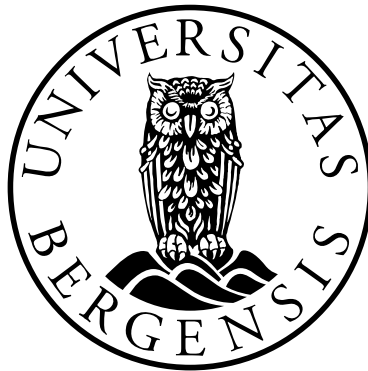# Functional level after Traumatic Brain Injury

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Functional level after Traumatic Brain Injury

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ABSTRACT

Objectives:

The objectives of the thesis were to describe the functional level (papers I and II) and self awareness of functional deficits (paper III) after moderate and severe Traumatic Brain Injury (TBI), and to evaluate the predictive impact of pre-injury and injury-related factors on functional level (papers I, II) and awareness of functional deficits (paper III).

Material and methods:

Papers I-II were cohort studies of 55 TBI patients (moderate = 21, severe = 34) and 65 TBI patients (moderate = 21, severe = 44). Their functional level was assessed by FIM (Functional Independence Measure) at admission and discharge from in-hospital sub-acute rehabilitation (paper I), and by FIM and GOSE (Glasgow Outcome Scale Extended) 12 months after injury (paper II). Possible predictors of FIM at discharge (paper I) and at 12 months (paper II) were analyzed in a regression model.

Paper III was a cohort study of 50 TBI patients (moderate = 17, severe = 33) assessed by Patient Competence Rating Scale (PCRS) 12 months after injury. Awareness of functional deficits was investigated by subtracting PCRS relative ratings (PCRS-R) from PCRS patient ratings (PCRS-P). Predictors of PCRS-P ratings and differences between patient and relative ratings were analyzed in a regression model.

Results:

At discharge from sub-acute rehabilitation, on average 53 (± 24) days post-injury, the FIM motor and cognitive scores had improved in both moderate and severe TBI patients, but 57% of those with moderate TBI and 91% of those with severe TBI still had impaired motor and cognitive function with a FIM score < 126 (paper I). The activity limitations were mild (FIM

109-126 = functionally independent) in 95% of moderate TBI patients and in 62% of severe TBI patients. During the period from discharge to 12 months after injury, the FIM motor score improved in severe TBI but not in moderate TBI patients, and the FIM cognitive score did not improve in any of the groups (paper II). At 12 months, 19% of moderate TBI patients and 40% of severe TBI patients still had impaired motor and cognitive function as assessed by FIM. The activity limitations were mild (FIM 109-126) in 95% with moderate and in 74% with severe TBI (paper II). Functional global outcome as assessed by GOSE showed "good recovery" in 52% with moderate TBI versus 33% in severe TBI, "moderate disability" in 33% with moderate TBI versus 31% in severe TBI, and "severe disability" in 14% with moderate TBI versus 36% in severe TBI. Longer stays at the rehabilitation unit, a short PTA period and a high GCS score at admission to rehabilitation were positive predictors of functional level (FIM) at discharge and 12 months follow-up (papers I and II).

Self-perceived function 12 months after injury was assessed by PCRS–P and compared to relative-perceived function (PCRS-R) with mean scores of 122/150 (95% CI = 115; 129) and 117/150 (95% CI = 110; 125), p = 0.93. The patients scored themselves slightly higher than their relatives in the domains of Activities of Daily Living (ADL) and cognitive function, but not in the domains of interpersonal and emotional function. The strongest predictor of PCRS-P was GCS at admission to rehabilitation (GCS rehab) (B = 3.314, p = 0.008), while others were GCS acute (admission acute hospital) (B = -1.771, p = 0.044), age (B = 0.510, p = 0.002), and PTA duration (B = -0.330, p < 0.001). Predictors of differences in PCRS-P and PCRS-R (overestimation of own function) were GCS acute (B = -3.530, p = 0.001), age (B = 0.304, p = 0.036), and PTA (B = -0.160, p = 0.020). Analyses of predictors in different domains showed that lower GCS rehabilitation predicted overestimation of ADL functioning (B = -0.526, p = 0.037), lower GCS acute was the strongest predictor of overestimation of cognition (B = -0.851, p = 0.001), and of emotional regulation (B = -1.042, p = 0.042) while

being married (12 months post-injury) was the strongest negative predictor of overestimation of interpersonal functioning (B = -3.622, p = 0.015).

Conclusions:

- The greatest improvement after moderate and severe TBI was in the sub-acute phase during the stay in a specialised rehabilitation unit

- A short PTA period, a high GCS score and FIM score at admission to rehabilitation, and a longer stay in the rehabilitation unit were positive predictors of functional level at discharge and 12 months after injury

- Residual disability was reported in 48% of moderate TBI patients measured by GOSE 12 months post injury

- A slight lack of awareness of dysfunction in the domains of ADL and cognitive function were reported 12 months after injury

- Higher age was a predictor of more severe awareness deficits 12 months after injury

- More severe injury (longer PTA) was a predictor of low self-perceived function though negatively associated with degree of awareness deficits 12 months after injury

LIST OF PAPERS

Paper I: Sandhaug M, Andelic N, Vatne A, Seiler S, Mygland Aa. Functional level during sub-acute rehabilitation after traumatic brain injury: Course and predictors of outcome. Brain Injury 2010; 24(5): 740-747.

Paper II: Sandhaug M, Andelic N, Berntsen SA, Seiler S, Mygland Aa. Functional level during the first year after moderate and traumatic brain injury: Course and predictors of outcome. J Neurol Res 2011;1(2): 48-58.

Paper III: Sandhaug M, Andelic N, Berntsen SA, Seiler S, Mygland Aa. Self and near relative ratings of functional level one year after traumatic brain injury. Disability and Rehabilitation 2011; 1-6.

LIST OF ABBREVIATIONS

ADL	Activities of Daily Living
ACRM	the American Congress of Rehabilitation Medicine
AIS	the Abbreviated Injury Scale
ANOVA	the Analyses of Variance test
CDC	the Centers for Disease control and Prevention
CT	Computed Tomography
DAI	Diffuse Axonal Injury
DRS	Disability Rating Score
DV	Dependent Variable
FIM	Functional Independence Measure
FIM-COG	the cognitive function in FIM
FIM-M	the motor function in FIM

GCS	Glasgow Coma Scales
GOSE	Glasgow Outcome Scale Extended
HISS	the Head Injury Severity Scale
ICD-10	the International Classification of Diseases
ICF	the International Classification of Disability and Health
ISS	the Injury Severity Scale
LOC	Loss of Consciousness
MRI	Magnetic Resonance Imaging
MVC	Motor Vehicle Crashes
NISS	the New Injury Severity Scale
PTA	Posttraumatic Amnesia
PCRS	Patient Competency Rating Scale
PCRS-R	Patient Competency Rating Scale – Relative
PCRS-P	Patient Competency Rating Scale – Patient
DiffPCRS	Difference in PCRS scores
TBI	Traumatic Brain Injury
TBIMS	The Traumatic Brain Injury Model Systems
TBINDSC	The Traumatic Brain Injury Model Systems National Data and Statistical Center
US	United States (of America)
VIF	Variance Inflation Factor

Contents

INTRODUCTION

TBI epidemiology

In general, the incidence rate of TBI (the occurrence of new cases in a specified period of time) requiring hospitalization appears to have decreased during the last 20 years. In three Norwegian studies conducted in 1974, 1979 and 1993 annual admission rates were 200, 236 and 169/100 000 population respectively (1, 2, 3). A study from the Southwestern Norway conducted in 2009 reported an annual incidence rate 157/100 000 population for hospital admitted head injury (4). A lower incidence of hospital admitted TBI patents, 83.3/100 000 population, was reported in a recent study from the Norwegian capital, Oslo (5). A similar decreasing trend in hospital admitted TBI is also observed in other European and the US countries (6, 7, 8). A recent estimate in the US is currently 79/100,000 (9). Variation observed in the incidence of different countries could be partially explained by differences in criteria used to define TBI or to identify patients (10). The effective implementation of prevention and safety programmes and the wider availability of emergency services and specialized trauma systems may also influence the decrease in incidence rates (11).

