Cranial Nerve Injuries In Patients With Moderate To Severe Head Trauma – Analysis of 91,196 Patients From The TraumaRegister DGU® Between 2008 And 2017

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Abstract

Background

Traumatic brain injury (TBI) constitutes a major cause of trauma-related disability and mortality. The epidemiology and implications of associated cranial nerve injuries (CNI) in moderate to severe TBI are largely unknown. We aimed to determine the prevalence of CNI in a large European cohort of TBI patients as well as clinical differences between TBI cases with and without concomitant CNI (CNI vs. control group) by means of a multinational trauma registry.

Methods

The TraumaRegister DGU[®] was evaluated for trauma patients with head injuries ≥ 2 Abbreviated Injury Scale, who had to be treated on intensive care units after emergency admission to European hospitals between 2008 and 2017. CNI and control cases were compared with respect to demographic, clinical, and outcome variables.

Results

1.0% (946 of 91,196) of TBI patients presented with additional CNI. On average, CNI patients were younger than control cases (44.3 ± 20.6 vs. 51.8 ± 23.0 years) but did not differ regarding sex distribution (CNI 69.4%; control 69.1%). Traffic accidents were encountered more frequently in CNI cases (52.3% vs. 46.7%; $p < 0.001$; chi-squared test) and falls more commonly in the control group (45.2% vs. 37.1%; $p < 0.001$). CNI patients suffered more frequently from concomitant face injuries (28.2% vs. 17.5%; $p < 0.001$) and skull base fractures (51.0% vs. 23.5%; $p < 0.001$). Despite similar mean Injury Severity Score (CNI 21.8 ± 11.3 ; control 21.1 ± 11.7) and Glasgow Coma Scale score (CNI 10.9 ± 4.2 , control 11.1 ± 4.4), there was a considerably higher rate of anisocoria in CNI patients (20.1% vs. 11.2%; $p < 0.001$). Following primary treatment, 50.8% of CNI and 35.5% of control cases showed moderate to severe disability (Glasgow Outcome Scale score 3-4; $p < 0.001$).

Conclusions

CNI as rare adjuncts to TBI should raise the suspicion of complicating skull base fractures and indicate higher rates of functional impairment following primary care.

Presentation At A Conference

Parts of this study were presented as an oral contribution at the 72nd annual meeting of the German Society of Neurosurgery, which was held online from June 6th to 9th, 2021. The meeting abstract is available at <https://www.egms.de/static/en/meetings/dgnc2021/21dgnc114.shtml> (doi: 10.3205/21dgnc114).

Background

From a global perspective, traumatic brain injury (TBI) constitutes a major cause of death and disability making this condition a pressing issue for public health services across the world [21]. Besides bodily restrictions, long-term effects predominantly comprise neuropsychiatric sequelae including personality changes, depression, anxiety, and cognitive impairment at multiple levels [10, 13, 16]. Head injuries were reported to account for 19.6% of all injuries that occurred in Germany in the year 1998 [41]. In view of a total TBI incidence rate for Central Europe as high as 332–337/100,000 persons per year, it is important to note that a majority of about 90% of these cases suffer mild head trauma [35, 41]. Hence, moderate to severe TBI may affect between 10 and 33.5 per 100,000 head of population per year in Germany [29, 35, 41]. Serious head trauma is known to be associated with a tremendously high in-hospital mortality. Maegele and colleagues stated a case fatality rate of 23.5% for this condition in a large retrospective multicenter analysis [29]. From the neurosurgical point of view, operations for injuries to the skull or brain account for about 45% of the essential global neurosurgical care [8]. A thorough review of the biomedical literature reveals a fundamental scarcity of large-scale data on the prevalence of cranial nerve injuries (CNI) in patients suffering from head trauma. To the best of our knowledge, the current body of literature mainly consists of a few series concentrating on pediatric and adult head injured patients with posttraumatic cranial nerve deficits [7, 22]. Therefore, we aimed to determine the frequency and impact of CNI in patients with moderate to severe head injury by means of a detailed evaluation of a comprehensive multinational trauma registry with a focus on the European context.

Methods

Guideline compliance and reporting standards

The present study is in line with the publication guidelines of the TraumaRegister DGU® of the German Trauma Society (TR-DGU) and registered as TR-DGU project ID 2019-021 [56]. Where possible, data presentation adheres to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines [12].

