Changes in Outcomes after Discharge from an Acute Hospital in Severe Traumatic Brain Injury

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Abstract

Neurological improvement occurs from the subacute to chronic phases in severe traumatic brain injury. We analyzed factors associated with improved neurological findings in the subacute phase, using data from the Japan Neurotrauma Data Bank (JNTDB). The subjects were 1345 patients registered in the JNTDB (Project 2015). Clinical improvement was evaluated by comparing the Glasgow Outcome Scale (GOS) at discharge and 6 months after injury. Of these patients, 157 with severe disability (SD) on the discharge GOS were examined to evaluate factors associated with neurological improvement in the subacute phase. Cases were defined as those with (group I) and without (group N) improvement: a change from SD at discharge to good recovery (GR) or moderate disability (MD) at 6 months after injury. Patient background, admission findings, treatment, and discharge destination were examined. In all patients, the favorable outcome (GR, MD) rate improved from 30.2% at discharge to 35.7% at 6 months after injury. Of SD cases at discharge, 44.6% had a favorable outcome at 6 months (group I). Patients in group I were significantly younger, and had a significantly lower D-dimer level in initial blood tests and a lower incidence of convulsions. In multivariate analysis, discharge to home was a significant factor associated with an improved outcome. Many SD cases at discharge ultimately showed neurological improvement, and the initial D-dimer level may be a predictor of such improvement. The environment after discharge from an acute care hospital may also contribute to an improved long-term prognosis.

Keywords: biomarker, discharge destination, outcome improvement, rehabilitation, traumatic brain injury

Introduction

The number of elderly patients with severe traumatic brain injury (TBI) has steadily increased in Japan.[1] Various new treatments for geriatric TBI have been developed based on the characteristics of elderly patients,[2,3] and this improved treatment has significantly decreased mortality from TBI; however, survivors with a poor outcome have also increased.[1]

Patients with severe TBI with poor outcomes at discharge from an acute care hospital are often transferred to a long-term care sanatorium that has no rehabilitation facilities, and thus, improvement is less likely. Disuse syndrome may then occur, and this leads to more bedridden patients and a major social loss. In the US, 15% of patients with severe TBI and disturbance of consciousness at ≥2 weeks that made them unable to follow an order had a favorable outcome 6 months after injury.[4] This indicates a risk of withdrawal of treatment early after injury based on persistent disturbance of consciousness.[4] Therefore, in treatment of severe TBI, establishment of indexes and goals for continuing treatment are important.

Several studies on long-term outcomes of severe TBI have found neurologic improvement at more than 6 months after injury.[5–7] In particular, the degree of improvement in the subacute phase is influenced by the environment of patients.[8] Therefore, it is dangerous to judge the long-term outcome based on neurological findings at discharge from an acute care facility and to decide on the strategy after the subacute phase, but this is common in Japan. This approach may cause a bedridden status in patients who actually have the ability to return to society.

In this study, outcomes were compared at discharge and 6 months after TBI using data from the Japan Neurotrauma Data Bank (JNTDB). Background data were investigated to search for factors influencing improvement of outcome, with the goal of developing an approach to ensure the best possible outcome in patients with severe TBI.

Materials and Methods

A prospective observational study was performed using the JNTDB, which was established by the Japan Society of Neurotraumatology in 1996 and is typically used for conduct of two-year projects.[9] The JNTDB includes patients with TBI with a Glasgow Coma Scale (GCS) score ≤8 within 48 h after injury or those who underwent craniotomy, and has information on more than 200 items, including trauma characteristics, diagnosis, treatment details, and outcomes. The JNTDB Project 2015 was conducted from April 2015 to March 2017 involving 1345 registered patients, including 1038 patients with known outcomes up to 6 months after injury, who were included in this study. Patient data regarding severe TBI are entered into the JNTDB Project 2015 from 32 collaborating clinical centers: Sapporo Medical University Hospital, Aomori Prefectural Central Hospital, Sendai City Hospital, Shinshu Ueda Medical Center, Chiba Emergency Medical Center, Chiba University Hospital, Kimitsu Chuo Hospital, The Jikei University Kashiwa Hospital, Showa University Hospital, Teikyo University Hospital, Nippon Medical School Hospital, Nihon University Hospital, National Disaster Medical Center, National Defense Medical College Hospital, Yokohama City University Medical Center, St Marianna University Hospital, Tokai University Hospital, Toho University Medical Center Ohashi Hospital, Nippon Medical School Tama Nagayama Hospital, Tokyo Medical and Dental University Hospital, Nagoya City University Hospital, Saiseikai Shiga Hospital, Kyoto Kujo Hospital, Nara Medical University Hospital, Osaka Mishima Emergency Critical Care Center, Hyogo Prefectural Kakogawa Medical Center,

Kagawa University Hospital, Yamaguchi University Hospital, Iizuka Hospital, Kurume University Hospital, Fukuoka University Hospital, and Japanese Red Cross Kumamoto Hospital. This project was submitted to and accepted by the institutional review board in each participating institute. Informed consent was obtained in the form of opt out on the website. Those who rejected were excluded.

