ORIGINAL ARTICLE

# Prediction of mortality in pediatric traumatic brain injury: Implementations from a tertiary pediatric intensive care facility

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## ABSTRACT

**BACKGROUND:** To explore the mortality risk factors of traumatic brain injury in pediatric intensive care unit admissions.

**METHODS:** Eighty-eight children (categorized using the Glasgow Coma Scale) between September 2014 and December 2016 were analyzed. Emergency department and intensive care course, treatment strategies, axonal injury, intubation and tracheostomy rates, length of intensive care and hospitalization, Rotterdam-CT scores, injury severity scores, and PRISM-III scores were recorded.

**RESULTS:** Older age was associated with trauma severity (p=0.010). Target serum osmolality was reached at 8.5 (3.5–40) hours in patients undergoing anti-edema therapy. ICP-monitoring rates was 8%; in absence of ICP-monitorization clinical follow-up was performed through repeated brain tomographies. Axonal injury was associated with prolonged intubation, intensive care and hospital stay (p<0.001, p<0.001, p=0.030). Six children required tracheostomy at 14.33±1.03 days; decannulations were performed within 6 months in five children.

**CONCLUSION:** Mortality rate was 12.5%; six patients progressed to brain death with organ donor approvals in five. Initial hypotension, lung contusion, injury severity scores and Rotterdam-CT scores were related with mortality. Rotterdam-CT score was determined as the independent risk factor for mortality; one increment in the score increased the odd of recovery by 20.334 times (%95 CI 1.999–206.879). ISS score was also borderline significant (p=0.052; OR:1.195 %95 CI 0.999–1.430).

**Keywords:** Brain edema therapy; children; mortality; pediatric critical care; Rotterdam-CT score; traumatic brain injury.

## INTRODUCTION

Traumatic brain injury (TBI) is one of the major causes of mortality and morbidity in children aged 1–19 years.[1,2] The Centers for Disease Prevention and Control, USA 2015 data estimates 475000 children <14 years of age sustain TBI annually with 37,000 hospitalizations and a mortality rate of 2,685 between 1999 and 2013.[3] There is limited data regarding TBI incidence in Turkey. Given the fact that traffic accidents constitute only a fraction of all trauma etiologies, latest Turkish Statistical Institute's 2016 data verifies 864 deaths and 55198 injuries related to traffic accidents in children.[4]

Prognosis depends on the severity of the primary injury and prevention of secondary insults, including hypoxemia, hypercarbia, hypotension, hyperthermia, seizure, and elevated intracranial pressure (ICP).[1] After initial management in the field and emergency department (ER), the primary goal of treatment in pediatric intensive care units (PICU) is to maintain age-appropriate cerebral perfusion pressure (CPP) and to minimize secondary injuries.[5,6]

As being one of the most referred pediatric trauma centers in the Mediterranean region, we conducted a retrospective study on PICU admissions between September 2014 and December 2016 to determine the characteristics of admissions and therapy strategies, and we evaluated the risk factors affecting the mortality and short term morbidity of TBI.

Cite this article as: Ongun EA, Dursun O. Prediction of mortality in pediatric traumatic brain injury: Implementations from a tertiary pediatric intensive care facility. Ulus Travma Acil Cerrahi Derg 2018;24:199-206.

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Ulus Travma Acil Cerrahi Derg 2018;24(3):199-206 DOI: 10.5505/tjtes.2017.37906 Submitted: 14.07.2017 Accepted: 17.10.2017 Online: 08.05.2018

## MATERIALS AND METHODS

Following IRB approval with waiver of consent, the electronic database of 88 children (age: 1 month–18 years) admitted to PICU between September 2014 and December 2016 was explored. Patients were categorized into three groups to define the severity of TBI based on initial Glasgow Coma Scale (GCS) at ER admission:[1] severe head trauma (GCS ≤8), moderate TBI (GCS: 9–12), mild TBI (GCS: 13–15). After initial categorization, patients with neurological deterioration were also noted. Data were analyzed for demographics and injury characteristics. Patients' vital signs, laboratory data, computed tomography (CT), intracranial and co-existing pathologies of other systems, treatment strategies, transfused blood products, and urgent surgical operations before PICU admission were recorded.

