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Associations Between Care Pathways and Outcome 1 Year After Severe Traumatic Brain Injury

Alison K. Godbolt, MD, MBChB; Maud Stenberg, MD; Marie Lindgren, MD; Trandur Ulfarsson, MD; Marianne Lannsjö, MD, PhD; Britt-Marie Stålnacke, MD, PhD; Jörgen Borg, MD, PhD; Catharina Nygren DeBoussard, MD, PhD

Objective: To assess associations between real-world care pathways for working-age patients in the first year after severe traumatic brain injury and outcomes at 1 year. **Setting and Design:** Prospective, observational study with recruitment from 6 neurosurgical centers in Sweden and Iceland. Follow-up to 1 year, independently of care pathways, by rehabilitation physicians and paramedical professionals. **Participants:** Patients with severe traumatic brain injury, lowest (nonsedated) Glasgow Coma Scale score 3 to 8 during the first 24 hours and requiring neurosurgical intensive care, age 18 to 65 years, and alive 3 weeks after injury. **Main Measures:** Length of stay in intensive care, time between intensive care discharge and rehabilitation admission, outcome at 1 year (Glasgow Outcome Scale Extended score), acute markers of injury severity, preexisting medical conditions, and post–acute complications. Logistic regression analyses were performed. **Results:** A multivariate model found variables significantly associated with outcome (odds ratio for good outcome [confidence interval], *P* value) to be as follows: length of stay in intensive care (0.92 [0.87-0.98], 0.014), time between intensive care discharge and admission to inpatient rehabilitation (0.97 [0.94-0.99], 0.017), and post–acute complications (0.058 [0.006-0.60], 0.017). **Conclusions:** Delays in rehabilitation admission were negatively associated with outcome. Measures to ensure timely rehabilitation admission may improve outcome. Further research is needed to evaluate possible causation. **Key words:** *health facility planning*, *outcome*, *rehabilitation*, *severe traumatic brain injury*

TRAUMATIC BRAIN INJURY (TBI) requiring hospitalization or causing death occurs with an incidence of about 235 per 100 000 in Europe,[1] which is significantly higher than the 103 per 100 000 reported from a synthesis of studies in the United States.[1] Severity is most commonly classified according to acute Glasgow Coma Scale (GCS) scores, with GCS score 13 to 15 considered mild, GCS score 9 to 12 moderate, and GCS score 3 to 8 severe. Most patients suffer mild

Author Affiliations: *Department of Clinical Sciences, Karolinska Institute, and University Department of Rehabilitation Medicine Stockholm, Danderyd Hospital, Stockholm, Sweden (Drs Godbolt, Borg, and DeBoussard); Department of Community Medicine and Rehabilitation, Rehabilitation Medicine, Umeå University, Umeå, Sweden (Drs Stenberg and Stålnacke); Department of Clinical Rehabilitation Medicine, County Council, Linköping, Sweden (Dr Lindgren); Department of Rehabilitation Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden (Dr Ulfarsson); and Department of Neuroscience, Uppsala University, Uppsala, and Department of Rehabilitation Medicine, Gävle and Sandviken Hospital, Sandviken, Sweden (Dr Lannsjö). Dr Godbolt was previously with Department of Rehabilitation Medicine, University Hosptial Uppsala and Uppsala University, Uppsala Sweden, during the intial stages of the study.*

Drs Godbolt and Nygren DeBoussard contributed equally to this work.

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PROBRAIN collaborators: The authors together with Dr Gudrun Karlsdottir, Department of Rehabilitation Medicine, Landspitalinn, University Hospital, Reykjavik, Iceland.

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Corresponding Author: *Alison Kate Godbolt, MD, MBChB, Department of Clinical Sciences, Karolinska Institute, and University Department of Rehabilitation Medicine Stockholm, Danderyd Hospital Stockholm, hus 39, plan 3, Danderyds sjukhus, SE-182 88 Stockholm, Sweden (alison.godbolt@ki.se).*

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injuries, with a severity ratio for mild/moderate/severe of 22:1.5:1.[1]

Although less common than mild and moderate TBI, severe TBI (S-TBI) may require a lengthy hospital stay and cause long-term disability. A European epidemiological study[2] found that brain injury was the commonest cause of permanent disability after injury. Analysis of factors impacting on outcome after S-TBI is therefore merited. Initial injury severity, post–acute complications, and any rehabilitation interventions all have the potential to impact on outcome. The literature on acute care and on rehabilitation for persons with S-TBI has, however, largely developed along separate paths: the acute care literature has focused on increasingly nuanced analysis of markers of acute injury severity of importance for predicting outcome (eg, CRASH[3] and IMPACT[4] studies) but largely ignored any impact of rehabilitation interventions, while the rehabilitation literature has relied on relatively simplistic definition of injury severity (eg, by acute GCS scores), to define study populations, without reference to recent developments in acute prognostic models.

Recovery of function after S-TBI[5] depends not only on spontaneous resolution of injury-related pathology (eg, resolution of edema, clearing of inflammatory infiltrate, resolution of disruption to functional networks) but also on neuroplasticity, which can be influenced by active rehabilitation interventions.[6] Besides contributing to improved function through optimization of neuroplastic processes, rehabilitation aids the patient in compensating for any persisting deficits and promotes prevention and treatment of complications, thereby minimizing activity limitations and maximizing possibilities for participation.