TraumaRegister DGU®

The TR-DGU was founded in 1993 (TraumaRegister DGU® 2014) [55]. The aim of this multi-center database is a pseudonymized and standardized documentation of severely injured patients. Data are collected prospectively in four consecutive time phases from the site of the accident until discharge from hospital: A) Pre-hospital phase, B) Emergency room and initial surgery, C) Intensive care unit and D) Discharge. The documentation includes detailed information on demographics, injury pattern, comorbidities, pre- and in-hospital management, course on intensive care unit, relevant laboratory findings including data on transfusion and outcome of each individual. The inclusion criterion is admission to hospital via emergency room with subsequent intensive care or reach the hospital with vital signs and die before admission to intensive care unit. The infrastructure for documentation, data management, and data analysis is provided by AUC - Academy for Trauma Surgery (AUC - Akademie der

Unfallchirurgie GmbH), a company affiliated to the German Trauma Society. The scientific leadership is provided by the Committee on Emergency Medicine, Intensive Care and Trauma Management (Sektion NIS) of the German Trauma Society. The participating hospitals submit their data pseudonymized into a central database via a web-based application. Scientific data analysis is approved according to a peer review procedure laid down in the publication guideline of TR-DGU. The participating hospitals are primarily located in Germany (90%), but a rising number of hospitals of other countries contribute data as well (at the moment from Austria, Belgium, China, Finland, Luxembourg, Slovenia, Switzerland, The Netherlands, and the United Arab Emirates). Currently, almost 30,000 cases from more than 650 hospitals are entered into the database per year. Participation in TR-DGU is voluntary. For hospitals associated with TraumaNetzwerk DGU®, however, the entry of at least a basic data set is obligatory for reasons of quality assurance.

Study population and course

The TR-DGU database was queried by two of the authors (RL, TH) for all moderately to severely head injured patients (by definition head injury with an Abbreviated Injury Scale (AIS) severity score of 2 or higher) with or without additional trauma to other body regions, who had been treated on intensive care units in European hospitals between 2008 and 2017. The Abbreviated Injury Scale is an internationally well-established scoring system for ranking injury severity that categorizes any individual lesion by anatomical region corresponding to its intensity on a 6-point scale ranging from 1 (= minor) to 6 (= maximum) [14, 57]. The diagnosis of any traumatic lesion was based on thorough clinical/neurological evaluation and widely applied emergency computed tomography scan. Patients who died within 48 hours following hospital admission were excluded from the analysis due to the risk of an incomplete diagnostic workup with potential underreporting of relevant lesions. Moreover, early transfer out (< 48h) patients were also excluded in order to prevent double counting of these cases from the receiving hospital. The detailed composition of the study cohort as well as all applied inclusion and exclusion criteria can be obtained from flowchart 1_ study population. A total of 91,196 patients fulfilled the inclusion criteria and constitute the study population. Thereupon two cohorts were built with regard to the presence or absence of documented concomitant CNI. The TR-DGU data collection system subsumes these neural lesions under the following AIS 2005 codes: 130299.2 (lesion of any cranial nerve) / 131605.3 (bilateral lesion of the facial nerve) / 131806.3 (bilateral lesion of the vestibulocochlear nerve). 946 of 91,196 (1.0%) head trauma patients presented with additional cranial nerve deficits (CNI group) while the remaining 90,250 patients did not (control group). Both cohorts were compared to each other with respect to demographics, trauma etiology & mechanism, injury severity, accompanying lesions, and functional outcome at hospital discharge. All reported figures refer to valid database entries. Missing values have not been replaced. Injury severity was assessed with the (New) Injury Severity Score as well as the head trauma specific Glasgow Coma Scale and Eppendorf-Cologne Scale scores [3, 4, 14, 17, 18, 33, 48]. The latter employs three parameters including motor response, pupil size, and pupil reactivity and has recently been shown to yield a significantly higher accuracy regarding traumatic brain injury presence and outcome prediction compared to the more commonly used Glasgow Coma Scale, which is also composed of three elements, namely eye opening, motor & verbal reaction [17, 18]. Furthermore, total hospital stay and direct treatment

costs were compared for both groups as further ancillary surrogate parameters. Treatment expenditures were calculated via the TR-DGU cost estimator established by Lefering and colleagues [27]. The Glasgow Outcome Scale score served as a primary measure of functional outcome and the patients' needs for subsequent inpatient rehabilitation or hospitalization following completion of acute care were determined as secondary variables [23].

