HIGH SCHOOL EDITION
Journal of Student Research
Volume 11 Issue 4 (2022)

Traumatic Brain Injuries

Emily Costa[1] and Candace Grisham[1]

[1] Santa Fe Christian High School, Solana Beach, CA
[#]Advisor

ABSTRACT

A traumatic brain injury (TBI) is an injury that disrupts the normal brain function, and is caused by a bump, blow, or jolt to the head or a penetrating head injury. TBI range from mild concussions, without a loss of consciousness, or to severe TBI, which can result in a deep coma or death. Types of TBI's that patients can sustain include concussions, hematomas, and CTE. The length of time that patients have symptoms depends on the TBI severity, with symptoms lasting a few days or even the rest of patient's life. Depending on the part of the brain that is injured in the accident, patients will have varying symptoms. This review article covers the different causes, diagnosis, and treatments of TBI's along with the types of TBI's that patients can sustain.

Introduction

Epidemiology

In the United States, traumatic brain injuries (TBI) are a common and widespread medical problem which are responsible for a third of all injury related deaths and over 50,000 deaths annually. Furthermore, TBI's are responsible for over 300,000 hospitalizations each year with over 80,000 resulting in long term disability. These numbers do not include the numerous TBI's each year that never reach healthcare and remain undiagnosed. The CDC has defined a traumatic brain injury as a "craniocerebral trauma, specifically, an occurrence of an injury to the head" (1). This can arise from a blunt or penetrating trauma with differing levels of force. Primary causes of traumatic brain injuries (TBI) vary from different ages, socioeconomic status and geographic regions. Low- and middle-income countries are found to have nearly three times the amount of TBIs compared to high income countries. The most common TBI varies in different age groups as well, with children and the elderly leading cause of TBI's being falls, and early adults leading cause being car accidents (2). Studies have found that TBI is less frequent in the female population, due to men being more frequent drivers then women. While TBI's are less frequent in women, it's more common for elderly women to have more complications and need neurosurgical intervention, compared to men in the same age group (3).

Brain Anatomy

The brain is made up of 3 major divisions which include the cerebrum, the cerebellum, and the brain stem. The cerebrum is the largest division of the brain and can be divided into two cerebral hemispheres. The left and right hemisphere are connected by the corpus callosum. Furthermore, these hemispheres of the cerebrum are subdivided into 4 lobes with both a right and left component. The frontal lobe is located anteriorly and involved in emotional regulation, reasoning, and problem-solving. The most posterior section of the frontal lobe contains the motor cortex which is the area in which movement arises. The partial lobe is posteriorly adjacent to the frontal lobe and is responsible for sensory information. This includes touch, temperature, pressure and pain. The temporal lobe, which is separated from the frontal lobe by the lateral fissure, has dedicated regions for

processing hearing, languages, and forming memories. Finally, the occipital lobe is the visual processing center of the brain. The occipital lobe receives and interprets visual information including depth and location of objects in space (4).

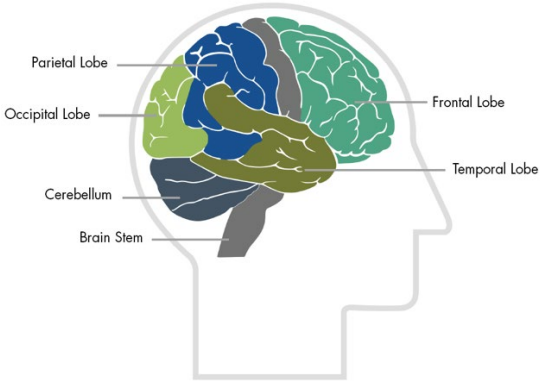

Figure 1 (5)

The cerebellum is located caudal to the temporal and occipital lobe. While it doesn't initiate motor commands, it modifies the commands of the descending pathways to make movements more accurate. With the input of vestibular receptors and proprioceptors, the cerebellum sends commands to motor neurons to shift the body's position in order to keep balance and good posture. The cerebellum also coordinates timing and force of muscle groups in order to allow for body movements. Finally, the cerebellum is instrumental in motor learning, allowing the brain to fine tune certain movements, such as cursive writing or painting (6).