Access to rehabilitation for patients surviving S-TBI is variable. A recent French study[7] found that more than a third of patients surviving S-TBI in Paris were not even referred to rehabilitation. In some countries, access to rehabilitation depends on the individual's medical insurance status and rehabilitation may be unavailable to uninsured patients.[8] In Sweden and Iceland, there is universal health insurance and as such no formal barriers to access to rehabilitation. However, acute and rehabilitation care have historically developed separately, without a planned, unified pathway of care. They also belong to different organizations, and clinical experience is that delays in admission to rehabilitation units are common.

Evidence is now emerging for the benefits of a continuous chain of care after S-TBI (from neurosurgical intensive care to inpatient rehabilitation to discharge). These were recently demonstrated in a Norwegian quasi-randomized study of S-TBI.[9] Better outcomes 1 year after injury were demonstrated for patients receiving early and continuous rehabilitation starting in the intensive care unit compared with a group of patients who received usual care (which also incorporated inpatient rehabilitation but not a defined, continuous pathway of care).

Elsewhere in Europe, Denmark has had a defined care pathway for patients after S-TBI for more than a decade, centralized to 2 national centers. Severely injured patients receive high priority regarding transfer to inpatient rehabilitation. Outcomes after introduction of this defined care pathway with centralized rehabilitation were better than outcomes for historical controls.[10]

In Sweden, rehabilitation after S-TBI may be offered in several forms.[11] Specialized inpatient rehabilitation is primarily offered in rehabilitation medicine departments based in, or with links to, university departments of rehabilitation medicine. These are found in each of the 6 healthcare regions and have traditionally offered specialized, post–acute rehabilitation to adults of working age. Inpatient rehabilitation also exists outside the regional units in several county hospitals, some of which have comprehensive rehabilitation programs. In some cases, these are integrated with geriatric services and as such lack a primary focus on the needs of working adults. Care pathways vary, and these county units may either act as step-down units for continued rehabilitation after discharge from specialized units or in some cases receive patients directly. There are no national guidelines regarding appropriate care pathways. An improved evidence base is needed to allow healthcare providers to support appropriate developments.

We performed a prospective observational study of care pathways and outcomes after S-TBI in Sweden and Iceland to assess associations between existing real-world care pathways and outcome after S-TBI. The hypothesis was that all of the following would be negatively associated with outcome: (*a*) acute injury severity, as assessed on day 1; (*b*) length of intensive care (influenced by acute injury and additionally mirroring secondary brain injury and early complications); (*c*) length of time between intensive care and rehabilitation admission (representing a break in the chain of care); and (*d*) number of intervening care units between discharge from intensive care and rehabilitation admission. Associations between preexisting medical problems and post–acute complications with outcome were also assessed.

METHODS

This study formed the part of a prospective, multicenter, observational study of patients who had sustained S-TBI (the "PROBRAIN" study).

Inclusion criteria were as follows:

1. Severe, nonpenetrating TBI, with a lowest nonsedated GCS score of 3 to 8 or Reaction Level Scale[12] (RLS) score of 4 to 8 in the first 24 hours after injury.

2. Age at injury 18 to 65 years.
3. Injury requiring neurosurgical intensive care, or collaborative care with a neurosurgeon in another intensive care unit.

Exclusion criteria were death or expected death within 3 weeks of injury. The 8-point RLS (see Table 1) is widely used in Sweden, and in some emergency departments and neurosurgical units, it is used instead of the GCS; RLS criteria were therefore necessary to allow recruitment of patients from those centers using this scale and thus to avoid selection bias. Scores on the GCS of 3 to 8 and on the RLS of 8 to 4 reflect similar severity of injury,[13] the RLS having been shown to have somewhat better interrater reliability than the GCS.[14] RLS scoring is in the opposite direction to GCS scoring, with the highest RLS score of 8 reflecting the most severe injuries.

Patients were recruited prospectively by rehabilitation physicians from January 2010 until June 2011, with extended recruitment until December 2011 at 2 centers. The participating centers provide neurosurgical care to more than 80% of the population of Sweden and the population of Iceland (total ~4.7 million adults aged 18-65 years). Neurosurgical intensive care units at 6 (of a possible 7) centers in Sweden and Iceland were contacted on a weekly basis to identify eligible patients. It was not possible to include the southern region of Sweden for logistical reasons.

The patient gave informed consent in cases where he or she had capacity. In the majority of cases, the patient lacked capacity and the patient's nearest relative gave consent to inclusion. The study was reviewed by the regional ethical review board in Stockholm.

After inclusion, acute prognostic and socioeconomic data were obtained from medical records. Additional background socioeconomic data and medical history were collected via interview of relatives (if the patient remained unable to participate) as soon as possible after inclusion. Patients were considered to have a coexisting medical problem at the time of injury if any of the following were present: hypertension, diabetes, cardiac disorder, psychiatric disorder, renal failure, chronic obstructive airways disease, other significant medical problem.