Intensive care course of the study included patients' vital signs and laboratory data, ICP-monitoring rates and if received, the anti-edema medications and duration that were required to attain the initial target serum osmolality (measured serum osmolality: 300–320 mosmol/L),[7,8] and the adverse effects related to hyperosmolar therapy (central pontine myelinolysis because of rapid increase in serum sodium, acute tubular necrosis, and hyperchloremic metabolic acidosis). To avoid medication-related side effects, intensive care protocol for patients who were administered mannitol and/or 3% NaCl included the following: if serum osmolality was >320 mosm/L, discontinue mannitol; if serum osmolality was 320–350 mosml/L, decrease the infusion rate of 3% NaCl; or if serum osmolality was >350 mosm/L, discontinue NaCl infusion. We also examined patient records for diabetes insipidus, anti-convulsive therapy (decision of initiating anti-seizure drug regimen was made by the pediatric neurologists based on the severity of parenchymal damage and neurological status of the patient without routine EEG monitoring) and if present, hemodynamic instability as well as transfused blood products and massive transfusion rates (administered upon the advice of Neff et al.;[9] 40 ml/kg of all blood products transfused per 24 h). Rate of neurosurgical operations during PICU admission, axonal injury observed in cranial magnetic resonance (MR) imaging, assessment of GCS of the patients based on the records at the time of admission to emergency care, injury severity score (ISS), Rotterdam computerized tomography scores (Ro-CT),[10] and PRISM-III scores after admission to PICU were performed. Finally, the total number of cranial CT scans (from the moment of ER admission to the hospital discharge), intubation and tracheostomy rates, length of PICU, and length of hospital stay were noted.

Statistics were analyzed using SPSS version 23. Descriptive analyses were presented as frequency (n), percentage (%), mean, standard deviation, and median, with minimum and maximum values. Categorical data was assessed using the chi-square test and Fisher's exact test. Shapiro–Wilks test was used to assess normality distribution. Continuous variables were analyzed using the Mann–Whitney U-test or Independent Samples t-test. One way ANOVA and/or Kruskal–Wallis tests were applied to compare the mean values or center of location parameters in three groups. Wilcoxon rank-sum test or paired samples t-test was used for statistical comparison. All the statistical tests were two-tailed, and P-values <0.05 were considered to be significant. Multivariate logistic regression was used to determine independent predictors of the studied outcomes.

## RESULTS

In total, 88 patients were enrolled in the study. The study population was categorized according to GCS on ER admission as severe TBI (42/88, 47.7%), moderate TBI (15/88, 17%), and mild TBI (31/88, 35.2%). Female/male ratio was 1:1.3 with a median age of 6 years (1–17 years) (Table 1). TBI severity and accompanying injuries of other organs were noted to increase by older age (p=0.010; p=0.007). Children with initial GCS <9 and neurological deterioration at follow-up required intubation at a rate of 69.3% to establish a secure airway. Length of MV stay was median 3 days (1–21 days). GCS was reciprocally associated with the length of MV and PICU stay (p=0.001; p=0.002), though it had no effect on the duration of hospitalization (p=0.155).

Accompanying pathologies of other organ systems and thoracic region injuries were observed more frequently in the severe TBI group (p=0.019; p=0.001). Table 2 shows intracranial pathologies and treatment-oriented data. Of the 20 children (22.7%) who required urgent neurosurgical interventions at ER (decompressive craniectomy/hematoma drainage/extraventricular drainage-EVD), only seven had been followed by ICP monitoring at PICU. In the absence of ICP monitoring, repeated brain CT scans were applied to children at a rate of median 2.5 (1–9) scans/per patient from ER admission to hospital discharge; however, only one patient underwent urgent surgical hematoma drainage because of the clinical signs of elevated ICP due to an enlarged epidural hematoma. The number of CT scans were inversely proportional to GCS (p=0.018, r=−0.304).

In case of brain edema or neurological deterioration, anti-edema therapy in the form of 20% Mannitol and/ or hypertonic saline (3% NaCl) were applied (Table 2). Note that only 11.3% of the study population received the first dose of anti-edema therapy at ER. After PICU admission, the median duration to achieve initial target serum osmolality was 8.5 h (3.5–40 h), and we did not observe any side effect related to hyperosmolar therapy (hypercloremic metabolic acidosis, acute tubular necrosis, or central pontine myelinolysis). Despite treatment, 21.6% of the patients presented clinical signs of elevated intracranial pressure. Anti-epileptic medication was initiated at the rate of 44.3%; however, seizures appeared in 15.9% of the study population (Table 2).

