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RESEARCH

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Paediatric traumatic brain injury: clinical presentation, treatment approaches, management strategies, and outcomes. Insights from the CENTER-TBI study

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Abstract

Objective This observational study aims to describe the characteristics and management of paediatric head-injured patients across different paediatric age groups, compared with adults.

Design Secondary analysis of the CENTER-TBI study.

Setting 65 centers in Europe between December 2014 and December 2017.

Patients Patients with traumatic brain injury (TBI) admitted to the hospital were divided into different age groups: paediatrics (pTBI, age ≤ 17 years), adults (18–65 years), and elderly (> 65 years). Paediatrics were further subdivided into three groups: toddlers (from 0 to 4 years), children (from 5 to 12 years), and adolescents (from 13 to 17 years).

Interventions None.

Measurements and main results 3,661 patients were included in the analysis (2,138 admitted to the intensive care unit (ICU) and 1,523 to the ward). Among these, 227 were paediatric (27 toddlers [0–4 years], 65 children [5–12 years], and 135 adolescents [13–17 years]). Most pTBI patients admitted to the ICU presented with mild injuries (Glasgow Coma Scale [GCS] 13–15; 66%), although severe injuries (GCS ≤ 8) were more common in adolescents (23.8%). Susceptibility to neuroworsening and seizures was low in the paediatric group (6% and 3.5%, respectively). Intracranial pressure monitoring was performed in 52 (39.4%) of 132 paediatric ICU patients. Paediatric patients received less intensive therapy targeted to the intracranial pressure (ICP) control particularly in toddlers.

Age below 18 years was associated with a lower risk of poor neurological outcomes at six months, particularly in adolescents and children (odds ratio (OR) = 0.31, 95% confidence interval (CI) = 0.15–0.58 $p < 0.001$ and OR = 0.29, 95% CI = 0.09–0.71, $p < 0.001$, respectively). In toddlers, the association was not statistically significant (OR = 0.48, 95% CI = 0.07–1.94, $p = 0.4$).

Conclusions Paediatric TBI differs significantly from non-paediatric cases, with predominantly mild injuries, lower neuroworsening rates, and less intensive management, especially in younger children. Outcomes at six months are

CENTER-TBI participants and investigators are non-authors collaborators.

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generally more favorable in paediatric patients, emphasizing the need for age-specific management strategies in TBI care.

Keywords Paediatric, Traumatic brain injury, Neurocritical care, Intensive care unit

Introduction

Paediatric traumatic brain injury (pTBI), affecting over 3 million children worldwide every year [1], is a significant contributor to mortality and morbidity rates in the first two decades of life, leaving a lasting impact on the lives of survivors [2, 3]. The distinct nature of TBI across various age groups [4, 5] complicates both its understanding and management. In toddlers, accidental falls are the primary cause of TBI, while adolescents encounter a different set of triggers, including road traffic incidents, sports-related incidents, and acts of violence [6].

Despite the high relevance of pTBI, current literature on traumatic brain injury has been predominantly focused on adults, with some recent analyses including the elderly. A significant gap in published evidence regarding pTBI exists [7, 8], leading to uncertainties and unresolved issues in this crucial area of medicine. The lack of comprehensive studies on pTBI highlights the need for dedicated research to better understand the unique aspects associated with paediatric head injuries [9].

The present study aims to descriptively characterize paediatric TBI management and outcomes across age groups within the intensive care unit (ICU) setting and to compare them with adult and elderly cohorts, acknowledging that differences in care intensity may partly reflect injury severity, institutional protocols, and developmental considerations. Given the challenges in clinical assessment across paediatric developmental stages, we included exploratory biomarker analysis to evaluate whether age-related differences in biomarker expression could reflect underlying pathophysiological variations and help refine age-specific management strategies.

Materials and methods

Study population

The Collaborative European NeuroTrauma Effectiveness in Research in Traumatic Brain Injury (CENTER-TBI) study, registered at clinicaltrials.gov (NCT02210221, 2014–12–19), is a prospective, multicenter, observational, longitudinal cohort study that enrolled traumatic brain injured patients. Data were collected between December 2014 and December 2017 across 65 participating centers in Europe.

The CENTER-TBI study had no age limit, however, the participating centers were not dedicated paediatric centers, and children were, therefore, part of the overall TBI population.

For the current sub analysis, only patients who were admitted to the ward or the ICU were included. Paediatric age subgroups were defined as toddlers (0–4 years), children (5–12 years), and adolescents (13–17 years) based on clinical relevance and sample size considerations. Although our age groups do not fully align with the National Institute of Child Health and Human Development (NICHD) classifications, further subdivision was avoided to preserve statistical power and interpretability. This pragmatic approach allowed for a more meaningful clinical comparison while preserving age-related distinctions across the paediatric spectrum.

The CENTER-TBI study (European Commission grant 602150) has been conducted following all relevant laws of the European Union (EU) and all relevant laws of the country where the recruiting sites were located. Informed consent by the patients and/or the legal representative/next of kin was obtained for all patients recruited (see https://www.center-tbi.eu/project/ethical-approval).

Data collection

Collected data includes demographic characteristics (age, sex), details on the cause and location of the injury, the severity of the injury (Glasgow Coma Scale [GCS], pupils' state, total Injury Severity Score [ISS] at hospital admission), the occurrence of secondary insults (seizures, neuroworsening, hypoxia, hypocapnia, hypotension), and the necessity for urgent surgery. Neuroworsening was defined as a documented decrease in GCS by ≥ 2 points, pupil asymmetry, or new neurologic deficit requiring escalation in care, in line with CENTER-TBI definitions.

Computed tomography (CT) abnormalities were classified using the Marshall CT classification to ensure comparability with the adult CENTER-TBI cohort and to maintain consistency with the standardized data dictionary.

Six specific serum biomarkers S100 calcium-binding protein B (S100B), neuron-specific enolase (NSE), neurofilament light (NfL), glial fibrillary acidic protein (GFAP), ubiquitin carboxy-terminal hydrolase L1 (UCH-L1), and protein Tau were measured in samples obtained within 48 h from hospital admission.

