https://doi.org/10.23934/2223-9022-2019-8-4-423-429

Features of the Clinical Course and Prognosis of Severe Traumatic Brain Injury Outcomes

Y.B. Vasilyeva, A.E. Talypov, M.V. Sinkin, S.S. Petrikov

Resuscitation Department
N.V. Sklifosovsky Research Institute for Emergency Medicine
3 Bolshaya Sukharevskaya Square, Moscow 129090, Russian Federation

*** Contacts:** Yekaterina B. Vasilyeva, Researcher of the Resuscitation Department, N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department. Email: vaskat17@mail.ru

BACKGROUND Traumatic brain injury (TBI) is one of the most important contemporary health issues. According to the World Health Organization, TBI is one of three leading causes of death in the world. Despite the development and widespread use of neuroimaging tools and instrumental research methods, clinical diagnosis of TBI is preferred. It is especially relevant at the prehospital stage when it is impossible to use instrumental diagnostic methods.

THE AIM OF THE STUDY To determine the clinical course features and prognosis of treatment outcomes in patients with various types of traumatic brain damage.

MATERIAL AND METHODS We studied the results of examination and treatment of 100 victims with a severe head injury hospitalized during the first days after receiving an injury and undergoing treatment at the N.V. Sklifosovsky Research Institute in 2008–2017. Depending on the type of brain injury patients were divided into 3 groups: Group 1 — isolated hematoma (n=20), Group 2 — hematomas and injuries of the brain (n=40), Group 3 — injuries of the brain (n=40). All patients underwent neurological examination, CT scan of the brain upon admission and over time within 12 days after trauma. In 30 victims, intracranial pressure (ICP) was monitored.

RESULTS We revealed features of the dynamics of individual neurological symptoms in patients with different types of brain damage. In patients with isolated hematomas, neurological status was represented mainly with clinic dislocation syndrome and contralateral hematoma hemiparesis, and clinical pattern significantly depended on intracranial hemorrhage. In patients with combination of hematomas and contusions, the neurological status and its dynamics were less dependent on the volume of the hematoma and were mainly determined by contusions of the midline structures of the brain. In patients with brain injuries, neurological status reliably correlated with injuries of midline structures.

CONCLUSION We revealed significant differences in neurological status, its changes over time and correlation with CT findings in patients with different types of traumatic brain injury.

Keywords: severe traumatic brain injury, acute subdural hematoma, acute epidural hematoma, brain contusion, traumatic intracranial hemorrhage, neurological examination, Glasgow Coma Scale, oculocephalic reflex

For citation Vasilyeva YB, Talypov AE, Sinkin MV, Petrikov SS. Features of the Clinical Course and Prognosis of Severe Traumatic Brain Injury Outcomes. *Russian Sklifosovsky Journal of Emergency Medical Care.* 2019;8(4):423–429. DOI: 10.23934/2223-9022-2019-8-4-423-429 (in Russ.)

Conflict of interest Authors declare lack of the conflicts of interests

Acknowledgments The study had no sponsorship

Affiliations

Yekaterina B. Vasilyeva	Researcher of the Resuscitation Department, N.V. Sklifosovsky Research Institute for Emergency Medicine
Aleksandr E. Talypov	Dr. Med. Sci., Chief Researcher, Neurosurgery Clinic, N.V. Sklifosovsky Research Institute for Emergency Medicine, https://orcid.org/0000-0002-6789-8164
Sergey S. Petrikov	Professor of RAS, Director of N.V. Sklifosovsky Research Institute for Emergency Medicine, https://orcid.org/0000-0003-3292-8789
Mikhail V. Sinkin	Candidate of Biological Sciences, Researcher of the Laboratory of Electron Microscopy, N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department, https://orcid.org/0000-0001-5026-0060

BS — Babinsky symptom
CT — computed tomography
DAI — diffuse axonal injury
EDH — epidural hematoma
GCS — Glasgow Coma Scale
GOS — Glasgow Outcome Scale
OCR — oculocephalic reflex
RTA — road ttraffic accident
SDH — subdural hematoma
TBI — traumatic brain injury
VBR2— second ventricular-brain ratio