**Table 1.** Demographics of the study population

| Variables | n (%) |
|---|---|
| Age (median) | 6 years (1–17 years) |
| Age groups | |
| <5 years | 36 (40.9) |
| 6–10 years | 25 (28.4 ) |
| 11–18 years | 27 (30.7) |
| Sex | |
| Females | 38 (43.2) |
| Males | 50 (56.8) |
| TBI Severity | |
| Mild (GCS: 13–15) | 31 (35.2) |
| Moderate (GCS: 9–12) | 15 (17.7) |
| Severe (GCS: ≤8) | 42 (47.7) |
| Mechanism of injury | |
| Vehicle | 16 (18.2) |
| Pedestrian | 27(30.7) |
| Motorcycle accident | 6 (6.8) |
| Fall (higher than 1.5 m) | 35 (39.7) |
| Other | |
| Fall (less than 1.5 m) | 3 (3.4) |
| Crush (television) | 1 (1.1) |
| Accompanying other organ systems injury | 63/88 children (71.6) |
| Thoracic region | 47/88 (53.4) |
| Pneumothorax/hemothorax | 12/47 (25.5) |
| Lung contusion | 38/47 (80.9) |
| Abdominal region | 25/88 (28.4) |
| Multiorgan injury | 9/25 (36) |
| Isolated hepatic injury | 9/25 (36) |
| Isolated splenic injury | 3/25 (12) |
| Isolated kidney injury | 3/25 (12) |
| Retroperitoneal bleeding | 1/25 (4) |
| Extremity injury | 49/88 (55.7) |
| Upper extremity fractures | 20/49 (40.8) |
| Lower extremity fractures | 29/49 (59.2) |
| Spinal cord injury | 23/88 (26.1) |
| Cervical spine fractures | 12/23 (52.2) |
| Thoracic spine fractures | 6/23 (26.1) |
| Lumbar/sacral spine fractures | 5/23 (21.7) |

GCS: Glascow Coma Scale; TBI: Traumatic brain injury.

**Table 2.** Intracranial pathologies and therapy strategies

| Variables | n (%) |
|---|---|
| Intracranial pathology | |
| Isolated subarachnoid hemorrhage | 25 (28.4) |
| Isolated epidural hematoma | 11 (12.6) |
| Isolated subdural hematoma/ | |
| Fluid accumulation | 13 (14.8) |
| Intraparenchymal hemorrhage | 7 (8) |
| Intraventricular hemorrhage | 2 (2.3) |
| Multi-localized hemorrhage | 30 (34.1) |
| Brain edema | 43 (48.9) |
| Midline shift | 19 (21.6) |
| Elevated intracranial pressure | 19 (21.6) |
| ICP monitoring | 7 (8) |
| Anti-edema therapy | 59 (67) |
| Mannitol alone | 9 (10.2) |
| Hypertonic saline alone | 13 (14.8) |
| Mannitol+Hypertonic saline | 37 (33) |
| Serum sodium at PICU arrival | 140.88±4.74 meq/L |
| Length of hypertonic saline | |
| therapy (median) | 4 (1–10) days |
| Length of mannitol therapy (median) | 3 (1–6) days |
| Reason of discontinuation for mannitol | |
| Neurological recovery | 25/46 (54.3) |
| Elevated serum osmolality | 15/46 (32.6) |
| Diabetes insipidus | 6/ 46 (13) |
| Target (measured) serum osmolality | 315±16.39 |
| Mannitol alone | 310.43±25.22 |
| Hypertonic saline alone | 310.22±9.12 |
| Mannitol+Hypertonic saline | 319.00±15.28 |
| Duration to reach target serum osmolality | 8.5 (3.5–40) hours |
| Diffuse axonal injury | 15 (17) |
| Diabetes insipidus | 9 (10.2) |
| Anti-seizure therapy | 40 (45.5) |
| Levetiracetam | 3 (38.6) |
| Phenytoin | 6 (6.8) |
| Clinical seizure | 14 (15.9) |
| Rate of brain computed tomography | |
| (median) | 2.5 (1–9)/person |

