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Brain Injury: Long term outcome after traumatic brain injury

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Introduction

Traumatic brain injury (TBI) is the number one cause of mortality and disability in young adults in modern Western societies. In Europe annually 1,6 million patients with TBI are admitted to hospital and 66.000 die. Direct healthcare costs related to TBI are estimated at € 2.9 billion per year. In Europe an estimated 8 million people experience some level of disability caused by TBI (Willemsevan Son, 2009). In the USA 1.6 million people sustain a TBI each year, approximately 50.000 people die from a TBI and 125.000 are disabled one year after injury. In 2000 it was estimated that the economic burden of TBI of all severities in the USA was about 60 billion dollars (Finkelstein, 2006).

Although impressive these figures underestimate the actual magnitude of the problem. Indirect costs, related to the loss of productivity, and intangible costs due to reduced quality of life, are not taken into account. Furthermore, these figures are based on hospital admissions only. Many patients, especially those with mild TBI, are not referred to emergency departments of acute hospitals and are not hospitalized. It is estimated that 80-90% of all treated TBI are considered mild (Stulemeijer, 2009). Often TBI co-incurs with multiple traumata and as such the patient may be registered as a polytrauma not as a TBI. The exact facts and figures on incidence, prevalence and long term consequences of TBI are obscure. It has been suggested that the incidence figures on TBI have to be multiplied by 5 or even 10, in order to include every unregistered patient. Goldstein already pinpointed this problem in 1990 by introducing the term 'the silent epidemic' (Goldstein, 1990). Ever since, TBI has been on the agenda of healthcare providers and in politics. TBI is a frequent disorder that may cause lifelong problems for those incurring it, for those caring for TBI patients and for society as a whole.

This chapter will provide an introduction on the (long term) consequences of brain injury. It is written from a clinical rather than a scientific perspective. Issues like psychometric evaluations of measurement scales, extensive referencing or detailed discussions on individual studies are not within the scope of this chapter. The interested reader is referred to some excellent websites such as of the Institute of Medicine (http://www.iom.edu), Evaluating the HRSA Traumatic Brain Injury Program (http://www.iom.edu/Reports/2006/Evaluating-the-HRSA-Traumatic-Brain-Injury-Program.aspx), the National Institute of Neurological Disorders and Stroke (www.ninds.nih.gov), to textbooks such as Medical Rehabilitation of Traumatic Brain Injury by Horn and Zasler or to November-December 2009 issue of the Journal of Head Trauma Rehabilitation which is dedicated to long term health outcomes after TBI.

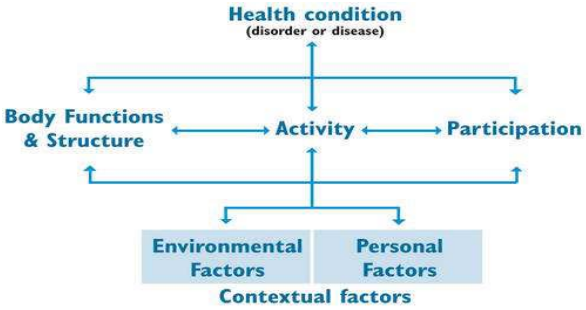
The International Classification of Functioning, Disability and Health

The International Classification of Functioning, Disability and Health (ICF) is a framework to measure health and disability at both individual and population levels. The ICF was endorsed by the World Health Organization in 2001. In the ICF model (see fig 1) the consequences of health

conditions are classified at the levels of body functions and structure and at the levels of daily activities and social participation (http://www.who.int/classifications/icf/en/). In the ICF model, disability results from the interaction between a person's functioning in a societal context. Therefore contextual factors are taken into account in the ICF model. The ICF model embeds almost 1500 categories that correspond to body functions, body structures, activities, participation and contextual factors. This is unpractical in daily clinical practice. Therefore the ICF checklist was developed with disease specific core sets. The TBI core set is currently being developed (Bernabeu et al, 2009).