Epidemiological studies have shown age-specific incidence of hospital-treated TBI, with highest rates in persons younger than four and older than 65 years (5, 7). According to national and international studies, TBI occur in males about twice as often as in women (3-5, 7). Falls are the leading cause of injury in Scandinavia and in the US, followed by traffic accidents, assaults and other injuries (3-5, 7). However, traffic accidents are the leading cause of injury in Southern Europe, and continue to be the main cause of severe and fatal injuries (7). Assaults are common cause of injury in males and associated with substance influence at the site of injury (3, 5).

In Europe, about 70-80% of patients are classified with mild TBI based on the Glasgow Coma Scale (GCS), and moderate and severe TBI with 10% each (7). In a recent Norwegian study the ratio of hospitalized patients with severe, moderate and mild TBI was 1:1.3:14 (5). Approximately 10-15% of patients have more severe injuries requiring specialist care (5, 12).

Severe TBI is associated with high mortality rates among hospitalized patients (30-50%). However, the overall rate of TBI mortality has generally decreased since the 1980s, and can be attributed to improved emergency and acute trauma services (Level I trauma centre) (11, 13).

TBI definition

In 1995, the Guidelines for Surveillance of Central Nervous System Injury by the Centers for Disease control and Prevention (CDC) published a TBI definition in an effort of standardization of the epidemiological case definitions (14, 15). TBI is defined as "damage to the brain tissue caused by an external mechanical force as evidenced by loss of consciousness due to brain trauma, amnesia, other neurological or neuropsychological abnormalities, skull fracture and diagnosed intracranial lesions or death" (16). A report from the British Society of Rehabilitation Medicine defined TBI as "brain injury caused by trauma to the head, including the effects of direct complications of trauma, notably hypoxemia, hypotension, intracranial hemorrhage and raised intracranial pressure" (17). In the codes of the International Classification of Diseases (ICD-10) specifying clinical features of brain injury, skull fractures, brain concussions, brain contusions, and other intracranial injuries, including subarachnoid, subdural, and extradural hematomas and diffuse injuries, are listed (18).

In the present work, TBI is defined as damage of brain tissue caused by external mechanical force (19).

TBI classification

The most commonly used clinical indices of TBI severity for adults is the Glasgow Coma Scale (GCS) assessing level of consciousness after TBI based on eye opening, motor and verbal responses. Mild TBI is defined as a state with GCS scores of 13-15, moderate 9-12 and severe 3-8 (20). Variation in the definition of mild TBI exists, and Scandinavian guidelines and recent studies defined moderate TBI as a GCS score of 9-13 (21). Other researchers suggest that persons with GCS score of 13-15 and intracranial lesions should be classified as moderate TBI because they have a similar course of recovery to those with GCS score of 9-12 (22).

Other scales that assess extracranial injuries and physiological instability are the Abbreviated Injury Scale (AIS) (23) and Injury Severity Score (ISS) (24). The AIS defines the severity of injury in different body regions, while the ISS quantifies the severity of multiple body region injuries based on the AIS codes. A new version of the ISS, the New ISS (NISS), exists and takes the three most severe AIS values irrespective of body region in full account of multiple injuries in the same body region (25).

In many TBI studies, description of the location or anatomical features of TBI in acute phase is done by the Marshall score for computed tomography (CT) findings (26). It classifies the presence or absence of a mass lesion and differentiates diffuse injuries by signs of increased intracranial pressure. A more recent and standardized CT-based classification is the Rotterdam score combining intracranial CT findings to predict outcomes (27). Magnetic resonance imaging (MRI) provide information about the neuroanatomy of the skull, brain tissue, and blood vessels and assess the extent of brain injury and the medical sequelae of traumatic brain injury (edema, intracranial bleeding, degeneration) (28). MRI has often been used for diagnostic purposes in follow-up studies for detecting diffuse axonal injuries (DAI). DAI is damage to the axons due to shearing, acceleration-declaration, and rotational forces on

the brain (29). It is classified into 1-3 stages of DAI; DAI 1-lesions confined to the lobar white matter; DAI 2-callosal lesions; and DAI 3-lesions in the dorsolateral brainstem (29, 30)

In addition, the presence and duration of posttraumatic amnesia (PTA) are often used as tools for classifying TBI (31). The term PTA is defined as the "time elapsed from injury until recovery of full consciousness and the return of ongoing memory" (32) or as "a period of clouded consciousness which precedes the attainment of full orientation and continuous awareness in persons recovering from head injuries (33). Persons in PTA suffer from anterograde amnesia, i.e. an inability to remember new experiences, and they often have a period of retrograde amnesia, i.e. loss of memory of events before injury (34).

In the thesis, TBI severity was classified as defined by the American Congress of Rehabilitation Medicine (ACRM) (35). Mild TBI was defined by an initial GCS score of 13-15, change in mental status without loss of consciousness (LOC), or LOC up to 30 minutes and PTA up to 24 hours. Moderate TBI was defined by GCS score of 9-12, LOC more than 30 minutes, but less than 6 hours. Severe TBI was defined by GCS score of ≤ 8 and LOC more than 6 hours. In the ACRM and WHO definitions, no minimal PTA duration is specified, and PTA duration of a few seconds qualifies. But if PTA duration exceeds 24 hours TBI should no longer be considered as mild (35). This ACRM definition has been widely used, especially in the field of rehabilitation and neuropsychology (35).

TBI care

TBI care is complex and includes specialized emergency, pre-hospital care, transport to an appropriate treatment centre, in-hospital acute care, early and later rehabilitation, vocational, educational and community support as well as long-term care (7, 36). Specialized emergency regional trauma systems have developed promoting fast air transport to level I trauma centres

for patients with severe TBI. These regional trauma centres have full-time intensive care, imaging (CT, MRI), neurosurgical, and other trauma subspecialists (36). In-hospital acute care for TBI patients is common when in need of observation of secondary neurological deterioration and complications to those with severe injury demanding intensive care management (36). The pathway toward acute inpatient rehabilitation or sub-acute care versus outpatient post-acute rehabilitation is commented later under the paragraph of "TBI rehabilitation". Vocational and educational support may be re-education, training and work services, and are important parts of the continuum of TBI care as returning to some sort of productive activity helps social reintegration and better life satisfaction (36). Community support are home and community based services for TBI people who are unable to live independently and who cannot rely on home supervision by family or friends. Provisions for transport, respite care to provide time-off for full-time caretakers, legal services, financial and estate planning, mental health services and treatment of substance abuse are other examples of community support in TBI care (36).