Diffuse axonal injury (diagnosed at cranial MR imaging) occurred at a rate of 17% among those who did not present the anticipated neurological recovery. It seemed to increase with the severity of brain injury (p=0.038), but the neurological deterioration at follow-up did not affect the frequency of diffuse axonal injury (p=0.325). However, it extended the length of MV stay, PICU stay, and the hospitalization (p<0.001, p<0.001, and p<0.001, respectively). In six of the axonal injury-diagnosed patients, tracheostomy cannulation was performed at an average of 14.33±1.03 days because of prolonged endotracheal intubation (Table 3). Tracheostomies' decannulation were performed within 6 months following hospital discharge in five children; only one child remained in the vegetative state and continued to receive home ventilation for >1 year.

Co-injuries to other organ systems were noted in 71.6% of the study group (Table 1). They were also related to prolonged MV, PICU, and hospital stays (p<0.001, p<0.001, p=0.030 respectively). Presence of lung contusion extended the length of stay in MV and PICU (p=0.002, p=0.002); however, it had no impact on hospital stay (p=0.104).

Observations on hemodynamics revealed that 31.8% of the children had presented age-specific hypotension at initial ER admission and received blood transfusions (Table 3). Hypotension was observed more frequently in severe TBIs and co-existing injuries of other organ systems (p=0.009, p=0.012). After the initial stabilization, 27.3% required urgent surgical intervention before PICU admission (Table 3). To maintain a hemoglobin level that was >8 g/dl, 37.5% of the children received blood transfusions during the first 48 h of PICU admission, while the massive transfusion rate against hemorrhagic shock was 8%. The ones with co-existing injuries of other organ systems and lower GCS seemed to require more frequent transfusions (p<0.001, p=0.001 respectively). Table 4 represents a comparison of variables within the GCS groups.

**Table 3.** Follow-up at emergency department and pediatric critical care unit

| | n (%) |
|---|---|
| Emergency department | |
| Initial hypotension at arrival | 28 (31.8) |
| Blood transfusion | 28 (31.8) |
| Neurological deterioration at follow-up | 21 (23.9) |
| Urgent surgery | 24 (27.3) |
| Neurosurgical procedures | 20 (22.7) |
| Orthopedic procedures | 2 (2.3) |
| Pediatric surgery procedures | 2 (2.3) |
| Pediatric critical care unit | |
| Blood transfusion within 48 h | 33 (37.5) |
| Massive blood transfusion | 7 (8) |
| Surgery Interventions (neurosurgery/ orthopedics/pediatric surgery) | 6 (6.8) |
| Intubation rates | 61 (69.3) |
| Length of mechanical ventilation (days) | 3 (1–21) |
| Tracheostomy cannulation | 6 (6.8) |
| Average tracheostomy cannulation timing (days) | 14.33±1.03 |
| Length of PICU stay (median) (days) | 4 (1–22) |
| Length of hospital stay (median) (days) | 10.5 (1–96) |
| Mortality | 11 (12.5) |
| Brain death | 6 (6.8) |
| Organ donor | 5 (5.7) |

Overall, 11 children (12.5%) died of TBI. To determine the independent risk factors for mortality, the variables that did not create multicollinearity with p<0.2 were included in multivariable logistic regression model at a ratio of 1/20 sampling cases. According to the model in which initial hypotension observed at ER, the presence of lung contusion, ISS score, and Ro-CT score were included as the variables, and only Ro-CT score was determined to be an independent risk factor for mortality. One increment in the score increased the odds of recovery by 20.334 times (95% CI: 1.999–206.879). ISS score was also found to be borderline significant (p=0.052; OR: 1.195; 95% CI: 0.999–1.430).

Brain death [diagnosis based on clinical findings indicating permanent loss of brain stem functions with apnea test and Single Photon Emission Tomography (SPECT)] occurred in six patients, five of whom became organ donors.

## DISCUSSION

Increased intracranial pressure as a leading cause of secondary brain damage on TBI prognosis is well established in literature.[6,11,12] The goal in pediatric critical care in TBI management is to maintain age-appropriate CPP by maintaining ICP <20 mmHg.[6,11,13] Despite the recommendations of the American Neurosurgery Association and Brain Trauma Association guidelines for ICP monitoring, the rates vary between 9.6% and 75%, and compliance to guidelines remains low because of either underestimation of the clinical importance of ICP monitoring or ignorance of the potential risks of invasive monitoring.[14,15] Our observations were concordant with previous reports, verifying low compliance; despite a relatively higher percentage of neurosurgical procedures (22.7%), ICP rates were merely 8%.