Data presentation and statistics

The registry-based data are presented descriptively. Metric variables are presented as mean values with standard deviation (SD) and counts as percentages. For mean values and percentages a 95% confidence interval (CI) was reported in the CNI group. Since the control group is very large (> 90,000 cases), statistical variation is extremely small in that group leading to rather narrow CI (less than ± 0.3 for percentages and less than 1/150 part of the SD for metric data). Therefore, CI were not reported for the control group. If the CI of the CNI group does not include the result of the control group, then this is approximately equivalent to a significant difference at 0.05 level. For selected clinically meaningful comparisons, however, a Chi-squared test was performed in the sense of targeted testing (significance level 0.01). To evaluate the impact of additional CNI on the functional outcome of TBI patients, we conducted a matched pair analysis. After exclusion of cases with a Glasgow Outcome Scale score of 1 (death) and 2 (persistent vegetative state), we matched the remaining TBI patients with and without CNI according to the following criteria: age group, sex, AIS head (2–6), AIS ≥ 2 for other body regions (face, thorax, abdomen, spine, extremities), trauma mechanism (traffic related, low fall, other), Glasgow Coma Scale score (3–8, 9–12, 13–15), and type of head injury (intracerebral bleeding, extraaxial bleeding, contusion, other). A Glasgow Outcome Scale score of 3–5 was found in 882 cases from the CNI group and for 787 of these cases a matching could be achieved (89.2%). A statistician was involved in the planning and execution of all calculations of this project. Statistical procedures were conducted with IBM SPSS Statistics (version 24, International Business Machines Corporation, Armonk, NY, USA) and GraphPad Prism (version 8.4.2, GraphPad Software, La Jolla California, USA).

Results

Prevalence of cranial nerve lesions following head trauma

946 of all 91,196 patients (1.0%; CI 1.0%-1.1%) with moderate to severe head injury (AIS ≥ 2) suffered from concomitant CNI.

Demographic data

On average, CNI patients were considerably younger compared to the control group (mean ages 44.3 years vs. 51.8 years). We found quite similar gender distributions for both cohorts with a predominance of male cases (CNI 69.4%; control 69.1%). Information on detailed epidemiological aspects of both study groups including further age differentiation into five distinct categories is provided in table 1_epidemiology.

Etiology and mechanism of trauma

When considering all types of traffic-related accidents, these were significantly more commonly encountered in CNI patients (52.3%) than in control cases (46.7%; $p < 0.001$; chi-square test). In contrast, high (> 3 meters) and low falls (< 3 meters) combined were more rarely seen in head trauma patients with cranial nerve deficits (CNI 37.1% vs. control 45.2%; $p < 0.01$; chi-square test). Criminal assault including gunshot, stabbing, and blow were seldom causal factors in both groups with blow being the most frequent of these three entities. The vast majority of patients sustained blunt injuries (CNI 97.1%; control 98.1%). In-depth data on trauma mechanisms and etiology broken down by different causes of head injury can be obtained from table 2_trauma etiology and mechanism.

Severity of injury

On the one hand, CNI and control patients revealed comparable mean Injury Severity Scores (CNI 21.8; control 21.1), Glasgow Coma Scale scores (CNI 10.9; control 11.1), Eppendorf-Cologne Scale scores (CNI 1.5; control 1.4), and days of intensive care (CNI 9.2; control 9.1) as well as total hospitalization (CNI 20.5; control 18.3). On the other hand, head trauma cases with accompanying cranial nerve lesions presented considerably more frequently with anisocoria (CNI 20.1%; control 11.2%; $p < 0.001$; chi-square test) and sluggish pupil reactivity (CNI 24.1%; control 17.5%; $p < 0.001$; chi-square test). Table 3_injury severity particularizes extensive information on all trauma severity measures inclusive of their respective levels of confidence.

Further associated injuries

A direct comparison between both cohorts indicated higher rates of concomitant facial lesions (AIS ≥ 2) in CNI patients (28.2%) as opposed to control cases (17.5%; $p < 0.001$; chi-square test). Especially damages to the eye and ear were more commonly seen in head trauma subjects with CNI. The exact prevalences for both groups concerning this matter are given alongside with numerous other kinds of specific injuries to the head and other body regions in table 4_concomitant injuries. Skull base fractures were exceptionally more frequent in CNI patients (51.0%) than in control cases (23.5%; $p < 0.001$; chi-square test), but also other types of viscerocranial fractures such as orbit, mandible, and LeFort I-III were more often encountered in CNI cases, as shown in table 4_concomitant injuries. Epidural hematoma, traumatic subarachnoid hemorrhage, and brain contusion occurred slightly more frequently in the CNI cohort, but injuries to the cerebral vasculature (extraordinarily rare) as well as other parts of the body emerged in similar ways in both groups.