TBI rehabilitation

Rehabilitation following TBI developed during World Wars I-II with the identification of neurocognitive and affective disorders by Poppelreuter, Goldstein, Russel and Luria (37-44). In the 1950s and 1960s, TBI rehabilitation concerned motor disorders within mechanical and orthopaedic frameworks, while behaviour-conditioning and psychoanalysis started under the influence of behaviourism (45). In the 1980s, holistic programmes and cognitive neuropsychology developed (46). Rehabilitation after TBI has derived from these works and focus on more home-based therapy in ADL and work skills (47-51).

TBI induces disturbances in different domains (physical, cognitive and social abilities) at different levels. Further, it involves disruption in the course of psychic state and the life plan of the person and often changes in personality and behaviour (52). The main goal of rehabilitation is to improve functional independence, re-entry to a community and return to work, as well as quality of life (52). Rehabilitation has been described as "a reiterative, active, educational, problem solving process focused on a patient's disability" with assessment, goal setting, intervention and evaluation (53). Rehabilitation following TBI is a continuous process that involves the identification of problems and needs, implementation of adequate interventions and evaluation of outcome (54). TBI rehabilitation is generally long consisting of three phases: (1) acute rehabilitation in the trauma hospital followed by (2) sub-acute (generally inpatient) rehabilitation, and (3) post-acute outpatient rehabilitation (52). Acute rehabilitation aims to reduce complications that can occur as a result of injury and promote functional recovery through multi-sensory stimulation (52, 55, 56). Sub-acute inpatient rehabilitation facilitates and accelerates recovery of physical and cognitive impairments, and compensates for disabilities (52, 57, 58). Post-acute rehabilitation includes outpatient therapy for physical, domestic and social independence, reduction of handicaps and re-entry to the community (52, 57, 58). Rehabilitation after TBI are organized in relation to these phases and are often carried out by a specialized brain injury rehabilitation team. The team is multidisciplinary and works on common goals for each patient, involves and educates the patient and family, has relevant knowledge and skills, and resolves most of the common problems faced by the patient (53). In papers I-III, all TBI patients received sub-acute interdisciplinary brain injury rehabilitation given by a specialized rehabilitation team: physiatrist, nurse, physiotherapist, occupational therapist, speech therapist, psychologist, and social worker.

In sum, rehabilitation after TBI is multi- and interdisciplinary management of a patient's functioning and health in order to minimize symptoms and disability. Its holistic view agrees with the framework of the International Classification of Functioning, Disability and Health (ICF) published by the World Health Organization (WHO) in 2001 that describes functional consequences of health and illness (59). It is a comprehensive model that classifies health-related function and dysfunction in the physical, psychological and societal aspects (i.e. bio-psychosocial perspective). The ICF framework is an interactional model where all components of the system are constantly influencing and modifying the others (60). Health condition (disorder or disease) is influenced by body functions and structure, activities, participation, environmental factors and personal factors. But, all these factors are also influenced by each other in a continuous interactive relationship (60).

TBI prognosis and prediction of functional level

In the 80s few publications were made on TBI rehabilitation. During the last decades there has been a growing interest addressing impairments, secondary conditions, course of recovery, and aspects of post-TBI function (61). The Brain Injury Association of America established in 1987 The TBI Model Systems (TBIMS). The Traumatic Brain Injury Model Systems National Data and Statistical Center (TBINDSC), is a central resource for researchers and data collectors within the TBIMS program. The primary purpose of the TBINDSC is to advance medical rehabilitation by scientific efforts to longitudinally assess the experience of individuals with TBI (62). The TBIMS examines the course of recovery and outcome following TBI in US population. The database includes 10 000 persons in follow-up studies of 20 years. So far, a summary of disability outcome assessed by FIM reports improvement in functional level from requiring moderate assistance at rehabilitation admission to modified independence at one and two years post-injury (62). Most improvement of disability and

functional level occur during inpatient rehabilitation. Improvement is continued one year post-injury, but a plateau of disability and functional level is reported between one and two years post-injury (62). Degree of injury and its consequences vary, but reduced physical function, cognitive function and reduced practical and social functioning are common sequela after TBI (19, 63-68). In moderate to severe cases of TBI, problems and limitations regarding ADL functioning, work functioning, as well as social functioning may be long lasting, sometimes life-long (63-70). Even in cases of mild to moderate TBI without significant intracranial injury one faces problems regarding work and social participation because of unregistered physical, cognitive and/or emotional sequelae due to subtle brain dysfunction and emotional reactions to trauma. Many of these patients have not received treatment or discharge information about how to handle and live their lives after a TBI (71).

After sub-acute rehabilitation 40% of severe TBI patients have persistent motor disabilities, 50% suffer from cognitive impairments, and 60% from psycho-affective changes (72-79). Within two years of injury 75-90% are working after mild TBI, 60-70% are working after a moderate TBI, and only 35-50% after severe TBI (80). Overall, 55-75% returns to the same job or equivalent, and 15-35% to a new job. After 7 years many have lost their jobs and the employment rate decreases to 27% (81). In other studies with severe TBI population 35% returned to work and 26% retired 7 years post injury, while in others 18% returned to work at 6 months, 31% at 12 months (82, 83). In a Japanese study of moderate to severe TBI no patients returned to work, while 39.5% were employed 6 months after discharge in a US study with mild to moderate TBI population (84, 85).

For the moderately injured TBI patient only most reports are made in the 1980s, and outcome was often determined at 3 and 6 months after injury. Follow-up studies beyond that period are lacking or have mixed severity TBI populations. We think it is important to look at the moderately injured as one group and not combined groups of mild-moderate or moderate-

severe. TBI is heterogeneous and injury severity has its own characteristics as mild, moderate, and severe. Therefore we focused on functional level in moderate TBI versus severe TBI in papers I and II.

Progress has been made in the evaluation of biomarkers, genetic factors, electrophysiological techniques, and neuroimaging. Still, no class I prognostic studies have been conducted (61). Prognosis and functional outcome depends on various trauma-related and individual factors. Research on time course and predictors of function is important to provide basis for realistic information to patient and relatives, and for program planning and design of interventions tailored to individual rehabilitation (86). Predictive modelling is however difficult due to the numerous complex clinical elements that occur and interplay (87). Most studies on predictors of functional level following TBI are carried out during the initial weeks or 6 months to years after injury. Some of these have reported that age, race, violent injury, initial Glasgow Coma Scale (GCS), duration of coma or post-traumatic amnesia (PTA), as well as length of stay at acute hospitalization, and rehabilitation length of stay (LOS) could predict functional outcome of patients (88-92). In a study 5 years after TBI, logistic regression analysis indicated that a variety of measures were predictive of employment and productivity (pre-injury productivity, age, education, discharge Disability Rating Score (DRS), discharge FIM score, rehabilitation length of stay (61). However, there is no single set of characteristics which has demonstrated to be uniformly accurate in predicting functional level. Therefore, in papers I and II we aimed at evaluating the impact of various trauma-related and other factors on short and long-term functional outcome.

We hope that this thesis will be a contribution to the needs addressed, as more knowledge about TBI rehabilitation outcome in Europe and especially in Scandinavia, was needed when our PhD project started.

TBI and self awareness of function

There are numerous reports of disability after TBI based on ratings by health personnel (93-94). How the patients perceive their own functional level is less described. To focus on the patient's perspective is important in everyday clinical practice to define the right goals and to achieve motivation and compliance with the rehabilitation process. A recent Norwegian study showed that patient perceived function at three months predicted function and participation one year after TBI, and suggested to focus on cognitive and interpersonal competency to enhance participation after TBI (86). Patient perceived function 12 months after injury is less studied, and to our knowledge predictors of self perceived function has not been published. Therefore, this was one of the aims of study III.