INTRODUCTION

Traumatic brain injury (TBI) is one of the most pressing public health problems in developed countries. According to the World Health Organization, injuries remain one of the three main causes of death among the world's population, TBI results in the death of 30-50% of victims under the age of 40, causing severe disability with a frequency of 15-20 per 100,000 people per year [1]. About 10 000 000 people per year worldwide have TBI leading to hospitalization. [2]

According to N.V. Sklifosovsky Research Institute for Emergency Medicine, the number of patients with TBI in Moscow admitted to the neurosurgery department, is 10 000-13 000 per year. In general, the incidence of head injury in Moscow is 1.2–1.4 cases per 1000 people per year [3].

The clinical picture of head injury is determined by the type and location of primary brain damage, as well as the severity of the dislocation syndrome. Indications for surgery for head injury are determined by the clinic and neuroimaging data.

We carried out a comparative analysis of the clinical course options and prognosis of treatment results in patients with various types of traumatic brain damage.

MATERIAL AND METHODS

The material of the work was the results of the examination and treatment of 100 victims of severe head injury, who were being treated at N.V. Sklifosovsky Research Institute for Emergency Medicine, from Jan 01, 2008 to Dec 31, 2017

The study included 20 patients with isolated epi- or subdural hematomas (Group 1), 40 patients with a combination of epi- or subdural hematoma with brain contusion (2nd group) and 40 patients with brain contusion (Group 3)

In Group 1, in 60% of the injured, the cause of the injury was a criminal situation, in 20% - a fall from a height of growth, that is, a low-intensity injury. In the 2nd and 3rd groups, the most common cause of brain damage was traffic accidents (RTA) (38% and 55% of the victims, respectively), i.e. high-intensity injury (Fig. 1).

Fig. 1. The incidence of various TBI mechanisms in patients with different types of brain damage

Computed tomography (CT) of the brain was performed in all victims upon admission to the hospital, and then in dynamics when clinical indications appeared. The type and volume of hematomas, the volume of brain contusion, the lateral size and the degree of axial dislocation of the brain stem, and the second ventricular-brain ratio (VBR2) were evaluated. Victims hospitalized more than 24 hours after injury were excluded from the study; with decresed alertness to 3 points by the Glasgow Coma Scale (GCS); with severe concomitant injury; in a state of severe alcohol or drug intoxication; with severe mental illness; with eyeball injury and severe facial skeleton injuries; with gunshot wounds to the brain. We also excluded the victims when CT signs of contusion were detected on the 1st – 3rd day after the injury or during the operation.

In the cohort analyzed, there were 81 men (81%) and 19 women (19%). The average age of patients was 36 (15–62) years. The most common causes of TBI were: RTA — 40 cases (40%), catatrauma — 14 (14%), criminal injury —14 (14%), fall from a height of growth —4 (4%). In 28 patients (28%), the mechanism of the injury remained unknown.

The depression of alertness was evaluated by GCS. The Glasgow Outcome Scale (GOS) was used to evaluate treatment outcomes. Unfavorable outcomes of treatment were considered as score 1-2, favorable as 3-5.

In assessing neurological status, we focused on the symptoms reported dislocation of brain stem according to classification of F. Plum and J.B. Posner (1986): the depression of alertness according to GCS, the diameter of the pupils, the safety of the oculocephalic reflex (OCR), limb paresis, postural reactions, Babinsky symptom (BS) [4]. We evaluated these signs upon admission to the hospital before the start of intensive therapy and drug sedation, and then on the 2nd, 4th, 6th, 8th, 10th and 12th days after the injury.

RESULTS

Among the victims of the 1st group, according to primary CT, epidural hematoma (EDH) was detected in 12 patients (60%), subdural hematoma (SDH) in 8 patients (40%). The volume of hematomas ranged from 59 to 190 cm^3 (128 ± 57 cm^3), the size of lateral dislocation was 8–13 mm (10.3 ± 6.3 mm), significant axial dislocation was in 16 patients (80%), the initial axial dislocation - in 4 (20%). The value of VBR2 was 6–12% (9 ± 2.5%) (Fig. 2).