Note that, in the absence of ICP monitoring, patient follow-up was achieved through repetitive CTs under the influence of neurological examinations; however, only one patient who presented neurological deterioration underwent neurosurgery (epidural hematoma drainage) following CT evaluation at PICU. Despite the routine radiological evaluation in adults, it rarely intervenes the course of therapy in neurologically stable pediatric patient causing unnecessary ionized radiation exposure.[16–18] Hill et al.[16] reported surgical intervention because of an enlarged intracranial hemorrhage in only one out of 95 patients (32.3%), who underwent repeated CTs in their study population. They concluded that repeated cranial imaging did not alter therapy, and standardized guidelines for repeated scanning at any age groups, including adults and children, were necessitated to be developed. Repeating neurological examination is a cheaper and safer method; the choice of radiological evaluation should be considered only if neurological deterioration occurs in those with mild/moderate TBI (GCS >8).[15,19] Long-term effects of ionized radiation in adolescent children are well established in previous reports; exposure to radiation because of a single dose brain

**Table 4.** Group comparisons according to TBI severity

| Variables | Severe (GCS ≤8) (n=42) | Moderate (GCS 9–11) (n=15) | Mild (GCS 12–15) (n=31) | p |
|---|---|---|---|---|
| Age (median) | 8.5 (1–17) | 3 (1.5–17) | 5 (1.5–17) | =0.010 |
| Age groups, n (%) | | | | |
| <5 years | 10 (23.8) | 10 (66.7) | 16 (51.6) | NA |
| 6–10 years | 16 (38.1) | 3 (20) | 6 (19.4) | |
| 11–18 years | 16 (38.1) | 2 (13.3) | 9 (29.03) | |
| Male sex, n (%) | 29 (69.05) | 6 (40) | 15 (48.4) | =0.075 |
| Mechanism of injury, n (%) | | | | |
| Vehicle | 9 (21.4) | 2 (13.3) | 5 (16.1) | |
| Pedestrian | 15 (35.7) | 4 (26.7) | 8 (25.8) | NA |
| Motorcycle | 5 (11.9) | 0 | 1 (3.2) | |
| Fall | 11 (26.2) | 9 (60) | 15 (48.4) | |
| Other | 2 (4.8) | 0 | 2 (6.5) | |
| Accompanying other organ system injury, n (%) | 36 (85.7) | 9 (60) | 18 (58.1) | =0.019 |
| Thoracic injury, n (%) | 30 (71.4) | 3 (20) | 14 (45.2) | =0.001 |
| Lung contusion, n (%) | 24 (57.1) | 2 (13.3) | 12 (38.7) | =0.012 |
| Abdominal injury | 16 (38.1) | 1(6.7) | 8 (25.8) | =0.063 |
| Extremity injury | 23 (54.8) | 5 (33.3) | 12 (38.7) | =0.121 |
| Spinal cord injury | 15 (35.7) | 1 (6.7) | 7 (22.6) | =0.076 |
| Brain edema, n (%) | 32 (76.2) | 6 (40) | 5 (16.1) | <0.001 |
| Midline shift, n (%) | 15 (35.7) | 1 (6.7) | 3 (9.7) | =0.007 |
| ICP monitoring, n (%) | 6 (14.3) | 1 (6.7) | 0 | NA |
| Increased intracranial pressure, n (%) | 17 (40.5) | 0 | 2 (6.5) | <0.001 |
| Serum sodium at PICU arrival, Mean±SD | 142.52±5.19 | 140.93±2.87 | 138.93±4.27 | =0.005 |
| Duration to reach target serum osmolality, Mean±SD | 12.93±5.55 | 20.75±12.96 | 16±5.80 | =0.216 |
| Diffuse axonal injury, n (%) | 10 (23.8) | 4 (26.7) | 1 (3.2) | =0.038 |
| Anti-seizure therapy, n (%) | 29 (69.05) | 4 (26.7) | 6 (19.4) | <0.001 |
| Clinical seizure, n (%) | 9 (21.4) | 3 (20) | 2 (6.5) | NA |
| Diabetes insipidus, n (%) | 9 (21.4) | 0 | 0 | NA |
| Emergency department, n (%) | | | | |
| Initial hypotension (at arrival) | 20 (47.6) | 2 (13.3) | 6 (19.4) | =0.009 |
| Blood transfusions | 20 (47.6) | 2 (13.3) | 6 (19.4) | =0.009 |
| Neurological deterioration | 5 (11.9) | 6 (40) | 10 (32.3) | =0.036 |
| Urgent surgical interventions | 16 (38.1) | 5 (33.3) | 3 (9.7) | =0.022 |
| Pediatric critical care unit, n (%) | | | | |
| Intubation rates | 42 (100) | 8 (53.3) | 11 (35.5) | <0.001 |
| Length of mechanical ventilation (days) (median) | 4 (1–21) | 1 (0–11) | 1 (0-7) | =0.001 |
| Tracheostomy cannulation, | 6 (14.3) | 0 | 0 | NA |
| Blood transfusions | 24 (57.1) | 3 (20) | 6 (19.4) | =0.001 |
| Massive blood transfusions | 7 (16.6) | 0 | 0 | NA |
| Brain CT scans, Mean±SD | 3.4±1.97 | 2.73±1.16 | 2.32±1.51 | =0.018 |
| Surgical intervention | 3 (7.1) | 1 (6.7) | 2 (6.5) | NA |
| Length of PICU stay (days), Mean±SD | 7.33±5.78 | 4.53±3.04 | 3.51±2.07 | =0.002 |
| Length of hospitalization (days) (median) | 16.5 (1–96) | 12 (5–35) | 8 (3–38) | =0.155 |
| Injury Severity Score (ISS) (median) | 15.5 (9–50) | 9 (9–34) | 9 (3–41) | =0.003 |
| Rotterdam-CT score, Mean±SD | 3.83±1.48 | 2.0±0.53 | 1.74±0.77 | <0.001 |
| PRISM-III score, Mean±SD | 12.93±10.34 | 2.33±1.98 | 1.74±2.19 | <0.001 |
| Mortality | 11 (26.2) | 0 | 0 | NA |
| Brain death | 6 (14.3) | 0 | 0 | NA |