One possible obstacle to evaluation of self perceived function and to achieve relevant goals is that TBI patients may have poor insight or lack of awareness of their deficits or strengths (93, 94). Awareness deficits - also called anosognosia - is defined as a disagreement between the patients' own perceived function as compared to what a near relative or clinician perceives - with the patient being less aware of their deficits (95). About 45% with moderate to severe TBI demonstrate awareness deficits in cognitive function, personality changes and abnormal behaviour process (96). Some studies show that TBI patients tend to underestimate their cognitive and behavioral impairments when compared with ratings of family members, clinician ratings, and their performance on neuropsychological testing (95). Other studies on self-awareness are contradictory (97, 98), though the data support low self-awareness with poorer vocational outcome (97). Awareness deficits are associated with worse functional outcome (99, 100), higher caregiver distress and poor compliance with rehabilitation (101). Most studies of awareness deficits concern inpatient rehabilitation settings, long-term follow-up and predictors of awareness deficits are less studied (95). Paper III was designed to increase our knowledge about these issues.

TBI research in Norway

Outcome data from Norway, Europe and the US that include patients in need of TBI rehabilitation are mostly based on follow-ups of severe TBI. However, some follow-ups of the whole TBI population including mild and moderate TBI have been published lately (102-105).

During the last decade there has been more focus on TBI research of moderate-to-severe injury in Norway, including epidemiology, disability, MRI imaging and neuropsychological outcome (4, 103, 106-109). In 2007, a report on neuropsychological function 23 years after mild TBI was published (106). The year after, a group of researchers investigated the relationship of "dose" of intracranial hypertension to outcome in severe TBI (110). Others again, reported on MMPI-2 profiles 23 years after pediatric mild TBI (111). In 2009, reports regarding post-concussion symptoms at 3 and 12 months after TBI, functional outcome and health related quality of life 10 years after moderate-to-severe TBI, and cognitive recovery one year after TBI were published (109,112,113). These were followed by studies of disability, competency in activities, cognitive impairment, validation of mortality prognostic modeling, as well as incidence of olfactory dysfunction across TBI in 2010-11 (103,107-108, 114-115).

Focus on TBI research in Norway increased as attention was directed towards a policy of continuum of care with reinforcement of the primary care and rehabilitation offered to TBI patients as recommended by the Norwegian Health Authorities (116).

However, less research is done on prediction of functional level during sub-acute TBI phase and one year after TBI. Thus the rationale of this thesis was as followed: In papers I-II, a patient cohort with moderate and severe TBI was followed during sub-acute rehabilitation and at 12 months after injury estimating course and predictors of functional level. Paper III

focused on the quantification of TBI patients' perception of their own function and identification of awareness deficits of long-term functional level after TBI. All three papers report on functional outcome according to the ICF components of body functions and structure, activities, and to some degree participation. The thesis is in line with recommendations by Bilbao et al that studies from different countries are required to provide better understanding of regional, national and international differences and needs in the area of brain injury rehabilitation (60). Hopefully, readers will find a Scandinavian thesis in the field of neurology, disability, physical medicine and rehabilitation valuable, though our material is smaller than studies from the larger European countries.

AIMS OF THE STUDY

Paper I:

a) To describe functional level and improvement as measured by Functional Independence Measure (FIM) in patients with moderate and severe TBI at admission and discharge from sub-acute rehabilitation

b) To evaluate the impact of pre-injury and injury-related factors (e.g. social-demographic and injury characteristics) as predictors of functional level at discharge from sub-acute rehabilitation

Paper II:

a) To describe the course of functional recovery during the first 12 months after moderate and severe TBI as measured by FIM

b) To examine the global outcome at 12 months as evaluated by Glasgow Outcome Scale Extended (GOSE)

c) To examine the influence of various factors as predictors on FIM outcome at 12 months

Paper III:

a) To see how TBI patients perceive their own function as measured by PCRS 12 months after injury

b) To examine self awareness of functional deficits by comparing PCRS ratings from patients and near relatives

c) To look at possible predictors of the discrepancy between patient and near relative ratings of functioning

MATERIALS AND METHODS

Setting

Department of Physical Medicine and Rehabilitation in Kristiansand is a department of the regional acute hospital (Sørlandet Hospital with locations in Kristiansand, Arendal and Flekkefjord) serving a population of 283 128 living in Vest-and Aust-Agder counties with specialized rehabilitation services. The department rehabilitates patients with TBI, stroke, progressive neurological disorders, bone amputations, multi-traumas, and orthopedic training. All TBI patients in need of rehabilitation (mostly severe and moderate injuries) are admitted

from the acute hospitals for sub-acute rehabilitation, and later followed by a specialized out-patient team. Among 25-35 TBI patients receive in-patient rehabilitation on a yearly basis.

Design

Papers I-III are prospective studies where we considered for inclusion consecutive patients with TBI admitted directly from acute care hospitals to the unit for neurological rehabilitation. The inclusion period was from December 2005 to June 2008 in paper I, while the inclusion periods in papers II-III were longer (December 2005 to November 2008) to increase the sample sizes to strengthen the statistical power.

Samples and recruitment procedure

Patients were admitted from Sørlandet Hospital (Kristiansand, Arendal and Flekkefjord) where they, after intensive care, had acute rehabilitation in either a Neurology department (25 patients/paper I, 31 patients/paper II, 25 patients/paper III) or a Surgery department (17 patients/paper I, 18 patients/paper II, 17 patients/paper III). We also included 13 patients from a cooperation project treated in a specific intensive rehabilitation unit at Oslo University Hospital, Ulleval (a Level I trauma centre). This project is a similar follow-up study of TBI patients from Eastern Norway where the same exclusion criteria were applied to them.

Exclusion criteria were age < 16 years, TBI classified as mild as defined by the American Congress of Rehabilitation Medicine (35), vegetative state (no response indicative of consciousness during the rehabilitation stay), and serious co-morbidities which would have interfered with assessment of TBI related impairments such as associated spinal cord injuries, previously diagnosed severe psychological disorders, and/or substance abuse. Vegetative state was listed as an exclusion criterion since The Regional Committee for Medical Research

Ethics did not approve written consent certified by a close relative if the patient was disabled from signing. During the autumn of 2005, we had information meetings about TBI and our PhD project with the doctors at Sørlandet Hospital and encouraged them to transfer all patients with moderate and severe TBI to rehabilitation.

Data collection

Data was collected during the acute hospital stay, rehabilitation stay, and at one year post-injury (papers II-III). The patient outcomes were assessed by clinical evaluation, interviews and self-reported questionnaires.

In paper I, 21 patients were classified as moderately injured (GCS 9-12) and 34 severely injured (GCS 3-8). One patient was excluded. In paper II, 65 patients were included initially and 10 of them were new subjects. Twenty-one patients had moderate TBI, while 44 were severely injured. The same patient was excluded as in paper I. Also, in the FIM and GOSE analyses the number of subjects was reduced to 63 (21 moderate TBI and 42 severe TBI) due to missing values in two patients. Seventy-four persons were considered for inclusion in paper III. Nine were excluded due to drop-outs (n=5), mild TBI (n=3) and death (n=1), and 15 were excluded due to incompletely answered PCRS sheets. We ended up with 50 included patients, 33 had severe TBI and 17 moderate TBI. New subjects were added in papers II-III due to inclusion of admitted consecutive TBI patients during the inclusion period. In paper III, all those with complete answered PCRS sheets were included: 16 moderate TBI patients from papers I-II, 32 severe TBI patients from papers I-II, and one new moderate TBI patient and one new severe TBI patient.

