

## Research Article

# Impact of Brain and Skull Injuries on Physiology, Infectious Complications and Outcomes in Patients with Polytrauma

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## Abstract

Brain and skull injuries in patients with polytrauma lead mostly to adverse outcomes. We investigated how such injuries influenced the physiology, infectious complications and outcomes. A total of 1465 patients with polytrauma were included in this retrospective cohort study with an Injury Severity Score (ISS)  $\geq 16$  and an age  $\geq 16$  years. The patients were subdivided into six groups according to the Abbreviated Injury Score (AIS) of the head. Marshall, Goris, Sequential Organ Failure Assessment (SOFA), Murray and Systemic Inflammatory Response Syndrome (SIRS) scores were calculated retrospectively. Infections were determined according to clinical signs and bacteremia. Data were analyzed using SPSS® 22.0; analysis of variance was used for continuous normally distributed data, the Kruskal–Wallis test was used for categorical data, and  $P < 0.05$  was considered significant. The Marshall score increased along with the head AIS ( $P < 0.01$ ). The Goris ( $P < 0.01$ ) and SOFA ( $P < 0.01$ ) score also increased significantly with increased head AIS. In the severe AIS groups the incidence of pneumonia was high (60%;  $P = 0.003$ ) without correlation with the AIS of the thorax. Ventilator-assisted days increased significantly ( $P < 0.01$ ) as well as the death rate ( $P < 0.01$ ) along with the head AIS severity. The mortality reached 80% in the group with the maximum head AIS. These injuries have an adverse impact on physiology and outcome in polytrauma patients without being associated with the overall injury pattern. However, there appeared to be side effects of intensive-care-unit therapy on the patients' physiology.

**Keywords:** Brain skull injury; Polytrauma; Marshall score; Goris score; SOFA score; SIRS score; Infection

## Abbreviations

AIS: Abbreviated Injury Scale; ANOVA: Analysis of Variance; APACHE: Acute Physiology and Chronic Health Evaluation; ATLS: Advanced Trauma Life Support; AUC: Area Under the Curve; CI: Confidence Interval; ICU: Intensive Care Unit; IRB: Institutional Review Board; ISS: Injury Severity Score; NISS: New Injury Severity Scale; ROC: Receiver Operator Characteristic; SD: Standard Deviation; SIRS: Systemic Inflammatory Response Syndrome; SOFA: Sequential Organ Failure Assessment

## Introduction

The proper management of patients with polytrauma is challenging and often involves an individual plan and time of treatment. Brain and skull injuries are very often a part of the injury pattern in such patients and contribute significantly to adverse outcomes. The proper management of acute isolated brain and skull injuries involves decompression and stopping the hemorrhage [1]. The patient's possible recovery depends on the amount of destroyed brain parenchyma and the degree of posttraumatic swelling with compression of the pons and medulla oblongata. As a monotraumatic injury, the management might be straightforward; however, the impact of a brain and skull injury on the patient's physiology under polytraumatic conditions remains unclear. Patients with polytrauma

are at high risk of suffering bleeding complications based on the coagulopathy of trauma-induced shock [2,3]. Sustained bleeding reduces the patient's temperature and oxygen transport capacity, and promotes anaerobic glycolysis leading to a decreased tissue pH. Sustained bleeding endangers perfusion and oxygenation of the brain tissue. Multilobular bleeding gives the surgeon multiple problems in the trauma bay. Even in the most experienced hands, brain and skull injuries remain difficult to treat, and the outcome is often uncertain [4]. Initially well-recovering patients may develop secondary damage such as bleeding or necrosis, and this can lead to further swelling of the brain and even to death [4]. Therefore, the management of brain and skull injuries takes precedence over other traumatic injuries. These might remain untreated, undergo a damage control procedure [5] or receive delayed definitive surgery. Taken together, the trauma and the treatment of brain and skull injury in a patient with polytrauma could have an impact on their physiology and susceptibility to infections because of delayed definitive care. The data on this topic are very scarce; however, knowing the nature of the most common complications could lead to improved treatment protocols in Intensive Care Units (ICUs). *The main goal in this retrospective cohort study was to investigate the nature of the impact of brain and skull injury on the physiology and infectious complications in patients with polytrauma.*