The Glasgow Outcome Scale (GOS) at discharge and 6 months after TBI was used to assess outcome, with good recovery (GR) and moderate disability (MD) defined as a favorable outcome. Patients with severe disability (SD) at discharge were classified into two groups with (group I) and without (group N) improvement to a favorable outcome at 6 months after injury. Patient background, GCS on admission, head CT findings, vital signs, blood tests, treatment, and discharge destination were compared between the two groups. Patient background, GCS on admission, and head CT findings were also compared according to the discharge destination from the acute care hospital.

Statistical analysis was performed by unpaired t-test or χ^2 test, with P <0.05 considered to be significant. Clinical variables were used in multivariate logistic regression analysis to identify independent predictors of improvement of outcome at 6 months after injury. A *P* value, 95% confidence interval (CI), and odds ratio (OR) are reported for significant variables in this analysis. Receiver-operating characteristic (ROC) curve analysis was used to estimate an optimal cutoff value of age for outcome change.

Results

The JNTDB Project 2015 included 1345 cases, of which 1038 (77.2%) with a recorded GOS at discharge and 6 months after injury were included in this study. The overall favorable outcome rate significantly increased from 30.2% at discharge to 35.7% at 6 months after injury (Fig. 1). For patients in a vegetative state (VS) at discharge, 98.8% still had a poor outcome at 6 months after injury; and of patients with a favorable outcome (GR, MD) at discharge, 95.9% were still classified as GR or MD at 6 months after injury (Table 1). In contrast, the SD rate decreased markedly after 6 months, with 44.6% of SD cases at discharge improving to a favorable outcome at 6 months after injury (Table 1). Therefore, we investigated predictors of a favorable outcome at 6 months after injury in 157 patients with SD at discharge.

Of the 157 patients, 70 (44.6%) showed improvement (group I) and 87 (55.4%) had no improvement (group N) (Table 2). Subjects in group I were significantly younger (51.9 ± 23.7 vs. 67.8 ± 20.8 years), and had a significantly lower rate of previous medical
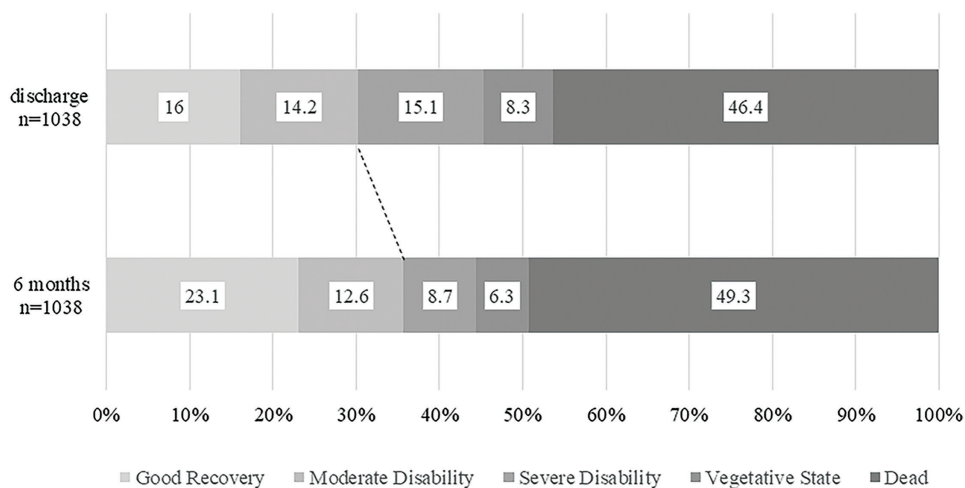
Fig. 1 **Clinical outcomes in 1038 patients at discharge and 6 months after injury measured by the GOS. Rate of favorable outcome has significantly increased from 30.2% to 35.7%. GOS: Glasgow Outcome Scale.**