TBI: Traumatic brain injury; ICP: Intracranial pressure; PICU: Pediatric intensive care units; CT: Computed tomography; SD: Standard deviation; NA: Not available.

tomography in a 1-year-old pediatric patient increases the mortality risk by 10-fold compared to that in an adult patient, and it adversely affects cognitive function and cataract upon reaching adulthood.[16,20] Our results indicate the necessity of further studies to compose standardized guidelines on decision of radiological evaluation.

20% Mannitol and 3% NaCl are hyperosmolar agents, proven to be effective in lowering intracranial pressure.[21] The goal of osmotherapy is to attain the target measured serum osmolality to lower intracranial pressure and maintain the achieved osmolality.[21] We confirmed that the medication were initiated with the admission to PICU in a majority of the children, and the duration to reach the target serum osmolality extended to 8.5 h (3.5–40 h). In the prospective randomized double blind study, Li et al.[22] demonstrated the serum osmolality for mannitol and 3% NaCl infusion was as 292.4±9.1 mosm/L and 294.1±6.6 mosm/L, respectively, and both these values were below the threshold levels at 6 h. As shown by Francony et al.,[23] 20% Mannitol and 7.4% NaCl infusions elevated serum osmolality only by 2%. Delays in achieving the target osmolality result in prolonged exposure to elevated ICP which are directly related to negative prognosis, and a multidisciplinary approach towards TBI management (medical staff responding in the field, ER physicians, and neurosurgeons) contributes to positive prognosis.[1,5] Therefore, we believe that osmotherapy, one of the main determinants in preventing secondary injuries, should be initiated at an earlier stage with an aggressive approach upon admission to the ER.