Intracranial pressure (ICP) monitoring and ICP values were collected when clinically indicated. The intensity of ICP treatment was evaluated using the 38-point Therapy Intensity Level (TIL) [10, 11].

Functional outcome was assessed using the 8-point Extended Glasgow Outcome Scale (GOS-E) [12]. A paediatric version was not available or validated at the time of data collection. For toddlers, functional independence was interpreted relative to age-appropriate developmental functioning.

The GOS-E was assessed by trained study personnel during a face-to-face visit, telephone interview, or postal questionnaire [13]. Unfavorable functional outcome was defined as a GOS-E ≤ 4, while good neurological recovery was defined as GOS-E ≥ 7. ICU mortality, mortality at six months, and length of stay in ICU were also evaluated as secondary outcomes.

Clinical data were collected using a custom web-based electronic case report form (eCRF) provided by QuesGen systems Inc., San Francisco, CA. For this sub analysis, data were extracted from the CENTER-TBI Core Version 3.0 using Opal.

Statistical analysis

Data are described with absolute and relative (%) frequency, median (I-III quartile), or mean (standard deviation, SD), where appropriate. Between age groups comparisons (toddlers vs children vs adolescents and paediatrics vs adults vs elderly) on baseline, management, and treatment characteristics were performed by chi-squared, Fisher's exact, or Kruskal–Wallis test, according to the nature of the variable. We used the Benjamini and Hochberg (BH) approach to correct for multiple testing and we reported the adjusted p-values.

The relationship between age and each of the six biomarkers was estimated using a linear regression model with a spline and results were reported along the corresponding 95% confidence intervals (95% CI), stratified by GCS (≤ 8 and > 8). Regarding the outcomes, the analysis of mortality was mainly descriptive due to the limited number of events in the paediatric population that prevented the possibility of building a regression model. On the contrary, a logistic regression model was performed to assess the association among the different age groups and the 6 months of poor functional outcome (GOS-E ≤ 4) considering adults as reference. The model was adjusted for the IMPACT core variables (i.e. age, pupils' reactivity, GCS motor), gender, and type of patients (ward or ICU) and results were shown as odds ratio (OR) of unfavorable outcomes with corresponding 95% CIs.

The tests were two-sided with a significant level of 0.05. All the analyses were conducted with the software R (version 4.2.1, "Beagle Scouts").

Ethical statement

Informed consent by the patients and/or the legal representative/next of kin was obtained, accordingly to the local legislations, for all patients recruited in the Core Dataset of CENTER-TBI and documented in the eCRF (see Supplemental Digital Content, SDC 1).

Results

Baseline characteristics of paediatric TBI patients

Among the 4,509 TBI patients enrolled in the CENTER-TBI core study, 3,661 (81.2%) were admitted to the ward or ICU. Within this subgroup, 227 (6.2%) were paediatric patients, comprising 27 (12%) toddlers, 65 (28%) children, and 135 (59%) adolescents (Figure S1 in Supplemental Digital Content, SDC).

Characteristics of injury and hospital admission are shown in Table 1. At admission, severe TBI was more frequent in adolescents (*n* = 28, 23.8%) than in children (*n* = 9, 18.8%) and toddlers (*n* = 3, 17.6%). At least one unreactive pupil was present in 18 (8%) pTBI. The ISS was higher in adolescents (median = 25, interquartile range [IQR] = 13–35.8) compared to children (median = 16, IQR = 10–25) or toddlers (median = 16 IQR = 9–22.5). A negative first CT (Marshall score 1-normal CT) scan was more frequent in toddlers (*n* = 12, 48%) and children (*n* = 26, 41.9%) compared to adolescents (*n* = 41, 32.5%), while pathological CT scans were more frequent in adolescents compared to the younger patients (Marshall scores 2, 3, and 4 resulted in *n* = 70, 55.6%, *n* = 9, 7.1%, and *n* = 2, 1.6%, respectively, Table 1).

Rates of secondary insults before admission to the emergency room were low overall: hypotension (*n* = 40, 17.6%), hypoxia (*n* = 27, 11.9%), neuroworsening (*n* = 14, 6.2%), seizures (*n* = 8, 3.5%), with no major differences across age groups (SDC, Table S2).

Management of paediatric TBI patients in the ICU

Among the 132 paediatric ICU patients, 52 (39.4%) underwent ICP monitoring, monitoring, mostly with intraparenchymal catheters (*n* = 44, 84.6%). Amidst 40 severe TBI cases (GCS ≤ 8), 28 (70%) were monitored for ICP (Table 2). A higher proportion was observed among the adolescent group (*n* = 37, 45.7%). Among toddlers, 3 of 16 (18.8%) received an ICP monitoring device. Paediatric group displayed a mean daily ICP value in the first week equal to 12.6 mmHg (SD = 10.8 mmHg) with lower values in the toddlers' group (mean daily ICP 10.16 mmHg, SD = 0.15 mmHg). ICP values distribution is shown in SDC, Figure S3.

As for the treatment of elevated ICP, a TIL extreme (TIL scale ≥ 10, TIL scale is detailed in SDC Table S4), was utilized in 30 paediatric patients (22.7%), with

Table 1 Baseline characteristics and injury profile of the paediatric population. Demographic, clinical, and imaging data are presented for the overall paediatric cohort and stratified by age group (toddlers, children, adolescents). The table includes Glasgow Coma Scale (GCS) scores, pupil reactivity, Injury Severity Score (ISS), cause and location of trauma, and early biomarker values

