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RADIOLOGY ROLE IN COMA, TRAUMATIC BRAIN INJURY AND BRAIN DEATH

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Abstract:

Introduction: *Coma most commonly occurs after acute traumatic brain injury, it is always alarming sign. The management depends on the type and severity of injury, immediate treatment may be life-saving. Brain death is another important term, the Uniform Determination of Death Act (UDDA) of 1980 proposed a legal definition of death. In this review, we will discuss the radiology role in diagnosis coma, traumatic brain injury, and brain death.*

Aim of work: *In this review, we will discuss the radiology role in diagnosis coma, traumatic brain injury, and brain death.*

Methodology: *We did a systematic search for radiological role in diagnosis of coma, traumatic brain injury and brain death using PubMed and Google Scholar search engines. The terms used in the search were: Coma, radiology, traumatic brain injury, pathophysiology, brain death.*

Conclusions: *Since past decade, the diffuse axonal injury was believed to be the cause of post-traumatic coma, when the CT showed no hematoma exerting a mass effect, and the patient remained comatose for six hours or more after the trauma. The initial aim of imaging the patients with traumatic head injury is to identify abnormalities for which management may be needed immediately. Studies have shown more evidence that focal brain injuries, such as hematomas, found by CT and conventional MRI, are poor predictors of the prognosis. Traumatic brain injuries are the most common causes of brain death in adults, in addition to spontaneous subarachnoid hemorrhage. The determination of brain death starts with detecting the cause.*

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INTRODUCTION:

Coma most commonly occurs after acute traumatic brain injury, it is always alarming sign. The management depends on the type and severity of injury, immediate treatment may be life-saving. Around nearly a quarter of a million patients are managed for traumatic brain injury in Germany alone yearly. Management recommendations must be always up to date in the light of advancing knowledge [1].

Traumatic brain injury (TBI) is simply an injury that happens to the brain due to trauma. It is considered a heterogeneous, dynamic pathophysiological process that begins starting from the moment of injury and continues over time with sequelae potentially seen even years later after the initial injury. There are many consequences to traumatic brain injury. The primary traumatic brain lesions may occur at the moment of impact include but not limited to contusions, haematomas, parenchymal fractures and diffuse axonal injury [2].

Brain death is another important term, the Uniform Determination of Death Act (UDDA) of 1980 proposed a legal definition of death, is still accepted worldwide. It is defined as an individual, who has sustained either irreversible cessation of circulatory and respiratory functions, or irreversible cessation of all functions of the entire brain, including the brain stem, is dead.[3]. Death is usually a consequence of either a cardiopulmonary arrest with irreversible cessation of respiration and circulation, or it is a consequence of irreversible loss of all functions of the brain, including the brain stem. The latter is defined as Brain Death. A patient determined to be brain dead is clinically and legally dead [4].

In this review, we will discuss the radiology role in diagnosis coma, traumatic brain injury, and brain death.

METHODOLOGY:

We did a systematic search for radiology role in coma, traumatic brain injury and brain death using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). Our search also looked for presentation, and treatment of appendicitis. All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: Coma, radiology, traumatic brain injury, pathophysiology, and brain death.

The definition of unconsciousness

The terms “unconsciousness” and “coma” are used frequently by international convention, without consideration of the duration of the condition of the illness [5]. It refers to the state of absent perception of oneself and one’s environment, from which one cannot be aroused. The Glasgow Coma Scale (GCS)[6], does not have a very precise definition of coma. An international working group of the Neurotraumatology Committee of the World Federation of Neurological Surgeons suggests the use of the following clinical definition of coma: a state in which the patient does not follow commands and does not open his or her eyes either spontaneously or in response to a noxious stimulus. Spontaneous movements are compatible with the definition of coma. In consideration, there are four main grades of coma depending on the severity of coma [7]. Coma, coma is diagnosed when the Glasgow Coma Score of 7 or less.

Coma Classification of the World Federation of Neurosurgical Societies:

- **Grade I** Coma without any of the neurological disturbances listed below
- **Grade II** Coma with lateralizing signs, unilateral fixed and dilated pupil, or hemiparesis
- **Grade III** Coma with pathological extensor responses
- **Grade IV** Coma with bilateral fixed and dilated pupils

Management of the comatose head-injured patient:

The current best method of choice for diagnosis of intracranial injuries is the CT scan of the head. CT of the entire body is also practical, as there are no other ways to exclude further, extracranial injuries such as bleeding in a comatose patient [8]. The benefit of this method is that it takes less time than x-rays and gives more information. The CT must be done as early as the insult happens, unless the vital signs, circulation, or breathing needs immediate lifesaving attention. Management of polytraumatized patients must be interdisciplinary meaning consulting different services. This is especially helpful when there’s suspicion of multiple injured organ systems. In some cases more than one surgery can be done at the same time if needed.