In studies comparing hyperosmolar therapies 3% NaCl infusions have been shown to decrease ICP better than mannitol infusions, and 3% NaCl is suggested as the first choice of drug in therapy at a dosage of 0.1–1 ml/kg/h infusion.[11,21,24] We found that the time required to reach the target serum osmolality in combination therapy (Mannitol + 3% NaCl) was shorter than that required by monotherapy (mannitol or 3% NaCl); however, our intention in this retrospective study was not to compare the efficiency of each hyperosmolar agent as the majority of the study population received combination therapy (62.7%). Instead, we identified drug-related potential side effects using clinical/laboratory and radiological data. Our results showed no side effects related to hyperosmolar drugs used for central pontine myelinolysis (due to rapid increase in serum sodium in hyponatremic patient) and hyperchloremic metabolic acidosis or acute kidney failure;[20] possibly because the administration of isonatremic 5% Dextrose and 0.09% NaCl solutions to protect children against hyponatremia or the dynamic therapy interaction (discontinue or decrease the infusion rate of drugs) to keep the serum osmolality below threshold levels (discontinue mannitol if serum osmolality <320 mosm/L; decrease 3% NaCl infusion rate if serum osmolality is 320–350 mosm/L, or discontinue NaCl if osmolality exceeds 350 mosm/L).

Mortality rates in children r is 9%–16% in multicentered cohort studies.[25,26] Low GCS (RR 3.06, 95% CI: 2.74–3.43), male gender (RR 1.17, 95% CI: 1.09–1.25), initial hypotension at admission (RR 1.83, 95% CI: 1.61–2.09), and ISS scores (RR 1.86, 95% CI: 1.41–2.45) have been identified as risk factors for mortality in adult studies.[27] Pupillary response at admission, hypothermia, mechanism of injury, hypotension, and hypoxia are directly related to survival.[28,29] In a pediatric series of 451 children obtained from the National Pediatric Trauma Registry database, mortality rate was reported as 61% in hypotensive alone and 85% in hypoxic and hypotensive children.[29] However, because of sedation and neuromuscular blocking agent treatment at arrival, limitations in the clinical predictors of outcome (more specifically GCS) in severe TBI have been described in previous studies.[13,30] Therefore, radiographic imaging (CT) and CT-derived scoring systems are also used as objective data to determine prognosis. Ro-CT is one of the radiographic scoring systems to predict hospital mortality and is also validated in children with moderate and severe TBI.[31,32] Liesemer et al.[32] reported that Ro-CT score may be used for risk stratification with incorporating variables as GCS, ISS, and mechanism of injury ($p<0.001$; OR: 0.91; 95% CI: 0.84–0.98). Our results also demonstrated Ro-CT score to be an independent risk factor predicting mortality in a model of initial hypotension at ER, lung contusion, higher ISS scores, and Ro-CT scores. One unit increment in Ro-CT score increased the odds of recovery by 20.334 times (95% CI: 1.999–206.879), and ISS score was found to be borderline significant ($p=0.052$; OR: 1.195; 95% CI: 0.999–1.430).

Axonal injury accompanies 50% of brain damage in hospitalized TBI population.[33] As a result of damage to brain parenchyma, cognitive, autonomic, motor, or sensory deficiencies develop upon injury and may result in inability to protect a secure airway and cause prolonged intubation which constitutes greater risks for long-term morbidity and mortality.[33] We also found an association between axonal injury and prolonged mechanical ventilation as well as PICU and hospitalization period. Six children required tracheostomy cannulation at 14.33±1.03 days because of inability to maintain a secure airway or ventilator dependency. The optimal timing of tracheostomy is controversial and varies from 7 to 10 days or even less in adults (3 days).[34,35] In pediatric series the cannulation timing is reported to be 10±8 days (0–38 days) for post-injury events; the decision of cannulation may be shortened to four days and early timing is associated with shorter intubation period, PICU admission and hospitalization.[35] Relatively extended duration in our study may be due to reluctance of families towards the procedure. When we investigated the long-term prognosis, decannulation was performed within 6 months in all the patients except for one who was still in a vegetative state. This favorable outcome possibly resulted from the nature of the underlying condition: prognosis in acute conditions is better than chronic events.[36]

International Registry in Organ Donation and Transplantation 2013 data reported Turkey' organ transplantation rates from donors and cadavers to be 46,64 and 5,05 per million and