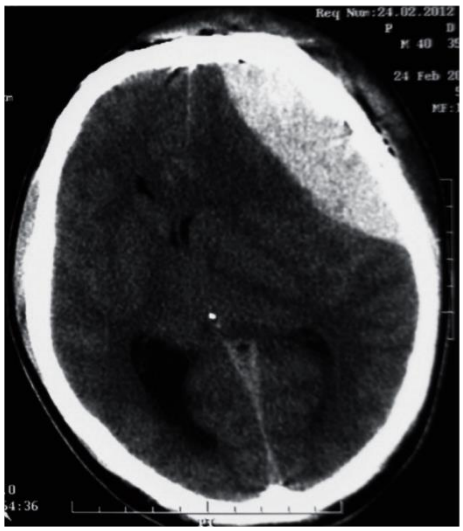

Fig. 2. CT scan of the brain, axial plane. Acute epidural hematoma in the left frontotemporal region of 90 cm^3 without concomitant foci of brain contusion

Among the victims of Group 2, SDH was detected in 26 patients (65%), EDH was detected in 14 cases (35%). The volume of hematomas ranged from 30 to 172 cm^3 (69.1 ± 42 cm^3). The volume of contusion ranged from 2 to 60 cm^3 (22 ± 17.6 cm^3). Injuries of midbrain structures (subcortical nuclei, corpus callosum), according to CT, were detected in 15 patients (37.5%), in 25 patients (62.5%) only contusion of cortical location were observed. The lateral dislocation was from 0 to 20 mm (9.2 ± 5.4 mm). CT signs of severe axial dislocation were detected in 6 patients (15%), significant axial dislocation was revealed in 17 (42.5%) patients, initial axial dislocation was found in 10 (25%) cases, there was no axial dislocation in 7 patients (17.5%). The value of VBR2 averaged 8.2 ± 3.2% (Fig. 3).

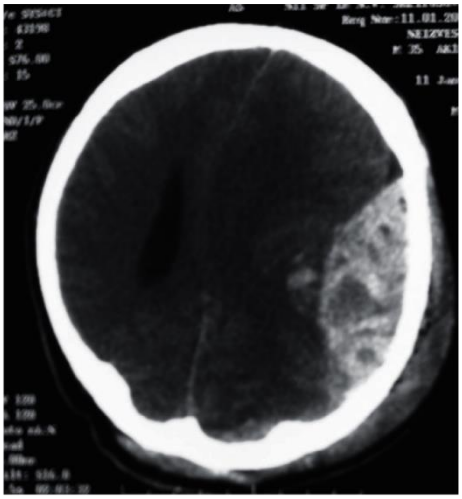

Fig. 3. CT scan of the brain, axial plane. Acute epidural hematoma in the left parietal-temporal region 110 cm3 small focal brain contusions in the projection of hematoma

Among the victims with isolated brain contusion (Group 3), according to the primary CT scan of the brain, the volume of contusion was 3–97 cm^3 (15.4 ± 21 cm^3 on average). Contusion of midline structures, according to CT, was detected in 14 patients (35%), in 26 cases (65%) only contusion of cortical location was revealed. Lateral dislocation of the brain was revealed in 34 patients. Its value was from 0 to 13 mm (2.5 ± 2.8 mm). CT signs of severe axial dislocation were detected in 10 patients (25%), signs of significant axial dislocation were revealed in 1 (2.5%) case, signs of initial axial dislocation were detected in 17 (42.5%) patients, and 12 patients (30 %) there were no signs of dislocation. The value of VBR2 was 6–15% (Fig. 4).

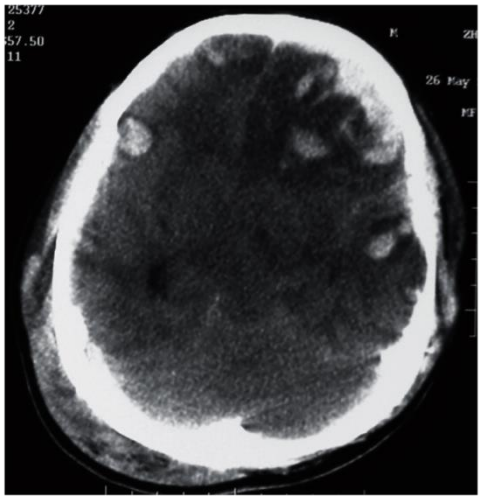

Fig. 4. CT scan of the brain, axial plane. Multiple foci of contusions in the hemispheres of the brain, lateral and axial dislocation, cerebral edema

ALERTNESS DEPRESSION

We detected alertness depression in all patients included in the study.

