The trajectories of overall disability in the first 5 years after moderate and severe

traumatic brain injury

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Abstract

Primary Objectives: To assess longitudinal trajectories of overall disability after moderate-

to-severe traumatic brain injury (TBI) and to examine whether those trajectories could be

predicted by socio-demographic and injury characteristics.

Methods: Demographics and injury characteristics of 105 individuals with moderate-to-

severe TBI were extracted from medical records. At the 1-, 2- and 5-year follow-ups, TBI-

related disability was assessed by the GOSE. A hierarchical linear model (HLM) was used to

examine functional outcomes up to five years following injury and whether those outcomes

could be predicted by: time, gender, age, relationship, education, employment pre-injury,

occupation, GCS, cause of injury, length of posttraumatic amnesia (PTA), CT findings, and

injury severity score, as well as the interactions between each of these predictors and time.

Results: Higher GOSE trajectories (lower disability) were predicted by younger age at injury

and shorter PTA, as well as by the interaction terms of time*PTA and time*employment.

Those who had been employed at injury decreased in disability over time, while those who

had been unemployed increased in disability.

Conclusion: The study results support the view that individual factors generally outweigh

injury-related factors as predictors of disability after TBI, except for PTA.

Key words: Traumatic Brain Injury, Disability, Outcome measures, GOSE

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Introduction

Traumatic brain injury (TBI) is a major cause of long-term functional disability in young adults (1-5). In a population-based study of individuals hospitalized after TBI in the US, 43% continued to have a disability one year after the injury (6). Similarly, one study from Glasgow, UK, reported that 53% of persons with mild-to-severe TBI remained disabled 5-7 years after injury as assessed by the Glasgow Outcome Scale extended (GOSE) (2). Another follow-up study 3-8 years after severe TBI found severe-to-moderate disability (GOSE <7) in the majority of patients (73 %) (7). An Australian study evaluating functional outcomes 10 years after TBI found that 48% of patients had severe-to-moderate disability (4). Studies of TBI outcomes have shown that trajectories of post-injury functioning and functional change may include periods of both improvement and decline over time (8;9). Thus, some patients with TBI may need more intensive and comprehensive health care and rehabilitative services over the long-term to maintain or regain functioning. Nevertheless, a statewide, population-based survey study from the US found that almost two-third of survivors after TBI received no additional services after discharge from the acute care hospital (10).

Numerous researchers have sought to identify factors that predict individuals' ability to regain a high functional level after TBI. Socio-demographic factors such as age (11;12), gender (11;13), education (4;14;15), pre-injury employment (14;16) and race (17;18) have been associated with the disability and recovery process. Moreover, injury severity variables also predict disability following TBI. Presence of intracranial lesions on CT scans has been associated with poorer functional outcomes in patients with moderate-to-severe TBI (19;20). Patients with shorter post-traumatic amnesia (PTA) and shorter length of acute hospitalization after TBI, less executive dysfunction and fewer memory problems showed better global functional outcomes after TBI (4;11;15).

However, few studies have investigated overall TBI related disability using a longitudinal research design or the factors influencing lapses and relapses in functioning over time. A study from Taiwan assessed the long-term global clinical outcomes of TBI patients from 1 week to 10 years post-injury and found that patients may have difficulties in social interactions and family relationships until 6 years post-injury (5). A recent study from the US described the temporal patterns of global outcomes over 1-20 years after moderate or severe TBI. The results showed that the GOSE trajectory initially increases and peaks approximately 10 years after the first GOSE assessment, and then decreases in the final years of the timeline (21).

As cultural, social, and vocational factors, health care and social security systems and disability policies may play an important role in the perception of disability over time, longitudinal studies from different countries are needed to provide a better understanding of long-term trajectories and predictors of TBI related disability at different time periods (22). To fill these needs, this longitudinal study was carried out, and the GOSE, a recommended core outcome measure of global level of function in TBI research, was used to assess the disability levels (23-26).

The main study aims were:

- (1) To assess the trajectories of disability in individuals with moderate-to-severe TBI through 1, 2, and 5 years post-injury.
- (2) To investigate whether the trajectories of disability could be predicted by sociodemographics and clinical indices of injury severity.

With these aims, we wanted to provide more precise information about trajectories of disability after TBI in a Norwegian context and investigate if individual level-factors (such as age, gender, education, employment pre-injury, and injury characteristics at hospital admission) may add complexity to the disability of TBI patients. We hypothesized that TBI-

related disability would decrease over the first 5 years post-injury and that individual factors would be associated with level of disability.

