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CHAPTER 6

Predictors of short-term outcome in brain-injured patients with disorders of consciousness ☆

J. Whyte[1,*], O. Gosseries[2], I. Chervoneva[3], M.C. DiPasquale[1], J. Giacino[4], K. Kalmar[4], D.I. Katz[5], P. Novak[6], D. Long[7], N. Childs[8], W. Mercer[8], P. Maurer[9] and B. Eifert[9]

[1]*Moss Rehabilitation Research Institute/Albert Einstein Healthcare Network, Philadelphia, PA, USA*
[2]*Coma Science Group, Cyclotron Research Center, University of Liege, Liege, Belgium*
[3]*Division of Biostatistics, Department of Pharmacology and Experimental Therapeutics, Thomas Jefferson University, Philadelphia, PA, USA*
[4]*JFK Johnson Rehabilitation Institute, Edison, NJ, USA*
[5]*Brain Injury Program, Braintree Rehabilitation Hospital, Braintree, MA; Department of Neurology, Boston University School of Medicine, Boston, MA, USA*
[6]*Sunnyview Hospital and Rehabilitation Center, Schenectady, NY, USA*
[7]*Bryn Mawr Rehab Hospital, Malvern, PA, USA*
[8]*Texas NeuroRehab Center, Austin, TX, USA*
[9]*Fachkrankenhaus Neresheim Hospital, Neresheim, Germany*

Abstract:

Objectives: To investigate predictors of recovery from the vegetative state (VS) and minimally conscious state (MCS) after brain injury as measured by the widely used Disability Rating Scale (DRS) and to explore differences in rate of recovery and predictors of recovery during inpatient rehabilitation in patients with non-traumatic (NTBI) and traumatic brain injury (TBI).

Design: Longitudinal observational cohort design and retrospective comparison study, in which an initial DRS score was collected at the time of study enrollment. Weekly DRS scores were recorded until discharge from the rehabilitation center for both NTBI and TBI patients.

Setting: Seven acute inpatient rehabilitation facilities in the United States and Europe with specialized programs for VS and MCS patients (the Consciousness Consortium).

Participants: One hundred sixty-nine patients with a non-traumatic (N = 50) and a traumatic (N = 119) brain injury who were in the VS or MCS states.

Interventions: Not applicable.

Main Outcome Measures: DRS score at 13 weeks after injury; change in DRS score over 6 weeks post-admission; and time until commands were first followed (for patients who did not show command-following at or within 2 weeks of admission).

☆ Both J. Whyte and O. Gosseries have contributed equally to this study.

*Corresponding author.
Tel.: 00 1 215 663-6872; Fax: 00 1 215 663-6113;
E-mail: JWHYTE@einstein.edu

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Results: Both time between injury and enrollment and DRS score at enrollment were significant predictors of DRS score at week 13 post-injury but the main effect of etiology only approached significance. Etiology was however a significant predictor of the amount of recovery observed over the 6 weeks following enrollment. Time between injury and enrollment was also a good predictor of this outcome, but not DRS score at enrollment. For the time until commands were first followed, patients with better DRS scores at enrollment, and those with faster early rates of change recovered command following sooner than those with worse DRS scores or slower initial rates of change. The etiology was not a significant predictor for this last outcome. None of these predictive models explained sufficient variance to allow their use in individual clinical decision making.

Conclusions: Time post-injury and DRS score at enrollment are predictors of early recovery among patients with disorders of consciousness, depending on the outcome measure chosen. Etiology was also a significant predictor in some analyses, with traumatically injured patients recovering more than those with non-traumatic injuries. However, the hypothesized interaction between etiology and time post-injury did not reach significance in any of the analyses suggesting that, within the time frame studied, the decline in prognosis with the passage of time was similar in the two groups.