There is no linear relationship between the domains 'Body Functions and Structure', 'Activity' and 'Participation'. Contextual factors may have a direct effect on this relationship. For example, the preferred coping style of the caregiver may affect the level of activities and participation of the patient (van Baalen et al, 2007). In comatose patients, treatment at the level of body functions often do not cause improved levels of participation or activity (Johnston et al, 1996 in Horn & Zasler). It is important to understand the structure of the ICF model. In daily clinical practice its application is not always obvious. Cognitive disorders and behavioral control represent impaired brain function (ICF domain body functions & structure). However, cognition can also be viewed as a basic activity of daily life.

Figure 1: the ICF model



Traumatic brain injury

A TBI occurs when a sudden trauma causes a closed or a penetrating head injury. The resulting brain damage can be focal – confined to one area of the brain – or diffuse – involving more than one area of the brain. A focal TBI usually is caused by sudden contact. Diffuse injury is more likely to be caused by an acceleration/deceleration trauma.

The severity of the TBI is determined by the nature, speed and location of the impact, and by complications such as hypoxemia, hypotension, intracranial hemorrhage or increased intracranial pressure. These complications may cause secondary injury, hours or even days after the trauma.

TBI is classified as mild, moderate or severe depending on a patient's level of consciousness and level of neurologic functioning. The Glasgow Coma Scale (GCS) is the most commonly used scale to determine severity (Table 1). The best eye opening response, the best motor response, and the best verbal response determines the score on a scale of 3-15 (EMV-score). The score represents the sum of the numeric scores of each of the categories. However, many prefer to document the score by its individual components. A patient with a Glasgow Coma Score of 15 would be documented as: E4-M6-V5, while an intubated patient would be scored as E4-M6-Vtube.

A TBI with a GCS of 13-15 is called a mild TBI, 9-12 a moderate TBI and 3-8 a severe TBI. The GCS has limited ability to predict outcome. The best motor response is probably the most significant predictor of outcome. Other classifications of injury severity include the duration of post-traumatic amnesia (PTA), and loss of consciousness (LOC) (table 2). The PTA reflects the

overall severity of the injury. PTA can be assessed with the Galveston Orientation and Amnesia Test (GOAT) or the Orientation Log (O-Log) (Frey et all, 2007).

Table 1: Glasgow Coma Scale (EMV score)

Eye opening (E)

1. None
2. To pain
3. To voice
4. Spontaneous

Motor response (M)

1. No response
2. Decorticate extension to pain
3. Decerebrate flexion to pain
4. Withdraws to pain
5. Localizing response to pain
6. Obeys verbal commands

Verbal response (V)

1. No vocalization
2. Incomprehensible sounds
3. Utters words, but not coherent
4. Disoriented conversations; confused
5. Alert and oriented; normal conversation

Total = E + M + V

Table 2

TBI score	**GCS**	**PTA**	**LOC**
Mild	13-15	<1 day	30 minutes
Moderate	9-12	>1 to <7 days	>30 minutes to <24 hours
Severe	3-8	>7 days	>24 hours

A *contusion* is a distinct area of swollen brain tissue, mixed with blood released from broken blood vessels. A contusion can occur in absence of skull fractures in response to shaking of the brain back and forth within the confines of the skull. This is called the 'coup - contrecoup mechamism'. Contusions are typically found on the inferior frontal lobes and poles of the frontal lobes, the lateral and inferior aspects of the temporal lobes and the cortex above and below the operculum of the sylvian fissures. In addition, rotational movements of the brain can cause *diffuse axonal injury* (DAI). The patient with DAI typically may be unconscious with little radiological findings on CT scanning. This results from microscopical damage to individual nerve cells (neurons) and loss of connections among neurons. Due to the rapid stretching of axons the cytoskeleton is damaged, disrupting cell function (Smith et al, 2003).