Patients then underwent prospective clinical assessment at 3 time points: 3 weeks (18-24 days), 3 months (75-105 days), and 1 year (350-420 days) after injury. Assessments took place in the patient's current care setting where possible (which in some cases was in the patient's home) or in a local outpatient department. Inclusion and follow-up were therefore designed to be independent of any decisions regarding care pathways and of any decision regarding admission to inpatient rehabilitation. The presence or absence of complications was recorded at each study time point. Those complications present 3 weeks after injury were considered in relation to possible delays in transfer to rehabilitation and outcome. The following possible complications were recorded: infection (meningitis, sepsis, wound infection, urinary tract infection, pneumonia, other stated infection), hydrocephalus, deep vein thrombosis, pulmonary embolism, heterotopic ossification, new fracture or new brain injury since the incident injury, other defined complication. The presence of tracheostomy, ongoing artificial ventilation, and administration of oxygen 3 weeks after injury were considered surrogates for respiratory complications in terms of difficulties in weaning from ventilation and/or persisting respiratory difficulties and were therefore also coded as representing complications. Data on care pathways were updated at follow-up to gather complete care pathway data during the first year after injury, as far as possible. Assessments were performed by rehabilitation physicians with assistance from rehabilitation nurses, psychologists, physiotherapists, and occupational therapists.

To control for acute injury severity, a validated acute prognostic model was used to obtain a composite representing risk of unfavorable outcome: the CRASH acute prognostic model[3] is an externally validated acute prognostic model, based on data from 10 008 patients worldwide. It incorporates 10 acute prognostic variables: age, pupil reaction, acute GCS scores, country, presence or absence of major extracranial injury, presence or absence of 5 specified acute computed tomographic

TABLE 1 *The Reaction Level Scale*[a]

1	Alert, with no delay in response (responds without stimulus)
2	Drowsy or confused, but responds to light stimulation
3	Very drowsy or confused, but responds to strong stimulation
4	Unconscious; localizes (moves a hand toward) a painful stimulus but does not ward it off
5	Unconscious; makes withdrawing movements following a painful stimulus
6	Unconscious; stereotypic flexion movements following painful stimuli
7	Unconscious; stereotypic extension movements following painful stimuli
8	Unconscious; no response to painful stimuli

[a]Patients with Reaction Level Scale score of more than 3 are unconscious.

brain findings. We used the online calculator for the CRASH prognostic model (available at http://www.crash2.lshtm.ac.uk/Risk%20calculator/index.html) to calculate the percentage risk of an unfavorable outcome (equivalent to Glasgow Outcome Scale Extended [GOSE] score of 1-4) at 6 months, for each patient, after conversion of RLS scores for those patients not assessed with the GCS. Ordering of severity with the RLS and the GCS has been shown to be consistent[15]; the RLS and the GCS are highly correlated ($r = -0.94$) and assess similar behavioral features reflecting consciousness.[13]

Outcome at 1 year was measured using the GOSE.[16] The GOSE has good interrater reliability[16] and validity[17] and is an established measure of global outcome after TBI. A standardized interview[16] was used to support good interrater reliability. To enable a logistic regression analysis (see later), it was necessary to dichotomize the GOSE findings into "good" and "bad" outcomes. This division was made in accordance with the definition of "good" and "bad" outcomes used in the CRASH study.[3] For those alive at 1 year, GOSE score 2 to 4 (vegetative state, lower and upper severe disability) was considered a "bad" outcome and GOSE score 5 to 8 (moderate disability or good recovery) a "good" outcome. Individuals with GOSE score 2 to 4 are dependent on others for activities of daily living. Those with GOSE score 5 to 8 are independent at home: individuals with GOSE score 5 to 6 have absent or reduced ability to work, and those with GOSE score 7 to 8 have some impact on social life and free-time activities.

As our focus was on evaluation of care pathways from acute care to rehabilitation, it was not meaningful to include patients who did not receive rehabilitation because they had died (ie, GOSE score 1) in the logistic regression analysis. Place of residence was also recorded at baseline and 1 year to contribute to evaluation of outcome.

Data analysis

Nonparametric methods were used as data were not normally distributed. Summary statistics (median, range) were obtained and correlations with outcomes were analyzed (Spearman ρ). To assess the possible respective impacts of injury severity (composite of acute prognostic variables according to the CRASH model), preexisting medical problems, duration of intensive care, the presence of complications at the 3-week assessment, and length of time between intensive care and rehabilitation admission, a logistic regression model was developed. Univariate analyses were performed for each variable, and those found to have a significant effect were taken forward to a multivariate analysis with a backward stepwise method. Statistical analysis was performed with SPSS (version 20).

RESULTS

Patient characteristics and completeness of follow-up

Demographic details and summary statistics on severity of injury are given in Table 2. Figure 1 shows a flowchart of follow-up, withdrawals and deaths.