The brainstem connects the cerebrum of the brain to the spinal cord and cerebellum. The brainstem is responsible for vital functions such as breathing, blood pressure, heart rate, consciousness, and sleep. It consists of 3 different components: the midbrain, the pons, and the medulla oblongata. The midbrain connects the pons and the diencephalon* and is associated with vision, hearing, motor-control, and sleep (7). The pons, located between the midbrain and the medulla oblongata, regulates many of the body's unconscious processes, including breathing. It also serves as an origination and termination point for important cranial nerves including the trigeminal nerve (facial touch and pain sensors) and abducens nerve (controlling eye movement) (8). Finally, the medulla oblongata, which connects the spinal cord and the pons, helps transmit signals between the spinal cord and the brain to control activities such as respiration and one's heartbeat (7). Similar to the other areas of the brain stem, there are critical cranial nerve entry and exit points from this brain involved in mouth/tongue movements as well as parasympathetic innervation (vagus nerve).(9)

The brain is covered with three layers of membrane known as the cranial meninges. These three layers are known as the dura mater, arachnoid mater, and the pia mater (10).The dura is the outermost cranial meninges and is composed of two layers. This allows for the dura to be a thick, fibrous membrane that's inelastic. The arachnoid mater is in-between the dura and the pia and is an avascular membrane that is involved in cerebrospinal fluid (CSF) metabolism in the subarachnoid space. The appearance varies depending on the location of the arachnoid mater, but it's generally a thin lucent membrane. The pia mater is the deepest layer of the cranial meninges and has 2 layers that follow the contours of the brain's sulci and gyri. The outer layer of the pia is the epipial layer and contains collagen fibers, while the inner layer is called the intima pia and contains elastic and reticular fibers. (11).

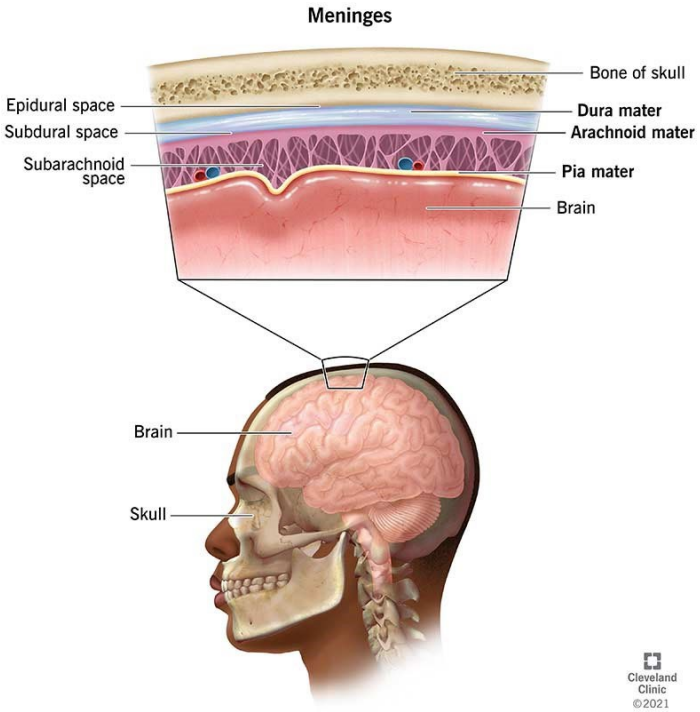

Figure 2 (10)

Types of TBI

There are 3 main types of hemorrhages: Epidural hematoma, Subdural Hematoma, and Subarachnoid Hemorrhage

Epidural Hematoma

An epidural hematoma can be arterial (carrying blood away from the heart) or venous (carrying blood towards the heart) in origin. Usually, an arterial epidural hematoma happens after a blunt trauma or penetrating injury to the head in the temporal region. This will likely lead to a skull fracture with damage to the middle meningeal artery leading to arterial bleeding in the potential epidural space, causing an arterial epidural hematoma. Similarly, a venous epidural hematoma occurs after a skull fracture, with the venous bleeding. The clinical presentation of these is a loss of consciousness after injury, and other symptoms include severe headaches, nausea, vomiting, and seizures. Importantly, patients can exhibit an insidious period of complete awareness with minimal deficits. This period can give a false sense of security to patients and doctors which may lead to a failure to diagnose (12).