Keywords: brain injuries; minimally conscious state; vegetative state; Disability Rating Scale; following command; prognosis; consciousness

Introduction

Outcome prediction is a frequent topic in the literature on neurologic recovery and rehabilitation. However, one may have several different purposes in mind in outcome prediction and each of these purposes places different performance requirements on the predictive model. Relatively gross aggregate prediction of rates of recovery may suffice for the purpose of planning healthcare services, estimating costs, or generating payment schemes. Similar gross aggregate models may highlight predictor variables that may have theoretical interest as possible causal factors in recovery. A much more demanding use of outcome prediction is to assist in the healthcare decision making for individual patients. Here one might wish to avoid ''wasting'' resources on someone who will not show substantial recovery, and to ensure that someone with good recovery potential receives services that will optimize that recovery. In this context, even a relatively accurate aggregate model may make inaccurate predictions about substantial numbers of individual cases. Outcome prediction may also differ in the time frame of interest. In many cases, the ''final outcome'' is of greatest interest to predict, but when the model is being used to allocate clinical services, one may be interested primarily in the outcome within the time frame that those services will be provided.

Prediction of outcome among patients with disorders of consciousness (DOC) is still difficult to establish individually. Moreover, most prognostic studies have begun on the day of injury when the diagnoses of vegetative (VS) and minimally conscious states (MCS) are not yet defined, and have studied the full range of injury severity. This provides little guidance to clinicians who see patients who have evolved from coma into the VS or MCS, and who wish to assess the likelihood of further progress, to determine the appropriate level of treatment intensity, and to provide guidance to caregivers in their decision making.

It is known that among patients with DOC one month after injury, those who show some minimal signs of consciousness have a better chance of recovery than patients who are still in a VS at that time, and the earlier the return of consciousness is detected, the better is the outcome (Giacino and Zasler, 1997; Giacino and Whyte, 2005; Whyte et al., 2005; Giacino and Kalmar, 1997). The etiology is also a relevant predictor of recovery.

Traumatic brain injury (TBI) tends to have a better outcome than non-traumatic etiology (NTBI) (especially anoxia) (The Multi-Society Task Force on PVS, 1994b). Moreover, the recovery phase lasts longer for a traumatic etiology: it has been suggested that the term *permanent vegetative state* should not be applied until 1 year after traumatic injury whereas for a non-traumatic injury, this diagnosis may be applied after only 3 months (The Multi-Society Task Force on PVS, 1994a, b). Note that the term *permanent* implies zero probability of recovery and can therefore give rise to serious decisions about the cessation of medication and nutrition.

Potential recovery is also linked to the location, extent, and nature of the brain damage as well as to the condition of the brain before the injury. Young age of the patient and the absence of medical history (such as alcoholism, drug use, or mental illness) lead to a better outcome (The Multi-Society Task Force on PVS, 1994b; Laureys et al., 2001). For patients with DOC of traumatic origin, the Disability Rating Scale (DRS) at 16 weeks post-injury, and the time at which commands were first followed, during the acute rehabilitation hospitalization, were related to the DRS score at rehabilitation admission, the time between injury and admission, and rate of DRS change during the first 2 weeks of rehabilitation (Whyte et al., 2005). New assessment methods, such as event-related potential (ERP) techniques, and evaluation with functional imaging modalities such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) scanning, offer promise in improving the precision of prognostic prediction, since they may help distinguish among patients with different neurophysiologic profiles (which confer different prognoses) at a time when behavioral assessments are at floor for all of them (Di et al., 2008; Owen et al., 2006; Schnakers et al., 2008; Kotchoubey, 2007). However, although these techniques appear to be able to identify a subgroup of VS patients with greater recovery potential or to identify subtle signs of consciousness not apparent on behavioral examination, they have not yet been used in systematic prediction at defined time points post-injury along with already known predictors.

Research on prediction of recovery from DOC is particularly challenging to conduct, at least in the United States, because intensive academically oriented healthcare services are severely restricted for this patient population after the first few weeks post-onset. This is based on a general pessimism that meaningful recovery is unlikely, the belief that the process of rehabilitation requires a level of voluntary participation that such patients cannot meet, and the sense that there is little evidence that intensive rehabilitation services can alter the outcome. Thus, such patients are generally dispersed to family homes or non-specialized nursing care facilities soon after injury, and, accordingly, lost to involvement in longitudinal research.