Follow-up rates were 98% at 3 weeks after injury (97% alive, 1% dead), 96% at 3 months after injury (92% alive, 4% dead), and 94% at 1 year after injury (88% alive, 6% dead). Patients who withdrew were similar to those

TABLE 2 *Patient characteristics (N = 114)*

Age at injury, median (range), y	42 (17-65)
Worst unsedated GCS[a] score during first 24 h, median (range)	5 (3-8)
Cause of injury, *n* (%)	
Transport accident	46 (41)
Fall	50 (44)
Other	13 (11)
Missing data	5 (4)
Length of stay in intensive care, median (range), d	17 (1-78)
Duration of ventilation, median (range), d	12 (0-101) (range, 0-36, with 1 outlier at 101 d)
Economic support at time of injury, *n* (%)	
Employed/self-employed full-time	57 (50)
Study grant	7 (6)
Unemployment benefit or social support	11 (10)
Sick pay	16 (14)
Other[b]	8 (7)
Part-time employment/self-employment	6 (5)
Unknown	3 (3)
Missing data	6 (5)
Previous brain injury requiring hospitalization, *n* (%)	18 (16)
Known drug or alcohol misuse at time of injury, *n* (%)	34 (28)
Gender, *n*	
Male	75
Female	26
Not recorded	13

Abbreviations: GCS, Glasgow Coma Scale; RLS, Reaction Level Scale.

[a]Or derived GCS score using conversion from RLS score (Table 1) for patients exclusively assessed with the RLS (n = 42).

[b]"Other" includes parental pay, pension, other economic support, combinations of other categories.

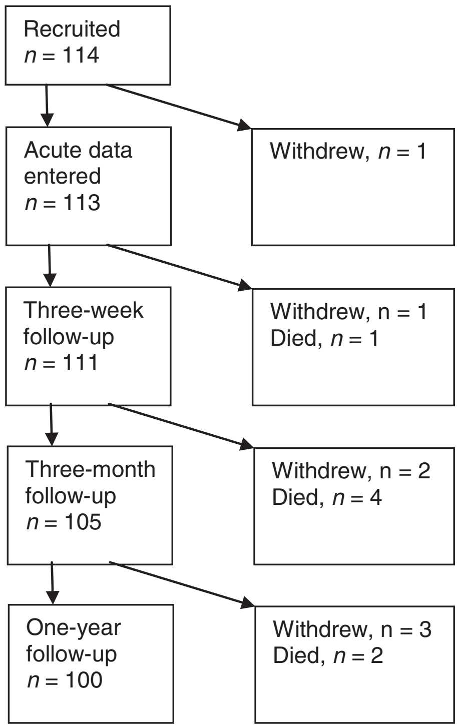

Figure 1. Flow of patients through the study.

who continued in terms of median age (30 vs 42 years; Mann-Whitney test, $P = .24$) and median acute GCS- or RLS-derived GCS scores (5 in both groups; Mann-Whitney test, $P = .55$). Because of a minor protocol violation, 1 patient was recruited shortly before his (or her) 18th birthday.

Care pathways: Intensive care length of stay and access to inpatient rehabilitation

Median length of stay in intensive care (LOSIC) during the acute period (ie, until the first discharge from intensive care) was 17 days (range, 1-78 days). Ninety-seven patients were transferred to an inpatient brain injury rehabilitation unit at some point during the first year after injury. Of these, 90 were alive and followed up at 1 year, 2 patients died after having received some inpatient rehabilitation but before follow up at 1 year, 4 had withdrawn from the study, and data were missing for 1. Another 5 patients died without having been transferred to a rehabilitation unit.

Eight surviving patients (7%) were known to not have been transferred to an inpatient brain injury rehabilitation service: 1 participated in early outpatient rehabilitation, 2 received nonspecialist rehabilitation in a nursing home or a geriatric unit, 1 received rehabilitation interventions within a neurology service, and 4 (3.5%) did not receive rehabilitation. One additional patient declined transfer to a rehabilitation unit, and care pathway data were missing for 3 patients (3%).

The 4 patients who did not receive rehabilitation were slightly older (median = 43 years; range, 24-59 years) than those receiving rehabilitation (median = 38.5 years; range, 17-64 years), with difference not significant (Mann-Whitney test, $P = .55$), and had slightly more severe injuries as assessed by the CRASH acute prognostic model, with a risk of a bad outcome based on acute prognostic variables being a median of 84.5% for those not receiving rehabilitation (range, 76%-95%) and a median of 72.5% (range, 23%-98%) for those receiving rehabilitation (not significant; Mann-Whitney test, $P = .14$). However, length of intensive care was shorter for those not receiving rehabilitation (median = 6 days; range, 5-17 days) than those receiving rehabilitation (median = 17 days; range, 1-78 days). Further analysis was not appropriate or possible, given the small group size.

For the 97 patients admitted to inpatient brain injury rehabilitation units during the first year after injury, median time from injury to first admission to inpatient rehabilitation was 28 days (range, 9-198 days). Median time from first discharge from intensive care to admission to inpatient rehabilitation was 13 days (range, 0-176 days), with a substantial proportion of patients waiting several weeks (see Table 3). The relationship between acute injury severity and the length of time between discharge from intensive care to admission to inpatient rehabilitation is shown in Figure 2 and was only weakly correlated. Only 23 of these patients (24%) were transferred directly from intensive care to rehabilitation.