Skull fractures, especially at the base of the skull, can cause cranial nerve injuries. The facial nerve, is the most commonly injured cranial nerve in TBI causing paralysis of facial muscles. Skull fractures can tear the membranes that cover the brain, leading to leaks of cerebrospinal fluid (CFS).

Intracranial CFS leaks may cause a subdural hygroma. Extracranial CFS leaks through the nose and ears allow air and bacteria to enter the skull, thus causing pneumocephalus or infections such as meningitis or brain abscess.

Intracranial hematoma is the most common cause of death and deterioration after TBI. An epidural hematoma involves bleeding into the area between the skull and the dura. A rupture of the middle meningeal artery due to a fractured temporal bone, is the usual cause of an epidural hematoma. It is an arterial bleeding with a fast increase in pressure and is life threatening in de acute phase after TBI. With a subdural hematoma, bleeding is confined to the area between the dura and the arachnoid membrane. Subdural hematoma's are caused by ruptured veins in the subdural space, don't grow as fast as epidural hematoma's but may act a mass lesions causing morbidity and mortality. Bleeding within the brain itself is called intracerebral hematoma.

In recent years hormonal problems from dysfunction of the pituitary following TBI have received much attention. *Pituitary dysfunction* may occur in the (sub-acute stage) after TBI and may develop within the first year post onset. Especially the growth hormone axis and gonadotrophic axis appear to be vulnerable after TBI. However, the incidence of pituitary dysfunction due to TBI is still debated (van der Eerden et al, 2010 and Schneider et al, 2007).

Many TBI patients have a *polytrauma*, injuries to other parts of the body in addition to the head and brain. Trauma victims often develop hypermetabolism or an increased metabolic rate, causing muscle wasting and the starvation of other tissues. Complications related to pulmonary dysfunction can include neurogenic pulmonary edema (excess fluid in lung tissue), aspiration pneumonia (pneumonia caused by foreign matter in the lungs), and fat and blood clots in the blood vessels of the lungs. Blunt trauma to the chest can also cause cardiovascular problems, including damage to blood vessels and internal bleeding, and problems with heart rate and blood flow. Blunt trauma to the abdomen can cause damage to or dysfunction of the stomach, large or small intestines, and pancreas. A serious and common complication of TBI is erosive gastritis, or inflammation and degeneration of stomach tissue. This syndrome can cause bacterial growth in the stomach, increasing the risk of aspiration pneumonia.

Traumatic brain injury: long-term sequelae

Problems with *cognition* (thinking, memory, and reasoning) and behavior or mental health (depression, anxiety, personality changes, aggression, acting out, and social inappropriateness) are amongst the most frequent sequelae after TBI.

Dikmen et al (2009) performed a systematic review to examine the relation between TBI and cognitive impairments 6 months or longer post injury. There was a clear evidence of an association between penetrating head injury and long-term cognitive impairments. Pre-injury intelligence, volume of brain tissue lost and the brain region damaged are important modifiers of this association. Severe TBI is clearly related to long-term cognitive defects and there is suggestive evidence that this is true for moderate TBI as well. There is insufficient evidence to determine a relationship between a single, mild TBI and long-term cognitive deficits. Stulemeijer et al (2007) that 39% of patients that suffered a mild TBI reported cognitive complaints 6 months post onset. Lower educational levels, emotional distress, personality and poorer physical functioning were related to cognitive complaints. This is not the case for injury characteristics. Furthermore, the self rated cognitive complaints were not related to outcome of neuropsychological testing. Especially in mild TBI patients, long term complaints may be related to premorbid traits and physical and emotional state factors rather than to actual cognitive impairments.