	Paediatrics *n* = 227	Toddlers *n* = 27	Children *n* = 65	Adolescents *n* = 135
Male	146 (64.3)	16 (59.3)	43 (66.2)	87 (64.4)
GCS score				
Mild (GCS 15–13)	139 (65.9)	11 (64.7)	46 (71.9)	82 (63.1)
Moderate (GCS 12–9)	26 (12.3)	3 (17.6)	6 (9.4)	17 (13.1)
Severe (GCS ≤ 8)	40 (21.8)	3 (17.6)	9 (18.8)	28 (23.8)
Baseline pupils				
Both reactive	205 (91.9)	25 (100)	61 (95.3)	119 (88.8)
One reactive	5 (2.2)	0 (0)	1 (1.6)	4 (3)
Both unreactive	13 (5.8)	0 (0)	2 (3.1)	11 (8.2)
Total ISS*	18 (10, 32)	16 (9, 22.5)	16 (10, 25)	25 (13, 35.8)
Marshall CT (%)				
1	79 (37.1)	12 (48)	26 (41.9)	41 (32.5)
2	111 (52.1)	10 (40)	31 (50)	70 (55.6)
3	13 (6.1)	1 (4)	3 (4.8)	9 (7.1)
4	3 (1.4)	0 (0)	1 (1.6)	2 (1.6)
5/6	7 (3.3)	2 (8)	1 (1.6)	4 (3.2)
Injury cause*				
Road traffic accident	110 (48.7)	5 (18.5)	25 (38.5)	80 (59.7)
Incidental fall	78 (34.5)	20 (74.1)	28 (43.1)	30 (22.4)
Other non-intentional injury	22 (9.7)	2 (7.4)	6 (9.2)	14 (10.4)
Violence/Assault	5 (2.2)	0 (0)	0 (0)	5 (3.7)
Other	11 (4.9)	0 (0)	6 (9.2)	5 (3.7)
Injury place*				
Street/Highway	118 (52.4)	7 (25.9)	24 (36.9)	87 (65.4)
Home/Domestic	40 (17.8)	18 (66.7)	15 (23.1)	7 (5.3)
Work/School	14 (6.2)	1 (3.7)	8 (12.3)	5 (3.8)
Sport/Recreational	40 (17.8)	1 (3.7)	15 (23.1)	24 (18)
Public location	11 (4.9)	0 (0)	3 (4.6)	8 (6)
Other	2 (0.9)	0 (0)	0 (0)	2 (1.5)
Biomarkers within 48 h				
S100B (ng/ml)	0.23 (0.25)	0.25 (0.23)	0.16 (0.15)	0.25 (0.28)
NSE (ng/mL)	26.74 (11.53)	30.72 (11.07)	27.95 (8.26)	26.00 (12.57)
GFAP (ng/ml)	12.88 (17.85)	4.29 (4.03)	13.08 (22.47)	13.34 (16.21)
UCH-L1 (pg/mL)	244.8 (338.73)	141.09 (140.8)	204.54 (316.44)	268.55 (356.32)
Tau (pg/ml)	8.13 (13.34)	4.39 (5.15)	6.74 (12.42)	8.97 (14.08)
NfL (pg/ml)	45.73 (63.36)	19.50 (16.67)	38.36 (45.78)	50.38 (70.35)

Results are expressed as n (%), mean (standard deviation, SD), or median (I-III quartile)

CT Computed tomography, *GCS* Glasgow Coma Scale, *ISS* Injury Severity Score, *S100B* S100 calcium-binding protein B, *NSE* Neuron specific enolase, *GFAP* Glial fibrillary acidic protein, *UCH-L1* Ubiquitin C-terminal hydrolase, *NfL* Neurofilament light chain

*A significant comparison among age groups (toddlers, children, adolescents) using the adjusted *p*-value

greater frequency in children ($n=9$, 25.7%) and adolescents ($n=20$, 24.7%). During the stay in the ICU, the pTBI mean TIL was 3.18 (SD = 4.16), and the mean maximum of 3.64 (SD = 4.91) in children. Of note, the lowest mean TIL of 1.23 (SD = 2.25) in toddlers (see SDC Table S3 and Table 2). No differences were found among paediatric groups in the ICP treatment. However, toddlers were treated more frequently with tier 1 interventions (i.e. elevated head position, temperature control, and optimization of sedation) (Fig. 1). Focusing on the

Table 2 Management and monitoring of paediatric TBI patients admitted to the ICU. Descriptive statistics on monitoring practices (e.g., ICP insertion), therapeutic interventions (e.g., mannitol, hypertonic saline, decompressive craniectomy), respiratory support, and laboratory parameters across paediatric age groups

	Paediatrics *n* = 132	Toddlers *n* = 16	Children *n* = 35	Adolescents *n* = 81
At the ICU				
ICP monitoring insertion	52 (39.4)	3 (18.8)	12 (34.3)	37 (45.7)
Duration of ICP monitoring (days)	6 (3, 12.3)	3 (3, 8.5)	8 (4, 12)	6 (2, 12.3)
Daily ICP levels (mmHg)	12.69 (10.8)	10.16 (1.5)	12.80 (5.2)	13.53 (15.2)
TIL extreme	30 (22.7)	1 (6.2)	9 (25.7)	20 (24.7)
Total TIL during the ICU stay	3.18 (4.16)	1.23 (2.25)	3.64 (4.91)	3.37 (4.03)
Mannitol dose	56 (24.7)	7 (25.9)	16 (24.6)	33 (24.4)
Hypertonic saline dose	65 (28.6)	8 (29.6)	19 (29.2)	38 (28.1)
Decompressive craniectomy	9 (4.0)	0 (0.0)	4 (6.2)	5 (3.7)
Intracranial surgery	20 (8.8)	3 (11.1)	9 (13.8)	8 (6.0)
Extracranial surgery	25 (11.2)	1 (3.7)	6 (9.2)	18 (13.6)
Mechanical ventilation	87 (46.5)	8 (40.0)	20 (35.7)	59 (53.2)
Tracheostomy*	17 (12.9)	0 (0.0)	0 (0.0)	17 (20.9)
Fluid loading	35 (40.2)	2 (28.6)	10 (40)	23 (41.8)
Need for vasopressor	41 (47.1)	3 (42.9)	9 (36)	29 (52.7)
Haemoglobin values (g/dL)*	11.75 (2.07)	10.62 (1.67)	11.16 (1.77)	12.18 (2.13)
Transfusion of red blood cells	11 (8.3)	2 (12.5)	4 (11.4)	5 (6.2)
Creatinine (μmol/L)	53.71 (19.37)	24.31 (5.40)	39.48 (9.15)	62.39 (16.63)

Results are expressed as *n* (%) or mean (standard deviation, SD) or median (I-III quartiles)

ICP Intracranial pressure monitoring, *ICU* Intensive care unit; *TBI* traumatic brain injury, *TIL* therapy intensity level

*A significant comparison among age groups (toddlers, children, adolescents) using adjusted *p*-value

hyperosmolar therapy among the paediatric group 56 (24.7%) patients received at least one dose of mannitol and 65 (28.6%) a dose of hypertonic saline. Hyperventilation treatment was more frequent in adolescents (40%) compared to children (24%) and toddlers (14.3). Urgent intracranial and extracranial surgeries were required in 20 (8.8%) and 25 paediatric patients, respectively (11.2%). A decompressive craniectomy (DC) was performed in 9 pTBI patients (4%) overall, with no such surgery required in toddlers, 4 surgeries in children (6.2%), and 5 in adolescents (3.7%), Table 2 and SDC Table S4.

