Table 5).

Table 5: Binary regression analysis of the injury pattern according to the death in each age group.

Group (a)	AIS Head	AIS Face	AIS Thorax	AIS Abdomen	AIS Spine	AIS Extr.	AIS Pelvis	AIS Skin	HL-test
Total	<0.001/1.843	<0.001/0.770	0.005/1.095	<0.001/1.153	0.945/0.993	<0.001/0.864	<0.001/1.184	0.021/0.858	<0.001
16-25	<0.001/1.927	0.017/0.779	0.259/1.082	0.002/1.237	0.189/0.897	0.247/0.914	0.545/1.062	0.219/0.842	0.374
26-35	<0.001/2.029	0.905/1.014	0.103/1.155	0.295/1.098	0.022/0.754	0.116/0.861	0.096/1.227	0.319/1.164	0.504
36-45	<0.001/2.525	0.001/0.655	0.966/1.004	0.555/1.055	0.091/0.847	0.027/0.794	0.035/1.333	0.986/1.004	0.150

46-55	<0.001/1.895	0.037/0.771	0.071/1.187	<0.001/1.378	0.209/0.877	0.087/0.826	0.720/1.047	0.238/0.787	0.193
56-65	<0.001/1.855	0.166/0.831	0.215/1.128	0.162/1.151	0.050/0.782	0.724/0.959	0.358/1.124	0.126/0.724	0.084
66-75	<0.001/1.590	0.004/0.622	0.187/1.127	0.069/1.250	0.874/1.017	0.536/1.076	0.474/1.108	<0.001/0.698	0.021
76-85	<0.001/1.847	0.261/0.814	0.316/1.142	<0.001/1.773	0.028/0.692	0.072/0.763	0.207/1.263	0.160/0.715	0.821
>85	0.044/1.879	0.591/1.562	0.209/1.703	0.679/0.875	0.508/1.383	0.941/1.026	0.092/2.329	0.175/0.495	0.156

Data are given as p-value/odds ratio; Hosmer-Lemeshow test (HL-test) gives the goodness of fit; good if p>0.05

Outcome

The ICU and Ventilator days were decreasing as a function of the age, harmonizing with the increasing ratio of death as a function of age in multiple trauma conditions (Table 6).

Table 6: The outcome according to each decade of the analyzed patient sample.

Group (a)	16-25	26-35	36-45	46-55	56-65	66-75	76-85	>85	p-value
Hospitalisation (d)	17.5 ± 15.7	20.3 ± 18.4	19.2 ± 20.7	19.5 ± 20.2	16.9 ± 17.5	13.6 ± 29.1	10.6 ± 12.7	6.3 ± 7.4	0.724*
ICU (d)	10.1 ± 11.6	9.3 ± 11.3	9.0 ± 11.5	9.7 ± 11.4	8.3 ± 10.0	6.2 ± 8.2	4.9 ± 6.6	3.4 ± 5.5	<0.00*
Ventilator (d)	6.8 ± 9.4	5.7 ± 8.2	5.7 ± 9.4	6.1 ± 8.6	5.0 ± 7.3	3.9 ± 6.6	3.0 ± 5.2	1.3 ± 1.9	<0.00*
Death (% of each decade)	25.5	18.3	23.6	23.4	32.1	43.1	53.9	71.4	<0.00†

Data are given as mean ± SD, Kolmogorov Smirnov p>0.05, *ANOVA, †χ², significant if p<0.05

Discussion

The exceptional situation of a multiple injured patient may mask leading injuries by alternated endocrine situation such as epinephrine and ACTH over secretion and the medication of the rescue teams [10]. This might lead to an increased awareness and a higher GCS calculation in this patient sample not mirroring the correct severity of traumatic brain injury (Table 4). The binary logistic regression revealed the traumatic brain injury as an independent predictor for death in all age groups indirectly indicating adverse dynamics of the traumatic brain injury in the multiple injury setting. Indeed, the skull as the worst accessible system and the dynamics of the injuries are hardly predictable. As demonstrated by the data the odds ratio reaches the maximum in the middle ages and increases the mortality rate by the factor 2,525 by each GCS point. The reason why the odds ratio was so high in this age group remains speculative. This high Odds ratio might be depicted by the middle aged not any more sportive patient with beginning chronic medication. This high odds ratio might not be correlated to the ISS or NISS, hence they were not really significantly differences between the single age groups. Certainly, a multifactorial cause of death has to be postulated in a multiple trauma setting. Compared to higher ages, the AIS-score of the head was continuously increasing according to the age groups, however, the odds ratio decreased

to approximately 1.8. This finding might be associated with the beginning cerebral atrophy due to patient's age as a kind of protection to intracranial mass processes such as bleedings. Obviously, as expected the mortality rate increased as a function of age and medical history as partly reflected by the APACHE II and TRISS score at admission. The high mortality of the youngest decade might be explained by its risk behaviors accompanied by the according AIS in each region. Taken together the traumatic brain injury is the killer number one in the multiple trauma setting. However, the GCS score has a not sufficient predictive quality in multiple trauma setting and does not reflect the reality of the head injury. Higher cerebral oxygen perfusion pressures, preemptive correction of hypo-coagulation and neuro-protective medication in multiple injured patients with traumatic brain injuries could improve the overall outcome accompanied by surgeons' around macrovigilance for adverse dynamics in brain trauma.

Conflict of Interest

The authors Ladislav Mica, Kai Sprengel, Clément ML Werner, Kai Oliver Jensen, Catharina Keller, Stefan H. Wirth and Hanspeter Simmen declare no conflict of interest and there will no conflict arise upon publication of this article.

Funding Source

No funding source was obtained.

Compliance with Ethical Requirements

The data were retrieved from patient records with the approval of the local institutional review board according to the University of Zürich IRB guidelines and the World Medical Association Declaration of Helsinki. The study was conducted according to our institutional guidelines for good clinical practice (Ethics Committee of the University Hospital of Zürich Permission: 'Retrospektive Analysen in der Chirurgischen Intensivmedizin' No. St. V. 01-2008).

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