Subdural Hematoma

A subdural hematoma happens when a vessel between the brain and skull is stretched, broken or torn, which leads to bleeding into the subdural space. It is most common for this type of hemorrhage to occur with blunt or penetrating head traumas. These hematomas also present with headaches, nausea, vomiting, motor deficits and decreased consciousness, however the lucid period (seen in epidural hemorrhages) is unlikely. A physical exam can also reveal neurological deficits, lethargy, and focal motor deficits (12).

Subarachnoid Hematoma

A subarachnoid hemorrhage is when there is bleeding into the subarachnoid and is a blunt trauma with or without penetrating injury which involves acceleration changes to the head. The bleeding occurs most commonly when cortical surface vessels are injured and bleed into the subarachnoid space. The most common symptom is called a "thunderclap headache" with patients having the worst headache of their lives. Some other symptoms are dizziness, nausea, seizures and a loss of consciousness (12).

Concussion

Concussions are most known as a mild subset of TBI's. A concussion happens when there is a direct blow to the head with acceleration/deceleration forces taking place. The force leads to the brain, which floats in a protective suspension of cerebrospinal fluid, to bump against the skull. This causes neuron damage along with possible bruising at the site of the impact. A concussion has different levels, so symptoms with a mild concussion may just lead to dizziness, while a more serious concussion can lead to an unconsciousness state. While computerized tomography CT scans and MRI's do not show any immediate abnormalities, it is shown that even one "silent concussion" has long term effects. It has been proven that even mild concussions can lead to axonal damage (13).

Second Impact Syndrome

A very dangerous subset of concussions is Second Impact Syndrome. This is when someone receives repeated concussions before the first one is healed. This is most common when an athlete returns to a sport before their first concussion is fully healed, due to the increased vulnerability of the brain. The mechanism of the injury is axon shearing, with rapid depolarization, neurotransmitter release, and ionic shifts. This results in dysregulation of cerebral blood flow which leads to a cerebral edema, causing the body to lose the ability to auto regulate intercranial and cerebral perfusion pressures (14). The mortality rate of Second Impact Syndrome is over 50%, with 100% of the cases ending with the patient having a permanent disability.

CTE

CTE is a progressive neurodegenerative disease which is caused by repetitive TBI's and head trauma. CTE is thought to result in executive dysfunction, memory impairment, depression, suicidal thoughts and actions, poor impulse control, and even dementia (15). While post- concussive symptoms are right after a concussion, CTE symptoms don't usually present themselves until years after the repetitive head traumas. CTE's unique neuropathological signature is the accumulation of phosphorylated tau proteins (p-tau) in the brain (16). The progression of CTE is divided into four separate stages called the McKee CTE staging scheme. The staging scheme is based on the density and regional deposition of p-tau, with stage 1 being the mildest and stage 4 being the most severe (17). While currently CTE is only able to being diagnosed with a post-mortem examination of the brain, there are many studies attempting to find ways to diagnose CTE in living patients.

Causes

There are three types of TBI's which can be categorized as closed head, penetrating, and explosive blast TBI (18).

The most common causes of closed head TBIs are car accidents, falls and sports activities, which all are associated with blunt impact. The blunt impact disrupts the normal function of the brain under the impact site, causing damage to the neuronal cells. Furthermore, brain displacements due to the impact also lead to the compression of brain tissue and reduction of cerebral blood flow (19).

The type and severity of the neurological damage of penetrating TBI's is dependent on the size, speed, route and strength of the external object penetrating the brain (18). Penetrating TBI's are most caused in civilian populations by high velocity objects, resulting in complex injures and high mortality. Low velocity penetrating TBI's are less common in the civilian population, but they have better outcomes due to localized primary injuries. These low velocity TBI's are usually caused by violence, accidents, or even suicide attempts (20).

Explosive blast TBI's are a recently new category of TBI's, and account for a high prevalence of combat-related TBI's, with explosive weaponry causing 73% of US military casualties in Operation Enduring Freedom and Operation Iraqi freedom (21). After an explosion, the brain is compromised from the rapid pressure shock waves generated from the explosion, which transmits energy from the skull into the brain (18). This is not the only effect from the explosion, as the shock wave causes internal damage and there may also be penetrating injuries from fragments of debris and injuries from the acceleration of the body away from the blast (21).