Turkish Transplant Foundation data announced organ donor rates as 23%.[37,38] However,pediatric data on brain death and organ donors is very limited in Turkey. One study conducted by Gencpınar and her colleagues confirmed the pediatric organ donor rate in 2015 as 46%, while Yalındağ Öztürk et al.[40] reported the rate of brain death as 1.1% and organ donor rate as 20%.[39] In this study, we diagnosed TBI-related brain death in six children (6.8%), of whom five became organ donors following family declarations. Although TBI-related brain death is only a small fraction of brain death etiology, recognizing the increase in donor trend at our center compared to previous years is inevitable.[39] Positive physician-family communication and raising public awareness towards organ donation undeniably play an important role in the escalating trend.[41]

Our study has some limitations: (i) retrospective nature of this study because of risks of potential bias, not allowing definite interpretations; (ii) a limited number of patients included owing to inclusion criteria for those admitted to PICU in 2-year period; (iii) evaluation of long-term cognitive functions on the study population was not possible; (iv) uncertainty about the time elapsed from the moment of trauma incident to PICU admission, which was quoted to be the most critical hours. However, recording all available data obtained through the length of stay (from the moment of ER arrival till the hospital discharge), duration and cessation of anti-edema therapy, and evaluation of potential side effects were stronger points of the study. Being one of the most referred centers in terms of trauma and neurocritical care in the Mediterranean region, the outcomes of our study will guide the clinical approach towards TBI on a nationwide scale.

## Acknowledgment

Authors thank Busra Gundogan Uzunay MD (Akdeniz University Faculty of Medicine, Department of Pediatrics, Antalya) for assistance in obtaining data.

Source of support: None
Conflict of interest: None declared.

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ORİJİNAL ÇALIŞMA - *ÖZET*

## Çocukluk çağı kafa travması olgularında mortaliteye etki eden faktörler: Üçüncü basamak çocuk yoğun bakım ünitesi uygulamaları

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AMAÇ: Çalışmanın amacı, travmatik beyin hasarı nedeniyle yoğun bakım yatışı yapılan çocuklarda morbidite ve mortaliteye etki eden faktörleri belirlemektir.

GEREÇ VE YÖNTEM: Eylül 2014–Aralık 2016 arasında 88 hasta değerlendirildi. Glaskow koma skoruna göre üç grupta incelenen hastaların acil servis ve yoğun bakım süreçleri, verilen anti-ödem tedavileri, hedef serum ozmolariteye ulaşma süreleri, aksonal hasar varlığı, entübasyon, trakeostomi oranları, yoğun bakım ve hastane yatış süreleri, Rotterdam-CT skorlaması, travma şiddet ve PRISM–III skorları kayıt edildi.

BULGULAR: Yaş arttıkça kafa travması şiddetinin arttığı görüldü (p=0.010). Beyin ödemi tedavisi alan hastalarda, hedef serum ozmolariteye (ölçülen) ulaşma zamanı 8.5 (3.5–40) saat idi. ICP monitorizasyon oranı %8 olup, monitorizasyon yapılamadığı durumda takiplerin tekrarlayan tomografiler ile yapıldığı ancak tedavi sürecini değiştirmediği saptandı. Aksonal hasarın entübasyon, yoğun bakım ve hastane yatış sürelerini uzattığı saptandı (p<0.001, p<0.001, p=0.030). Altı hastaya 14.33±1.03 günde trakeostomi açıldı; beşinin trakeostomileri ilk altı ay içinde kapatıldı.

TARTIŞMA: Mortalitenin %12.5 olduğu görüldü; hipotansiyon, akciğer kontüzyonu, travma şiddet ve Rotterdam-CT skorlarının mortalite ile ilişkili idi. Rotterdam-CT skorunun sağ kalımda etkili bağımsız risk faktörü olduğu (p=0.001), skordaki bir birimlik artışın sağ kalım oranını 13.235 kat artırdığı (%95 GA 2.792–62.735); travma şiddet skorunun ise sınırda anlamlı olduğu saptandı (p=0.052; OO: 1.195 %95 GA 0.999–1.430). Beyin ölümü tanısı alan altı hastanın beşi hasta organ donorü oldu.

Anahtar sözcükler: Beyin ödemi tedavisi; çocuk; mortalite; Rotterdam CT skoru; travmatik beyin hasarı; yoğun bakım.

Ulus Travma Acil Cerrahi Derg 2018;24(3):199-206 doi: 10.5505/tjtes.2017.37906