TBI is strongly associated with several neurologic disorders 6 months or more after injury (Bazarian et al, 2009). *Seizures* are associated with most types of TBI. About 25 percent of patients with brain contusions or hematomas and about 50 percent of patients with penetrating head injuries

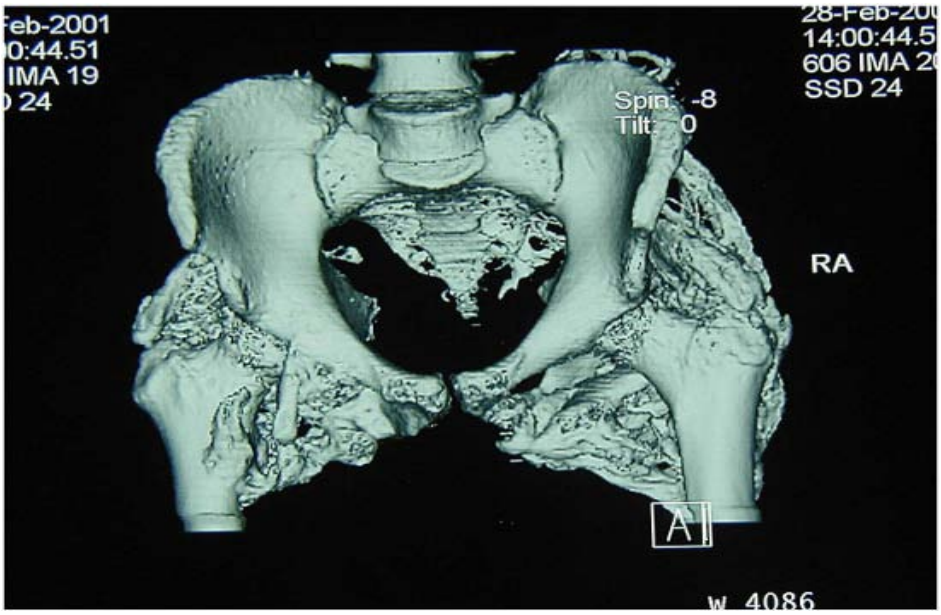
will develop seizures within the first 24 hours of the injury. These immediate seizures do not seem to be linked to the development of post-traumatic epilepsy (recurrent seizures occurring more than 1 week after the initial trauma). After penetrating TBI 32%-53% suffer from seizures. After a closed TBI the seizure risk varies with the initial TBI severity. Compared to the healthy population the risk increases 17-95 times after severe TBI, 2,9 to 6,6 times after moderate TBI and 1,5 times in mild TBI resulting in LOC or PTA.

Neurodegenerative disorders such as *dementia of the Alzheimer's type* (DAT) and Parkinsonism are related to mild and moderate TBI. DAT is a progressive, neurodegenerative disease characterized by dementia, memory loss, and deteriorating cognitive abilities. A moderate TBI increases the risk of DAT with a hazard ratio (HR) of 2.32. In case of a severe TBI the HR for DAT is 4.51. For the sake of ease, one could say that the risk for DAT in patients with a moderate TBI is 2.32 times compared to those who have not suffered a TBI. *Parkinsonism* may develop years after TBI as a result of damage to the basal ganglia. It is characterized by tremor or trembling, rigidity or stiffness, slow movement (bradykinesia), inability to move (akinesia), shuffling walk, and stooped posture. The association between TBI and parkinsonism has not been studied as extensively as in DAT. However significant associations between PD and TBI have been established. Professional career boxers have in increased risk for *dementia pugilistica* also called chronic traumatic encephalopathy or the punch-drunk syndrome. Mild cases may present with slurring dysarthria, gait ataxia, disequilibrium and headache. Symptoms begin anywhere between 6 and 40 years after the start of a boxing career, with an average onset of about 16 years. Mental and physical abilities may decline resulting in dementia and parkinsonism.

Language and communication problems are common in TBI patients. Aphasia may occur in 19%, dysarthria in 30% and dysphagia in 17% (Safaz et al, 2008). Some experience difficulty with the more subtle aspects of communication, such as body language and emotional, non-verbal signals called prosodic dysfunction.