Studies have not support any other indications on whether any further sedating or intracranial-pressure-lowering drugs given to the unconscious patient would improve the prognosis. In the past barbiturates was believed to do so [9], however, this was not confirmed by a many studies [10]. Sedation to secure

the airway might be required for practical reasons. Invasive intracranial pressure (ICP) monitoring may be helpful in providing a useful early warning of rising ICP; if it is performed via an intraventricular catheter, the ICP can be decreased by drainage of cerebrospinal fluid (CSF).

Maintaining the cerebral perfusion pressure (CPP) in the normal values is effected majorly by avoiding arterial hypotension, rather than by decreasing the ICP with medications. In very critical cases, medications usually do not lower the ICP significantly.

Prognosis

Marshall et al [11], suggested a prognosis classification of posttraumatic CT findings, however, there is no obvious association found between the CT findings of initially comatose patients and the prognosis of their management. There is similarly no obvious association between the extent of brain injury seen in CT and the prognosis [10].

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MRI usually shows traumatic lesions in the brain (specifically helpful when the injury affects the brainstem) in much greater information than CT. So, it is more useful for to determine the prognosis [8]. But it is time consuming and not better than CT at revealing the bony and intracranial traumatic lesions that need surgical management [14].

Since the MRI was invented it has been clear that brainstem lesions are of major prognostic

Significance when it comes to mortality, and morbidity in patients with traumatic brain injury. The MRI findings can be used for a four-level classification of the severity of traumatic brain injury almost 70% of patients with a grade I injury survived without functional impairment, while only between 20-25% of patients with a grade II injury survived. All patients with grade III or grade IV injury had functional impairment.

The pathophysiology of coma:

There has been disagreement on the diagnostic evaluation, treatment, and prognosis of comatose head injured patients, the dilemma around this controversy surrounds the question, “Which brain structures are responsible for coma?”. Epidural hematoma can be followed in many cases by a lucid interval and then by acute coma that resolves when the hematoma is removed [15] has been explained as reflecting reversible brainstem dysfunction due to compression [15]. There is another concept of the organic cause of coma is due to the histopathological observation of massive neuronal injury, with axonal lesions extending far into the white matter of the cerebral hemispheres.

Since past decade, the diffuse axonal injury was believed to be the cause of post-traumatic coma, when the CT showed no hematoma exerting a mass effect, and the patient remained comatose for six hours or more after the trauma. Multiple histopathological case reports concluded that brainstem injury was rarely involved and not the cause of coma [16]. Therefore, Coma was attributed to damage of neural pathways that ascend from the brainstem in the setting of diffuse axonal injury to the hemispheric white matter. With this concept maintaining the upper hand, the contrary notion that coma, pupillary areflexia, and pathological extensor responses are signs of brainstem damage was vehemently disputed as recently as 2002 (the “brainstem damage saga”) [16].

There are other teams and definitions used, but usually the reported neuropathological findings that conflicted with this interpretation [17], including findings from patients who had remained comatose from the time of the accident until death: all, without exception, had brainstem injuries.

This histological finding is supported by a study involving serial MRI scans in comatose cases. A statistically significant correlation was found between coma and brainstem lesions in the first 8 days. All patients who were still in coma within 8 days had structural brainstem damage on MRI. An association of bilateral pontine injury with especially high mortality described as over 88%.

In addition, traditionally the pupillary areflexia and pathological flexor and extensor responses were considered the clinical signs of brainstem dysfunction, were in fact significantly associated with structural brainstem lesions commonly seen on MRI. So, the recent finding recommends a patient with post-traumatic coma is because of brainstem dysfunction rather than hemispheric axonal disruption[15]. This conclusion is extremely significant, it has been shown that there is no way to reconnect torn axons, but brainstem compression can be counteracted by lowering the ICP. However, a more effective way to lower ICP than any medications is the surgical evacuation of a hematoma that is exerting a mass effect, and/or an extensive decompressive hemicraniectomy. Those options should be widely available to all comatose patients

Imaging assessment of traumatic brain injury:

Traumatic brain injury (TBI) is injury that occurs to the brain due to trauma. It is considered a dynamic and complex pathophysiological process that causes temporal change commencing with primary parenchymal damage, which is followed by a myriad of systemic and local effects including but not limited to hypoxia, hypotension, hypercarbia, brain swelling±compression, that add to cause secondary brain damage. Trauma is commonly the major cause of death in young people less than 40 years old in the Western world, and TBI accounts for more than 40 % of these deaths [18].

Imaging studies is vital to the treatment of patients with traumatic head injury as it can help with providing a fast assessment of primary damage can give information about potentially avoidable, secondary effects and may also provide markers, which may help to predict outcome.