Diagnosis

There are many ways to diagnose a TBI, and one way that can help the diagnosis that athletes can complete before an injury is baseline neuropsychological testing. This data can be used when an athlete is suspected of having a concussion, and their baseline results can be compared to the post-accident results. The most popular baseline to be used is ImPact (Immediate Post-concussive Assessment and Cognitive Test), which is used by professional, collegiate, and high-school athletes. While this test can be helpful, some athletes lack integrity with the baseline testing, with some athletes preforming poorly on their baseline in order to affect the return-to-play decision in their favor (22).

Another way to determine if a patient has a TBI is using the Glasgow Coma Scale. This test is one of the most used TBI scoring systems, and tests patients' eye-opening response, verbal response, and motor response. While comparing pupil sizes along with motor strength and sensation are important parts of the test, eye opening has the most weight because it suggests a more reassuring outcome if the patient can open their eyes spontaneously (23). This test was originally designed for "repeated bedside assessment" in a neurosurgical unit to see patients' change in state in consciousness and to measure the "duration of a coma". Now the test is now widely used to use patients' altered level of consciousness to predict patients' clinical outcomes and is a vital part of trauma and life support courses. While this test is a great tool, the creators warn that, "We have never recommended using the GCS alone, either as a means of monitoring coma, or to assess the severity of brain damage or predict outcome." (24).

MoCA is a cognitive screening instrument developed to detect mild cognitive impairment. This cognitive test is 10 minutes long and assesses cognitive areas including memory, language, executive functions, visuospatial skills, calculation, abstraction, attention, concentration, and orientation (25). While MoCA is most used for screening for dementia, dementia has been found to be a co-morbidity of CTE, with CTE patients being two to four times as likely to develop dementia(26).

Neuroimaging has become a vital part of diagnosing TBI's. Imaging has allowed surgeons to localize injuries and determine extracranial landmarks to help plan incisions and burr holes, when necessary, along with determining the aggressiveness of their surgical approach (27). While non-contrast CTs are the primary choice

for TBI neuroimaging, MRIs provide more detail, allowing for the identification of small, focal intercranial legions (28).

Computed Topography (CT) is an imaging technique which uses x-rays to build cross section images of the body. It uses the density of the tissue that the x-ray passes through to make this image (25). CT scans are the primary choice for TBI neuroimaging due to their ability to detect trauma related fractures, hemorrhages, intracranial injury, extra-axial fluid collection, brain tissue swelling, and foreign bodies. An advantage of CT scans is they have 24-hour availability in most emergency medical facilities, fast imaging and allows for patients with ferromagnetic substances like shrapnel (28).

Magnetic resonance imaging (MRI) is an imaging modality which uses non-ionizing radiation to create images. Using this technique, the patient lays in a large metal tube, and a radio waves antenna sends signals to the body which a radiofrequency receiver then detects. These signals are then converted into an image by a computer attached to the scanner (29). While MRI scanners are slower and more expensive than CT scans, they detect 10-25% of abnormalities that CT scans miss. 48-72 hours after injuries MRI prove to be more useful, as they can better detect hematomas over time. They are also able to identify small contusions, along with identifying lesions in patients who have normal CT scans (30).

Treatment

Surgical Medical Intervention

Surgical medical intervention is used when there is a significant volume of blood from either an epidural or subdural hematoma (23). To treat an epidural hematoma (EDH) surgically, a craniotomy is preformed over the desired region that evacuates the hematoma and cauterizes the bleeding blood vessel. While EDH are usually less severe underlying brain injuries, subdural hematomas (SDH) are usually more severe brain injuries. The severe brain injuries that are associated with SDH need decompressive craniotomy's to be performed. Without the removal of the bone flap, the evacuation of the subdural hematomas in a patient with a cerebral edema can result in deterioration after surgery (31).

Non-Surgical Medical Intervention

Head Elevation

After a TBI, head elevation can have rapid effects on the patient. This is due to intracranial pressure (ICP) being reduced by the displacement of CSF from the intracranial compartment, and the promotion of venous outflow. While the ICP is reduced, the cerebral blood flow (CBD) is unaffected (23).