A variety of care pathways were experienced by the cohort. Considering those patients who were eventually transferred to inpatient rehabilitation ($n = 97$), the most common care pathway was from intensive care to a neurosurgical ward to a rehabilitation unit ($n = 25$). Nearly as many patients were transferred directly to a rehabilitation unit from intensive care ($n = 23$), and a similar number from intensive care to a surgical ward to a rehabilitation unit ($n = 20$). The remaining 29 patients (30% of those eventually transferred to rehabilitation) received a wide variety of different care pathways, receiving care on between 1 and 5 different intervening care units after intensive care discharge and before eventual transfer to a rehabilitation unit. These intervening care units encompassed the following specialties: internal medicine and its specialties (including infectious diseases and neurology), surgery and its specialties (including neurosurgery [here excluding patients who thereafter went straight to rehabilitation], plastic surgery, otolaryngology, hand surgery, orthopedics), psychiatry, geriatrics (despite patients being younger than 65 years), short periods in short-stay nursing homes (4 patients), and readmissions to intensive care (3 patients).

TABLE 3 *Time between discharge from intensive care and admission to inpatient rehabilitation*

Time between discharge from intensive care and admission to inpatient rehabilitation	Intervening care form (for cases with >1 intervening care unit, the first unit after intensive care is given in the table)					
	N (total)	Medical or surgical acute ward	Neurosurgical ward	Geriatric ward	Missing	Acute care ward with rehabilitation
0 (= direct transfer to inpatient rehabilitation)	23					
<1 wk	11	7	3	0	0	1
1 to <2 wk	14	9	5	0	0	0
2 to <3 wk	16	6	9	1	0	0
3 to <4 wk	8	3	5	0	0	0
4 to <5 wk	3	1	2	0	0	0
5 to <6 wk	7	4	2	1	0	0
≥6 wk	13	6	5	1	1	0
Missing data on interval	2					
Total	97					

During the period between discharge from intensive care and admission to rehabilitation, patients received care in a median of one other care unit (range, 1-5). The number of intervening care units was not significantly associated with outcomes at 1 year.

Outcomes

Of the 100 patients alive and followed up 1 year after injury (including those who did not receive inpatient rehabilitation), 36 had a bad outcome (GOSE score = 2, 3, or 4), 62 had a good outcome (GOSE score = 5,

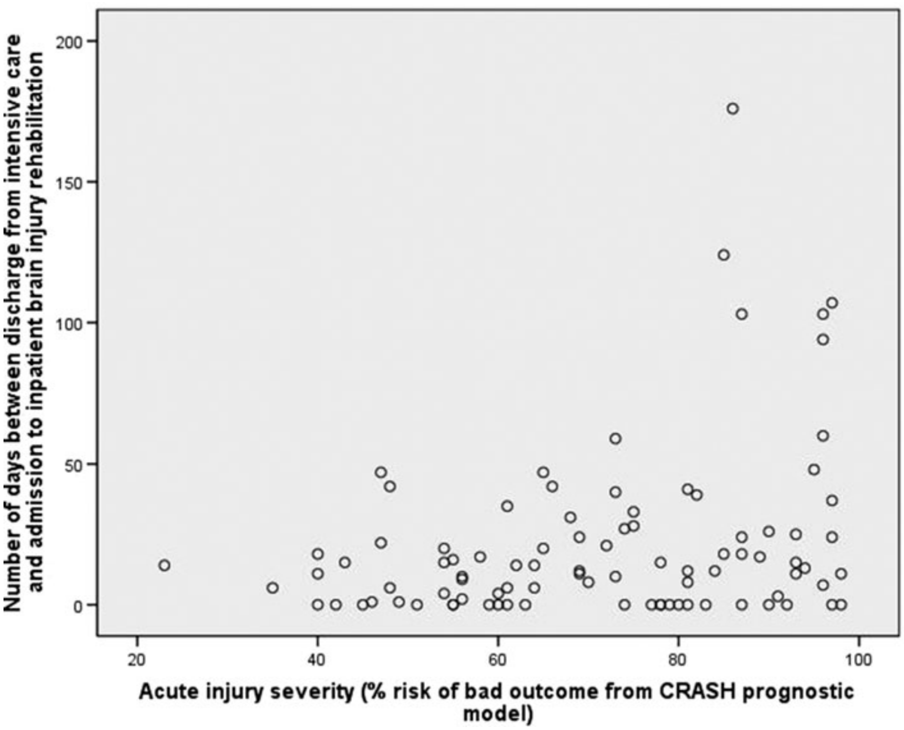

Figure 2. Delays between discharge from intensive care and admission to inpatient rehabilitation, related to acute prognostic markers.

TABLE 4 *Outcomes and place of residence, 1 year after injury*

GOSE score at 1 y	Total number of patients	Place of residence 1 y after injury		
		Own home	Care home	Not yet decided/other
1 = dead	7	Not applicable		
2 = vegetative state	7	1	5	1
3 = lower severe disability	23	14	9	0
4 = upper severe disability	6	5	1	0
5 = lower moderate disability	12	12	0	0
6 = upper moderate disability	12	9	1	2
7 = lower good recovery	21	21	0	0
8 = upper good recovery	17	17	0	0
Withdrew from the study	7			
Followed up but GOSE data missing	2			
Total	114			

Abbreviation: GOSE, Glasgow Outcome Scale Extended.