Materials and Methods

Participants

A longitudinal cohort study was conducted including patients with acute TBI who had been admitted from 2005 to 2007 to the Trauma Referral Centre for the Southeast region of Norway, covering a population of nearly 2.6 million people. Patients were assessed in the acute phase (baseline) and followed up at 1, 2 and 5 years after injury. Inclusion criteria were (a) age 16-55 years, (b) residence in eastern Norway, (c) admission with ICD-10 diagnosis S06.0-S06.9 within 24 hours of injury, and (d) presence of moderate-to-severe TBI with a Glasgow Coma Scale (GCS) score of 3-12 (27) at admission or before intubation. Exclusion criteria were (a) previous neurological disorders/injuries, (b) associated spinal cord injuries, (c) previously diagnosed severe psychiatric or substance abuse disorders, and (d) unknown address or incarceration. For additional details, see study by Forslund et al. (28).

Overall, 133 individuals with TBI met the inclusion criteria. Twenty-four (18%) patients died in acute or post-acute care, and four (3%) refused further participation, leaving 105 (79%) individuals at the 1-year follow-up. One patient died and four dropped out between the 1- and 2-year follow-ups; thus of all patients who initially met the inclusion criteria, 100 (75%) participated at the 2-year follow-up. Two patients died between the 2- and 5-year follow-up, and four patients dropped out leaving 94 (71%) patients at the 5-year follow-up. The attrition rate from the 1- to 5-year follow-up was 11%. No significant differences were found in demographics and injury characteristics between individuals assessed and those lost to the 5-year follow-up.

Measures

The independent variables used in this study were: Gender (male vs. female), age at time of injury (in years), relationship status at hospital admission (partnered [married/cohabitant] vs. single), education (≤12 years vs. >12 years), employment status preinjury (employed vs. unemployed), occupation prior to admission (blue collar [physical work] vs. white collar [nonphysical work/being a student]), acute GCS 3-12, cause of injury (traffic accident vs. other), length of PTA (number of days), CT head Marshall scores (less severe [no visible injury or small intracranial injury, scores 1-2]) and more severe [significant intracranial abnormalities, scores 3-5]) (29) on the "worst" CT scan within the first 24 h, and Injury Severity Score (ranges from 1-75 [best to worst]) (30). If a person was unemployed pre-injury, the occupation prior to unemployment status was used.

The dependent variable in this study was the Glasgow Outcome Scale Extended (GOSE) (24;31). The GOSE measures overall disability (independence, work, social and leisure activities, family and friendship and return to normal life) after TBI and divides patients into the following outcome categories: 2 = (vegetative state), 3 = (lower severe disability and complete dependence on others), 4 = (upper severe disability and some dependency on others, but can be alone for eight hours), 5 = (lower moderate disability, living independently and working at a lower level of performance/sheltered work), 6 = (upper moderate disability and returning to previous work with adjustments), 7 = (lower good recovery with minor physical or mental deficits), and 8 = (upper good recovery that implies full functional recovery). The GOSE was administrated at the follow-ups in structured face-to-face interviews conducted by the two last authors. Due to the longitudinal functioning focus of the project, individuals categorized as dead (GOSE=1) were removed from the modeling.

Procedure

Pre-injury, injury-related, and acute phase factors were extracted from medical records. At the 1-, 2- and 5-year follow-ups, a physiatrist performed the assessments and interviews of patients at the outpatient department. Several patients made requests that the assessments and interviews should be conducted in the patients' homes, and this was followed. The study was approved by the Regional Committee for Medical Research Ethics, East Norway, and the Norwegian Data Inspectorate. All participants gave their written informed consent to participate in the study.

Data Analyses

Skewness diagnostics for the GOSE outcome variable and multicollinearity diagnostics for the predictors were first run. Then, descriptive statistics were used to present demographics and injury related variables, and the GOSE disability categories. Results were presented as percentages and/or means with standard deviations (SDs).

A hierarchical linear model (HLM) was performed to examine whether linear trajectories of GOSE scores over 1, 2, and 5 years post-TBI could be predicted by: time, gender, age, relationship status at admission, education, employment status pre-injury, occupation prior to admission, acute GCS score, cause of injury, length of PTA, CT head Marshall score, and injury severity score, as well as the interactions between each of these predictors and time. These variables were all entered simultaneously as fixed effects into the HLM, and all continuous predictor variables were centered to have a mean of 0 or all categorical predictors were given a reference point of 0 before being entered into the HLM. GOSE scores at each of the three time points were entered as the dependent variable. Main effects would indicate that GOSE scores over time vary as a function of the predictor variable (i.e., in overall height across the time points), whereas significant predictor*time interactions

would indicate that GOSE trajectories changed differentially over time as a function of one of the predictors (i.e., different slopes). Statistically significant fixed main effects or interaction effects on GOSE scores were then graphed across each of the three time points. In these figures, if the predictor was continuous, a median-split procedure was used to generate separate lines as a function of the predictor, although the continuous nature of the predictor was retained in the actual hypothesis testing and reporting of statistical significance.