Hyperventilation

Hyperventilation lowers ICP by reducing the intraarterial carbon dioxide partial pressure, resulting in vasoconstriction, which is the narrowing of blood vessels. This results in the reduction of cerebral blood volume in the brain (23). Prophylactic hyperventilation is not generally recommended, as vasoconstriction lowers CBF, so hyperventilation is only utilized during brief periods of acute neurological deterioration (32).

Hyperosmolar Theory

Hyperosmolar solutions are effective in reducing ICP with TBI's. Mannitol is a widely used hyperosmolar solution and is paired with hypertonic saline solutions to help lower ICP (33). Hyperosmolar therapy also causes a change in blood rheology allowing for an increase in CBF. Hyperosmolar therapy can be administered to patients in the form a bolus or an infusion (23).

Therapeutic Cooling

Therapeutic cooling is used with patients with TBI's to perform mild induced hypothermia (MIH) on patients. This is proved to cause neuroprotection in patients, along with reduced secondary cerebral insults post TBI. When used to control brain edema, MIH can reduce patients' ICP. This method is best used on patients with elevated ICP and who have a focal TBI rather than those with a diffuse injury (34).

ICP Monitoring

The use of ICP monitoring for TBI patients is to prevent and treat secondary ischemic injury. Since the brain is encased by a skull which doesn't expand, an increase in ICP may hinder CBF and lead to cerebral ischemia. Since increased ICP can have such a detrimental impact on patients and cause secondary brain injury, ICP monitoring is a very important tool to see if surgical intervention is needed. Intracranial monitors are used to monitor patients' ICP (35).

Research Advancements in The Field

While currently CTE can only be diagnosed postmortem, there are imaging technologies being developed to allow the monitoring of CTE progression. These new machines would allow researchers to detect small but important brain changes from CTE, prior to CTE symptoms, in order to take preventative measures. The stronger devices will allow for physicians to detect brain injuries without gross lesions and be able to detect minor TBIs from pathological changes (36). Another study is being done trying to create an immunotherapy to help target phosphorylated tau proteins in the brain which are a result of CTE. The main goal of the immunotherapy is to only target these p-tau, and not affect the functional tau proteins in the brain (37).

Acknowledgments

I would like to thank Candace Grisham for mentoring me through researching and writing this paper. She made me feel supported and excited to improve not only my research skills, but also helping me create useful brainstorms and outlines before I even started my research.

References

1. Brain Injury Medicine: Principles and Practice - Douglas I Katz, MD, Ross D Zafonte, DO, Nathan D Zasler, MD, FAAPM&R, FAADEP, DAAPM - Google Books [Internet]. [cited 2022 Jul 14]. Available from: https://books.google.com/books?hl=en&lr=&id=Td100Pun9dYC&oi=fnd&pg=PA45&dq=TBI+epidemiology&ots=laj1j4NsLL&sig=1ezuTOBPyjwOYKvnVyZxnP3UTMc#v=onepage&q=TBI%20epidemiology&f=false
2. Epidemiology of Traumatic Brain Injury - Physiopedia [Internet]. [cited 2022 Jul 17]. Available from: https://www.physio-pedia.com/Epidemiology_of_Traumatic_Brain_Injury
3. Munivenkatappa A, Agrawal A, Shukla DP, Kumaraswamy D, Devi BI. Traumatic brain injury: Does gender influence outcomes? International Journal of Critical Illness and Injury Science [Internet]. 2016 Apr 1 [cited 2022 Jul 17];6(2):70. Available from: /pmc/articles/PMC4901830/
4. Lobes of the brain - Queensland Brain Institute - University of Queensland [Internet]. [cited 2022 Jul 18]. Available from: https://qbi.uq.edu.au/brain/brain-anatomy/lobes-brain
5. Brain Function | Centre for Neuro Skills [Internet]. [cited 2022 Jul 19]. Available from: https://www.neuroskills.com/brain-injury/brain-function/