The initial aim of imaging the patients with traumatic head injury is to identify abnormalities for which managemnt may be needed immediately. CT scan remains the best imaging and modality of choice for initial assessment because it is easy to access, fast (especially useful in agitated patients) and for its high sensitivity in detecting acute bleeding lesions which need surgical procedures [19]. CT scan has been improving significantly with the recent advent of volume rendering three-dimensional reformats, also can provide valuable details on skull fractures. Guidelines in United Kingdom are offered via the National Institute for Health and Care Excellence. The use of CT has increased significantly with an overall reported incidence of intracranial abnormalities of about more than 9% [20].

MRI limitations include but not limited to access, feasibility with patient monitoring and potential instability, long acquisition time and degradation by motion artefact, is typically reserved for the identification of injuries that might explain clinical symptoms that remain unresolved despite initial CT. The use of MRI sequences might have a better definition the extent of existing intracranial injury. As an example, susceptibility-weighted imaging (SWI) provides exquisite information on microhaemorrhages that are usually poorly discerned on CT or on conventional T2-weighted and T1-weighted sequences and diffusion-weighted imaging (DWI) delivers inforamition for areas of acute infarction.

Advanced MRI techniques such as diffusion tensor imaging (DTI) which is used to map fibers tracts and detects pathway's sites of disruption, and functional MRI (fMRI) which is used to detect intrinsic connectivity networks during task-evoked paradigms and also during rest. These techniques might add highly relevant details regarding coexistent structural and functional brain damage and might determine prognoisis.

The Use of Imaging in Determining Patient Outcome:

CT scan:

As we mentioned the CT scan is the initial imaging modality of choice, researchers have attempted to construct classification systems based on initial CT findings to determine prognosis. Marshall et al[11] suggested a descriptive scoring system based on the presence or absence of a space-occupying lesion, intracranial abnormalities and findings of raised intracranial pressure with subsequent validation [21]. But, this system was very broad in its differentiation between diffuse injuries and mass lesions and lacked specification of the type of mass lesion.[22] Therefore there has been concerns that the system might mask those individuals who have DAI in addition to a mass lesion.[22] Maas and his colleagues, sought to offer prognosis prediction in patients with moderate and severe head injury based on CT findings within no more than four hours of injury proposed a modification of the Marshall criteria [11]. The authors redefined the existing criteria through adding more information analysis of the presence of mass lesions and the status of the basal cisterns, and generated two additional parameters: subarachnoid and intraventricular haemorrhage. The authors concluded that better discrimination was acquired through the analysis of individual components of the criteria, including the additional haemorrhagic parameters, rather than through the analysis of the collective parts [23].

MRI:

Studies have shown more evidence that focal brain injuries, such as haematomas, found by CT and conventional MRI, are poor predictors of the prognosis [24]. The additional presence of DAI (typicaly poorly portrayed on conventional imaging) can explain this discrepancy, and additional MRI sequences that can better define the extent of DAI may help add better prognostication. In a study of patients with closed head injury (not limited to DAI), Schaefer demonstrated that the volume of parenchymal lesions depicted with DWI shows a stronger correlation with clinical outcome than FLAIR and T2-weighted sequences. Researchers have also aimed to assocaite clinical outcome with the apparent diffusion coefficient (ADC, a

quantitative marker of restricted diffusion obtained with DWI acquisition). In patients with DAI, Zheng and colleagues found that mean ADC can be associated with the duration of coma [25], this suggests that DWI might predict clinical prognosis. While the use of gradient-echo depicted microbleeds as a surrogate marker of DAI has also provided greater clinical insight into microstructural brain damage but might underestimate the full extent of parenchymal injury. The potential for DTI and fMRI to map and associate disruption in fibre tracts and regional connections have leaded to the examination their biomarker feasibility.

f MRI as a biomarker of outcome following TBI:

The idea behind functional MRI is based on the detection of changes in blood oxygenation as a marker of neuronal activity [26]. Recently the most common way of acquiring fMRI is by the blood-oxygen-level-dependent (BOLD) method, in which changes in blood oxygen levels provides an endogenous contrast agent. Deoxyhaemoglobin and oxyhaemoglobin have different magnetic characteristics and changes in their relative proportions can cause temporary change in the signal shown on MRI of the target brain region relative to surrounding parenchyma [20].

Intrinsic connectivity networks are believed to be present in constant, but with their activity being manipulated by changes in behavioural state. fMRI might be used to study intrinsic connectivity networks while performing task-evoked paradigms and also during rest (so-called 'resting-state networks'). So, fMRI can be done in the comatose patient and in patients who might respond to tasks.

Brain Death:

Traumatic brain injuries are the most common causes of brain death in adults, in addition to spontaneous subarachnoid hemorrhage. In pediatric population, nonaccidental trauma is the most common cause of brain death [27]. Every hospital should have a policy for diagnosis of brain death. A recent survey found that almost half of US hospitals require training for those determining brain death [28] 49% of the surveyed need that a neurologist or neurosurgeon be involved, However, this is not mandatory by the AAN guideline. Though the AAN strongly recommend the presence of a neurologist [29].