During their ICU stay 87 (46.5%) pTBI needed mechanical ventilation: 59 (53.2%) were adolescents, 20 (35.7%) were children and eight (40%) were toddlers. The mean $PaCO_2$ was 34.9 mmHg (SD = 4.85), SpO_2 was 99% (SD 2%) and PaO_2 was 94.99 mmHg (SD = 8.98), and tracheostomies were required in 17 (12.9%) paediatric patients, all performed on adolescents (p = 0.002) (SDC Table S3, Table 2).

The mean heart rate (HR) was 99 bpm (SD = 23.5), toddlers reached a mean value of 131 bpm (SD = 25.8), children 101 bpm (SD = 19.3), and, at least, adolescents 93 bpm (SD = 19.7). Fluid loading was used in 35 (40.2%) paediatric patients (in 28.6% of the toddlers, 40% of the children, and 41.9% of the adolescents). Furthermore, 41 (47.1%) pTBI needed vasopressor: 3 (42.9%) were toddlers, 9 (36%) were children and 29 (52.7%) were adolescents. During the first week haemoglobin levels were different among paediatric age groups and the values ranged between 10.62 g/dL (SD = 1.67) in toddlers and 12.18 g/dL (SD = 2.13) in adolescents ($p < 0.001$). Eleven paediatric patients required red blood cell (RBC) transfusion with no statistically significant differences among the age groups. Toddlers had a lower creatinine value compared to children and adolescents. A similar trend was observed in sodium levels. The mean value was 141.09 mmol/L: children and adolescents had the same values (141 mmol/L, SD = 3.3) compared to toddlers' lower value whose value was slightly lower (139.5 mmol/L, SD = 3.9).

Four adolescents underwent gastrostomy tube positioning. Complications during the ICU stay were rare in paediatric patients with an occurrence of 28% overall events. The most frequent thereby were respiratory failure ($n = 13$, 9.8%) and ventilation-associated pneumonia ($n = 11$, 8.3%), more often in adolescents than in the other age groups (SDC Table S3).