The HLM used full information maximum likelihood estimation (FIML) to account for missing data, which allows participants with missing data points to be retained in the HLM. Intercept for random effect, variance components covariate type and maximum likelihood methods were used; otherwise no random effects were included at the participant level. And within-person residuals were treated as independent. An HLM was used in the calculation of growth curves over traditional analyses (e.g., repeated measures analyses of variance or regressions) because of its robustness to longitudinal missing data. FIML allows the calculation and prediction of latent, longitudinal trajectories of disability level after TBI in the current sample. HLM can transcend a many problems hindering regression analyses via a more accurate estimate of standard errors, maximizing predictive precision.

Results

The skewness coefficient for the GOSE across all time points was -.97, which does not indicate that skew was present for this variable. Similarly, bivariate correlations among all predictors in the model suggested that the largest correlation of r = -.52 (PTA and GCS) did not exceed the .70 cutoff for multicollinearity among the predictors. As a result, the predictors and outcome variable are generally suitable for HLM. The mean age of the 105 patients at the injury time was 30.9 (SD=11.2) and 78% were males. The mean GCS at the admission was 7.2 (SD=3.2). Demographics and injury-related characteristics are presented in Table 1.

- Insert table 1 here.-

The distribution of patient frequency in the GOSE disability categories is presented in Table 2. The proportion of patients in the severe disability groups decreased from 12% to 7 % from 1 to 5 years post-injury whereas the proportion of patients in the group representing upper level of moderate disability increased from 34 % to 39 %. The highest difference in the proportions was found in the group representing the upper level of good recovery from 10 % at 1-year to 23 % at 5-year, respectively. A similar distribution patterns were shown when analyzing the GOSE trajectories in 94 patients presented at the 5-year follow-up.

- Insert table 2 here.-

All statistically significant and non-significant fixed effects from the HLM, as well as their b-weights and *p*-values appear in Table 3.

--Insert Table 3 here.—

Younger individuals with TBI had higher GOSE scores (less disability) over time than older individuals (p = 0.036; Figure 1).

--Insert Figure 1 here.--

The time*employment interaction term was statistically significant (p = 0.021), suggesting that participants who had been employed at the time of injury showed improvements in GOSE scores over time, while those who had been unemployed at the time of injury showed declines in GOSE scores (Figure 2).

--Insert Figure 2 here.--

Longer length of PTA was associated with lower GOSE scores across the three time points (p < 0.001; Figure 3).

--Insert Figure 3 here.--

Also, the time*PTA interaction term was statistically significant (p = 0.022). When considering the nearly parallel lines in Figure 3 for the time*PTA interaction, this interaction

effect could have been significant because very high or very low PTA values might have acted as influential observations and had a substantial impact on the results. Also, PTA was the most significant predictor in the HLM, therefore giving its interaction with time the greatest chance of being statistically significant of all the predictors. As a result of not being able to ascertain the direction of this interaction, or whether it is a statistical artifact as opposed to a true effect, it will not be interpreted further.

Discussion

The overall results of this study support the view that individual factors (age, prior employment status) outweigh the injury-related factors as predictors, except for PTA. Thus, the study results were in line with our hypothesis. Trajectory analyses using HLMs indicated that GOSE scores remained relatively stable across 1, 2, and 5 years post-TBI. Consequently, our assumption that TBI-related disability would decrease over the first 5 years post-injury was not confirmed. This is inconsistent with findings of a US study involving 3,870 adults with moderate or severe TBI that showed improvement in the GOSE during the first 10 years post-injury (21). Another US study of 13,500 adults who received acute inpatient rehabilitation, in contrast and supporting the current findings, showed that more than half of patients were moderately or severely disabled at 5 years after TBI, with more than one-third of patients having deteriorated from a global outcome attained 1 or 2 years post-injury (32). Similarly, a follow-up study of 301 patients with TBI demonstrated no meaningful functional changes in 76% of patients while 7% declined from 1 to 5 years post-injury (33). Recently published 2-year follow-up study of 52 patients with moderate and severe TBI from South of Norway found a plateau of GOSE recovery after 1 year post-TBI (34).