Functional outcome

Following primary treatment, a remarkably higher percentage of head trauma patients with cranial nerve damage was disabled to a greater or lesser extent (Glasgow Outcome Scale score 3–4: CNI 50.8%; control 35.5%; $p < 0.01$; chi-square test). This finding was in parallel with the increase in the need for subsequent rehabilitation for these individuals upon completion of primary care (CNI 35.1%; control 27.3%; $p < 0.01$; chi-square test). Table 5_outcome depicts detailed data on the functional status of both cohorts at the

time of hospital discharge. The additionally performed matched pair analysis confirmed that with otherwise similar injury severity and circumstances, TBI patients with concomitant CNII were significantly more likely to have moderate to severe functional disability at hospital discharge (Glasgow Outcome Scale score 3–4: CNII 51.6%; matched controls 40.2%; 787 matched pairs; $p < 0.01$; chi-square test). Table 6_matched pair analyses provides comprehensive information regarding the matching variables and functional outcome of the two groups.

Discussion

This study aimed to determine the prevalence of CNII following moderate to severe head trauma in Europe. We found, based on a multinational trauma registry analysis, that one out of hundred (1.0%) TBI cases sustained concomitant CNII and these nerve lesions were associated with considerably younger patient age. In general, there is a scarcity of information on CNII prevalence after TBI, but our findings are consistent with the insights of Coello and colleagues, who report on an incidence of 0.3% of CNII with similar age distribution in a large sample of more than 16,400 patients suffering from mild head trauma defined as a Glasgow Coma Scale score of 14–15 [7]. In this study, the olfactory, facial, and oculomotor nerves (cranial nerves III, IV, and VI) were most commonly injured and about three out of four CNII patients presented with single nerve palsies which is backed by a vast body of literature [24, 26, 32, 34, 42]. Another survey revealed cranial neuropathies affecting visual capacity and/or ocular movement in 1.9% of pediatric inpatient cases hospitalized for severe head trauma resulting from falls [52]. To some extent, investigations from other world regions showed substantially higher CNII prevalences complicating head injuries, ranging between 9.1% and 12.6% for adults and up to 22.4% in children [24, 31, 34]. Noteworthy, premature comparisons between these analyses and our findings should not be drawn, because previous studies partly lack data on head trauma severity or, in elementary contrast to our patients, comprised primarily of either stab wounds or gunshot injuries, such as is the case with the aforementioned pediatric series. On the contrary, our study sample consisted almost entirely of blunt trauma cases (98%) which impressively demonstrates the impact of the underlying trauma mechanism on the prevalence of CNII following head injury. Generally speaking, more severe head injuries are more likely to elicit cranial nerve deficits [38]. Therefore, it is not surprising that CNII were identified in 75% of autopsies of fatal traffic-related head trauma cases, primarily in the form of root avulsion [30]. Different from TBI without CNII, which revealed a stronger association with high or low falls, more than half of all CNII evaluated in our study occurred within the context of traffic accidents. Falls have been widely recognized as the most frequent cause of TBI in the western world with even increasing numbers over the years in parallel with the aging of the population [29, 35, 47]. On the other side, many series focusing on the specific subset of TBI patients with concomitant CNII stated road accidents as leading cause of these types of injury, which is in accordance with our results [2, 24, 37, 40]. Despite similar overall and head injury severity in both groups, head trauma cases with accompanying CNII presented considerably more frequently with anisocoria and sluggish pupil response to light compared to their TBI counterparts without diagnosed cranial nerve deficits. This is an obvious finding, as the iris sphincter muscle, also known as pupillary sphincter, is innervated by parasympathetic fibers originating from the Edinger-Westphal nucleus in the