In victims of Group 1, an almost linear relationship was found between the volume of the hematoma and depression pf alertness. With its decrease to a deep coma, the median of the hematoma volume was 150 cm^3 , to a moderate coma - 120 cm^3 , to stupor - 75 cm^3. Most patients from Group 1 had a good or satisfactory treatment outcome. One victim died. He had a disresorptive hydrocephalus in the postoperative period. We found no significant correlation relationship between the degree of vigorous existence and outcome of treatment. Consciousness was restored within 1 to 7 days after surgery.

In the victims of Group 2, there was no statistically significant relationship between the volume of the hematoma and the state of consciousness. So, with a decrease to a deep coma, the median volume was 60 cm^3 , a moderate coma - 35 cm^3, stupor - 110 cm^3. However, we found a statistically significant relationship between the degree of wakefulness and the outcome of treatment. In all victims operated on in stupor or stunning, treatment outcomes were good or satisfactory, while in 82% of patients operated on in a coma, the outcome of treatment was permanent vegetative status or death.

In patients of Group 3, a weak correlation was observed between the volume of contusion and alertness depression, which depended much more on the location of contusion and the severity of cerebral edema. For example, among patients who came in a coma, we found signs of contusion of the median structures in 62% of patients, and among victims in stupor only 6%. Depression to deep coma was noted in all patients with VBR2 less than 8%, while with VBR2 more than 10%, most of the victims were stunned.

In the victims of Group 3, we did not reveal a significant correlation between the degree of wakefulness before surgery and the outcome of treatment. Among those operated on in stunning and stupor, a fatal outcome or vegetative state was recorded in 61% of the patient, and in patients who were operated on by suppressing wakefulness to a coma - 59%.

ASSESSMENT OF PUPIL DIAMETER

Changes in pupil diameter were detected in 73 patients. In the Group 1, in all patients with a hematoma volume of more than 100 cm^3, we observed anisocoria due to the expansion of the ipsilateral pupil by more than 5 mm. Symptom regressed in 50% of patients by the 12th day after the injury, and in the remaining victims anisocoria persisted until the discharge.

In Group 2, we observed anisocoria on both ipsi- and contralateral side with respect to the location of the intracranial hematoma in 63% of patients, and the uniform narrowing of both pupils to less than 5 mm - in 20%. The dependence of the anisocoria on the volume of the hematoma was not statistically significant, however, we observed this symptom in all patients with a hematoma volume of 90 cm^3 or more. In 24% of patients with anisocoria on the 3rd – 6th day after the injury, a fatal outcome occurred, in 68% - unilateral expansion of the pupils persisted until the end of the study. Narrow pupils (diameter less than 5 mm) were detected in 20% of patients; on the 10th day after the injury, 50% of them died. Treatment outcomes in patients with altered pupils were statistically significantly worse: in patients with narrow pupils, adverse outcomes were 100%, with anisocoria - 64%, with normal pupils - only 29%.

In the victims of Group 3, we also observed anisocoria and evenly narrowed pupils, however, since most of the victims had bilateral brain contusion and not significant lateral dislocation, it was not possible to assess the degree of mydriasis relative to the main lesion site. In patients with anisocoria, the lateral dislocation exceeded 8 mm, and in patients with narrow pupils it was 4 mm or less. The timing of the restoration of the shape of the pupils depended on the severity of cerebral edema. On the 12th day after the injury, the pupil diameter returned to normal values in patients with VBR2 more than 12% of cases, and in all patients with VBR2 less than 8% of the size changes persisted for more than 12 days. Treatment outcomes in patients with altered pupils were 38% worse.