Because many of the available outcome studies follow a sample from the time of injury, so that a large proportion of the sample (those with milder injury) regain consciousness quickly, predictors of outcome in this rapidly recovering population may not apply to the sample with prolonged DOC. Other studies have followed patients with DOC for longer intervals, but typically restrict their prediction to the return of consciousness as a dichotomous variable (e.g., Multi-Society Task Force), shedding little light on the overall level of functional recovery. In this context, therefore, it is important to examine whether those patients with DOC who are available for study show sufficient recovery during the subacute period to suggest greater rehabilitation potential than is currently appreciated. In addition, if predictors of their short-term outcome are sufficiently accurate to guide individual service decisions, then these could be used to help tune rehabilitation admission criteria to accept the individuals with the greatest potential to benefit, and to avoid admitting individuals who will fail to make progress, and may present difficult placement problems. In this context, then, a number of important outcome questions need to be addressed. (1) As a group, how much recovery do patients admitted with DOC make in the subacute period? (2) Are there variables, available at the time that admission decisions are being made, that can help predict the amount of functional recovery that will occur in the time span over which rehabilitation services might be delivered? (3) Are there differences in the factors that predict recovery for patients with traumatic versus non-traumatic injuries during this interval?

We hypothesized that substantial recovery would be seen in a large proportion of patients who present with DOC in the first few weeks after brain injury. We also hypothesized, based on prior studies and our own previous work with a pure sample of individuals with traumatic brain injuries, that the etiology of injury (in particular traumatic vs. non-traumatic), the time post-event at which the patient was admitted to rehabilitation, and the functional level at which they were admitted, would all predict differences in the short-term recovery seen over the ensuing weeks.

Methods

Participants in this research were enrolled from the Consciousness Consortium (CC), which consists of a set of facilities in the United States and Europe that have specialized programs for the care and rehabilitation of patients with DOC, and an interest in conducting research in this area. The CC began a longitudinal descriptive study in 1996, and reported the results of the traumatic sample ($n = 124$) in 2005 (Whyte et al., 2005) which laid the groundwork for a randomized controlled treatment study currently underway (Giacino and Whyte, 2003; Whyte, 2007). Here we report the data for the non-traumatic sample also enrolled by CC facilities, and also analyze comparative results for the two subsamples.

Participants

Participants were enrolled in the study between December 1996 and June 2001 when they were admitted to one of the seven CC-member rehabilitation centers. Admission criteria were a severe acquired brain injury of traumatic or non-traumatic etiology and a DRS score on admission greater than 15, with no more than inconsistent command-following. These score criteria were chosen because all patients in VS or MCS should have DRS scores of at least 16, but lack of consistent command following helps ensure that those who have emerged from MCS are excluded. One hundred forty-eight (148) traumatic and 77 non-traumatic patients diagnosed as vegetative or minimally conscious on admission were entered into the longitudinal database. However, because specific variables required for the analyses were missing from some participants, the number of participants included in this report is smaller (see Table 1 for details).

Note that there is a bias of selective admission in rehabilitation centers. Indeed, acute inpatient rehabilitation facilities tend to select, to varying degrees, candidates who are believed to have a

Table 1. Outcome variables

	Traumatic brain injury (TBI)			Non-traumatic brain injury (NTBI)			Definition
	No. of subjects	Mean/median/SD	Min./max.	No. of subjects	Mean/median/SD	Min./max.	
DRS_{13}	99	18.14/20/5.65	5/28	36	19.72/20.5/4.3	9/26	DRS score at week 13 post-injury
$Change_{DRS6}$	99	4.96/4/4.23	−2/11	36	2.86/2.5/2.93	−1/16	[DRS score at enrollment]–[DRS score 6 weeks later]
T_{Follow}	71	62.04/30/79.72	0/473	37	42.27/27/44.73	0/196	[Date of command following or date of discharge if not following commands]−[date of 2 weeks post-admission]

chance of recovery and who will benefit from intensive therapy. Admission is therefore based, at least informally, on various prognostic factors that are perceived to be positive indicators of functional improvement (e.g., recent injury, possible signs of consciousness, etc.). Thus, this is not a population-based study, although it is relevant to decision making in the types of facilities in which the study was conducted.

The study was determined by the relevant Institutional Review Boards to be exempt from the need for individual informed consent because it involved only anonymous recording of observational data but no changes in clinical care.