Table 1 Changes in GOS from discharge to six months

	GOS	Total	Six months				
			GR	MD	SD	VS	Dead
Discharge	GR	166	160 (96.4%)	5 (3.0%)	1 (0.6%)		
	MD	147	61 (41.5%)	74 (50.3%)	9 (6.1%)		3 (2.1%)
	SD	157	18 (11.5%)	52 (33.1%)	71 (45.2%)	8 (5.1%)	8 (5.1%)
	VS	86	1 (1.2%)		9 (10.5%)	57 (66.3%)	19 (22.1%)
	Dead	482					482 (100%)

GOS: Glasgow Outcome Scale, GR: good recovery, MD: moderate disability, SD: severe disability, VS: vegetative state.

events (less medical history) (57.1% vs. 72.4%) and a significantly higher rate of traffic accidents as a cause of TBI (64.3% vs. 37.9%) (Table 2). There were no significant differences in sex (male: 67.1% vs. 65.5%), GCS score at admission (8.32 ± 3.71 vs. 7.66 ± 3.35), pupillary abnormalities (27.1% vs. 26.2%), and transport time from injury (170 ± 405 vs. 229 ± 476 min) between the two groups (Table 2). To determine the relationship between age and group, an ROC curve was generated. The area under the ROC curve for age was 0.710 (95% CI = 0.627–0.792, p <0.001), with sensitivity of 67.8% and specificity of 67.1% at a cutoff age of 66.5 years.

There were also no significant differences between groups I and N for disease types and cerebral hernia findings on CT at admission, and for vital signs at admission (Table 2). In blood tests, only D-dimer differed significantly, with a lower level in group I (37.8 ± 34.3 vs. 62.3 ± 80.2) (Table 2). The incidence of convulsion was significantly lower in group I during the treatment and clinical course (11.4% vs. 24.1%) (Table 2).

Interestingly, group I also had a significantly shorter hospital stay (36.8 ± 22.1 vs. 56.1 ± 45.2) and a higher rate of discharge to home (70.6% vs. 11.0%) (Table 2). In a multivariate model, duration of hospital stay (OR = 1.03; 95% CI = 1.01–1.06) and discharge to home (OR = 0.06; 95% CI = 0.02–0.20) were both associated with an improved outcome (Table 3).

Patients discharged from the acute care hospital to home were significantly younger than those discharged to another hospital (Table 4). Sex, GCS score at admission, pupillary abnormalities, disease types, and cerebral hernia findings on CT at admission were not significantly related to the discharge destination (Table 4).

Discussion

The rate of favorable outcomes of patients with TBI in the JNTDB Project 2015 was significantly higher at 6 months after injury compared to that at discharge, and many SD cases at discharge had improved at

Table 2 Comparison of baseline factors between improved and non-improved outcome groups among patients with SD at discharge

	Improved outcome	Non-improved outcome	p value
Number of patients	70 (44.6%)	87 (55.4%)	
Age (years)	51.9 ± 23.7	67.8 ± 20.8	<0.001*
Sex (male)	47 (67.1%)	57 (65.5%)	0.830
Medical history (positive)	40 (57.1%)	63 (72.4%)	0.045*
GCS	8.32 ± 3.71	7.66 ± 3.35	0.569
Pupillary abnormalities	19 (27.1%)	22 (26.2%)	0.894
Mechanism of injury (traffic accident)	45 (64.3%)	33 (37.9%)	0.001*
Transport time from injury (min)	170 ± 405	229 ± 476	0.410
CT findings			
Diffuse injury	27 (38.6%)	27 (31.0%)	0.323
SAH	51 (72.9%)	65 (74.7%)	0.792
IVH	10 (14.3%)	14 (16.1%)	0.755
Perimesencephalic cistern compression	28 (40.0%)	46 (52.9%)	0.108
Midline shift (mm)	3.84 ± 5.23	5.46 ± 7.40	0.111
Vital signs on admission			
Blood pressure (systolic) (mmHg)	141.8 ± 35.9	151.1 ± 33.4	0.094
Heart rate (bpm)	87.3 ± 23.6	90.9 ± 25.6	0.375
Respiratory rate (bpm)	20.1 ± 6.9	20.7 ± 5.8	0.601
Body temperature (°C)	36.3 ± 1.1	36.2 ± 1.2	0.793
Blood examination			
pH	7.36 ± 0.08	7.37 ± 0.12	0.581
$PaCO_2$ (mmHg)	44.6 ± 12.2	41.7 ± 12.1	0.168
PaO_2 (mmHg)	194.1 ± 132.4	177.5 ± 138.1	0.484
Blood sugar (mg/dl)	175.5 ± 115.3	178.4 ± 71.9	0.854
Platelet count ($\times 10^4$/µl)	29.1 ± 45.3	22.5 ± 19.0	0.252
PT–INR	1.15 ± 0.38	1.96 ± 6.52	0.333
APTT (sec)	29.3 ± 7.9	31.2 ± 6.9	0.132
Fibrinogen (mg/dl)	251.1 ± 82.6	261.1 ± 103.6	0.563
D-dimer (µg/ml)	37.8 ± 34.3	62.3 ± 80.2	0.023*
Treatment and clinical course			
ICP monitoring	32 (45.7%)	38 (43.7%)	0.799
Ventricular drainage	3 (5.5%)	9 (14.1%)	0.120
Craniotomy	57 (81.4%)	68 (78.2%)	
Body temperature management	31 (44.3%)	28 (32.2%)	0.120
Talk and deteriorate	11 (15.7%)	23 (28.7%)	0.057
ICP_{max} (mmHg)	25.1 ± 13.4	25.4 ± 18.4	0.941
Convulsions	8 (11.4%)	21 (24.1%)	0.003*
Status at discharge			
Duration of hospital stays (days)	36.8 ± 22.1	56.1 ± 45.2	0.001*
Discharged to home	48 (70.6%)	9 (11.0%)	<0.001*