ASSESSMENT OF THE OCULOCEPHALIC REFLEX

In the Group 1, the disappearance of OCR was noted in all patients with a hematoma volume of more than 100 cm^3. The severity of the violation statistically significantly depended on the volume of the hematoma: in patients with violated OCR, on the one hand, the median was 120 cm^3, in patients with the termination of the registration of the OCR on both sides, it was 145 cm^3. In 86% of the injured, the movements of the eyeballs fully recovered on the 6th day after the injury.

In Group 2, the dependence of OCR on the volume of the hematoma was less pronounced than in the first group, and the interdependence on the volume and location of brain contusion was statistically significant: all patients with a hematoma volume of 110 cm^3 or more had a lack of mobility of eyeballs in the study of OCR with a volume of contusion more than 25 cm^3, and in patients with a volume of contusion more than 35 cm^3 disorders were bilateral. In all patients with contusion of the median structures, we revealed a bilateral disappearance of OCR. Treatment outcomes in these patients were statistically significantly correlated with the persistence of OCR.

In Group 3, 57.5% of the victims revealed a bilateral disappearance of the OCR, unilateral - in 12.5%. In 94% of patients we revealed injuries of the median structures. Most patients did not have a symptom dynamics, and treatment outcomes were unsatisfactory: 44% of patients died, and a vegetative status developed in 30%.

ASSESSMENT OF THE SEVERITY OF PARESIS OF LIMBS

In Group 1, paresis of the extremities was statistically significantly dependent on the volume of hematoma, lateral and axial dislocation: in patients with hemiparesis, the median volume of the hematoma was 110 cm^3, the median of lateral dislocation was 8 mm, in patients with tetraparesis - 150 cm^3 and 17 mm, respectively. Of the 9 patients who had tetraparesis, on the 2nd – 6th day, ipsilateral hemiparesis, associated with dislocation of the brain stem, regressed, and contralateral hemiparesis, caused by damage to the motor cortex of the adjacent hematoma, persisted until discharge from the hospital, the depth of paresis was less.

In Group 2, the presence and severity of paresis depended both on the volume of the hematoma and on the volume and location of brain contusions. We observed hemiparesis in 30% of patients. The volume of hematomas in them was 110 cm^3 and more, while the contusion foci were of small volume (median 12 cm^3) and only cortical location. Treatment outcomes were positive in 67% of patients. In patients with tetraparesis, the volume of hematomas was less than in patients with hemiparesis, and did not exceed 80 cm^3 (median 45 cm^3), and the volume of contusion was greater (median 30 cm^3). In all patients with tetraparesis during CT, contusion of the median structures of the brain were revealed. Treatment outcomes were unfavorable in 86% of those affected.

In Group 3, the development of limb paresis was not statistically significantly dependent on the volume of damage, but statistically significantly correlated with the presence of contusion in the median structures. However, in patients with hemiparesis, the volume of contusion was greater than in other patients, and amounted to 40 cm^3 or more, lateral dislocation - 6 mm or more, contusion of median structures was in 50% of patients. In 100% of patients with tetraparesis, we revealed contusion of the median structures. Treatment outcomes were unfavorable in 60% of patients with tetraparesis and in 59% of patients with hemiparesis. In patients without motor disorders, treatment outcomes were significantly better, and only 33% had adverse outcomes.

ASSESSMENT OF MUSCLE TONE AND POSTURAL REACTIONS

Violation of muscle tone and pathological postural reactions in Group 1 were observed in patients with a hematoma volume of 125 cm^3 or more with a significant or severe axial dislocation. We detected diffuse muscle hypotension in 40% of patients, decortication rigidity in 5%, and diffuse increase in muscle tone in 10% of patients. The dynamics of symptoms was positive, and treatment outcomes were favorable in 91% of patients.

In Groups 2 and 3, violations of muscle tone and their dynamics were similar and depended only on the presence of bruises in the median structures. Pathological postural reactions were observed more often than in Group 1 - in 20% and 8% of the victims, respectively. In 10% of the victims of Group 2 and 13% of the victims of Group 3 postural reactions arose only on the 3rd – 6th day after the head injury. The outcome of treatment in 86% of patients with postural reactions was vegetative status.