## Materials and Methods

### Patient sample

One thousand four hundred and five patients with polytrauma admitted consecutively to the emergency room of the University Hospital of Zürich (Switzerland) in the period 1996–2011 were included in this retrospective cohort study. The inclusion criteria were an Injury Severity Score (ISS)  $\geq 16$  points, age  $\geq 16$  years, and admission within at least 24 h of incurring the polytrauma. The cohort was subdivided into six groups (Table 1) according to the Abbreviated Injury Scale (AIS) of the head. All patient data were collected retrospectively. All data were retrieved from patient records with the approval of the local institutional review board according to the University of Zürich guidelines as well as the World Medical Association Declaration of Helsinki. The study was conducted according to our guidelines for good clinical practice (Permission: "Retrospektive Analysen in der Chirurgischen Intensivmedizin" Nr. St. V. 01-2008).

### Diagnostic protocols

Unstable patients underwent resuscitative procedures according to the Advanced Trauma Life Support (ATLS) standards of the American College of Surgeons. Hemodynamically stable patients received diagnostics according to the clinical findings or a whole-body Computed Tomography (CT) scan in uncertain situations. Hemodynamically unstable patients received focally oriented diagnoses with immediate problem solving according to the ATLS protocols.

### Primary care

The treatment of all patients admitted was done according to the ATLS guidelines and previously assessed trauma management protocols after appropriate indications had been identified [6–8].

### Scoring systems

The maximal values during hospitalization of the Murray, Goris, Marshall, and Sequential Organ Failure Assessment (SOFA) scores were used to evaluate the physiological impairment of the patient [9–12]. The acute physiology and chronic health evaluation (APACHE II) score was used to evaluate the overall physiological impairment of the patient at admission [13]. The ISS and the new injury severity scale (NISS) were used to define the severity of any trauma [14,15]. The 2005 version of the AIS was used to describe injuries in specific anatomical regions.

### Laboratory parameters

Blood lactate, pH, hematocrit and base excess were measured at regular intervals using a blood-gas analyzer (ABL 800 Flex; Radiometer GmbH, Thalwil, Switzerland).

### Statistical analysis

Data are presented as the mean  $\pm$  Standard Deviation (SD) for continuous variables and as percentages for categorical variables. Cases with an incomplete data set were discarded from this study. A two-tailed Kolmogorov–Smirnov test was used for normality testing; if  $P < 0.05$ , the data were considered as normally distributed. The data for the AIS groups of the brain and skull injuries were compared using the Kruskal–Wallis test for categorical data and with one-way Analysis of Variance (ANOVA) for continuous data. The data

were considered significant when  $P < 0.05$ . Pearson's correlation was calculated and was given as Pearson  $r$  with the corresponding  $p$ -value (2-tailed). The predictive quality of brain and skull injuries for any increase in the Goris, SOFA, Murray and Marshall scores was subjected to Receiver Operator Characteristic (ROC) analysis, and results are reported as the area under the curve (AUC)  $\pm$  standard error with a corresponding Confidence Interval (CI) of 95%. The data were analyzed using SPSS for IBM statistical software (version 22.0; IBM Corp., Armonk, NY, USA).

## Results and Discussion

### Patient sample

All patients admitted to the trauma bay who met the inclusion criteria were included in this study. The admission data were subjected to the Kolmogorov–Smirnov test, and all data tested positively for normality ( $P < 0.05$ , for all noncategorical data; Table 1). There were significantly more men than women ( $P < 0.001$ ). There was no significant difference in age between the groups. The mean age was  $42.8 \pm 19.1$  years at admission (range between study groups, 40.8–49.4). According to the AIS of the head the ISS values (range between study groups,  $27.9 \pm 10.2 - 69.0 \pm 13.3$ ;  $P < 0.001$ ) and NISS grades (range between study groups,  $31.8 \pm 11.8 - 72.4 \pm 6.7$ ,  $P < 0.001$ ) increased significantly (Table 1). Interestingly, the AIS values from the different anatomical regions, especially the thorax (range between study groups,  $0.9 \pm 1.4 - 2.9 \pm 1.3$ ,  $P < 0.001$ ) and abdomen (range between study groups,  $0.0 \pm 0.0 - 2.3 \pm 2.2$ ,  $P < 0.001$ ) decreased significantly according to the increasing AIS head score and reached their minima in group 6 at  $0.9 \pm 1.4$  and  $0.0 \pm 0.0$ , respectively (Table 1). The APACHE II score increased along with the AIS head score (range between study groups,  $10.2 \pm 6.7 - 20.3 \pm 8.0$ ), reaching a maximum in AIS group 5 at  $20.3 \pm 8.0$  ( $P < 0.001$ ; Table 1). The pH, lactate, base excess and hematocrit values were significantly different between the six study groups but without any particular association with the AIS scores (Table 1).