6, 7, or 8), and data on GOSE were missing for 2. Details of GOSE findings are given in Table 4. Predictions from the CRASH acute prognostic model correlated only poorly with actual outcome at 1 year (Spearman ρ correlation coefficient = −0.12*)*. However, both LOSIC (correlation coefficient = −0.49) and length of time between intensive care and admission to rehabilitation (correlation coefficient = −0.30) showed somewhat stronger correlations with outcomes. The number of intervening care units between intensive care and rehabilitation was, however, not significantly related to outcomes at 1 year.

The results of logistic regression analyses (see Table 5) show odds ratios and confidence intervals for adjusted and unadjusted values of these factors on outcome (dichotomized GOSE) at 1 year. A separate analysis of the impact of extracranial injury on outcomes found a nonsignificant effect ($P = .61$), and as this variable is already part of the CRASH composite, it is not included in Table 5. Correlation matrices were inspected to evaluate possible multicolinearity, which was not found to any important degree (highest correlation of 0.27 between LOSIC and time between intensive care and admission to rehabilitation). In summary, the logistic regression model demonstrated that LOSIC, length of time between intensive care and rehabilitation admission, and the presence of post–acute complications contributed significantly to the variation in outcome and together explained 52% of the variation in the model. The CRASH composite (representing acute injury severity) and the presence of preexisting medical problems were not significantly related to outcome (Table 5). Furthermore, Mann-Whitney tests found that time between intensive care and rehabilitation admission was not significantly different for patients with and without complications at 3 weeks ($P = .11$), or for patients with and without major extracranial injury ($P = .59$), or for patients with and without preexisting medical conditions ($P = .64$).

Length of stay in inpatient rehabilitation

Length of inpatient rehabilitation stay was significantly inversely related to outcome, a bad outcome being associated with a longer stay in inpatient rehabilitation (Mann-Whitney test, $P = .001$). Median length of inpatient rehabilitation stay was 34 days (range, 3-127 days) for patients with a good outcome and 64 days (range, 2-315 days) for patients with a bad outcome. This variable was not incorporated into the regression model because of the high likelihood of confounding: within a healthcare system where there are no formal restrictions on length of stay, patients with persistent severe deficits leading eventually to worse outcome are likely to be the subject of more prolonged attempts at rehabilitation.

DISCUSSION

Our study supports previous findings[9] that delays between discharge from intensive care and admission to a rehabilitation unit are negatively associated with outcome a year after injury. Further investigation of the role of timely admission to rehabilitation after S-TBI is warranted, as this could thus be considered in itself as a potential treatment intervention to optimize outcome. Further studies replicating or expanding on these findings are needed. A traditional randomized controlled trial to assess early rehabilitation admission as a treatment intervention would, however, present significant

TABLE 5 *Stepwise logistic regression analysis with odds ratio for good outcome 1 year after injury (GOSE score >4)*[a]

	Unadjusted					Adjusted				
	n (missing)	Odds ratio	95% CI	*P*	Variation explained[b]	*n* (missing)	Odds ratio	95% CI	*P*	Variation explained[b]
Acute injury severity (CRASH composite[c])	83 (7)	0.98	0.96-1.01	0.21	2.6%	Excluded from model as not significant				
Preexisting medical conditions	86 (4)	0.98	0.41-2.33	0.96	0%					
Length of stay in intensive care	86 (4)	0.89	0.83-0.95	<0.001	31%	83 (7)	0.92	0.87-0.98	0.014	52%
Time between discharge from intensive care and admission to inpatient rehabilitation	85 (5)	0.97	0.95-0.99	0.01	15%		0.97	0.94-0.99	0.017	
Complications at 3 wk	85 (5)	0.04[d]	0.005-0.29	0.002	31%		0.058	0.006-0.60	0.017	

Abbreviations: CI, confidence interval; GCS, Glasgow Coma Scale; GOSE, Glasgow Outcome Scale Extended.
[a]Analysis of surviving patients followed up to 1 year who received inpatient rehabilitation ($n = 90$).
[b]Evaluated using the "CRASH model" (see text), which incorporates 10 acute prognostic variables: age, pupil reaction, acute GCS scores, country, presence or absence of major extracranial injury, presence or absence of 5 specified acute computed tomographic brain findings.
[c]Variation explained = Amount of variation explained by the model. (Model summary, Nagelkerke R^2).
[d]This odds ratio should be interpreted with caution due to the low number of cases in 1 cell (only 1 patient without complications had a bad outcome).

ethical and methodological challenges that may be difficult to overcome. Further studies with pragmatic designs appropriate to complex interventions,[18] for example, quasi randomization[9] and independent reviews of the existing evidence in the light of ethical and methodological realities, will be necessary to provide evidence-based foundations from which healthcare providers can develop optimal care for patients with S-TBI.