SYMPTOM OF BABINSKY

Bilateral Babinsky (BS) in patients of Group 1 was observed in severe or significant axial dislocation. On the 3rd – 5th day after the injury, in all the victims on the ipsilateral side with respect to the hematoma, BS regressed. The persistence of BS on the contralateral side was noted in patients with hematomas with a volume of more than 110 cm^3 and lateral dislocation of 10 mm or more. The presence of unilateral BS statistically significantly correlated with contralateral hemiparesis. Of the 11 victims who had no BS upon admission to the hospital, 64% recovered completely, 2 patients were discharged with recovery to severe, and 2 to moderate disability.

In Group 2, all patients with bilateral BS had contusion of the median structures, and VBR2 was less than 7%. In 34% of patients, bilateral BS occurred on the 2nd – 5th day after the injury. The abscence of the symptom in this group appeared as poor prognosis in terms of survival: 64% of patients died, of whom 58% died early after injury.

In Group 3, bilateral BS upon admission was identified in 33% of the victims, but in 18% it developed unilaterally or bilaterally on the 3rd – 8th day after the injury. We did not reveal the dependence of this symptom on the parameters of the lesion. Treatment outcomes in patients with and without symptom did not differ significantly: 59% and 61% of deaths, respectively.

DISCUSSION

The types of brain damage to a large extent depend on factors such as the acceleration value and the duration of exposure to the traumatic agent.

The shear stress resulting in deformation and damage to brain tissue axonal cyto skeleton, develops, as a rule, in the combination of angular and linear acceleration in trauma of high intensity. This mechanism of TBI leads to multiple brain damage. A short exposure time (less than 30 ms) and a high acceleration (head hit on a hard surface) leads to rupture of the cortical and parasinous veins and the formation of subdural hematomas [5]. A longer traumatic effect (more than 30 ms) at the same value of acceleration (for example, hitting a car's soft panel) leads to shear forces in the brain tissue and the formation of diffuse brain damage (Fig. 5) [6].

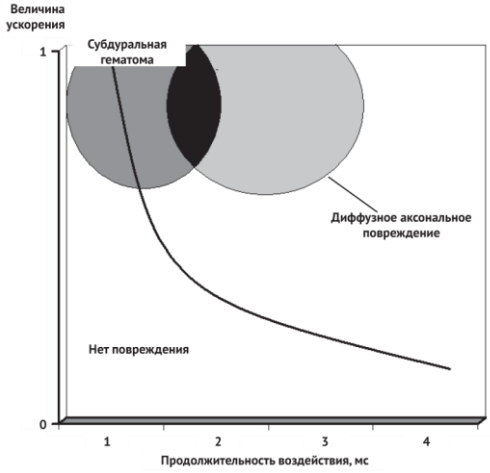

Fig. 5. Scheme of head injury development depending on acceleration and duration of the traumatic effect. (According to Reilly P.L, 2001)

From a clinical point of view, the initial loss of consciousness and coma, as well as various kinds of alertness depression at a later date, such as a prolonged vegetative state or cognitive disorders can be caused by both focal brain injury and diffuse, though more common in on last case [7]. A decrease in the alertness depression is the most important symptom in assessing the condition of a patient with a head injury. From a clinical point of view, both initial unconsciousness and later unconscious states, such as a permanent vegetative state or persistent cognitive impairment, can be characteristics of both focal TBI and the result of dislocation syndrome, cerebral edema, and diffuse axonal injury (DAI) [8]. The same can be said of other neurological symptoms observed in patients with TBI - with similar clinical manifestations, their pathogenesis may vary, which dictates different treatment tactics [9]. For example, a symptom complex, including deep coma, anisocoria, abscence of OCR, tetraparesis, decortication rigidity, and bilateral BS, can be observed in the presence of a large volume intracranial hematoma or foci of brain contusion, progressive dislocation of the brain stem, and also contusion of the brain located in nuclei, in DAI [10–12]. At the same time, treatment tactics will be different. In the first two cases, the patient needs emergency decompression trepanation of the skull, removal of the hematoma, and in the third - intensive care in the intensive care unit. Quick and correct diagnosis significantly increases the victim's chances of a favorable outcome [13]. Modern diagnosis of head injury is impossible without neuroimaging methods, however, our analysis of the clinical symptoms showed that it is possible to suspect a particular type of damage based on information about the mechanism of injury and analysis of only 7 signs determined during the initial neurological examination. Such prediction at the prehospital stage will accelerate the provision of neurosurgical care to victims of head injury due to the preparation of the operating team for the admission of the victim to the emergency room, which may ultimately help reduce the number of adverse outcomes of severe brain injury.