### Scoring each patient's health

The Marshall score increased along with the AIS head scores, as could be expected, reaching a maximum in group 6 at  $9.6 \pm 3.4$  ( $P < 0.001$ ; Table 2). The Goris score (range between study groups,  $3.6 \pm 2.1 - 7.2 \pm 1.5$ ;  $P < 0.001$ ) and SOFA score (range between study groups,  $5.5 \pm 4.4 - 11.8 \pm 3.2$ ;  $P < 0.001$ ) also increased along with the AIS head scores but did not correspond to the injury pattern shown in Table 1 (Table 2). Pulmonary function estimated by the Murray score revealed no significant differences between the head score groups ( $P = 0.263$ ). The SIRS score was similar over all head score groups (range,  $2.1 \pm 1.1 - 2.2 \pm 1.2$ ,  $P = 0.715$ ). The maxima of the Goris, SOFA, and Murray scores revealed no clear tendencies. The predictive quality of brain skull injuries for the rise of the investigated scores was only for the Goris score significant (AUC:  $0.606 \pm 0.021$ ;  $P < 0.001$ ) (Figure 1).

### Infectious complications

Analysis of infections revealed only a significant increase in pneumonia along with the AIS head scores, with a maximum incidence of 60% (range, 13–60%;  $P = 0.003$ ; Pearson's  $r = .049$ ; Table 3). Bacteremia showed a maximum incidence of 15% in group 5 (overall range, 0–12%;  $P = 0.016$ ; Pearson's  $r = 0.077$ ) with significant

**Table 1:** Patient sample characteristics at admission.

AIS head score group	0	1	2	3	4	5	6	P-value	Total
<i>n</i>	380	77	114	204	285	395	10	0.072†	1465
Age (y)	42.6 ± 17.4	40.8 ± 17.6	41.7 ± 19.1	41.3 ± 18.3	45.2 ± 19.8	42.7 ± 20.5	49.4 ± 25.0	0.224*	42.8 ± 19.1
Sex (male/female)	285/95	55/22	81/33	143/61	194/91	300/95	10/0	0.001†	1068/397
AIS face	0.3 ± 0.8	0.6 ± 1.0	0.6 ± 1.2	0.9 ± 1.1	0.9 ± 1.2	0.7 ± 1.2	0.9 ± 1.5	< 0.001*	0.6 ± 1.1
AIS thorax	2.4 ± 1.7	2.9 ± 1.3	2.3 ± 1.6	2.4 ± 1.5	2.1 ± 1.6	1.7 ± 1.7	0.9 ± 1.4	< 0.001*	2.2 ± 1.7
AIS abdomen	2.3 ± 2.2	2.1 ± 1.8	1.8 ± 1.9	1.2 ± 1.8	0.9 ± 1.6	0.9 ± 1.6	0.0 ± 0.0	< 0.001*	1.4 ± 1.9
AIS extremities	2.0 ± 1.6	2.1 ± 1.4	2.2 ± 1.4	2.0 ± 1.4	1.5 ± 1.4	1.2 ± 1.3	0.7 ± 1.2	< 0.001*	1.7 ± 1.4
AIS pelvis	0.9 ± 1.4	0.9 ± 1.4	1.0 ± 1.4	0.9 ± 1.4	0.5 ± 1.0	0.5 ± 1.1	0.0 ± 0.0	< 0.001*	0.7 ± 1.3
AIS skin	0.5 ± 0.9	0.6 ± 0.7	0.9 ± 0.9	0.7 ± 0.9	0.5 ± 0.7	0.4 ± 0.8	0.4 ± 0.5	< 0.001*	0.5 ± 0.8
ISS	29.4 ± 10.3	28.9 ± 8.6	27.9 ± 10.2	29.0 ± 10.5	32.4 ± 10.2	38.9 ± 11.8	69.0 ± 13.3	< 0.001*	32.6 ± 11.8
NISS	38.2 ± 14.2	33.6 ± 10.4	31.8 ± 11.8	32.3 ± 12.2	39.2 ± 9.5	53.2 ± 12.0	72.4 ± 6.7	< 0.001*	41.1 ± 14.7
APACHE	13.8 ± 10.0	11.1 ± 8.2	10.2 ± 6.7	14.9 ± 9.6	14.9 ± 8.6	20.3 ± 8.0	20.1 ± 10.3	< 0.001*	15.5 ± 9.4
Blood pH	7.27 ± 0.17	7.31 ± 0.12	7.33 ± 0.08	7.28 ± 0.16	7.31 ± 0.12	7.29 ± 0.13	7.31 ± 0.12	.004*	7.29 ± 0.14
Blood lactate (mmol/L)	3.7 ± 3.2	2.7 ± 2.1	2.8 ± 2.0	3.3 ± 3.0	3.1 ± 2.6	3.5 ± 2.9	3.5 ± 2.5	.025*	3.4 ± 2.9
Base excess (mmol/L)	-5.67 ± 7.05	-3.48 ± 4.12	-3.23 ± 4.02	-5.13 ± 6.48	-3.44 ± 5.41	-4.83 ± 5.33	-5.53 ± 4.86	< 0.001*	-4.64 ± 5.94
Hematocrit (%)	30.6 ± 9.4	32.5 ± 8.0	33.6 ± 8.4	31.9 ± 9.3	33.8 ± 8.4	32.6 ± 9.0	30.7 ± 10.6	< 0.001*	32.2 ± 9.0