Independent variables

Pre-injury socio-demographic, injury and post-injury patient characteristics were collected in all three papers. See table 1 for an overview.

Table 1. Independent variables Paper I – III.

Predictor	Paper I	Paper II	Paper III
Gender M/F	x	x	x
Age	x	x	x
Civil status pre-injury (alone/ live with)	x	x	x
Civil status 12 months post- injury (alone/ live with)			x
Education (< 12/> 12 years)	x	x	x
Previous head injuries (yes/no)	x	x	
Place of acute care (neurology/surgery/level 1 trauma center)	x	x	
Injury mechanism (traffic accidents/falling/violence, sports, other)	x	x	
Brain injury localization on CT head scans (frontal/non-frontal region)	x	x	x
Injury severity (severe/moderate)	x	x	x
Other injuries (none/≥ 1)	x	x	
Alcohol/drug influence at time of injury (yes/no)	x	x	x
PTA duration (days)	x	x	x
Length of stay in acute hospital (LOS acute days)	x	x	
Length of stay in rehabilitation hospital (LOS rehab days)	x	x	x
Glasgow Coma Scale at admission to acute hospitalization (GCS acute)	x	x	x
Glasgow Coma Scale at admission to the rehabilitation unit (GCS rehab)	x	x	x
Functional Independence Measure (FIM) admission to rehabilitation unit	x		

Outcome measures

Functional Independence Measure (FIM) was used to assess functional outcome in papers I-II. The validity and reliability of the scale to assess functioning has been documented (117). The FIM has also previously been shown to be both valid and reliable for measuring functional outcome after TBI (118). The FIM is an 18-item rating scale assessing self-care, bowel and bladder management, mobility, communication, cognition, and psychosocial adjustment (119). Each item is rated on a scale from 1 (total assistance) to 7 (complete independence) (120). The FIM consists of two subscales, FIM Motor (FIM-M) and FIM Cognitive (FIM-COG). The FIM-M consists of 13 items of motor function and movement (score range 13-91) and the FIM-COG 5 items regarding the processing of information, interaction with others, and communication (score range 5-35), giving a total FIM score range of 18 to 126. A total FIM score (sum of FIM-M and FIM-COG) of $\leq$ 108 indicates limitation in activities and need for assistance from another person while scores of 109-126 indicates functional independence. The FIM scoring was performed by a certified interdisciplinary team (physician, nurse, occupational therapist, and physiotherapist) during the first week after admission and the last week before discharge and at 12 months follow-up. For this study, differences of 2 or more FIM units were considered to be clinically important (17).

Glasgow Outcome Scale Extended (GOSE) was used as measure of global outcome in paper II. The validity and reliability to assess global outcome had been documented for TBI population (121). The GOSE measures a combination of neurological functioning and dependence on others with eight outcome categories ranked 1 to 8: score 8 = good recovery, score 7 = good recovery with minor physical or mental deficits, score 6 = moderate disability and return to previous work with some adjustments, score 5 = moderate disability and work at a lower level of performance, score 4 = severe disability and for some activities dependent upon others, score 3 = severe disability and completely dependent on others, score 2 =

vegetative state, score 1 = death (122). The GOSE has been reported to be a good method for assessment of upper range of outcome, and sensitive for detection of good recovery or moderate disability in moderate TBI (121). The GOSE scoring was performed as face-to-face interviews by a certified interdisciplinary team (physician, nurse, occupational therapist, and physiotherapist) 12 months after injury.

In paper III the dependent outcome variables were the patient ratings and differences between patient and relative ratings of perceived competency and awareness 12 months after the injury as measured by **Patient Competency Rating Scale (PCRS)**. The PCRS is a 30-item self-report questionnaire assessing competency in activities of daily living, cognitive and interpersonal functioning, and emotional regulation (123). It was developed to assist in assessment of self-awareness in patients following brain injury. The ratings indicate how difficult it is for the patient to do each activity on a 5-point Likert scale (ranging from 1, "Can't do", to 5, "Can do with ease"). Total PCRS ratings range from 30 to 150, and higher ratings indicate higher levels of competency. The PCRS questions can be sorted into domains of ADL, cognition, interpersonal and emotional functioning. The total ADL and cognitive ratings range from 8 to 40 while the total interpersonal and emotional domains range from 7 to 35. The PCRS has a good internal consistency and test-retest reliability (123).

Statistics

Paper 1: Variables in moderate and severe TBI groups were compared statistically using Independent Samples T-test, Chi-square and Mann-Whitney U Test were appropriate. For ordinal raw scores of the FIM, Wilcoxon Signed Rank Test was used for comparison of individual changes within the severity groups from admission to discharge (124).

The dependent variable in our regression analysis was FIM at discharge from the rehabilitation unit. Independent variables were compared to FIM at discharge by using Spearman's Rank Order Correlation, Kruskall-Wallis Test, Mann-Whitney U Test, Independent Samples T-test or ANOVA. Independent variables with p values < 0.05 in pre-analyses were then entered into a multiple linear regression model to quantify their predictive impact on FIM at discharge. FIM score at admission to sub-acute rehabilitation was included as a covariate to adjust for the baseline level. Five variables were included in the final model due to a conservative approach of allowing one predictor for every 10 participants (n = 54). Seven predictors had p-values < 0.01, out of these five variables were selected since they made the strongest prognostic model (adjusted R square = 0.860).

Paper II: FIM variables from three assessment periods in moderate and severe TBI groups were compared statistically using Mixed Model Analyses and Friedman test for comparison of individual changes within the severity groups from rehabilitation admission to one year after injury (124). GOSE results in both severity groups were compared statistically using Chi-square.

The dependent variable in our regression analysis was FIM 12 months after injury. The patient characteristics considered for use as independent variables are shown in Table 1. These independent variables were compared to FIM 12 months after injury by using Spearman's Rank Order Correlation, Kruskall-Wallis Test, Mann-Whitney U Test, Independent Samples T-test or ANOVA. In the pre-analyses subjects were divided into two groups of either acute treatment at a general surgery department (48 subjects) or a neurosurgery intensive care department (15 subjects). FIM score at admission to sub-acute rehabilitation was included as a covariate to adjust for the baseline level. Independent variables of clinical importance or with p values < 0.05 in pre-analyses were then entered into a multiple linear regression model to quantify their predictive impact on FIM at discharge.

Initially, 11 variables of clinical interest or $p < 0.05$ were entered in the multiple regression analysis (gender, age, drug/alcohol, injury severity, PTA duration, LOS acute, LOS rehab, GCS acute, GCS rehab, FIM adm, other injuries). Complications were not included as a predictor because of 11 missing responses. Due to a conservative approach of allowing one predictor for every 10 participants (n = 63), the 6 variables with lowest p-values were re-entered.

Paper III: We investigated agreement between patient and relative ratings in all TBI patients, by subtracting relative ratings from patient ratings (PCRS-P minus PCRS-R), and assessed the difference by a paired sample t-test.

To identify possible predictors of PCRS ratings we performed regression analyses with the following 6 dependent variables: PCRS-P total score, difference in PCRS total score (DiffPCRS total score) for patients and relatives (total PCRS-P minus total PCRS-R), differences in the total sub sum scores (DiffPCRS sum sub scores) in the domains of ADL, cognition, interpersonal and emotional functioning. Independent variables were entered into 6 stepwise multiple linear regression models to quantify their predictive impact on the dependent outcome variables.