The determination of brain death starts with detecting the cause. This is determined by taking history, performing clinical examination, and conducting imaging studies. Clinicians therefore must take pause when the circumstances are unclear or when imaging appears normal. CT scan findings after neurologic injury can include but not limited to hemorrhage, edema, mass lesions, or ischemia. Sometimes imaging might be normal in the first 24 to 48 hours or longer in situations of hypoxic injury and central nervous system (CNS) infection.

Even if the circumstances of the neurologic injury are obvious and imaging is abnormal, a regimented, detailed and precise clinical examination is central. Neurologic findings might be reversible; for example in many reports of transtentorial herniation being reversed with aggressive critical care techniques [30,31]. Thus the physicians must approach severe neurologic injury without bias or supposition.

Cerebral Angiography

Angiography is invasive, expensive and needs prolonged travel to the angiography suite, is not readily available and interpretable at many centers. The right technique for cerebral angiography is illustrated in the AANPP guideline and includes high-pressure injection into the aortic arch, contrast medium should reach both anterior and posterior circulations, no intracerebral filling at the level of entry of the carotid or vertebral artery to the skull. The external carotid circulation should be seen as a positive control [32].

Cerebral Scintigraphy

Scintigraphy, also known as nuclear flow testing or SPECT, the mechanism behind it lies in using a gamma-emitting radioactive tracer instilled into the venous system and detected by a radio counter in nuclear medicine. It is considered reliable in comparison to cerebral angiography.[33] Nuclear scintigraphy needs instrumentation, a highly expert radiologistand the expensive radioisotope that must be reconstituted by a specialty pharmacy [34,35].

Transcranial Doppler Ultrasonography

Transcranial doppler ultrasonography (TCD) is considered as a noninvasive, bedside, and a fast method in performing as well as interpreting, however, there has been little evidence on the advantages of TCD as an ancillary test, as it does not necessarily quantify cerebral blood flow. TCD depends on the technician and the interpreter. It needs visualization of each hemisphere and demonstration of an abnormal flow pattern. TCD is helpful only if a reliable signal is found. More than 15% of patients are not good candidates for TCD due to increased thickness of cranial vaults or other technical limitations [36].

Computed Tomography Angiography

Computed tomography angiography (CTA) was previously used as an ancillary test in the diagnosis of brain death in 1998. It was reported to have one hindered percents specificity [37]. It is used widely in worldwide especially in European countries as an ancillary test to diagnose cessation of cerebral blood flow [29,28]. CTA is widely available, cheap, easy to acquire, minimally invasive, and quick, but needs expert interpreter.

Magnetic Resonance Angiography

To determine and diagnose brain death by MRA, it be based on the same criteria as CTA. MRA has not been used as an ancillary test in brain death. Similarly to MRI the patient must be transported to the radiology suite, examination time is longer than CT or HMAO-SPECT, and the patient and monitors must be MRI-compatible [39].

Whatever the imaging modality is used, radiologists and others who interpret the tests hold a vital role in brain death diagnosis. The radiologic study is usually used as the final examinations detect brain death. The time of death is often recorded as the time the report is finalized. It is recommended that radiologists refer strictly to brain blood flow testing. It is recommended to avoid the terminology "consistent with brain death" [40]. This way will let the radiologist to maintain the appropriate relationship with respect to the process of brain death detection.

CONCLUSION:

Coma most commonly occurs after acute traumatic brain injury, it is always alarming sign. Traumatic brain injury (TBI) is simply an injury that happens to the brain due to trauma. Brain death is another important term, the Uniform Determination of Death Act (UDDA) of 1980 proposed a legal definition of death, The terms "unconsciousness" and "coma" are used frequently by international convention, without consideration of the duration of the condition of the illness [5]. It refers to the state of absent perception of oneself and one's environment, from which one cannot be aroused. The Glasgow Coma Scale (GCS). The current best method of choice for diagnosis of intracranial injuries is the CT scan of the head. Since the MRI was invented it has been clear that brainstem lesions are of major prognostic
significance when it comes to mortality, and morbidity. Since past decade, the diffuse axonal injury was believed to be the cause of post-traumatic coma, when the CT showed no hematoma exerting a mass effect, and the patient remained comatose for six hours or more after the trauma. The initial aim of imaging the patients with traumatic head injury is to identify abnormalities for which management may be needed immediately. Studies have shown more evidence that focal brain injuries, such as hematomas, found by CT and conventional MRI, are poor predictors of the prognosis. Traumatic brain injuries are the most common causes of brain death in adults, in addition to spontaneous subarachnoid hemorrhage. The determination of brain death starts with detecting the cause.

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