Data are given as the mean ± SD. \*ANOVA, †Kruskal–Wallis.

**Table 2:** The analysis of physiological scoring systems and the days when they peaked.

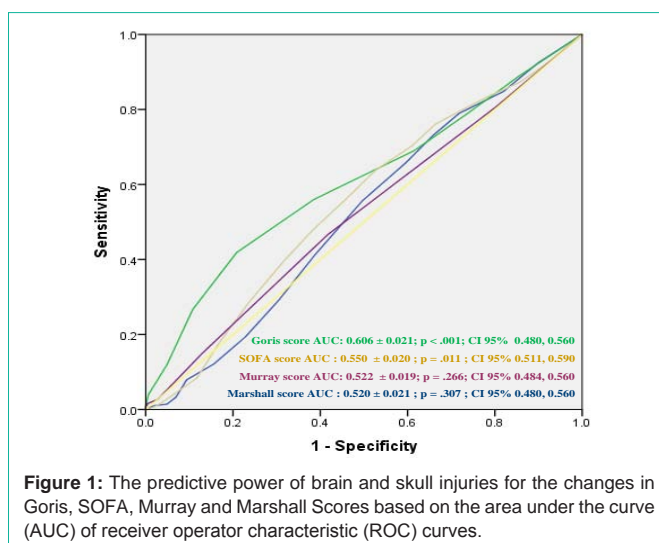
AIS head	0	1	2	3	4	5	6	P-value
Marshall score	4.9 ± 3.9	4.3 ± 3.3	3.9 ± 3.8	5.6 ± 3.4	5.1 ± 3.4	6.4 ± 2.7	9.6 ± 3.4	< 0.001*
Day of Marshall score maximum	1.4 ± 2.2	1.5 ± 1.7	1.8 ± 2.1	2.0 ± 2.5	2.3 ± 3.4	1.9 ± 3.0	3.2 ± 3.1	0.005*
Goris score	3.6 ± 2.1	3.6 ± 2.3	3.4 ± 2.3	4.3 ± 2.3	4.5 ± 2.5	5.3 ± 2.3	7.2 ± 1.5	< 0.001*
Day of Goris maximum	1.2 ± 1.9	1.3 ± 1.7	1.7 ± 2.4	1.6 ± 2.3	1.9 ± 3.2	1.5 ± 2.4	1.8 ± 1.9	0.042*
SOFA score	5.5 ± 4.4	5.5 ± 3.8	4.9 ± 4.5	7.0 ± 4.2	7.1 ± 4.3	8.6 ± 3.4	11.8 ± 3.2	< 0.001*
Day of SOFA score maximum	1.3 ± 2.1	1.4 ± 1.5	1.7 ± 2.2	1.9 ± 2.4	1.9 ± 2.7	1.5 ± 2.1	3.0 ± 1.9	< 0.001*
Murray score	1.4 ± 1.0	1.1 ± 0.9	1.5 ± 1.5	1.4 ± 1.0	1.4 ± 1.1	1.5 ± 1.4	1.9 ± 1.2	0.263*
Day of Murray score maximum	1.8 ± 2.5	2.0 ± 2.5	2.8 ± 3.5	2.7 ± 4.3	2.8 ± 4.0	2.0 ± 2.8	3.3 ± 3.1	0.007*
SIRS score	2.1 ± 1.2	2.3 ± 1.1	2.1 ± 1.1	2.2 ± 1.2	2.1 ± 1.3	2.1 ± 1.4	1.7 ± 1.9	0.715*
Day of SIRS score maximum	2.1 ± 2.9	2.9 ± 5.0	2.2 ± 2.6	2.8 ± 3.6	3.2 ± 4.6	2.4 ± 3.8	2.3 ± 2.7	0.023*