The Disability Rating Scale (DRS)

The DRS is a measure of impairment, disability (now referred to as "activity"), and handicap (now referred to as "participation") across the span of recovery to track an individual from coma to community (Rappaport et al., 1982). The first three items of the DRS ("Eye Opening," "Communication Ability," and "Motor Response") reflect impairment ratings whereas cognitive ability for "Feeding," "Toileting," and "Grooming" reflect the level of disability and, finally, the "Level of Functioning" item reflects handicap, as does the last item, "Employability". The DRS is scored from 0 (no disability) to 29 (extreme VS). Note that this scale does not disentangle VS from MCS because it was constructed before the development of the MCS criteria (Giacino et al., 2002).

Data collection

For those patients who met the enrollment criteria for this study, demographic information, injury history and early complications, and admission DRS score were recorded. DRS scoring was repeated weekly as long as the patient remained at the facility. Data were recorded on paper forms and then faxed or mailed to the data center at the Moss Rehabilitation Research Institute, where they were entered into a computer database. For these analyses, the database was queried for demographic information (age, gender, ethnicity), the cause of injury (traumatic or non-traumatic brain injury), the time between the injury and the admission to the rehabilitation facility, the DRS score on admission, the weekly DRS score until discharge, and the time between the admission and the first command following (if not present at admission).

Three outcomes were addressed in the analyses: the DRS score at 13 weeks after injury (DRS_{13}), the change in DRS score over 6 weeks post-admission ($Change_{DRS6}$), and the time until commands were first followed for patients who did not show command following at or within 2 weeks of admission (T_{Follow}). Patients that did not follow commands during admission were censored at the discharge time. The operational definition of each outcome is reported in Table 1. DRS score at 13 weeks post-injury was chosen because the largest sample was available at that time and DRS score over 6 weeks post-enrollment was selected because it is the average length of stay in the rehabilitation facilities. For practical relevance, T_{Follow} would ideally be calculated from the time of admission since a clinician admitting a patient wants to know whether and when he/she will begin to follow commands thereafter. Moreover, calculating this index from the time of injury would be problematic in this sample, since many injured individuals would have recovered command following much earlier, but would not be included in the sample. However, because the rate of functional improvement in the first 2 weeks after admission was used as one of the predictor variables (see below for details), in fact we attempted to predict recovery of command following from that point forward.

Of the participants meeting the enrollment criteria, only those who had complete data for the outcome and predictor variables were used in each analysis (see Tables 1 and 2). This resulted in an effective sample of 135 (99TBI, 36NTBI) for the DRS_{13} and $Change_{DRS6}$ analyses and 108 (71TBI, 37NTBI) for the T_{Follow} analysis. Out of these 108 patients, 48 were censored at the time of discharge. Seventy-four (74) participants (50TBI, 24NTBI) were included in all of the analyses.

Table 2. Predictor variables

	DRS_{13} and 6-week change		T_{Follow}	
	TBI ($N = 99$)	NTBI ($N = 36$)	TBI ($N = 71$)	NTBI ($N = 37$)
Continuous variables	Mean/median/SD	Mean/median/SD	Mean/median/SD	Mean/median/SD
Age	31.58/28/14.09	40.78/39.5/16.33	28.79/26/12.54	36.89/35/14.85
$\mathrm{Log}T_{enroll}$	5.55/5.39/0.55	5.44/5.51/0.49	5.59/5.39/0.59	6.05/5.73/1.29
(T_{enroll})	(50.4/42/20.15)	(45.75/45.5/14.18)	(52.37/42/23.07)	(115.49/53/186.19)
DRS_{enroll}	22.85/23/2.23	23.06/23/2.57	23.84/24/2.14	23.84/24/1.72
Nominal variables	No. of subjects (%)	No. of subjects (%)	No. of subjects (%)	No. of subjects (%)
Gender				
Male	67 (67)	15 (41.7)	54 (76.06)	13 (64.86)
Female	32 (32.3)	21 (58.3)	17 (23.94)	24 (35.14)
Ethnicity				
White	77 (77.8)	29 (80.5)	61 (85.91)	28 (75.68)
Non-white	22 (22.2)	7 (19.4)	10 (14.09)	9 (24.32)

Abbreviations: $\mathrm{Log}T_{enroll}$: $\log_2$ transformation of T_{enroll}; T_{enroll}: date of command following–date of enrollment; DRS_{enroll}: DRS score at enrollment.