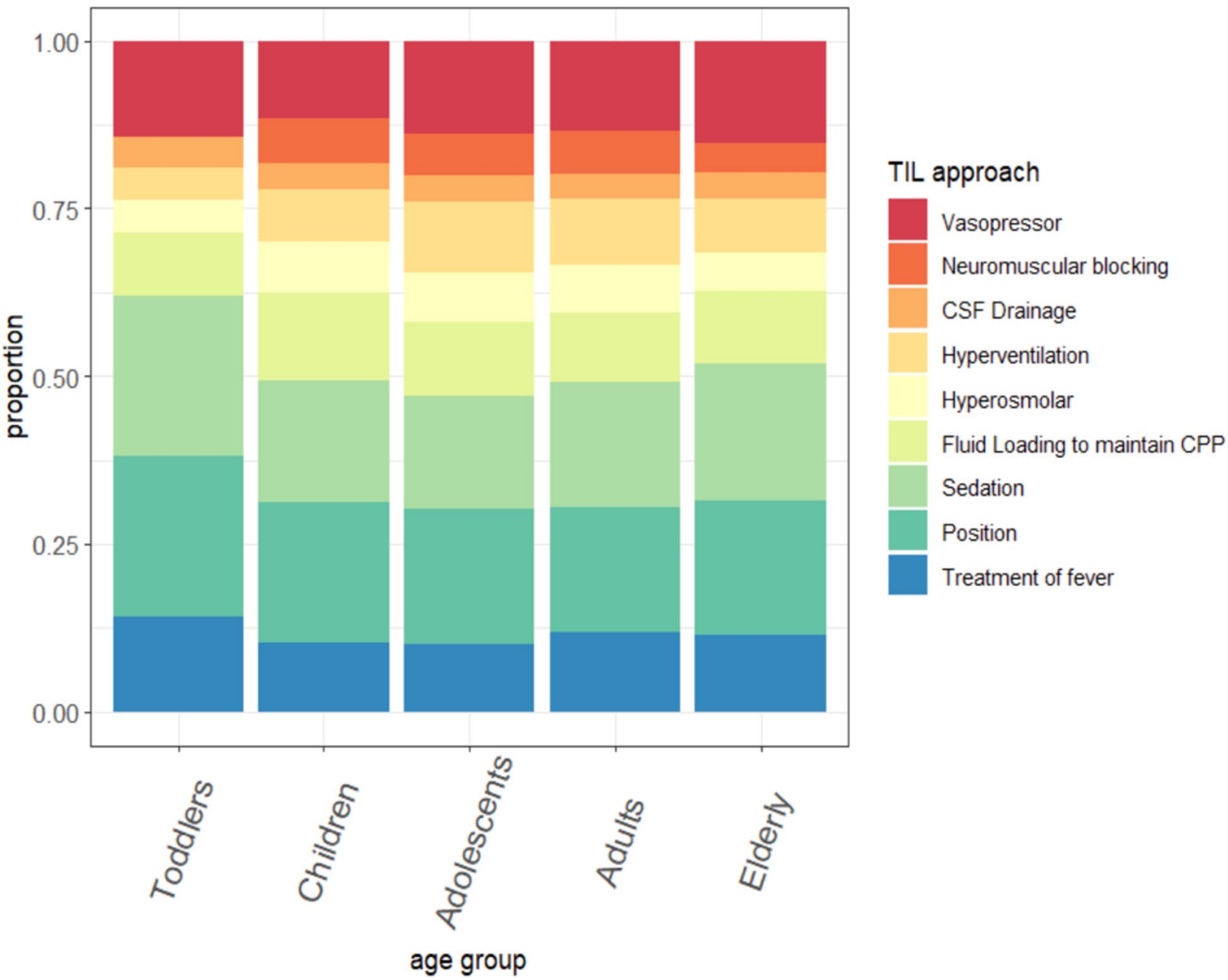

Fig. 1 Therapy intensity levels (TIL) stratified by paediatric age groups. Stacked bar plot illustrating the distribution of specific therapeutic interventions used for ICP management across paediatric subgroups (toddlers, children, adolescents). Lower-intensity measures (Tier 1) were more frequently applied in younger children, while higher TIL scores were observed predominantly in adolescents. Abbreviations: TIL = Therapy Intensity Level; CSF = Cerebrospinal fluid drainage; CPP = Cerebral perfusion pressure

Short and long-term outcomes analysis

Among the paediatric group, ICU and mortality at 6 months was higher in toddlers (4.8% vs 1.6% in children and 3.3% in adolescents) and unfavorable outcome (GOS-E ≤ 4) was slightly more frequent in adolescents (10.7%) than in toddlers (9.5%) and children (8.1%) (Table 3 and SDC Figure S4). Highest incidence of good neurological recovery (GOS-E ≥ 7 at six months) was detected in the paediatric population (63.9%; thereby 66.7% in toddlers, 54.8% in children, and 68%

Table 3 Short- and long-term outcomes in paediatric TBI patients. Key outcome metrics including ICU mortality, 6-month mortality, GOS-E-based functional outcome, and hospital length of stay are reported across paediatric age strata

Outcomes	Paediatrics	Toddlers	Children	Adolescents
ICU mortality	6 (2.9)	1 (4.8)	1 (1.6)	4 (3.3)
Mortality at 6 months	6 (2.9)	1 (4.8)	1 (1.6)	4 (3.3)
Unfavorable GOS-E	20 (9.8)	2 (9.5)	5 (8.1)	13 (10.7)
Good recovery at 6 months	131 (63.9)	14 (66.7)	34 (54.8)	83 (68)
Length of stay in hospital (days)	11.87 (18.38)	8.10 (13.77)	9.20 (14.92)	13.93 (20.42)

Results are expressed as n (%) or mean (standard deviation, SD) or median (I-III quartiles)

TBI Traumatic brain injury, *GOS-E* Glasgow Outcome Scale Extended, *ICU* Intensive care unit in adolescents) compared to adults (47.6%) and elderly patients (41.2%) ($p < 0.001$) (SDC Table S3). The proportion of GOS-E at six months among the age groups is detailed in SDC.

Results from the logistic regression model on unfavorable outcomes (GOS-E ≤ 4) are shown in Fig. 2. Pupils' reactivity and GCS motor were associated with higher odds of poor outcomes. Moreover, an age below 18yo was associated with lower odds of poor outcomes (OR = 0.31, 95% CI = 0.15–0.58, $p < 0.001$ in adolescents; OR = 0.29, 95% CI = 0.09–0.71, $p < 0.001$ in children; and OR = 0.48, 95% CI = 0.07–1.94, $p = 0.4$ in toddlers, Fig. 2). Finally, the odds of poor neurological outcome were significantly higher in patients admitted to ICU (OR = 3.90, 95% CI = 3.05–5.03, $p < 0.001$).

Biomarkers and Comparison with adults and elderly

Regarding the different biomarkers, GFAP, Tau, NfL, and UCH-L1 levels increased with age, while NSE showed the opposite trend and decreased with age. Higher biomarker values were observed in patients with a GCS ≤ 8 compared to those with a GCS > 8. (SDC, Figure S2). Mean values for each biomarker are detailed in Table 1 and Supplemental Table S1.

In depth comparison of paediatric data with adults and elderly is presented in SDC.

Discussion

This study offers a detailed analysis of pTBI using data from the CENTER-TBI cohort, highlighting distinct age-related differences in presentation, management, and outcomes compared to adult and elderly patients.

Our core results can be summarized as follows: adolescents show a clinical severity and management profile similar to that of adults; adherence to paediatric TBI guidelines is only partial; toddlers and younger children receive a lower intensity of care yet experience better outcomes; and biomarker analyses reveal distinct age-related pathophysiological patterns. A key finding is that adolescents mirror adults in injury severity and treatment needs, while toddlers and children show distinct profiles—such as lower ISS scores, more frequent normal