Heterotopic ossification (HO) is pathologic ectopic bone formation commonly located in the soft tissue around the big joints, causing range-of-motion limitation, pain, and periarticular warmth, swelling and erythema. It may complicate neurological disorders including traumatic brain injury (TBI), spinal cord injury, stroke and burns. The incidence of HO in TBI ranges from 7.3% to 76% (Simonson, 2007). Hendricks et al (2007) established that the occurrence of heterotopic ossification is related to the severity of the brain injury. Coma duration, diffuse axonal injury, spasticity and systemic infections all are associated with an increased risk of HO. Especially the presence of autonomic dysregulation is important as is has a high positive and negative predictive value.

Figure 2: A case of severe heterotopic ossification of both hips causing ankylosis in a young female after severe TBI



Social functioning after traumatic brain injury

Social outcome or participation after TBI is a multilayered concept that encompasses domains such as mobility, domestic life, interpersonal interactions and relationships, and community, social and civic life. Information about the course and prognosis of participation after TBI is necessary to determine which patients are at risk for an unfavourable outcome and to optimize the use of limited health care and social resources. For TBI patients and their relatives, early information on prognosis is important for adequate coping and anticipating long term consequences. However, most studies have focused on short-term outcome, 6 months to 1 year post onset. Temkin et al (2009) performed a systematic review on social functioning after TBI observed at least 6 months after the injury. They conclude that there is a dose-response relationship between the severity of the injury and social outcomes. However there is insufficient evidence to determine at what level of severity the adverse effects are demonstrated. Willemse-van Son performed a 3 years prospective study on patients with moderate and severe TBI and used the Community Integration Questionnaire (CIQ) as primary end-point. At three months post injury a decline had occurred compared to the pre-injury situation regarding home integration, social integration, and productivity. Substantial improvement occurred in the first year post-injury. Improvement continued from year 1 to 3 years post injury. Age, the post-acute Barthel Index and the pre-injury CIQ scores were the major determinants of community integration three years post-injury. It seems as if clinical determinants regarding TBI severity like the GCS-score, abnormalities on CT scanning and hypoxia, hypotension or hypothermia in the acute stage predict short term outcome rather than long term outcome.

These findings were substantiated in 2 systematic reviews on activity limitations and participation restrictions 6 months and one year post-injury (Husson et al, 2010 and Willemse-van Son, 2009). Strong evidence for predicting outcome at six months was found for GCS on admission, GCS motor score, midline shift on CT scan, subdural haematoma and pulsatility index. For ongoing disability one year post-injury, older age, pre-injury unemployment, substance abuse, and severe disability at rehabilitation discharge were strong predictors. Pre-injury unemployment, longer posttraumatic amnesia, substance abuse, and more disability at rehabilitation admission, were strong predictors for being unproductive one year post-injury.

Although these profiles are best evidence for prognosis of restrictions in activities and participation one year after TBI, they seem to be of limited value. Most factors are not modifiable by prevention

or treatment. Hence, it is not possible to change the course and prevent a future worse outcome. Further, the identified prognostic factors are of limited value in planning adequate and costeffective long-term care. In the Rotterdam TBI study, the presence of unmet needs in patients with moderate and severe TBI was assessed three to five years post-injury with the shortened version of the Impact on Participation and Autonomy Questionnaire (Willemse-van Son, thesis 2009). 17% of the patients reported long-term unmet needs. Most unmet needs concerned work (31%), education (45%), and supporting others (46%).

Overall it can be concluded that much information is needed on long term outcome at the level of activities and participation after mild, moderate and severe traumatic brain injury. Which patients are at risk of losing their jobs, of developing marital or parental difficulties? Who is at risk of developing substance abuse, will become dependent in transportation or leisure activities or will depend heavily on the caregiver? What patient can be helped by treating his depression or post traumatic stress disorder and what patient will benefit from structured day time activities. These are examples of unanswered questions that are of paramount importance in clinical practice. As long as these issues are not dealt with, traumatic brain injury patients as well as their caregivers should be followed-up over long periods of time.

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