The characteristics of the patients in both analyses sets are shown in Table 2.

Data analysis

The independent variable *time to enrollment* (T_{enroll}) was log transformed ($\mathrm{Log}T_{enroll}$), since the assumption of linear association with the outcome was more appropriate on the log scale. NTBI and TBI were analyzed jointly to allow evaluation of the difference in outcomes by etiology. Different statistical models were used for the different outcomes. DRS at week 13 and the change in DRS scores 6 weeks post-admission were analyzed on a total of 135 observations using the robust MM regression (Yohai, 1987), since distributions of residuals from the standard multiple regression models exhibited heavy tails compromising the normality assumption. Etiology, admission DRS, and time to enroll (log base 2 transformed) as well as gender, age, and ethnicity were considered as predictors of DRS at week 13 and change in DRS scores 6 weeks post-admission. The interactions between etiology and admission DRS, etiology and time to enroll, and admission DRS and time to enroll were also considered in the models. The final models included the etiology, admission DRS, and time to enroll and controlled for potentially important age difference. Other demographic variables, which were not significantly associated with outcome, were excluded from the models.

For the last outcome, the time until commands were first followed, the analyses were performed on a partially overlapping sample because some patients in the previous analyses had already followed commands before admission and because some patients were admitted after 13 weeks post-injury. A Cox proportional hazards model was initially fitted to the time from admission to follow commands. Etiology, admission DRS, and time to enroll (log base 2 transformed) as well as gender, age, and ethnicity were considered as predictors. The interactions between etiology and admission DRS, etiology and time to enroll, and admission DRS and time to enroll were also considered in the model. Data from 169 patients were available for these analyses. Because the proportional hazards assumptions were not satisfied, the 2-week rate of change in DRS was also introduced into Cox model, which improved the overall model fit. In the earlier work (Whyte et al., 2005), the 2-week rate of change in DRS was found to be a strong predictor of the time to follow commands in TBI patients. Time from 2 weeks post-admission until commands were followed was then modeled. The final Cox model was based on 108 patients who also had 2-week rate of change in DRS available and did not follow commands within the first 2 weeks of admission. Etiology, admission DRS, and time to enroll (log base 2 transformed) as well as gender, age, and ethnicity were considered as predictors. The interactions between etiology and admission DRS, etiology and time to enroll, and admission DRS and time to enroll were also considered in the model.

Results

DRS score at week 13

None of the demographic variables was significantly associated with DRS score at week 13, but age was retained in the model because of prior research suggesting that age may influence the pace of neurologic recovery (Millis et al., 2001; Ritchie et al., 2000). Both time between injury and enrollment ($\mathrm{Log}T_{\mathrm{enroll}}$) and DRS score at enrollment ($\mathrm{DRS}_{\mathrm{enroll}}$) were highly significant predictors of DRS score at week 13 post-injury. The main effect of etiology approached significance (difference = 1.4, 95% CI: −0.2, 3.0; $p = 0.083$). However, the interactions between etiology and DRS at enrollment and time to enrollment were not significant. Table 3 reports the slopes for the different predictors from the final model. The model implies that an increase of 1 point in DRS at enrollment translates on average into a 1.2 point increase in DRS at week 13 (note that higher DRS scores indicate worse outcomes). Meanwhile doubling of the time to enrollment (1 unit increase of the $\mathrm{Log}T_{\mathrm{enroll}}$) implies a 3.7 point increase in DRS at week 13. Thus, this analysis did not provide strong evidence for a difference in the recovery pattern between TBI and NTBI patients during this time frame. Finally, the R^2 is 0.355 for this robust regression model.