6. Cerebellum (Section 3, Chapter 5) Neuroscience Online: An Electronic Textbook for the Neurosciences | Department of Neurobiology and Anatomy - The University of Texas Medical School at Houston [Internet]. [cited 2022 Jul 19]. Available from: https://nba.uth.tmc.edu/neuroscience/m/s3/chapter05.html
7. Basinger H, Hogg JP. Neuroanatomy, Brainstem. StatPearls [Internet]. 2022 Jul 6 [cited 2022 Jul 25]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK544297/
8. Pons: What It Is, Function & Anatomy [Internet]. [cited 2022 Jul 19]. Available from: https://my.clevelandclinic.org/health/body/23003-pons
9. Brainstem [Internet]. [cited 2022 Jul 25]. Available from: https://www.strokeeducation.info/brain/brainstem/
10. Meninges: What They Are & Function [Internet]. [cited 2022 Jul 25]. Available from: https://my.clevelandclinic.org/health/articles/22266-meninges
11. Ghannam JY, Kharazi KA al. Neuroanatomy, Cranial Meninges. StatPearls [Internet]. 2021 Jul 31 [cited 2022 Jul 25]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK539882/
12. Joshi NK, Okuda Y. Intracranial Hemorrhage. Simwars Simulation Case Book: Emergency Medicine [Internet]. 2022 Feb 21 [cited 2022 Jul 19];159–63. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470242/
13. Galgano M, Toshkezi G, Qiu X, Russell T, Chin L, Zhao LR. Traumatic Brain Injury: Current Treatment Strategies and Future Endeavors. Cell Transplantation [Internet]. 2017 Jan 1 [cited 2022 Jul 19];26(7):1118. Available from: /pmc/articles/PMC5657730/
14. May T, Foris LA, III CJD. Second Impact Syndrome. StatPearls [Internet]. 2021 Jul 6 [cited 2022 Jul 19]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK448119/
15. Chauhan CS, Jadon G. An Overview-Chronic traumatic encephalopathy (CTE)An Overview-Chronic traumatic encephalopathy (CTE) SYNTHESIS, CHARACTERIZATION AND ANTI-INFLAMMATORY ACTIVITY OF SOME HYDRAZONE DERIVATIVES View project Ethosomes-A Phyto Drug Delivery System: Recent Approach On Trans Dermal Drug Delivery System View project Dipal R Patel ACDIMA BioCenter. 2018 [cited 2022 Jul 21]; Available from: https://www.researchgate.net/publication/327829072
16. Fesharaki-Zadeh A. Chronic traumatic encephalopathy: A brief overview. Frontiers in Neurology. 2019;10(JUL):713.
17. Alosco ML, Cherry JD, Huber BR, Tripodis Y, Baucom Z, Kowall NW, et al. Characterizing tau deposition in chronic traumatic encephalopathy (CTE): utility of the McKee CTE staging scheme. Acta Neuropathologica [Internet]. 2020 Oct 1 [cited 2022 Jul 21];140(4):495–512. Available from: https://link.springer.com/article/10.1007/s00401-020-02197-9
18. Ng SY, Lee AYW. Traumatic Brain Injuries: Pathophysiology and Potential Therapeutic Targets. Frontiers in Cellular Neuroscience. 2019 Nov 27;13:528.
19. Sahler CS, Greenwald BD. Traumatic Brain Injury in Sports: A Review. Rehabilitation Research and Practice. 2012;2012:1–10.
20. Kazim SF, Shamim MS, Tahir MZ, Enam SA, Waheed S. Management of penetrating brain injury. Journal of Emergencies, Trauma and Shock [Internet]. 2011 Jul [cited 2022 Jul 24];4(3):395. Available from: /pmc/articles/PMC3162712/
21. Cernak I, Noble-Haeusslein LJ. Traumatic brain injury: An overview of pathobiology with emphasis on military populations. Journal of Cerebral Blood Flow and Metabolism [Internet]. 2010 Oct 7 [cited 2022 Jul 24];30(2):255–66. Available from: https://journals.sagepub.com/doi/10.1038/jcbfm.2009.203
22. Erdal K. Neuropsychological Testing for Sports-related Concussion: How Athletes Can Sandbag their Baseline Testing Without Detection. Archives of Clinical Neuropsychology [Internet]. 2012 Aug 1 [cited 2022 Jul 25];27(5):473–9. Available from: https://academic.oup.com/acn/article/27/5/473/4407