brainstem and traveling along the third cranial nerve to their destination [50]. As already described earlier in this paper, the oculomotor nerve is among the most frequently affected cranial nerves in the context of TBI. Cranial nerve deficits and particularly anisocoria and/or fixed dilated pupils were, among other variables, identified as predictive for abnormal computed tomography findings (e.g. intra- or extraaxial hematoma) in head trauma patients [39]. Our analysis revealed a common combination between CNI and face injuries including ear and eye as well as skull base and viscerocranial fractures. There is ample evidence for this association in the epidemiological literature [5, 11, 15, 24]. A long-term follow-up study on a pediatric head trauma cohort led to the insight that, in addition to the severity of the injury, fractures involving the base of the skull, its foramina and channels are the main determinants for the frequency of CNI [22]. While acute TBI-related CNI are caused primarily by nerve compression and/or traction, late injuries presumably arise from ischemia-induced nerve edema and delayed fracture repairing with excessive ossification [1]. A single institution study found a significant correlation between certain fracture patterns and specific CNI [25]. Occipital fractures appeared often together with olfactory nerve injuries and sphenoid/ethmoid fractures with oculomotor nerve damage. Furthermore, temporal bone fractures and facial nerve palsies commonly coexisted. Finally, maxillary fractures were frequently associated with trigeminal nerve lesions. The strong interlocking of temporal bone fractures and facial nerve palsies is well documented, but there remain uncertainties regarding the exact proportion of nerve injuries in these patients with differing incidences between 7% and 50% [2, 6, 54]. The majority of temporal bone fractures are known to be longitudinal, whereas only a small share of 10–30% is transversely oriented. The categorization of the type of fracture is important because damages to the facial and/or cochlear nerve are much more likely encountered following transverse fractures [53, 54]. Our findings indicate that TBI patients with additional CNI, unlike those without, are more at risk of experiencing a worse functional outcome with higher degrees of moderate to severe disability and need for further rehabilitation interventions following primary care. This is well in line with previous studies. While overall mortality of severe head trauma has decreased over the last decades [41, 47], accompanying lesions especially of the lower cranial nerve group are still associated with high death rates owing to their close relation to human basic life functions such as swallowing and protective reflexes [24]. Disturbances or loss of vision (cranial nerves II/III/IV/VI), facial movement (cranial nerve VII), and hearing ability (cranial nerve VIII) mainly contribute to the high degrees of reported posttraumatic disability following CNI [9, 24]. Moreover, the common involvement of the olfactory nerve/bulb resulting in dys-, par-, and anosmia further deteriorates the health-related quality of life in TBI individuals and has also been related to the development of depressive disorders in the long term after head trauma [20]. With regard to the functional recovery from CNI, the rehabilitative potential of ocular movement as well as facial nerve palsies is considered to be high (sometimes with a substantial delay), whereas it is rated considerably lower for the olfactory, optic, and vestibulocochlear nerves [19, 26, 28]. Coello and colleagues recognized the predictive value of skull base fractures for poor functional recovery of CNI [7]. In general, traumatic CNI is less likely to recuperate than cranial nerve impairment in the context of vascular disease [36]. In view of the therapeutic approach to ocular motor CNI, many methods of treatment including surgical correction, botulinum toxin injection, prisms, and steroid medication have been applied and reported apart from observation and watchful waiting [43–46].

Limitations And Strengths

First of all, the registry-based concept pursued forces a retrospective study design. Taking into account the principal goal of the TR-DGU, which is the creation of a comprehensive database on severely injured patients, one can easily imagine that non-life-threatening lesions such as CNI might be overlooked in the acute treatment phase that primarily focuses on the stabilization of the patients' vital functions [25]. This potential bias toward underreporting of CNI could be further aggravated by other patient and diagnostic factors alike, including impaired consciousness following head trauma, the lack of routine electrophysiological and/or elaborated smell testing, and finally the well-established use of emergency cranial computed tomography instead of magnetic resonance imaging in polytrauma patients. The latter imaging method, in comparison with the former, is known to offer better soft tissue contrast and hence enables the radiologist to identify cranial nerves and their lesions adequately, which are usually not seen on routine computed tomography scans [49, 51]. Putting these factors together, the herein reported prevalence of CNI in moderate to severe TBI should be understood and interpreted as minimum value. Furthermore, due to the different aforementioned primary objective of the TR-DGU, we were not able to obtain specific information on which cranial nerves were affected more or less frequently. Additionally it should be mentioned that no long-term follow-up is available for both study cohorts, as data collection is terminated upon hospital discharge in accordance with the statutes of the registry. On the other hand, the study has many strengths. First of all, the analysis is based on a large transnational database and comprises of more than ninety-one thousand patients with moderate to severe TBI. Moreover, the included patients underwent a comprehensive clinical and complementary radiological computed tomography based examination. Apart from the completeness of the clinical information, there is a high degree of representativeness owing to the participation of local, regional and national trauma centers [58]. These two factors clearly contribute to the transferability of the findings to daily clinical practice.