DRS score improvement over the 6 weeks post-enrollment

Etiology was a significant predictor of the amount of recovery observed over the 6 weeks following enrollment. On average TBI patients had 2.0 points (95% CI: 0.4, 3.5; $p = 0.011$) greater improvement in DRS scores over the 6-week interval than NTBI patients. In this analysis, time until enrollment, but not DRS score at enrollment was a significant predictor of recovery. Table 4 reports the slopes for the different predictors in the final model. The model implies that doubling of the time to enrollment (1 unit increase of the log base 2 transformed time to enroll) implies ~1.9 point reduction in the DRS change over this interval. Once again, the interaction between etiology and $\mathrm{DRS}_{\mathrm{enroll}}$ and $\mathrm{Log}T_{\mathrm{enroll}}$ was not significant. Thus, although NTBI patients showed less recovery, during this interval, this lesser degree of recovery was not accounted for by a more prominent decline in prognosis with the passage of time. Note that the R^2 for this robust regression model is only 0.094.

Time to follow commands

The final model was reduced to two significant predictors plus etiology, because models incorporating additional non-significant covariates did not yield adequate goodness-of-fit test results. As noted in Table 5, with inclusion of the 2-week rate variable, etiology was not a significant predictor of the time until commands were followed.

Table 3. Results for the robust regression model for DRS at week 13

	Slope or difference[a]	95% confidence limits		p-value
		Lower	Upper	
Etiology[a]	1.4	−0.2	3.0	0.083
$\mathrm{Log}T_{\mathrm{enroll}}$	5.4	3.6	7.2	<0.0001
$\mathrm{DRS}_{\mathrm{enroll}}$	1.12	0.9	1.5	<0.0001
Age	0.0	−0.1	0.0	0.565

[a]Difference between TBI and NTBI groups.

Table 4. Results from the robust regression model for the change in DRS scores 6 weeks post-admission

	Slope or difference[a]	95% confidence limits		p-value
		Lower	Upper	
Etiology[a]	2	0.4	3.5	0.011
$\mathrm{Log}T_{\mathrm{enroll}}$	−1.87	−3.12	−0.62	<0.003
$\mathrm{DRS}_{\mathrm{enroll}}$	−0.14	−0.42	0.15	0.358
Age	0.03	−0.01	0.08	0.184

[a]Difference between TBI and NTBI groups.

Table 5. Results from the Cox model for time to follow commands from 2-week admission

	Hazard ratio	95% hazard ratio confidence limits		p-value
		Lower	Upper	
Etiology	1.14	0.66	1.98	0.637
$\mathrm{DRS}_{\mathrm{enroll}}$	0.87	0.77	0.99	0.033
2-week rate	11.26	1.65	76.67	0.013

However, both $\mathrm{DRS}_{\mathrm{enroll}}$ and the 2-week rate of change were significant predictors. Patients with lower (better) DRS scores at enrollment, and those with faster early rates of change recovered command following sooner than those with higher DRS scores or slower initial rates of change.

Discussion

These results demonstrate that considerable recovery is possible during the typical time frame of acute rehabilitation care, for both TBI and NTBI patients. Overall 83.7% of patients improved their DRS score by at least 1 point over the 6 weeks of observation (84.8% of TBI and 80.5% of NTBI), and 61.1% of those who were not following commands at admission began to follow them prior to discharge (67.6% TBI and 48.6% NTBI). How much rehabilitation services enhance this recovery is unknown, but these findings suggest that the majority of patients who are admitted to acute rehabilitation will demonstrate meaningful recovery.

These results also confirm, in a sample of TBI and NTBI patients followed in a comparable manner, that time between injury and enrollment is a key predictor of recovery, with the passage of time reducing the chances of recovery. This was true for DRS_{13} and for 6-week change, but not for the time until commands were followed. However, in the latter analysis, direct measurement of the rate of recovery, captured by the 2-week change variable, may have reduced the significance of the more indirectly predictive T_{enroll} variable. The DRS score at enrollment was predictive of the DRS score at 13 weeks post-injury, but not of the amount of recovery that would be seen over a defined interval, suggesting that the admission DRS score is primarily a predictor of functional *status* rather than functional *change*, whereas the time until enrollment is particularly relevant to the probability of *change*. DRS at enrollment was also predictive of the time at which commands would be followed. This may indicate that, at equivalent rates of change, patients who start at a better functional level need less improvement (and hence less time) to reach the criterion of command following.