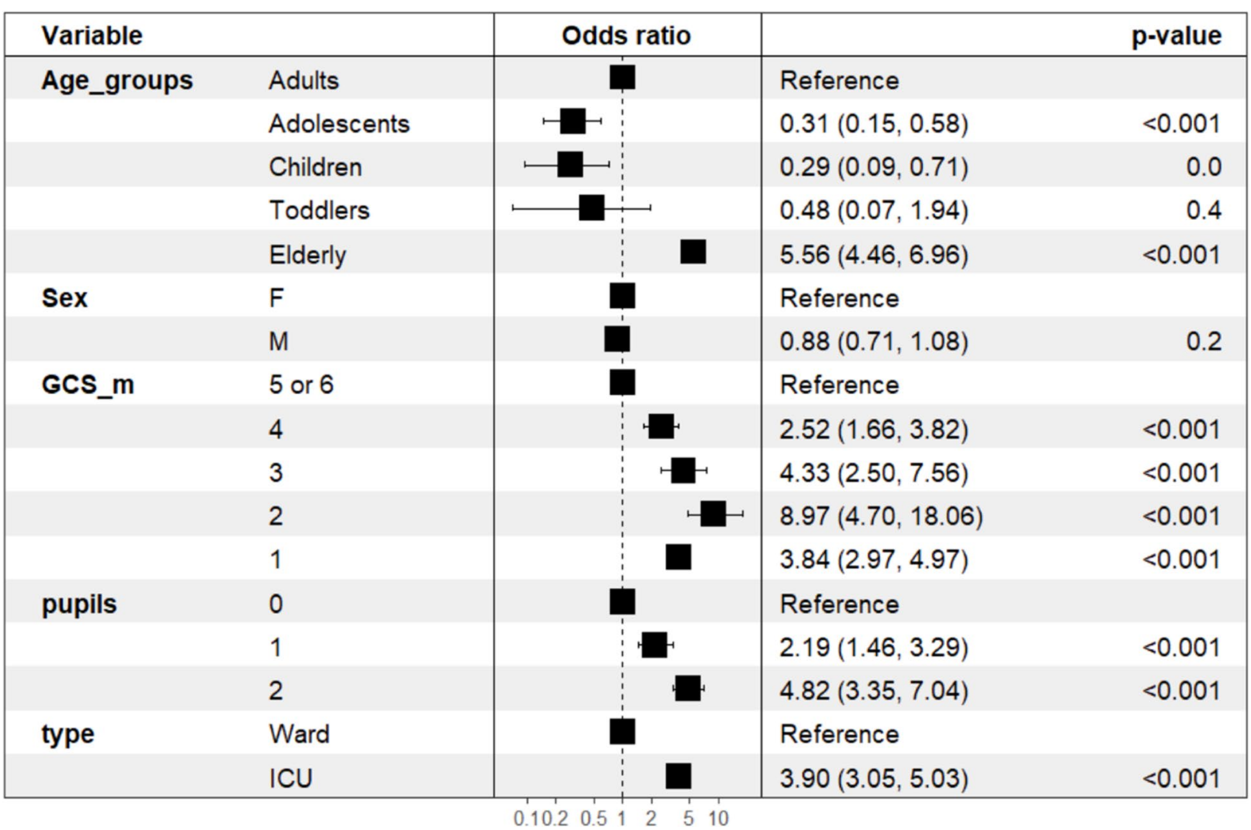

Fig. 2 Multivariable logistic regression model for unfavorable outcome (GOS-E ≤ 4) at 6 months. Odds ratios with 95% confidence intervals are shown for relevant predictors of poor functional outcome. Age below 18 years was associated with a lower odds of unfavorable outcome, especially in children and adolescents. Abbreviations: GOS-E = Glasgow Outcome Scale – Extended; GCS_m = Glasgow Coma Scale motor; ICU = Intensive Care Unit

CT scans, and lower ICP values. These findings underscore that pTBI is not a uniform condition and support the need for age-specific strategies [14–19]. The limited use of ICP monitoring and decompressive craniectomy in younger children further highlights the need for evidence-based guidelines tailored to paediatric subgroups [20–26].

Although the third edition of the Brain Trauma Foundation paediatric TBI guidelines [7] was published after the study period, our evaluation of adherence refers to the 2012 second edition [27], whose recommendations on ICP monitoring and hyperosmolar therapy are conceptually similar.

The 2012 and 2019 paediatric TBI Guidelines [7, 8] recommend ICP monitoring for patients with a GCS score ≤ 8, aiming to maintain ICP below 20 mmHg. In this study, ICP monitoring was performed in only 39.4% of paediatric.

ICU patients, with a higher prevalence among adolescents compared to children and toddlers. Specifically, ICP monitoring was performed in 70% of severe cases, implying partial but not poor adherence, especially considering that two-thirds of paediatric ICU admissions were for mild injuries.

These findings suggest that ICP monitoring is underutilized, particularly in younger children, despite guideline recommendations. This discrepancy may reflect clinical hesitation due to the invasiveness of the procedure or uncertainty about its necessity in younger paediatric populations [22–24].

The guidelines outline a tiered approach to ICP management. Paediatric patients received less aggressive ICP-directed therapy than adults, likely reflecting differences in injury severity and clinical decision-making rather than inherently lower treatment requirements. Hyperventilation, for example, was more commonly used in adolescents than in children and toddlers. Additionally, decompressive craniectomy was performed in only 4% of paediatric cases, with no toddlers undergoing the procedure. This suggests that the need for aggressive ICP management is lower in younger children or that surgical interventions may be underutilized. The limited use of decompressive craniectomy raises questions about whether surgical interventions should be more aggressively considered in paediatric TBI or whether alternative strategies should be prioritized. The guidelines recommend the use of mannitol or hypertonic saline to control elevated ICP. We found that 24.7% of paediatric patients received mannitol, while 28.6% received hypertonic saline. These rates are comparable to those observed in adult populations [21]. In this study, both mannitol and hypertonic saline were used in roughly equal proportions. Recent paediatric TBI guidelines favor hypertonic saline over mannitol due to limited paediatric evidence for the latter, and the pattern observed here likely reflects practice variability during the 2014–2017 period. The guidelines recommend maintaining a partial pressure of carbon dioxide between 35–40 mmHg. The average $PaCO_2$ in paediatric patients was 34.9 mmHg. However, adolescents exhibited a trend toward more aggressive ventilation strategies, potentially reflecting their closer physiological resemblance to adults [28]. This variation raises concerns about the need for stricter adherence to ventilation targets, particularly in younger paediatric patients, where excessive hyperventilation could lead to secondary ischemic injury [19–23].

Short- and long-term outcomes further illustrate the advantages of younger age in TBI recovery. ICU mortality was lowest in toddlers, followed by children and adolescents. At six months, paediatric patients exhibited the highest rates of good neurological recovery compared to adults and elderly patients. Adolescents demonstrated a slightly higher risk of unfavorable outcomes than younger paediatric groups, aligning with their closer resemblance to adult TBI profiles [15, 18, 19, 29].