A better understanding of which patients are at risk of functional deteriorations across longitudinal trajectories might help in applying the proper rehabilitation services and more

effective use of resources along the acute, early and post-acute TBI care. In our previous study on the same TBI population, we assessed the self-perceived health care needs in patients with moderate-to-severe TBI five years after the injury (35). Eighty-four percent of patients reported independence in daily life activities at the 5-year follow-up. A comprehensive rehabilitation services was still in use in 17% of patients. Furthermore, we found that patients with less severe disability (GOSE 6-8) one year after the injury reported more unmet needs for health care and rehabilitation services five years post-injury than those with more severe disability (GOSE 2-5) (35). These findings highlighted the importance of the follow-up of TBI patients over long time to capture patient needs and to prevent functional deterioration.

Variations in the data collected and a lack of consistency in methodology make comparisons between different studies difficult. However, it is worth mentioning that most of the significant predictors of the trajectories of overall disability found in this study were in line with previous research on outcomes after TBI (3;4;7;11). Regardless, we found interesting trends in significant predictors across the timelines. Of particular note is that women and men had no differences in long-term outcomes after TBI across the three time points. The anecdotal observations from clinical practice that women tend to experience better outcomes than men after TBI, as well as findings from the US examining functioning during discharge from acute TBI (36) were not confirmed in this study. Our results are also not in line with number of studies that showed gender influence on TBI outcomes such as a meta-analysis of outcome studies from mild-to-severe TBI that found poorer outcomes in women for 85% of the measured variables, including disability and subjective symptoms (37).

Age at the time of injury was a significant predictor in this study. Younger individuals recovered better and carried less disability over time than older individuals. The influence of age has previously been reported for baseline GOSE scores as well as for the rate and extent of improvement over time (21). However, deterioration in global outcome was not age-related

in the previously mentioned US study (32). This is in contrast to the larger decline from 2 to 5 years in subjects above 30 years old in the present study. We can only speculate that perhaps a greater focus on education and return to work in the younger subjects over time and/or advices to move to disability pension in the older age group contributed to this result.

The interaction term of employment status at the time of injury and time was also a significant predictor of GOSE trajectories. Participants who were employed at the time of injury had better overall functioning over time while those who were unemployed at the time of injury were more disabled and declined in overall function, particularly from 2 to 5 years post-injury. No differences in initial injury severity between these two groups were found. A previous study found that the probability of being employed one year after injury was 95 % lower for pre-injury unemployed patients (16). As reviewed by Willemse-van Son et al. (11), prior unemployment might reflect disability, activity limitations, participation restrictions, and less productivity after TBI. Our previous findings of reduced community integration for participants who were unemployed at the time of injury (38) may reflect unemployed patients having fewer resources and opportunities after the injury.

And finally, longer length of PTA was associated with worse functional outcomes at all time points, perhaps because of the stability in and high GOSE scores among the patients with shorter length of PTA. Other studies also found that the duration of PTA, as the direct consequence of clinical injury severity, was associated with the disability level after TBI (4;15). No significant predictors were found for the other injury characteristics in this study.

Study limitations and future directions

Because this study included individuals with moderate-to-severe TBI between 16-55 years old, the results may not be generalizable to individuals with different demographic and injury characteristics. Moreover, the use of a global measure of functional outcome such as

the GOSE may also limit the current study to extrapolate different domains of functional

disability following moderate-to-severe TBI. Future studies should incorporate more detailed

measures of severity of intracranial injuries such as the MRI evaluation, functional measures

and broader range of predictors, such as time-varying factors and social support at the

community level to better understand the long-term impact of injury on various functional

outcomes and tailor rehabilitation programs to meet the long-term needs of this population.

Conclusion

Findings support the view that disability after moderate-to-severe TBI remains fairly

constant over the first five years after injury, although improvements were apparent in

patients with specific demographic and injury characteristics. It is clear that younger age and a

productive lifestyle before injury are beneficial to functional outcomes years after injury.

These findings may help rehabilitation professionals to plan targeted rehabilitation programs

for patients with specific demographic characteristics. Further studies are required to

determine effects of environmental and time-varying factors on disability trajectories over

time.