Conclusions

CNI are relatively rare concomitant lesions in moderate to severe TBI, affecting approximately one percent of these cases in the European context. Despite their infrequency, CNI represent an important type of injury because of the essential neurological functions cranial nerves perform in the human body. Therefore, primary care physicians should carefully examine all twelve pairs of cranial nerves at an early stage, as lesions of these neuroanatomical structures may indicate additional skull base and facial fractures, on the one hand, and are a predictor of poorer neurologic functional outcome, on the other. Rapid identification of CNI, in conjunction with intensified neurorehabilitation measures, could potentially improve the functional outcome of this specific patient group.

Abbreviations

AIS - Abbreviated Injury Scale

CNI - cranial nerve injury

TBI - traumatic brain injury

TR-DGU - TraumaRegister DGU® of the German Trauma Society

Declarations

Ethics approval

The present study adheres to the publication guidelines of the TraumaRegister DGU® and was registered as TR-DGU project (ID 2019-021) upon approval by the institutional review board.

Consent for publication

Not applicable.

Availability of data and materials

All epidemiological data presented in this publication were retrieved from the TraumaRegister DGU®. The datasets are available from the registry on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

The authors received no specific funding for this work.

Authors` contributions

TH conceived the study. TH and RL collected and analyzed data. All authors contributed to the manuscript and approved the final text prior to submission.

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Tables

Table 1_epidemiology. Sex and age distribution of head trauma patients ± concomitant cranial nerve injury (CNI). * Control group value not covered by 95% confidence interval (CI) of CNI group. SD=standard

deviation.

	CNI group	control group
number of patients	946	90,250
share of the total population (%)	1.0 (CI 1.0-1.1)	99.0
male sex (%)	69.4 (CI 64.2–75.0)	69.1
mean age (years $\pm$ SD)	44.3 $\pm$ 20.6 (CI 43.0-45.6)*	51.8 $\pm$ 23.0
1–15 years of age (%)	6.5 (CI 5.0-8.3)*	4.7
16–59 years of age (%)	68.7 (CI 63.5–74.2)*	54.5
60–69 years of age (%)	10.5 (CI 8.5–12.8)	12.6
70–79 years of age (%)	10.8 (CI 8.8–13.1)*	15.5
80 + years of age (%)	3.5 (CI 2.4–4.9)*	12.6

Table 2_trauma etiology and mechanism. Trauma etiology and mechanisms recorded in subjects with head injury $\pm$ associated cranial nerve injury (CNI). * Control group value not covered by 95% confidence interval (CI) of CNI group.

	CNI group	control group
all traffic accidents (%)	52.3 (CI 47.7–57.2)*	46.7
car/lorry accident (%)	19.5 (CI 16.8–22.6)	17.6
motorcycle accident (%)	10.6 (CI 8.6–13.0)*	8.4
bicycle accident (%)	13.6 (CI 11.3–16.2)	12.2
pedestrian traffic accident (%)	7.2 (CI 5.5–9.1)	7.4
other traffic accident (%)	1.4 (CI 0.7–2.4)	1.1
fall > 3 meters (%)	14.1 (CI 11.8–16.7)	14.5
fall < 3 meters (%)	23.0 (CI 20.0-26.3)*	30.7
blow (%)	4.3 (CI 3.1–5.9)	3.6
shot (%)	0.7 (CI 0.2–1.4)	0.4
stab (%)	0.8 (CI 0.3–1.6)	0.3
other (%)	4.9 (CI 3.6–6.5)	3.8
blunt (%)	97.1 (CI 90.8–100.0)	98.1
penetrating (%)	2.9 (CI 1.9–4.2)	1.9

Table 3_injury severity. Severity of trauma is illustrated by means of (New) Injury Severity Score ((N)ISS), Glasgow Coma Scale score (GCS), Eppendorf-Cologne Scale score (ECS), intensive care unit (ICU) & total hospital stay as well as direct treatment expenditures for head trauma patients with and without cranial nerve injury (CNI). * Control group value not covered by 95% confidence interval (CI) of CNI group. ** ECS data were not available in all CNI cases (n=642/pupil size; n=588/pupil reactivity; n=848/motor response). CNI=cranial nerve injury. SD=standard deviation.