FINDINGS

1. The clinical picture of traumatic brain injury and its dynamics are largely dependent on the type of brain damage.

2. In patients with isolated hematomas, the clinic and the dynamics of symptoms are statistically significantly dependent on the volume of the hematoma.

3. In patients with a combination of hematomas with brain contusion and isolated brain contusion, the clinical picture is largely determined by the location of the contusion foci.

REFERENCES

1. Fleminger S, Ponsford J. Long term outcome after traumatic brain injury. *BMJ*. 2005; 331(7530):1419–1420. PMID: 16356951. https://doi.org/10.1136/bmj.331.7530.1419
2. World Health Organization. *The World health report: 2003: shaping the future.* Geneva: World Health Organization; 2003. Available at: https://www.who.int/whr/2003/en/ [Accessed Oct 22, 2019]
3. Talypov AE. Khirurgicheskoe lechenie tyazheloy cherepno-mozgovoy travmy: dr. med. sci. diss. synopsis . Moscow; 2015. Available at:: http://www.neurosklif.ru/Text/Thesises/88.pdf [Accessed Oct 22, 2019] (In Russ.)
4. Posner JB, Saper CB, Schiff N, Plum F. *Plum and Posner's Diagnosis of Stupor and Coma.* 4th ed. Oxford University Press; 2007.
5. Kleiven S. Why most traumatic brain injuries are not caused by linear acceleration but skull fractures are. *Front Bioeng Biotechnol*. 2013;(1):15. PMID: 25022321 https://doi.org/10.3389/fbioe.2013.00015
6. Gennarelli TA, Thibault LE, Adams JH, Graham DI, Thompson CJ, Marcincin RP, et al. Diffuse axonal injury and traumatic coma in the primate. *Ann Neurol*. 1982;12(6):564–574. PMID: 7159060 https://doi.org/10.1002/ana.410120611
7. Reilly PL. Brain injury: the pathophysiology of the first hours. 'Talk and Die revisited'. *J Clin Neurosci*. 2001;8(5):398–403. PMID: 11535003 https://doi.org/10.1054/jocn.2001.0916
8. Potapov AA, Gaytur EI. Biomekhanika i osnovnye zven'ya patogeneza cherepno-mozgovoy travmy. In: Konovalov AN, Likhterman LB, Potapov AA (eds.). *Klinicheskoe rukovodstvo po cherepno-mozgovoy travme*. Vol.1. Moscow: Antidor Publ.; 1998. pp.152–168. (In Russ.)
9. Krylov VV, Talypov AE, Levchenko OV. (eds.) *Khirurgiya tyazheloy cherepno-mozgovoy travmy.* Moscow: ABV-press Publ.; 2019. (In Russ.)
10. Adams JH, Graham D., Gennarelli TA. Head injury in man and experimental animals: neuropathology. *Acta Neurochir Suppl (Wien)*. 1983;32:15–30. PMID: 6581702 https://doi.org/10.1007/978-3-7091-4147-2_2
11. Smith DH, Meaney DF, Shull WH. Diffuse axonal injury in head trauma. *J Head Trauma Rehabil*. 2003;18(4):307–316. PMID: 16222127 https://doi.org/10.1097/00001199-200307000-00003
12. Marshall LF, Gautille T, Klauber M. Eisenberg HM, Jane JA, Luerssen TG, et al. The outcome of severe closed head injury. *J Neurosurg*. 1991;75(Suppl.):S28–S36. https://doi.org/10.3171/sup.1991.75.1s.0s28
13. Gennarelli TA, Adams JH, Graham DI. Diffuse axonal injury: a new conceptual approach to an old problem. In: Baethmans A, Go KG, Unterberg A. (eds.) *Mechanisms of secondary brain damage.* New York: Plenum Press; 1986.pp.15–28.

Received on 08.05.2019

Accepted on 23.06.2019