Data are given as the mean ± SD. \*ANOVA.

correlation to the AIS head scores ( $P = 0.005$ ; Table 3). The other infectious foci were randomly distributed between the six AIS head score groups (Table 3).

## Outcomes

The analysis of time spent in the ICU revealed significant differences (range between study groups,  $5.8 \pm 5.6 - 7.8 \pm 9.0$  days;  $P = 0.004$ ; Pearson's  $r = 0.016$ ; Table 4). Analysis of the ventilator-associated days showed a clearer picture with a significant increase according to the AIS head score (range between study groups,  $2.4 \pm 3.4 - 4.7 \pm 4.9$  days;  $P < 0.001$ ; Pearson's  $r = 0.146$ ; Table 4). The numbers of hospitalization days were inversely related to the AIS head scores, with the lowest AIS head score group having the longest hospitalization (range between study groups,  $20.4 \pm 19.0 - 7.6 \pm 10.5$  days;  $P < 0.001$ ; Pearson's  $r = -0.273$ ; Table 4). The mortality rate also showed an increase to 80% in group 6 (overall range, 5–80%,  $P < 0.001$ ; Pearson's  $r = 0.380$ ; Table 4).



**Figure 1:** The predictive power of brain and skull injuries for the changes in Goris, SOFA, Murray and Marshall Scores based on the area under the curve (AUC) of receiver operator characteristic (ROC) curves.

**Table 3:** Analysis of the infection rate in the patient sample.

AIS head	0	1	2	3	4	5	6	P-value	Pearson's r/P
Pneumonia	17%	13%	19%	16%	15%	23%	60%	0.003 <sup>†</sup>	0.049/0.072
Abdominal infection	2%	0%	3%	1%	2%	1%	0%	0.586 <sup>†</sup>	-0.002/0.933
Wound infection	6%	1%	4%	6%	6%	7%	20%	0.294 <sup>†</sup>	0.020/0.474
Bone infection	1%	0%	0%	1%	1%	1%	0%	0.881 <sup>†</sup>	0.004/0.891
Urinary tract infection	7%	4%	5%	4%	5%	8%	10%	0.705 <sup>†</sup>	0.005/0.848
Catheter infection	4%	3%	5%	4%	6%	8%	0%	0.143 <sup>†</sup>	0.065/0.020
Central nervous system infection	2%	4%	4%	3%	2%	3%	0%	0.834 <sup>†</sup>	0.006/0.815
Bacteremia	6%	7%	7%	4%	8%	12%	0%	0.016 <sup>†</sup>	0.077/0.005

Data are given as the percentage of patients in each AIS head group. <sup>†</sup>Kruskal–Wallis tests. Pearson's correlation coefficient with the corresponding AIS head group is given with the corresponding significance two tailed.

**Table 4:** Analysis of outcomes.

AIS head score	0	1	2	3	4	5	6	P-value	Total	Pearson's r/P
ICU [days]	5.8 ± 5.6	7.9 ± 5.6	5.9 ± 6.2	7.8 ± 9.0	7.3 ± 8.3	5.9 ± 7.8	5.9 ± 7.3	0.004 <sup>*</sup>	6.5 ± 7.4	0.016/0.534
Ventilator [days]	2.4 ± 3.4	3.6 ± 4.8	2.3 ± 3.4	4.4 ± 6.6	4.4 ± 6.9	4.3 ± 5.9	4.7 ± 4.9	< 0.001 <sup>*</sup>	3.7 ± 5.7	0.146/0.001
Hospitalization [days]	20.4 ± 19.0	20.3 ± 13.3	18.3 ± 13.7	17.9 ± 15.2	14.7 ± 13.3	9.0 ± 11.4	7.6 ± 10.5	< 0.001 <sup>*</sup>	15.6 ± 15.5	-0.273/0.001
Death [% of each group]	17	5	9	18	32	65	80	< 0.001 <sup>†</sup>	32	0.380/0.001

Data are given as the mean ± SD. <sup>\*</sup>ANOVA, <sup>†</sup>Kruskal–Wallis. Pearson's correlation coefficient with the corresponding AIS head group is given with the corresponding significance if P < 0.05.