	CNI group	control group
mean ISS ($\pm$ SD)	21.8 $\pm$ 11.3 (CI 21.1–22.5)	21.1 $\pm$ 11.7
mean NISS ($\pm$ SD)	29.8 $\pm$ 13.3 (CI 28.9–30.7)*	26.9 $\pm$ 14.9
mean GCS ($\pm$ SD)	10.9 $\pm$ 4.2 (CI 10.6–11.2)	11.1 $\pm$ 4.4
circulatory shock at admission (%)	7.9 (CI 6.2–10.0)	7.1
mean intubation time (days $\pm$ SD)	4.5 $\pm$ 8.2 (CI 4.0–5.0)	4.9 $\pm$ 9.1
mean ICU time (days $\pm$ SD)	9.2 $\pm$ 11.6 (CI 8.4–10.0)	9.1 $\pm$ 11.7
mean hospital stay (days $\pm$ SD)	20.5 $\pm$ 17.0 (CI 19.4–21.6)*	18.3 $\pm$ 17.9
mean treatment costs (Euro $\pm$ SD)	19,579 $\pm$ 19,398 (CI 18,317 – 20,840)	18,624.1 $\pm$ 20,084.3
mean ECS** ($\pm$ SD)	1.5 $\pm$ 1.9 (CI 1.4–1.6)	1.4 $\pm$ 1.9
ECS_pupil size_normal_0** (%)	75.1 (CI 68.5–82.1)*	83.4
ECS_pupil size_anisocoric_1** (%)	20.1 (CI 16.8–23.9)*	11.2
ECS_pupil size_bilaterally dilated_2** (%)	4.8 (CI 3.3–6.9)	5.4
ECS_pupil reactivity_brisk_0** (%)	68.2 (CI 61.7–75.2)	74.8
ECS_pupil reactivity_sluggish_1** (%)	24.1 (CI 20.4–28.5)*	17.5
ECS_pupil reactivity_fixed_3** (%)	7.7 (CI 5.6–10.2)	7.7
ECS_motor response_normal_0** (%)	50.5 (CI 45.8–55.5)	54.3
ECS_motor response_specific_1** (%)	30.2 (CI 26.6–34.1)*	26.0
ECS_motor response_nonspecific_2** (%)	6.6 (CI 5.0–8.6)	5.6
ECS_motor response_none_3** (%)	12.7 (CI 10.4–15.4)	14.1

Table 4_concomitant injuries. Additional traumatic involvement of other body regions, facial sensory organs, osseous structures, brain parenchyma and blood vessels. The anterior cerebral circulation includes the internal carotid, middle cerebral, and anterior cerebral artery. The posterior cerebral circulation comprises of the vertebral, basilar, and posterior cerebral artery. * Control group value not covered by 95% confidence interval (CI) of CNI group. AIS=abbreviated injury scale. CNI=cranial nerve injury.

	CNI group	control group
face_AIS ≥ 2 (%)	28.2 (CI 24.9–31.8)*	17.5
neck_AIS ≥ 2 (%)	2.3 (CI 1.5–3.5)*	1.1
thorax_AIS ≥ 2 (%)	39.9 (CI 35.9–44.1)	38.5
abdomen_AIS ≥ 2 (%)	10.9 (CI 8.9–13.2)	10.2
pelvis_AIS ≥ 2 (%)	8.8 (CI 7.0–10.9)*	11.4
spine_AIS ≥ 2 (%)	19.0 (CI 16.3–22.0)*	23.8
arm_AIS ≥ 2 (%)	30.2 (CI 26.8–33.9)*	26.5
leg_AIS ≥ 2 (%)	14.9 (CI 12.5–17.6)	16.4
eye (%)	4.7 (CI 3.4–6.2)*	1.7
ear (%)	7.5 (CI 5.9–9.5)*	1.4
nose (%)	6.1 (CI 4.7–7.9)	6.4
mouth (%)	0.6 (CI 0.2–1.4)	0.4
orbit (%)	13.0 (CI 10.8–15.5)*	8.6
zygoma (%)	7.5 (CI 5.9–9.5)	6.0
mandible (%)	6.3 (CI 4.8–8.2)*	2.6
LeFort I-III (%)	16.6 (CI 14.1–19.4)*	9.4
skull base (%)	51.0 (CI 46.5–55.7)*	23.5
mandibular joint (%)	0.6 (CI 0.2–1.4)	0.2
brain_contusion (%)	27.3 (CI 24.0–30.8)*	22.1
brain_edema (%)	8.4 (CI 6.6–10.4)	7.5
brainstem (%)	2.4 (CI 1.5–3.6)	1.8
artery_anterior cerebral circulation (%)	0.8 (CI 0.4–1.7)	0.5
artery_posterior cerebral circulation (%)	0.3 (CI 0.1–0.9)	0.3
cerebral vein/venous sinus (%)	1.2 (CI 0.6–2.1)*	0.4
epidural hematoma (%)	12.7 (CI 10.5–15.2)*	9.0
subdural hematoma (%)	29.8 (CI 26.4–33.5)	31.7
subarachnoid hemorrhage (%)	37.2 (CI 33.4–41.3)*	31.7
Intracerebral hemorrhage (%)	14.4 (CI 12.1–17.0)	14.6