23. Galgano M, Toshkezi G, Qiu X, Russell T, Chin L, Zhao LR. Traumatic Brain Injury: Current Treatment Strategies and Future Endeavors. Cell Transplantation [Internet]. 2017 Jan 1 [cited 2022 Jul 26];26(7):1118. Available from: /pmc/articles/PMC5657730/
24. Riechers RG, Ramage A, Brown W, Kalehua A, Rhee P, Ecklund JM, et al. Physician knowledge of the Glasgow Coma Scale. Journal of Neurotrauma. 2005 Nov;22(11):1327–34.
25. Bell D, Nadrljanski M. Computed tomography. Radiopaedia.org [Internet]. 2010 Mar 14 [cited 2022 Aug 8]; Available from: http://radiopaedia.org/articles/9027
26. Julayanont P, Nasreddine ZS. Montreal Cognitive Assessment (MoCA): Concept and clinical review. Cognitive Screening Instruments: A Practical Approach [Internet]. 2016 Jan 1 [cited 2022 Jul 27];139–95. Available from: https://link.springer.com/chapter/10.1007/978-3-319-44775-9_7
27. Lee B, Newberg A. Neuroimaging in Traumatic Brain Imaging. NeuroRx [Internet]. 2005 [cited 2022 Jul 28];2(2):372. Available from: /pmc/articles/PMC1064998/
28. Evaluation of the Disability Determination Process for Traumatic Brain Injury in Veterans. Evaluation of the Disability Determination Process for Traumatic Brain Injury in Veterans. 2019 May 20;
29. Bell D, Jones J. MRI. Radiopaedia.org [Internet]. 2009 Jun 5 [cited 2022 Aug 8]; Available from: http://radiopaedia.org/articles/6317
30. Evaluation of the Disability Determination Process for Traumatic Brain Injury in Veterans. Evaluation of the Disability Determination Process for Traumatic Brain Injury in Veterans. 2019 May 20;
31. Surgical management of acute subdural hematomas - PubMed [Internet]. [cited 2022 Aug 12]. Available from: https://pubmed.ncbi.nlm.nih.gov/16710968/
32. Darby JM, Yonas H, Marion DW, Latchaw RE. Local “inverse steal” induced by hyperventilation in head injury. Neurosurgery [Internet]. 1988 [cited 2022 Aug 13];23(1):84–8. Available from: https://pubmed.ncbi.nlm.nih.gov/3140047/
33. Knapp JM. Hyperosmolar therapy in the treatment of severe head injury in children: mannitol and hypertonic saline. AACN Clin Issues [Internet]. 2005 [cited 2022 Aug 13];16(2):199–211. Available from: https://pubmed.ncbi.nlm.nih.gov/15876888/
34. Urbano LA, Oddo M. Therapeutic hypothermia for traumatic brain injury. Current Neurology and Neuroscience Reports [Internet]. 2012 Oct 27 [cited 2022 Aug 13];12(5):580–91. Available from: https://link.springer.com/article/10.1007/s11910-012-0304-5
35. Traumatic Brain Injury | Brain Cancer Research | Henry Ford Health - Detroit, MI [Internet]. [cited 2022 Aug 13]. Available from: https://www.henryford.com/hcp/research/basic-science/neurosurgery/traumatic-brain-injury
36. Turner RC, Lucke-Wold BP, Robson MJ, Omalu BI, Petraglia AL, Bailes JE. Repetitive traumatic brain injury and development of chronic traumatic encephalopathy: A potential role for biomarkers in diagnosis, prognosis, and treatment? Frontiers in Neurology. 2013;3 JAN:186.
37. Lu KP, Kondo A, Albayram O, Herbert MK, Liu H, Zhou XZ. Potential of the Antibody Against cis–Phosphorylated Tau in the Early Diagnosis, Treatment, and Prevention of Alzheimer Disease and Brain Injury. JAMA Neurology [Internet]. 2016 Nov 1 [cited 2022 Aug 13];73(11):1356–62. Available from: https://jamanetwork.com/journals/jamaneurology/fullarticle/2553320