## Discussion

Brain and skull injuries are very often associated with accompanying injuries and are very common in patients with polytrauma [16]. Higher AIS scores of the head at admission were associated with increased AIS values from other anatomical regions, suggesting a higher whole body impact upon trauma. However, these higher head AIS values were associated with lower AIS values from other anatomical regions, suggesting a direct isolated impact on the head. Unfortunately, the head tends to be involved in any kind of trauma in humans because of its mass and the weak neck muscles. The analysis of the Murray score showed no significant differences between the six study groups. An increase in this score could be expected according to the AIS head score because of ICU-associated brain therapy with hyperventilation and changing blood gases. Furthermore, significant differences were only found in the Goris and SOFA scores, which increased according to the severity of brain and skull injury. This association with the injury pattern might only partly explain the continuous rise of the Goris and SOFA scores, especially because in the higher AIS head score groups, there were low AIS scores for the abdomen and thorax. This suggests that there were physiological changes associated with brain and skull injury therapy such as hyperventilation with hyperoxygenation and the extensive use of norepinephrine to assure sufficient cerebral tissue oxygenation and perfusion pressure. The Glasgow Coma Scale [17] is usually artificially lowered to 3 by sedation during brain and skull therapy to stabilize neuronal networks and to reduce their electric activity. Rheological properties of the blood might be improved with a reduced hematocrit and a lower international normalized ratio for blood clotting; however, this reduced hematocrit usually results from the anemia associated with critical illness [18]. These alterations in blood properties might be accepted clinically to a certain extent; however, they play a role in deciding the Goris and SOFA scores. Interestingly, the injured brain is an organ with high levels of cytokine production

by astrocytes and microglia, but this does not influence the SIRS score [19], which might be masked by ICU treatment of the brain and skull injuries. The heart rate, hyperventilation and temperature (usually hypothermia) are changed during brain and skull therapy. The Goris, SOFA and SIRS scores reached their maxima at about the second day of treatment in the ICU, suggesting side effects of the therapies used. The same was shown by the ROC analysis, with a low ability to predict the severity of the brain and skull injuries on physiological scores. The analysis of infectious complications as frequent problems during the management of patients with polytrauma showed a good correlation only for urinary tract infections and bacteremia. However, this distribution seemed to be random, without any particular association with the severity of brain and skull injuries.

### Outcomes of therapy for brain and skull injuries

Controlled ventilation was required for the patients with more severe brain and skull injuries, which was mirrored by the increasing numbers of days on ventilation according to the higher AIS head scores. Interestingly, the duration of hospitalization decreased with the severity of brain and skull injuries. This might be reflected by the mortality rate, as brain and skull injuries contribute to the mortality of patients with polytrauma when a certain severity is reached. We can speculate about the extent to which the physiological changes are caused by the brain and skull injury or are side effects of ICU therapy. These data indicate that the higher the AIS head score, the more such therapy-related factors contributed to the scoring systems used in this study. Reflections made on improvement of the therapy of traumatic brain injuries might not show the golden path but a harsh way between Scylla and Charybdis.

### Conclusive Clinical Recommendations

The Physiological changes and infectious complications in this study might be rated as paratherapeutic and are only evitable by proper nursing and hygiene of the ICU patient. Rigorous hygiene



and supportive systemic therapy could reduce the adverse effects of a brain skull injury in polytrauma patients.

## Hypothetical Sources of Bias

All patients were selected retrospectively. The documentation of all parameters followed Good Clinical Practice guidelines. The collection of data was performed by many different persons under the guidance of the personnel selecting the patients for treatment. The time period of 15 years could have led to a bias in the treatment of brain and skull injuries, and several parameters have changed during this time. The scores and values were calculated from a single Excel spreadsheet (Microsoft, Office 2010, Redmond, WA, USA).

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