The organizational and structural challenges involved in allowing timely transfer to rehabilitation should not be underestimated: colocation of neurosurgical and early-phase rehabilitation units, increased staffing levels and training, and increased cross-disciplinary collaboration at all organizational levels are some areas for improvement. The challenge for healthcare professionals is to convey needs for complex interventions to healthcare commissioners.

From our data, it is not possible to determine whether short periods of a day or two between discharge from intensive care and admission to rehabilitation have a negative effect on outcome. Indeed, establishing that the patient is indeed neurosurgically and medically stable enough for transfer to rehabilitation seems a clinically reasonable strategy. However, the delays identified in this study were not short, with nearly as many patients waiting longer than a month ($n = 22$) as being transferred directly ($n = 23$). During the period between intensive care and inpatient rehabilitation, nearly a third of patients received care on units that would not be expected to have specific knowledge of recovery after TBI, for example, medical, geriatric, and general surgical wards. Some patients even received a short period of care in short-stay nursing homes before the initial rehabilitation stay.

Several patient- and injury-related factors may impact on the likelihood of timely transfer to rehabilitation and are possible confounders when considering relationship between delay in rehabilitation and outcome. These include coexisting medical problems, extracranial injuries, and post–acute complications. The presence of coexisting medical problems and major extracranial injury did not to have a significant relationship to outcome and were not significantly related to time between intensive care discharge and rehabilitation admission. Our findings did, however, add support to the role of post–acute complications in contributing to poorer outcome. The association between time to rehabilitation admission and outcome remained, however, significant even when complications were accounted for, as demonstrated by the logistic regression model. Interestingly, patients with complications did not have a significantly longer time between intensive care discharge and rehabilitation admission than those without complications.

Experience suggests that bottlenecks at certain stages, specifically delays in discharge from rehabilitation to appropriate social care, back up and prevent timely transfer of patients to inpatient rehabilitation. These delays may be undocumented and as such hidden, especially within a healthcare system where length of stay is not directly influenced by external funders: rehabilitation professionals informally have an understanding that available postrehabilitation care is in some cases suboptimal, and length of rehabilitation stay may therefore be extended on a case-to-case basis in an attempt to avoid negative effects from this. A defined chain of care for all patients suffering from S-TBI would contribute to optimization of care for all patients and support difficult discharge decisions and allow adequate follow-up. For some patients, a degree of continued medical instability (not requiring intensive care but exceeding that which can be safely managed in existing rehabilitation facilities) may be another contributing factor. A willingness to work across organizational boundaries (both within healthcare services and between health and social care) and to introduce central standards within fragmented health and social care systems is also essential to be able to counter such delays.

Given the evidence for effectiveness of rehabilitation,[19] it is positive that the majority of patients did eventually receive inpatient brain injury rehabilitation. A previous retrospective study[20] of a comparable group of patients with S-TBI receiving care in 2003-2004 at 3 neurosurgical centers in Sweden found that 17% were never admitted to rehabilitation. It is reassuring that only 7% of patients in this study did not receive inpatient rehabilitation.

The association between longer LOSIC and worse outcome can be understood by considering LOSIC as a proxy for the contributions of complications during the intensive care period and of secondary brain injury during the post–acute phase after S-TBI. A recent French study[21] also found LOSIC to be an independent predictor of outcome at 1 year. LOSIC is somewhat susceptible to local variations in policy regarding discharge from intensive care. However, pressure on intensive care beds is extremely high at all centers, leading to discharge as soon as clinically possible, and likely minimizing the contribution of local variations in policy.

Our hypothesis that acute prognostic factors would be associated with outcome at 1 year has face validity and has been insufficiently considered in previous studies focusing on rehabilitation. We incorporated such acute prognostic variable into our data collection primarily to allow evaluation of any additional contribution of delayed rehabilitation admission. We chose to use the CRASH model to predict the risk of unfavorable outcome from acute prognostic variables in order to provide a composite of known important negative factors related to injury severity and patient factors on day 1. This model was developed from a study of more than 10 000 patients worldwide and has been externally validated against another large data set of more than 8000 patients. It was thus unexpected that this composite was not significantly related to actual outcome in our patients. Several factors may explain this apparent paradox. Assessment of outcome was at 6 months in the CRASH model but at 1 year in our study. There is increasing evidence that recovery in fact continues after 6 months postinjury,[22] and the CRASH model may be missing improvements that have an important long-term impact on patients' functioning. Another factor is that the CRASH model included patients who died in the group with unfavorable outcome, and as our study evaluated the impact of rehabilitation care pathways, it was not meaningful to include patients who died before any rehabilitation was received. In addition, the CRASH study omitted any consideration of rehabilitation interventions when considering outcome and it is unknown what proportion of CRASH patients received any rehabilitation. If the proportion was low, then the CRASH findings may not be generalizable to patients who do receive timely rehabilitation. Timing of assessment of acute GCS scores for inclusion in the CRASH model is not specified, other than that an inclusion criteria was GCS score of 3 to 14 within the first 8 hours after injury. We included patients with a lowest unsedated GCS score of 3 to 8 within the first 24 hours, that is, over a somewhat longer time window, which could also lead to discrepancies. The CRASH model has also recently been shown to overestimate rates of unfavorable outcome in patients receiving intracerebral pressure–targeted neurosurgical treatment[23] (according to the Lund concept[24]), which is common in Sweden.