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Variable	n (%)	Total n
Age at injury		105
Mean (SD)	30.9 (11.2)	
Gender		105
Male	82 (78.1)	
Female	23 (21.9)	
Relationship status		105
Partnered	33 (31.4)	
Single	72 (68.6)	
Education level		104
≤12 years	59 (56.7)	
>12 years	45 (43.3)	
Employment status		105
Yes	85 (81.0)	
No	20 (19.0)	
Occupational status		105
Blue collar	53 (50.5)	
White collar	52 (49.5)	
Injury cause		105
Traffic accident	61 (58.1)	
Other	44 (41.9)	
Glasgow Coma Scale (GCS)		105
Moderate (9-12)	34 (32.4)	
Severe (3-8)	71 (67.6)	
Post-traumatic amnesia (PTA)		97
0-18 days	58 (59.7)	
19 + days	39 (40.3)	
CT Head Marshall Score	, ,	
Score 1-2	49 (46.6)	105
Score 3+	56 (53.4)	
Injury Severity Score	, ,	
Score 0-29	47 (44.7)	105
Score 30 +	58 (55.3)	
Total length of hospital stay (LOS acute hospitalization	` /	105
and inpatient rehabilitation)		
Mean (SD)	71.8 (58.7)	

Table 2. The distribution of patient frequency (%) in the GOSE disability categories at 1-, 2- and 5-year follow-ups.

	1- year	2 - year	5 - year
	(n = 105)	(n = 100)	(n = 94)
GOSE level 2	1 (1 %)	1 (1 %)	1 (1 %)
GOSE level 3	7 (7 %)	5 (5 %)	4 (4 %)
GOSE level 4	4 (4 %)	4 (4 %)	2 (2 %)
GOSE level 5	17 (16 %)	14 (14 %)	12 (13 %)
GOSE level 6	36 (34 %)	37 (37 %)	37 (39 %)
GOSE level 7	29 (28 %)	23 (23 %)	17 (18 %)
GOSE level 8	11 (10 %)	16 (16 %)	21 (23 %)

GOSE, Glasgow Outcome Scale Extended.

Table 3. Predictors of GOSE trajectories at 1, 2, and 5 years after injury.

Predictor Variable	b-weight	Std. Error	df	t	<i>p</i> -value	95% Co	onfidence Interval
Tredictor variable	0-weight	Elloi	uı	ι	p-value	Upper	Lower
T	5.04	0.22	101.70	10.11	**0 000		
Intercept	5.84	0.32	181.70	18.11	**0.000	5.20	6.47
Time	-0.16	0.19	181.85	-0.87	0.387	-0.54	0.21
Sex (male=0, female=1)	-0.20	0.20	178.43	-1.00	0.317	-0.60	0.20
Time*Sex	-0.19	0.12	177.34	-1.65	0.1	-0.42	0.04
Age at Injury	-0.02	0.01	179.11	-2.11	*0.036	-0.04	0.00
Time*Age at Injury Relationship Status (single=0,	-0.01	0.01	179.79	-1.19	0.237	-0.02	0.00
partnered=1)	0.01	0.20	179.50	0.07	0.945	-0.39	0.42
Time*Relationship Status	0.04	0.12	178.31	0.31	0.756	-0.20	0.27
Education (≤12 years=0, >12 years=1)	0.08	0.11	179.89	0.76	0.451	-0.13	0.29
Time*Education	-0.04	0.06	180.32	-0.67	0.505	-0.17	0.08
Employment at Injury (no=0, yes=1)	0.33	0.22	181.42	1.55	0.123	-0.09	0.76
Time*Employment at Injury Occupation (blue collar=0, white	0.30	0.13	183.15	2.33	*0.021	0.05	0.55
collar=1)	0.11	0.19	180.06	0.59	0.557	-0.27	0.50
Time*Occupation	0.11	0.11	178.86	0.98	0.328	-0.11	0.33
Glasgow Coma Scale	0.04	0.03	179.62	1.31	0.191	-0.02	0.10
Time*Glasgow Coma Scale	0.00	0.02	181.03	-0.08	0.934	-0.04	0.03
Cause of Injury (other=0, traffic=1)	-0.08	0.19	179.01	-0.42	0.678	-0.45	0.29
Time*Cause of Injury	-0.12	0.11	179.76	-1.05	0.296	-0.33	0.10
Posttraumatic Amnesia	-0.02	0.00	178.96	-5.21	**0.000	-0.02	-0.01
Time*Posttraumatic Amnesia	0.00	0.00	177.82	2.31	*0.022	0.00	0.01
CT Head Injury Score	-0.10	0.08	179.22	-1.18	0.24	-0.26	0.07
Time*CT Head Injury Score	-0.01	0.05	180.13	-0.29	0.776	-0.11	0.08
Injury Severity Score	0.00	0.01	179.15	-0.01	0.989	-0.01	0.01
Time*Injury Severity Score	0.00	0.00	178.20	-0.27	0.788	-0.01	0.01

^{*} *p* < 0.05; ** *p* < 0.01.

Figure 1. Effect of age on GOSE trajectories.