In all models of this thesis, variables were controlled for collinearity statistics by estimating Variance Inflation Factor (VIF), distribution of the residuals for normality and influential data points were examined using histograms and Cook's distance. None of the variables had VIF greater than 10, indicating no presence of multicollinearity.

All data were analysed using SPSS versions 15.0 (papers I-II) and 18.0 (paper III) and results were considered significant at the $p < 0.05$ level.

Ethics

All studies were conducted according to the Declaration of Helsinki, approved by the Regional Committee for Medical Research Ethics, South-East Norway. The Norwegian Data Inspectorate endorsed the project. Patients gave their written consent.

SUMMARY OF RESULTS

Papers I-II: **Functional level during sub-acute rehabilitation and the first year after traumatic brain injury: Course and predictors of outcome.**

Most common types of intracranial injuries were contusions (60% in paper I and II).Traffic accidents accounted for 42% and 48% of the injuries, 40% and 37% occurred from falls, and 18% and 12% from sports and violence.

At discharge from the unit of neurological rehabilitation (paper I), 5% of patients with moderate TBI were still in PTA phase versus 16% in those with severe TBI (p = 0.020). Mean PTA duration in days in moderate TBI was 11 (± 14) versus 44 (± 44) (p < 0.001) in severe TBI. Mean length of sub-acute rehabilitation stay was 28 (± 23) days for all patients (range, 4-96). Fifty-seven percent of moderate TBI patients and 91% of severe TBI patients still had activity limitations with a FIM score < 126. The limitations were mild (FIM 109-126) in 95% with moderate TBI and in 62% with severe TBI. The activity limitations were severe (FIM < 72) in 24% with severe TBI. Only one patient did not improve. In the period from discharge to 12 months after injury (paper II) the mean FIM motor score improved in severe TBI but not in moderate TBI patients. The mean FIM cognitive scores did not improve in any of the groups. At 12 months, 95% with moderate TBI had a FIM score from 109-126 (functionally

independent) compared to 74% with severe TBI. Functional global outcome as assessed by GOSE was "good recovery" in 52% with moderate TBI versus 33% in severe TBI, "moderate disability" in 33% with moderate TBI versus 31% in severe TBI, and "severe disability" in 14% with moderate TBI versus 36% in severe TBI.

Predictors of functional level at discharge from rehabilitation were Glasgow Coma Scale (GCS) score at rehabilitation admission (B = 5.991), FIM total score at rehabilitation admission (B = 0.393), length of stay (LOS) in the rehabilitation unit (B = 0.264), and length of Post-Traumatic Amnesia (PTA) (B = -0.120). Together, these predictors explained 86% of variance of FIM total scores at discharge. High positive B-values illustrate better functional outcome, while higher negative B-values illustrate worse functional outcome. In paper II predictors of functional level the first year after TBI were Glasgow Coma Scale (GCS) score at rehabilitation admission (B = 5.234), length of stay (LOS) in the rehabilitation unit (B = 0.419), and length of Post-Traumatic Amnesia (PTA) (B = -.211). The predictors explained 47% of the FIM variance.

Among patients with moderate TBI, 100% were discharged to their homes. Among patients with severe TBI, 61% were discharged to their homes, 27% to nursing homes and/or other care facilities, and 11% to other local rehabilitation facilities at one year follow-up.

Paper III: **Self and near relative ratings of functional level one year after traumatic brain injury.** The average patient PCRS sum score was 122 (95% CI = 115; 129) as compared to a sum score of 117/150 (95% CI = 110; 125) given by their relatives (p = 0.93). The patients scored themselves slightly higher than their relatives in the domains of ADL and cognitive function, but not in the domains of interpersonal and emotional function. The strongest predictor of PCRS-P was a high GCS score at admission to the rehabilitation unit (B = 3.314, p=0.008). Age was a significant predictor with a positive B coefficient for the PCRS-P (B=

0.510, p = 0.002) and was also a positive predictor for the difference between patient and relative ratings for the total PCRS score (B = 0.304, p = 0.036) and the domains cognitive (B = 0.142, p < 0.001) and emotional (B = 0.068, p < 0.001), meaning that higher age predicted an overestimation of function. PTA duration was a significant predictor with a negative B-coefficient for the PCRS-P (B = -0.330, p < 0.001), and was also a predictor with negative B-coefficient for the difference in total PCRS score (B = -0.160, p = 0.020) and the domains cognitive (B = -0.048, p < 0.001) and emotional (B = -0.050, p = 0.002).

DISCUSSION

Methodological considerations

Subjects:

Seventy-four patients with moderate and severe TBI had a rehabilitation stay at the unit of neurological rehabilitation during the inclusion period from December 2005 to November 2008. Of these, 73% were included in paper I, 85% in paper II and 68% in paper III. Differences in number of percents are due to exclusions and further admissions of new patients during the research period.

One should be careful in generalizing our results with the overall TBI population as our cohort was limited to those considered as in need of specialized TBI rehabilitation. Such studies may lead to overestimation of the severity of TBI related disability (125).

A limited number of moderate TBI was included as those patients are probably often discharged from the acute hospital directly to their homes because they do not report TBI related problems in need of further follow-up.

One of the major limitations of this study was the small sample size. Compared to other international TBI studies, our papers may have small samples, but results of clinical relevance have been reported. Due to the sample sizes our results need to be validated up against a larger sample of unselected moderate and severe TBI patients. However, strength of the study was the few drop-outs.

Design:

The data in papers I-III were sampled with a prospective cohort design implying that certain criteria for the data collection were established in advance securing the relevance and completeness of the data.

Outcome variables:

FIM is reported to have a ceiling effect at one-year post injury (126). The FIM-COG has limited sensitivity to cognitive disability in high functional level TBI patients which therefore may be underestimated in our studies (119, 127). Neuropsychological tests would have been preferable for better description of cognitive functional recovery after TBI. Still, we chose to use FIM as it is widely used in TBI and other populations in need of rehabilitation, and our project was not designed to evaluate the neuropsychological outcome after TBI.

 GOSE is a global measure of function, but criticized for ceiling effects and for being insensitive to subtle, functionally limited deficits in cognition, mood and behavior (128). However, we performed structured interviews as it improves inter-rater reliability of the GOSE (128). In paper II it was a supplementary assessment to FIM in measuring global function as it is reported to be a good method of upper range outcome, and sensitive for detection of good recovery or moderate disability in moderate TBI (121). GOSE is often considered to be a better assessment on long-term global function after TBI than FIM as the

GOSE measures impairments, activity limitations and participation restrictions while the FIM measures activity limitations in motor and self-care skills.

PCRS is a self-evaluation questionnaire assessing competency in daily life (129). We chose PCRS as assessment method in paper III as it was originally designed to evaluate self-awareness of functioning in daily life after TBI. Its validity and reliability has been documented (130,131). The UK national TBI study suggests using self-evaluation questionnaires to detect TBIs impact on functioning over time and problems of daily life (132). Since PCRS has not been much applied for this purpose in the TBI literature, our evaluation of outcome prediction is important (86). We agree with Sveen et al in that PCRS provides useful information about competency in important areas of daily life from a subjective perspective (86). It may be questioned whether a self-evaluation scale lacks reliability due to lack of insight among people with TBI. Still, we share the view of Sveen et al in letting the patient's own voice be heard in the assessment process (86). The extent of lack of awareness is probably underestimated in our study due to ceiling effect of the PCRS in later TBI stages as reported in other studies (109).