Our study's biomarker analysis offers additional insights into the neurobiological differences between age groups. Biomarker analysis revealed an age-related trend, with GFAP, Tau, NfL, and UCH-L1 levels increasing with age, while NSE levels decreased, reflecting distinct neurobiological responses to injury across the lifespan [25, 26, 28, 30]. The higher levels of GFAP, Tau, and NfL in the elderly suggest greater susceptibility to axonal degeneration and astroglial damage, likely due to reduced neuroplasticity, impaired repair mechanisms, and a greater burden of secondary neuroinflammatory processes. In contrast, the higher NSE levels in paediatric patients indicate greater neuronal metabolic activity and susceptibility to early excitotoxic stress, possibly due to higher neuronal turnover, greater reliance on glycolysis, and a predominance of necrotic rather than apoptotic cell death following injury [31, 32]. These age-related trajectories highlight fundamental differences in TBI pathophysiology across age groups, suggesting that younger brains may experience more immediate metabolic stress, while older brains exhibit more chronic neurodegenerative responses. However, evidence on age-related susceptibility to secondary brain insults is mixed. Some studies report lower systemic and intracranial insult burden in children [33, 34], whereas others suggest equal or greater vulnerability due to immature autoregulation [35]. The lower incidence observed in our cohort may therefore reflect less intensive monitoring rather than intrinsic resistance. Given the potential for biomarkers to improve age-specific patient stratification and guide therapeutic decisions, their integration into clinical practice should be explored in future guideline updates.

While this study provides valuable insights, several limitations should be noted. The CENTER-TBI dataset involves a heterogeneous patient population from multiple centers, introducing variability in clinical practices. The inclusion of paediatric patients managed in adult trauma centers may limit the generalizability of findings to dedicated paediatric settings. Due to the limited number of paediatric cases, especially in the youngest age groups, we adopted broader paediatric age bands that do not correspond exactly to standard developmental stages. This may mask developmental differences, particularly between infants and older toddlers or between early and late adolescents. Interpretation in toddlers should be cautious given the small sample size. Future paediatric TBI studies should aim for more granular age stratification. The limited number of moderate-to-severe paediatric TBI cases and outcome events constrains the strength of inferential statistics and limits multivariable modeling, especially for mortality. Another major limitation is the use of the adult validated Marshall CT classification scale. We acknowledge that paediatric-specific CT scores may offer improved prognostic discrimination. Moreover, GOS-E scale is not validated for children under 17 years. This restricts the interpretability of paediatric functional outcomes, especially in toddlers and young children. Future research should use validated paediatric measures such as the GOS-E Peds. These findings should therefore be interpreted as exploratory and hypothesis-generating rather than confirmatory. Nonetheless, the study remains one of the largest multicenter ICU cohorts reporting paediatric TBI care patterns across Europe. Future studies should address these gaps by developing age-specific management protocols, refining paediatric ICP thresholds, validating biomarkers for clinical decision-making, and evaluating long-term neurodevelopmental outcomes.

Although this analysis draws on ICU data from 2014–2017, it remains relevant due to the continued lack of large-scale multicenter paediatric TBI datasets. While practices may have evolved slightly since then, the underlying differences in pathophysiology, monitoring, and therapeutic intensity across paediatric age groups continue to underscore the need for tailored strategies.

Conclusion

Paediatric TBI exhibits clear age-related differences, with adolescents resembling adults more closely than younger paediatric groups. Overall, paediatric patients have better outcomes than adults and elderly patients, with lower rates of secondary insults, reduced need for intensive therapies, and higher rates of neurological recovery. These findings highlight the importance of tailored treatment approaches and the need for further research to optimize pTBI management strategies, particularly in the youngest patients. Additionally, the study also suggests partial implementation of guideline-recommended monitoring and surgery in children and highlights the potential role of biomarkers in future age-specific management strategies. Addressing these knowledge gaps through further research may lead to more effective, evidence-based paediatric TBI management strategies.

Supplementary Information

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Supplementary Material 1.

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Clinical trial number

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Authors' contributions

Conceptualization and study definition: Giuseppe Citerio. Funding acquisition: Giuseppe Citerio. Patients' enrolment: CENTER-TBI participants and investigators. Data verification: Francesca Graziano. Access to raw data: Giuseppe Citerio, Francesca Graziano. Formal analysis: Francesca Graziano, Paola Rebora, Stefania Galimberti. Project administration, Data access and verification: Giuseppe Citerio. Writing—original draft: Giuseppe Citerio, Francesca Graziano, Angelo Guglielmi. Writing—review and editing: All the authors. The final responsibility for the decision to submit for publication: Giuseppe Citerio.

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Data availability

The data supporting the study findings are available upon reasonable request after approval of a proposal from the corresponding author (GC). Data collected for the analysis will be made available to others, including deidentified individual participant data and a data dictionary defining each field in the set. Related documents, such as the study protocol, statistical analysis plan, and informed consent form, will also be available.

Declarations

Ethics approval and consent to participate

The CENTER-TBI study was performed according to the Helsinki Declaration and the International Conference on Harmonization for Good Clinical Practice. Since comatose patients could not provide informed consent during study recruitment, each center referred to local/national law on the lack of capacity.

If the patients regained capacity at the follow-up visit, they had to either provide informed consent to use the acute and follow-up data or refuse to participate in the research. Ethical approval for the study was obtained from the Medical Ethics Committees of each participating center, and informed consent was obtained from all participants following local regulations (https://www.center-tbi.eu/project/ethical-approval). For this sub-analysis, no further ethical approval was required.

Consent for publication
Written informed consent for the publication of these data has been previously obtained.

Competing interests
The authors declare no competing interests.