Values are presented as mean ± standard deviation. *Significantly different compared between two groups at p <0.05. SD: severe disability, SAH: subarachnoid hemorrhage, IVH: intraventricular hemorrhage, PT–INR: prothrombin time–international normalized ratio, APTT: activated partial thromboplastin time, ICP: intracranial pressure, ICP_{max}: maximum ICP.

Table 3   Multivariate predictors of improved outcome

Variable	OR, 95% CI	p value
Age	1.03, 0.99–1.06	0.109
Medical history	0.60, 0.18–2.01	0.403
Mechanism of injury	0.47, 0.17–1.35	0.161
D-dimer	1.01, 0.99–1.02	0.120
Convulsions	0.49, 0.12–2.08	0.332
Duration of hospital stays	1.03, 1.01–1.06	0.011*
Discharged to home	0.06, 0.02–0.20	<0.001*

*Significantly different compared between two groups at p <0.05. OR: odds ratio, CI: confidence interval.

6 months. In general, the GOS-extended (GOS-E) is recommended as a primary outcome measure at 6 months after injury, but not at discharge,[10] and long-term outcomes of TBI may improve over 5 years in some patients.[5–7,11] A primary outcome measure at 6 months after injury makes it difficult to assess a correct outcome.[12] However, since we followed the primary outcome measure recommendation, outcomes were evaluated until 6 months after injury, and longer-term outcomes were not examined. Despite this relatively short follow-up period, the discharge destination from an acute care facility was still a predictor of improved outcome. However, because there is no detailed information on how to assign discharge destinations and subacute treatment, discharge to home is not essential for outcome improvement. Long-term improvement requires continuous rehabilitation in the subacute to chronic phases,[13] and this finding suggests that the discharge environment is also important.

Of cases with an unfavorable outcome (SD + VS) at discharge, 29.2% improved to a favorable outcome (GR + MD). Using GOS-E between 3 and 6 months after injury, Wilkins et al.[7] found that 42.86% of patients with an initially unfavorable outcome (lower SD or worse) improved to a favorable outcome (upper SD or better), which is a slightly higher rate than in our study. This might be due to the younger age of the patients in Wilkins et al.[7] compared to that of our patients (35.06 ± 15.11 vs. 58.46 ± 24.60 years), since younger patients with TBI have been shown to have a higher rate of improvement of long-term outcomes.[11,14] There was also a difference in the outcome evaluation method. Using GOS, we defined MD or better as a favorable outcome, which is a slightly stricter criterion than that used in GOS-E. Also, we found that the outcome improved to favorable in 44.6% of SD cases at discharge, but in only 1.2% of VS cases. Previous studies of long-term outcomes of TBI have also found few cases with improvement from VS.[15] Overall, these findings suggest that an improved long-term outcome of TBI is most likely in young patients with SD on GOS at discharge.

To investigate factors associated with improvement to a favorable outcome in patients with SD at

Table 4   Comparison of patient characteristics depending on discharge destination with SD at discharge