Difference scores, obtained by subtracting PCRS-R from PCRS-P (PCRS-P minus PCRS-R), were used as a marker of impaired awareness of deficits in paper III (133). It is reported that different forms of impaired self- awareness of deficits may exist after TBI and may be similar to what is observed in aphasia (133). According to Kertesz et al various patterns of recovery are observed over time in aphasic patients (134). As with brain injured, type and pattern of impaired awareness may vary across patients resulting in varying recovery patterns (133). Prigatano has argued that human awareness is a brain function influencing both cognitive and affective states, and patients with impaired self-awareness demonstrate disturbances in both (135).

In this section a discussion of the standard statistical analyses are left out in favor of the pros and cons of a more comprehensive method, the multiple linear regression analysis used in all three papers.

Multiple regression analysis explores the relationship between one continuous dependent variable and a number of independent variables or predictors (136). It is based on correlation and can tell how well a set of variables is able to predict a particular outcome. The strength of multiple regression analysis is that it provides information about the model as a whole (all subscales), and the relative contribution of each of the variables that make up the model (individual subscales) (136). Further, it allows testing whether a variable contributes to the predictive ability of the model, over and above those variables already included in the model. In our case, multiple regression analysis was used to statistically control for additional variables when exploring the predictive ability of the model. The main types of research questions that multiple regression analysis addresses are (136):

- How well a set of variables is able to predict a particular outcome

- Which variable in a set of variables is the best predictor of an outcome

- Whether a particular predictor variable is still able to predict an outcome when the effects of another variable are controlled for

The three main types of regression analyses are standard, hierarchical and stepwise. Standard multiple regressions were used in papers I-II because we had a set of variables and wanted to know how much variance in a dependent variable they were able to explain as a group or block. This approach also reports how much variance in the dependent variable each of the independent variables explained (136). In paper III, the statistical SPSS program was

provided with a list of independent variables and selected which variables it would enter, in which order they go into the equation, based on statistical criteria (136).

One negative aspect is that the method is not well suited on small samples and where the distribution of scores is skewed. With a small sample size one may obtain a result that is not generalizable (136). Therefore, we used a conservative approach in papers I-II to increase our confidence in the quality of the analyses: with the number of subjects at least ten times the number of included variables. In paper III our approach was also conservative in choosing a stepwise method by the program ware itself. Further, Adjusted R Square was reported to provide a better estimate of the true population value in all three papers (136).

One must also check for multicollinearity and singularity. "Multicollinearity exists when the independent variables are highly correlated (r=.7 and above)" (136). Singularity occurs when one independent variable is a combination of other independent variables, for instance when both subscale scores and the total score of a scale are included. As cons of multiple regression analyses, multicollinearity or singularity, do not contribute to a good regression model (136). Another problem is outliers as multiple regression analysis is sensitive to very high or very low scores. We checked for outliers as part of the initial data screening process and used additional procedures for detecting outliers included in the multiple regression programs. Other various aspects of the distribution of scores and the nature of the underlying relationship between the variables are normality, linearity and homoscedasticity. Meaning that the residuals should be normally distributed about the predicted dependent variable (DV) scores (normality), the residuals should have a straight-line relationship with predicted DV scores (linearity), and the variance of the residuals about the predicted DV scores should be the same for all predicted scores (homoscedasticity) (136). In all our models variables were controlled for collinearity statistics by estimating Variance Inflation Factor (VIF), distribution

of the residuals for normality and influential data points were examined using histograms and Cook's distance.

Functional level during sub-acute rehabilitation and the first year after TBI

The FIM total mean score at admission for the entire sample was 88 (± 37), improving to 107 (± 30) at discharge (p < 0.001) (paper I), with further improvement of 114 (± 25) at one year after injury (p < 0.001) (paper II). It is expected from the natural course after TBI that most of the spontaneous recovery from injury happens initially (137). As expected, moderate TBI patients had milder motor and cognitive impairments at admission to the sub-acute rehabilitation, than patients with severe TBI (89). Overall, functional recovery as judged by FIM was quite good in moderate TBI, with a total score from 109-126 in 95% at discharge. However, 12 of 21 patients did not reach full total score on FIM. The average motor score was normal; while the cognitive score was 3 points below full subscales score. It is noteworthy that more than half of moderate TBI patients had cognitive residual disability at discharge from sub-acute rehabilitation. Previous studies have documented by neuropsychological assessment that cognitive recovery after moderate and severe TBI is more rapid the first 5 months after injury and continues at a slower rate the next 7 months (5).

The observed gain in the FIM-M score was lower in paper I than in studies from US and Australia (115,138). This may be explained by longer LOS in the US (49 days) and Australian (62 days) studies than in paper I (32 days). Another reason that may explain this association is that rehabilitation facilities keep patients who are making a lot of progress and discharge people when they stop improving. During the period from discharge from the rehabilitation unit to 12 months after injury, there was an improvement in mean FIM motor score in severe TBI but not in moderate TBI patients. In paper I, cognitive function showed clinically

important recovery in the severe TBI group, but less than the observed improvement in Corrigan's study (5 vs. 11 points) (117). This can partly be explained by the better admission cognitive function in our patients (20 vs. 15 points), although discharge scores were at the same level. Mean scores of cognitive function did not improve in any of the groups in paper II. The lack of statistically significant improvement in these mean FIM scores may in part be due to a low number of patients, since individual total scores improved in the majority of both moderate and severe TBI patients. As reported in the literature, the FIM was developed to track progress in functional status during inpatient rehabilitation and has a ceiling effect at one-year post injury (139). Lack of improvement in the later phase found in this study may also in part be due to the fact that FIM is not sensitive enough to detect changes in either upper functional level or light cognitive dysfunction (137). Our results in papers I-II raise a question of whether more intensive rehabilitation than what was offered is needed during the post-acute phases after TBI. After discharge from sub-acute rehabilitation, our patients were offered standardised visits from our specialised brain injury rehabilitation team at three months post-discharge and 12 months post-injury. In addition, the majority of our patients were offered visits, telephone contact, assistance and education by the interdisciplinary team at home or in other institutional settings when considered necessary. In paper I, the impact of pre-injury and injury-related factors on short-term recovery following TBI rehabilitation was also investigated. As expected, the direction of B coefficient was positive for GCS rehabilitation, FIM admission, and negative for PTA meaning that patients with less severe injury had better functional level. B coefficient was also positive for LOS meaning that a longer stay in rehabilitation unit is associated with a better functional level at discharge. This agrees with a report from Cowen et al who found that a longer inpatient rehabilitation LOS was associated with significantly higher gains in both FIM-M and FIM-COG scores (89). Even though longer stays are associated with better recovery, a logical circular argument may

be that longer stays are also associated with a more serious injury and a lower starting point. However, the regression model should ideally correct for this and show the role of LOS as an independent predictor of functional level at discharge. An obvious confounding factor is however that a longer stay increases the overall spontaneous recovery magnitude. Still, it is important to notice the great improvement in level of function at discharge in the severe TBI group. Paper II shows that the same factors are predictors of functional outcome at 12 months after injury. GCS at admission to rehabilitation turned out to be the strongest predictor (B = 5.234). This may implicate that GCS score at admission to rehabilitation is a strong predictor of outcome after TBI, in addition to PTA which has been reported as the strongest predictor in other studies (140, 141).