Table 5_outcome. Comparison of outcome measures for patients with head trauma ± concomitant cranial nerve injury (CNI). * Control group value not covered by 95% confidence interval (CI) of CNI group. ** Patients dying within 48 hours after hospitalization were excluded from the analysis according to the prespecified exclusion criteria. GOS=Glasgow Outcome Scale.

	CNI group	control group
GOS 1_death > 48 h** (%)	2.1 (CI 1.2–3.2)*	9.4
GOS 2_ persistent vegetative state (%)	2.2 (CI 1.3–3.4)	2.9
GOS 3_ severe disability (%)	13.7 (CI 11.4–16.3)	11.9
GOS 4_moderate disability (%)	37.1 (CI 33.3–41.3)*	23.6
GOS 5_good recovery (%)	45.0 (CI 40.7–49.5)*	52.2
discharge_home (%)	51.0 (CI 46.5–55.7)	48.2
discharge_rehabilitation (%)	35.1 (CI 31.4–39.1)*	27.3
discharge_other hospital (%)	9.4 (CI 7.6–11.6)*	11.8
discharge_death or other (%)	4.5 (CI 3.3–6.1)*	12.7

Table 6_matched pair analysis. Comparison of matched head trauma patients with and without concomitant cranial nerve injuries (CNI) in terms of hospital length of stay and functional outcome (787 matched pairs). * Matching criterion. ** Wilcoxon matched pairs test. *** Chi-square test. AIS=abbreviated injury scale. GCS=Glasgow Coma Scale. GOS=Glasgow Outcome Scale. ICU=intensive care unit. ISS=Injury Severity Score. SD=standard deviation.

	CNI	matched controls	p value
mean age (years $\pm$ SD)	43.8 $\pm$ 19.7	43.6 $\pm$ 20.0	*
male sex (n, %)	555 (70.5)	555 (70.5)	*
mean ISS ($\pm$ SD)	20.6 $\pm$ 10.4	20.9 $\pm$ 10.9	
all traffic accidents (n, %)	400 (50.8)	400 (50.8)	*
low fall (n, %)	177 (22.5)	177 (22.5)	*
head_AIS 2 (n, %)	179 (22.7)	179 (22.7)	*
head_AIS 3 (n, %)	261 (33.2)	261 (33.2)	*
head_AIS 4 (n, %)	263 (33.4)	263 (33.4)	*
head_AIS 5 (n, %)	83 (10.5)	83 (10.5)	*
head_AIS 6 (n, %)	1 (0.1)	1 (0.1)	*
GCS 3–8 (n, %)	171 (21.7)	171 (21.7)	*
GCS 9–12 (n, %)	123 (15.6)	123 (15.6)	*
GCS 13–15 (n, %)	377 (47.9)	377 (47.9)	*
GCS unknown (n, %)	116 (14.7)	116 (14.7)	*
mean intubation time (days $\pm$ SD)	3.6 $\pm$ 7.1	5.3 $\pm$ 8.8	< 0.001**
mean ICU time (days $\pm$ SD)	8.0 $\pm$ 10.4	9.7 $\pm$ 11.5	< 0.001**
mean hospital stay (days $\pm$ SD)	19.8 $\pm$ 16.8	19.9 $\pm$ 18.3	0.425**
GOS 3_severe disability (n, %)	104 (13.2)	96 (12.2)	
GOS 4_moderate disability (n, %)	302 (38.4)	220 (28.0)	
GOS 5_good recovery (n, %)	381 (48.4)	471 (59.8)	< 0.001***

Figures

Figure 1

The flowchart delineates detailed inclusion and exclusion criteria for the study population. *Of note, *no intensive care* and *death within 48 h* are not mutually exclusive categories. AIS=abbreviated injury scale. TR-DGU=TraumaRegister DGU®.