	Discharge to home	Discharge to other hospital	p value
Number of patients	57 (36.3%)	100 (63.7%)	
Age (years)	48.6 ± 25.3	67.6 ± 19.3	<0.001*
Sex (male)	39 (68.4%)	65 (65.0%)	0.663
Medical history (positive)	32 (56.1%)	71 (71.0%)	0.059
GCS	8.66 ± 3.71	7.57 ± 3.36	0.076
Pupillary abnormalities	18 (31.6%)	23 (23.0%)	0.286
Mechanism of injury (traffic accident)	35 (61.4%)	43 (43.0%)	0.027*
CT findings			
Diffuse injury	23 (40.4%)	31 (31.0%)	0.236
SAH	37 (64.9%)	79 (79.0%)	0.053
IVH	8 (14.0%)	16 (16.0%)	0.742
Perimesencephalic cistern compression	22 (38.6%)	52 (52.0%)	0.106
Midline shift (mm)	3.74 ± 5.10	5.30 ± 7.21	0.151
Improvement of outcome at 6 months after injury			
Improved outcome	48 (84.2%)	22 (22.0%)	<0.001*

Values are presented as mean ± standard deviation. *Significantly different compared between two groups at p <0.05. GCS: Glasgow Outcome Scale, SAH: subarachnoid hemorrhage, IVH: intraventricular hemorrhage.

discharge, background factors were compared between patients who did and did not improve from SD. Patients with improvement were significantly younger, which is consistent with previous reports,[11,14] and had fewer previous medical events and a higher rate of traffic accidents as a cause of injury, both of which may be related to the younger age. The serum D-dimer level on admission was also significantly lower in patients with improved outcomes. We previously reported that the D-dimer level on admission reflects the severity of TBI.[16–18] Since neurological findings of head injury, such as consciousness, change with time, it is difficult to identify the time period in which findings can be judged as true brain injury. However, the serum D-dimer level on admission is considered quantitatively to represent the severity of TBI[17] and can be used as a predictor of long-term outcome. The incidence of convulsion during the course was also significantly lower in improved cases. This may be because convulsion causes secondary brain injury, which is likely to worsen the outcome.[19]

Post-traumatic amnesia and clinical markers of injury severity (initial motor GCS, elevated intracranial pressure, craniotomy, focal hemorrhage on CT) have been proposed as predictors of the long-term outcome of TBI,[11] which makes it important to evaluate the severity of TBI. The outcome may also be associated with serum levels of interleukin-6, glial fibrillary acidic protein (GFAP), and progesterone,[20] and utilization of these serum biomarkers is likely to increase.

Continuous rehabilitation from the early phase after injury is important for improvement of the long-term outcome of severe TBI.[13] Subdivision of medical care in many countries now results in many patients being transferred from an acute care facility to another hospital or to a recovery ward immediately after completion of acute-phase treatment with the goal of rehabilitation and recovery. In contrast, patients with a predicted poor outcome may be transferred to a long-term care sanatorium with less opportunity for rehabilitation. A patient with SD at completion of acute-phase treatment may be judged to be likely to have a poor outcome, but in this study, 44.6% of these cases improved to a favorable outcome after discharge. This is an important finding for staff engaged in acute-phase medical care of TBI. It indicates that an equal opportunity for rehabilitation should be given to SD cases due to the high possibility of an improved long-term outcome.

In this study, 70.6% of patients with improved outcomes were discharged to home, and this rate was significantly higher than that in patients who did not improve. Only two options, "home" and "hospital", were available for the discharge destination in the database, and therefore, the lifestyle and rehabilitation for patients at home or the type of hospital and degree of rehabilitation are uncertain. A detailed comparison of rehabilitation and lifestyle in the subacute and chronic phases remains as a future task. However, our results show a relationship with discharge to home. Similarly, a study of long-term outcomes after surgery for chronic subdural hematoma in elderly patients showed a significantly more favorable rate in patients discharged to home compared to those transferred to another hospital.[5] Thus, it may also be necessary to investigate environmental and psychogenic factors of motivation that improve long-term outcomes of TBI in patients living at home in the recovery phase.

In this study, discharge to home was associated with improved outcomes, but the details of how the discharge destination was determined are unknown. The GOS at discharge was SD for all patients in the study, but there is still a wide range of requirements from full care to partial care among SD cases. Differences in neurological symptoms at discharge may affect the location of discharge destinations. Patients discharged to home had lower severity injury and were significantly younger but had no other differences compared to those discharged to another hospital. Thus, differences in situations among patients classified as SD need to be considered at discharge.

About half of patients with TBI with SD at discharge from an acute care facility improved to GR or MD by about 6 months after injury. The rate of discharge to home was higher in patients with improved outcomes, which may indicate the importance of environment in the subacute phase. Appropriate management in the subacute phase also leads to improvement of long-term outcome of patients with TBI. Therefore, decisions on treatment strategy should be made with consideration of both long-term and short-term outcomes. Identification of predictors of long-term outcomes, such as serum biomarkers, is needed to determine appropriate acute- and subacute-phase treatment strategies.

Conflicts of Interest Disclosure

All authors have no conflicts of interest to declare.

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