The GCS is the most widely used clinical measurement of TBI severity (142). GCS scores in the acute phase provide guidance for early care and predict early outcome such as mortality and morbidity (142-146). GCS is also used in predicting late global outcome such as functional level and return to employment (147, 148). There is controversy about which GCS score should be recorded since interventions in the early medical management of moderate and severe TBI, may complicate GCS assessment and provide inaccurate prognostic predictions for some patients (142, 148).

In our regression analysis PTA duration turned out to be a weak predictor of functional level (B = -0.211) at 12 months after injury. In contrast to this, others have found PTA duration to be the strongest predictor of functional outcome, and more predictive than GCS at rehabilitation admission (149-151). Still, its predicative accuracy and clinical utility is limited by the large outcome variability (87, 90,150, 152-155). Two PTA durations of 4 and 8 weeks emerged as global outcome threshold points that should aid prognosis accuracy after TBI (141).

Our results showed some discrepancy between functional level as assessed by GOSE and FIM at 12 months, especially in the group with moderate TBI. By using GOSE we found that 47% of our moderate TBI patients were still moderately or severely disabled at 12 months, whereas FIM detected reduced cognitive scores in only 24% and motor scores in 14%. Further, 95% of moderate TBI patients had a mean FIM total score indicating functional independence, while only 52% of the moderates achieved good recovery as assessed by GOSE at 12 months. Our results may however support those studies which demonstrate that although neuropsychological impairment at baseline usually resolves within three months, moderately injured may still have selective cognitive deficits (attention and memory) one year after injury (113, 122, 156-157).

Self and near relative ratings of functional level after TBI

In reference to our study aims, we evaluated patient perceived functioning (PCRS-P), awareness of own deficits (differences in PCRS-P and PCRS-R), and predictors of self-perceived function and awareness of functional deficits.

In patient perceived functioning (PCRS-P) we found a mean PCRS sum score of 122. A score of 120 indicates that patients believe that they can perform the various activities fairly easily while total scores of 140-150 indicates that patients believe they can do the activities very well with no difficulty (133). Thus, our patients reported moderate belief in self competency which is in accordance with another study (158).

The total PCRS scores given by patients and relatives did not differ significantly. This might represent improved awareness of deficit during the first 12 months after injury as reported in other studies (158, 159). The sub scores in the domains of ADL and cognition showed significantly higher score by patients than relatives, indicating a slight overestimation of own

function by the patients in these domains. These findings were unexpected and in contrast to other studies (130, 158). Patients with severe TBI have impaired memory and their problems in remembering how many and how often they have difficulties in performing ADL may have influenced study results.

According to Sveen et al (103), the functional aspects of cognition may be more directly related to the brain injury in contrast to the interpersonal and emotional problems that may develop over time. However, the domains of interpersonal and emotional functioning patients' and relatives' scores showed small discrepancies in this study. This finding agrees with previous studies reporting that the improvement of awareness during the first year after injury is most pronounced for the behaviour and emotions with significant reduction in discrepancy scores between patients and relatives (158).

In the domain of emotional regulation there were 4 single questions with different scores; one with a negative value – i.e. underestimation of own function (controlling laughter), and 3 with positive values – i.e. overestimation of own function (adjusting to change, accepting criticism, controlling temper). Underestimation of emotional regulation such as "controlling laughter" in our study is also found by others (130), and can be explained as a way in which TBI patients try to minimize their behavioural limitations (130). It is argued that patients themselves are aware of the difficulty, but able to control the emotion to such an extent that their relatives were unaware of the difficulty (130). Otherwise, it is possible that injury severity and the initial disturbance in consciousness contribute to this dysfunction in post-acute TBI patients (133). The latter may be true in our paper as the results may be related to the patient selection as two thirds of patients suffered from severe TBI. Another possible explanation is that as ability improves tasks become less difficult to accomplish which can lead to higher self-rating in post-acute phase of TBI (158). In practical terms, we found no consistent discrepancy in

how patients and their near relatives interpret competency in social interaction. We found that a high GCS at admission to rehabilitation was the strongest predictor of self-perceived function (PCRS-P) at 12 months after injury. Acute GCS and age showed the same pattern in the way that both a low acute GCS and a high age was associated with a high self-perceived function (PCRS-P), but also with a larger difference between patient and relative ratings (PCRS-P minus PCRS-R, total, cognitive and emotional) 12 months after injury. Taken together, this indicates that older and more severely injured patients overestimated their own function due to deficient awareness of functional deficits.

A longer PTA after injury was associated with a lower self- perceived function (PCRS-P) 12 months post-injury, consistent with previous findings of PTA duration as good measure of TBI severity and a predictor of long-term prognosis. PTA has even been suggested as more valuable than the depth or duration of coma or neuroimaging findings (31, 152,160). We also found that a longer PTA was a weak but significant negative predictor of discrepancies between patient and relative ratings in the cognitive and emotional domains, meaning shorter PTA predicted more severe awareness deficits. This may imply that lack of insight in own deficits is not restricted to those with the most severe injuries. Further, it may to some extent explain parts of the social problems among moderately injured. Perhaps moderate deficits are more difficult for the patient to perceive due to coping strategies while patients are more self-aware of major deficits.

The study is based on patients who were able to understand questions, and to verbalize their understanding of their deficits. An objective assessment of personality, emotional status and executive functioning by psychological and neuropsychological tests is not performed, and our study does not include a prospective follow-up over time.

CONCLUSIONS

- Functional level (FIM) improved from admission to discharge and one year after injury for all TBI patients

- Less than half of moderate TBI patients reached a normal functional level as assessed by FIM at discharge from sub-acute rehabilitation

- Residual disability was reported in 47% of moderate TBI patients as assessed by GOSE 12 months post injury

- A short PTA period, a high GCS score and FIM score at admission to rehabilitation and a longer stay in the rehabilitation unit were positive predictors of functional level at discharge and 12 months after injury

- TBI patients had a moderate belief in self competency 12 months after injury

- A slight lack of awareness of dysfunction in the domains of ADL and cognitive function were reported 12 months after injury

- Higher age was a predictor of more severe awareness deficits 12 months after injury

- More severe injury (longer PTA) was a predictor of low self-perceived function though negatively associated with degree of awareness deficits 12 months after injury

IMPLICATIONS AND FUTURE ASPECTS

Our thesis and other studies suggest that significant functional, emotional, behavioural and social difficulties occur after TBI, and severity of injury and pre-morbid factors predict functional level. Still, it is unclear whether these results are applicable to all persons with TBI. In which areas are rehabilitation effective, and for which particular subgroups of TBI individuals?

Future research of larger samples with unselected moderate and severe TBI patients is needed to validate prediction of TBI prognosis. Our results suggest a need for more research on the effect of more intense and long-lasting cognitive training and rehabilitation overall in the post-acute TBI phase.

Scandinavian follow-up studies of course and predictors of outcome 5-10 years after TBI are important in order to evaluate the system of TBI care and future long-lasting prospects for the injured and their relatives.

National standardisation of TBI rehabilitation in programmes, methods, classifications and assessments should be implemented and multi-centre research of TBI outcome should be performed in the future.

In future research it would be interesting to assess if there is a systematic reproducibility in self and informant ratings of social and community reintegration one year after moderate and severe TBI.
More focus should be attained towards the implications of moderate injuries in future research of TBI rehabilitation programmes and community re-integration.

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