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References
1. Coulter IC, Forsyth RJ (2019) Paediatric traumatic brain injury. Curr Opin Pediatr 31(6):769–774
2. Figaji A (2023) An update on paediatric traumatic brain injury. Childs Nerv Syst 39(11):3071–3081
3. Sookplung P, Vavilala MS (2009) What is new in paediatric traumatic brain injury? Curr Opin Anaesthesiol 22(5):572–578
4. Dewan MC, Mummareddy N, Wellons JC, Bonfield CM (2016) Epidemiology of global paediatric traumatic brain injury: qualitative review. World Neurosurg 91:497-509.e1
5. Andelic N (2013) The epidemiology of traumatic brain injury. Lancet Neurol 12(1):28–29
6. Taylor CA, Bell JM, Breiding MJ, Xu L (2017) Traumatic brain injury-related emergency department visits, hospitalizations, and deaths — United States, 2007 and 2013. MMWR Surveill Summ 66(9):1–16
7. Kochanek PM, Tasker RC, Carney N, Totten AM, Adelson PD, Selden NR et al (2019) Guidelines for the Management of paediatric Severe Traumatic Brain Injury, Third Edition: Update of the Brain Trauma Foundation Guidelines. Pediatr Crit Care Med 20(3S):S1-82
8. Sigurtà A, Zanaboni C, Canavesi K, Citerio G, Beretta L, Stocchetti N (2013) Intensive care for paediatric traumatic brain injury. Intensiv Care Med 39(1):129–136
9. Stocker RA (2019) Intensive care in traumatic brain injury including multimodal monitoring and neuroprotection. Med Sci 7(3):37
10. Maas AIR, Harrison-Felix CL, Menon D, Adelson PD, Balkin T, Bullock R et al (2011) Standardizing data collection in traumatic brain injury. J Neurotrauma 28(2):177–187
11. Bhattacharyay S, Beqiri E, Zuercher P, Wilson L, Steyerberg EW, Nelson DW et al (2024) Therapy intensity level scale for traumatic brain injury: clinimetric assessment on neuro-monitored patients across 52 European intensive care units. J Neurotrauma 41(7–8):887–909
12. Wilson L, Boase K, Nelson LD, Temkin NR, Giacino JT, Markowitz AJ et al (2021) A manual for the Glasgow outcome scale-extended interview. J Neurotrauma 38(17):2435–2446
13. Wilson JTL, Pettigrew LEL, Teasdale GM (1998) Structured interviews for the Glasgow outcome scale and the extended Glasgow outcome scale: guidelines for their use. J Neurotrauma 15(8):573–585
14. Serpa RO, Ferguson L, Larson C, Bailard J, Cooke S, Greco T et al (2021) Pathophysiology of paediatric traumatic brain injury. Front Neurol 12:696510
15. Keenan HT, Clark A, Holubkov R, Ewing-Cobbs L (2023) Longitudinal developmental outcomes of infants and toddlers with traumatic brain injury. JAMA Netw Open 6(1):e2251195
16. Ciurea AV, Gorgan MR, Tascu A, Sandu AM, Rizea RE (2011) Traumatic brain injury in infants and toddlers, 0–3 years old. J Med life 4(3):234–243
17. Myhre M, Grøgaard J, Dyb G, Sandvik L, Nordhov M (2007) Traumatic head injury in infants and toddlers. Acta Paediatr 96(8):1159–1163
18. Adamo MA, Drazin D, Smith C, Waldman JB (2009) Comparison of accidental and nonaccidental traumatic brain injuries in infants and toddlers: demographics, neurosurgical interventions, and outcomes: clinical article. J Neurosurg Pediatr 4(5):414–419
19. Popernack ML, Gray N, Reuter-Rice K (2015) Moderate-to-severe traumatic brain injury in children: complications and rehabilitation strategies. J Pediatr Health Care 29(3):e1-7
20. Keenan HT, Nocera M, Bratton SL (2005) Frequency of intracranial pressure monitoring in infants and young toddlers with traumatic brain injury&ast. Pediatr Crit Care Med 6(5):537–541
21. Figaji AA (2017) Anatomical and physiological differences between children and adults relevant to traumatic brain injury and the implications for clinical assessment and care. Front Neurol 8:685
22. Alkhoury F, Kyriakides TC (2014) Intracranial pressure monitoring in children with severe traumatic brain injury : National Trauma Data Bank-based review of outcomes. JAMA Surg 149(6):544–548
23. Allen BB, Chiu YL, Gerber LM, Ghajar J, Greenfield JP (2014) Age-Specific Cerebral Perfusion Pressure Thresholds and Survival in Children and Adolescents With Severe Traumatic Brain Injury &ast. Pediatr Crit Care Med. 15(1):62–70
24. Adamo MA, Drazin D, Waldman JB (2009) Decompressive craniectomy and postoperative complication management in infants and toddlers with severe traumatic brain injuries: clinical article. J Neurosurg Pediatr 3(4):334–339
25. Nagy L, Morgan RD, Collins RA, Kharbat AF, Garza J, Belirgen M (2023) Impact of timing of decompressive craniectomy on outcomes in paediatric traumatic brain injury. Surg Neurol Int 14:436
26. Ardissino M, Tang A, Muttoni E, Tsang K (2019) Decompressive craniectomy in paediatric traumatic brain injury: a systematic review of current evidence. Childs Nerv Syst 35(2):209–216
27. Kochanek PM, Carney N, Adelson PD, Ashwal S, Bell MJ, Bratton S et al (2012) Guidelines for the Acute Medical Management of Severe Traumatic Brain Injury in Infants, Children, and Adolescents-Second Edition. Pediatr Crit Care Med. 13(NA):S1-2
28. McLaughlin C, Darcy D, Park C, Lane CJ, Mack WJ, Bliss DW et al (2019) Timing of tracheostomy placement among children with severe traumatic brain injury: a propensity-matched analysis. J Trauma Acute Care Surg 87(4):818–826
29. Ferrazzano PA, Rebsamen S, Field AS, Broman AT, Mayampurath A, Rosario B et al (2024) MRI and clinical variables for prediction of outcomes after paediatric severe traumatic brain injury. JAMA Netw Open 7(8):e2425765
30. Lugones M, Parkin G, Bjelosevic S, Takagi M, Clarke C, Anderson V et al (2018) Blood biomarkers in paediatric mild traumatic brain injury: a systematic review. Neurosci Biobehav Rev 87:206–217
31. Oris C, Pereira B, Durif J, Simon-Pimmel J, Castellani C, Manzano S et al (2018) The biomarker S100B and mild traumatic brain injury: a meta-analysis. paediatrics 141(6):e20180037
32. Ryan E, Kelly L, Stacey C, Duff E, Huggard D, Leonard A et al (2022) Traumatic Brain Injury in Children. Pediatr Emerg Care 38(3):e1139–e1142
33. Mansfield RT (1997) Head injuries in children and adults. Crit Care Clin 13(3):611–628

34. Bruce DA (1990) Head injuries in the paediatric population. Curr Probl Pediatr 20(2):66–107
35. Figaji AA, Zwane E, Fieggen AG, Argent AC, Roux PDL, Siesjo P et al (2009) Pressure autoregulation, intracranial pressure, and brain tissue oxygenation in children with severe traumatic brain injury: clinical article. J Neurosurg Pediatr 4(5):420–428

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