The effects of etiology on outcome in this study were more complex. NTBI patients had significantly or marginally worse outcomes in terms of 6-week change and DRS_{13}, respectively, but etiology was not a significant predictor of time until commands were followed. As mentioned above, the inclusion of the 2-week rate of change in the latter model, necessitated for statistical reasons, may have reduced the significance of less direct predictors such as time post-injury or etiology. Even though NTBI patients had somewhat poorer outcomes than TBI patients, depending on the outcome measure chosen, the specific prediction that the prognosis of NTBI patients would decline more precipitously over time (i.e., an interaction between etiology and LogT_{enroll}) was not supported. This is in contrast to prior studies suggesting that the ‘‘window of recovery’’ is shorter for NTBI than for TBI patients (The Multi-Society Task Force on PVS, 1994b). However, the differential impact of time may be more dramatic in the 3–12 month range, whereas these data were collected primarily in the early weeks post-injury.

In the aggregate, these results confirm the importance of etiology, initial functional status, and time since injury in determining outcome in individuals with DOC. However, the majority of the variance in individual outcome remains unaccounted for. The final models described here account for approximately 35.5% of the variance in DRS_{13}, and about 9% of the variance in 6-week change. Thus, these predictors cannot be used with confidence to predict the outcomes of individual patients or to make admission decisions, without a high risk of error in both directions.

This study has a number of important limitations. Most importantly, it was conducted on a select referral sample, not a population-based sample. Thus, the large proportion of patients who recover in hours or days after injury are not included in the analysis. But even if one focuses on those patients who might be considered for rehabilitation care because they are still suffering from DOC several weeks post-injury, this remains a biased sample, since it involved only those patients who were admitted to rehabilitation services but not those who were not referred or were referred but not admitted. The specific clinical factors used in making those admission decisions are unknown, but surely may have included some subtle prognostic factors. In particular, since clinicians are generally aware of the more negative prognosis of NTBI patients reported in the literature, they may have had more stringent admission screening of non-traumatic referrals than of traumatic referrals. This, in turn, may have led to smaller differences in outcome based on etiology than might be seen in a less selected sample. This implicitly assumes, however, that some of the variance in recovery not accounted for by the predictors used in this study, was accounted for by unmeasured variables available to clinical decision makers, rather than simply being altogether unexplained. There is no direct evidence for a more stringent admission screening of NTBI patients since, for example, their DRS scores at enrollment were actually slightly worse than those of the TBI patients. Finally, the relatively short-term nature of this study, constrained by the current realities of acute inpatient rehabilitation stays in the United States, meant that a substantial number of patients were not following commands by the time of discharge and were censored in the Cox analysis. Longer intervals of follow up and larger samples, particularly of those with non-traumatic injuries might have more clearly informed the pattern of recovery.

Conclusion

In this selected sample of patients with DOC, referred and approved for inpatient rehabilitation admission, significant recovery was seen over the hospital stay, with the majority of patients with both traumatic and non-traumatic injuries demonstrating improvements in DRS scores and, among vegetative patients, the development of command following. The time between injury and rehabilitation admission and the DRS score at admission were each predictive of two of the three outcomes. Etiology was predictive of amount of functional improvement seen over 6 weeks of hospitalization, but less so of the DRS score at 13 weeks post-injury or the time until commands were followed. In the one model in which early rate of change was included, it was strongly predictive of outcome while etiology was not, suggesting that the clinical trajectory, itself, is highly predictive. None of the predictive outcome models accounted for sufficient variance to be used in individual clinical decision making.

Abbreviations

CC	Consciousness Consortium
$\mathrm{Change}_{\mathrm{DRS6}}$	change in DRS score over 6 weeks post-admission
DOC	disorders of consciousness
DRS	Disability Rating Scale
DRS_{13}	Disability Rating Scale score at 13 weeks after injury
$\mathrm{DRS}_{\mathrm{enroll}}$	Disability Rating Scale score at enrollment
ERP	event-related potential
fMRI	functional magnetic resonance imaging
$\mathrm{Log}T_{\mathrm{enroll}}$	log transformation of the time between injury and enrollment
MCS	minimally conscious state
NTBI	non-traumatic brain injury
PET	positron emission tomography
PVS	persistent vegetative state
TBI	traumatic brain injury
T_{enroll}	time between injury and enrollment
T_{Follow}	time until commands were first followed for patients who did not show command following at or within 2 weeks of admission
VS	vegetative state

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