That the number of intervening care units between intensive care and inpatient rehabilitation was not associated with outcome was also unexpected. A high number of transfers could, however, have negative effects for both patients and relatives, due to lack of continuity, even if these were not associated with outcome per se.

The association between longer rehabilitation stay and worse outcome was expected. Reverse causality is likely in a healthcare system where length of stay is determined by individual clinicians. This may be due to both a real need for a longer period of rehabilitation (due to more severe deficits and slower improvement in patients with more severe injuries) and difficulty arranging another medium- to long-term discharge placement for these patients (due to persistent deficits and need for supervision, nursing care, and personal care).

A challenge for future development of an optimal chain of care for these patients is to develop smoother bridges between health and social care. The reality is that ongoing health and social care needs for these patients are closely interwoven over an extended period, with social and healthcare components so closely related that it is not possible (or meaningful) to separate out which is which. Provision of one component (health or social care) without consideration and collaboration regarding availability, delivery, and future planning with respect to the other may lead to wasted resources, suboptimal outcomes, and possibly even increased costs. Patients may have ongoing needs for specialized preventative care (eg, consistent use of orthotics, careful positioning as part of spasticity management, pressure sore prevention, appropriate bowel and bladder management) and some potential for continued slow improvement with continued slow-stream rehabilitation interventions in collaboration with social care providers. Within the Swedish tradition of high taxation and a strong welfare state, such difficulties are more likely to be due to weaknesses in interagency working than to differences in patients' premorbid socioeconomic status. Research on these aspects is needed, but the complexity is such that it may be difficult to capture all relevant aspects within traditional study designs.

LIMITATIONS

Because of the observational nature of the study, it is possible that other unknown, unmeasured variables could explain the observed association between care pathways and outcome and as such causality cannot be inferred. Further studies are needed. Although the prospective multicenter design, independent of care pathways, guards against selection bias, some eligible patients may have been missed if they were admitted to and discharged from intensive care between the authors' weekly contacts. This would likely impact primarily on recruitment of less severely injured patients. Completeness of follow-up (94%, 88% alive, 6% dead) is acceptable, especially given the necessity of obtaining consent from relatives at study start, due to injury-induced lack of capacity. Some degree of error is possible due to derivation of acute GCS scores from RLS scores for those patients not assessed with the GCS. This could have caused some slight overestimation of injury severity, particularly for patients with RLS score of 4 to 5. Proponents of the RLS in Sweden highlight its superior interrater reliability compared with the GCS and the avoidance of the GCS's problems with scoring for intubated patients. However, the exclusive use of the RLS does complicate application of established prognostic models, such as CRASH, and hampers direct application of evidence from studies of patients assessed with the GCS.

Clinicians who assessed outcome at 1 year were not systematically blinded to acute prognostic data, which is a source of potential bias and thus a study limitation. This type of study has many inherent logistical difficulties, requiring as it did follow up of patients over a very wide geographical area and over a period of time to minimize other sources of bias. Within reasonable study resources, it was not possible to arrange blinded follow-up at all locations and at the same time protect completeness of follow-up and interrater reliability. The time interval between the assessments at 3 months and 1 year can reasonably be expected to go some way to protect against this bias, as the relatively long time would make it unlikely that examiners would remember data from the acute phase at the time of follow-up. We acknowledge this limitation.

CONCLUSION

Greater time between intensive care discharge and rehabilitation admission was associated with bad outcome at 1 year. Longer duration of intensive care and the occurrence of post–acute complications were additional factors impacting on outcomes. Measures to establish timely rehabilitation admission may improve outcomes. Health economic studies on possible additional costs of delay to rehabilitation admission, both during the initial period of hospitalization and in terms of longer-term care requirements, would be of interest.

REFERENCES

1. Tagliaferri F, Compagnone C, Korsic M, Servadei F, Kraus J. A systematic review of brain injury epidemiology in Europe. *Acta Neurochir (Wien)*. 2006;148:255–268; discussion 268.
2. Polinder S, Meerding WJ, Van Baar ME, et al. Cost estimation of injury-related hospital admissions in 10 European countries. *J Trauma*. 2005;59:1283–1290.
3. Perel PA. Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients. *BMJ*. 2008;336:425–429.
4. Murray GD, Butcher I, McHugh GS, et al. Multivariable prognostic analysis in traumatic brain injury: results from the IMPACT study. *J Neurotrauma*. 2007;24:329–337.
5. Chen H, Epstein J, Stern E. Neural plasticity after acquired brain injury: evidence from functional neuroimaging. *PM & R*. 2010;2:S306–S312.
6. Turner-Stokes L, Disler PB, Nair A, Wade DT. Multidisciplinary rehabilitation for acquired brain injury in adults of working age. *Cochrane Database Syst Rev*. 2005:CD004170.
7. Jourdan C, Bayen E, Bosserelle V, et al. Referral to rehabilitation after severe traumatic brain injury: results from the PariS-TBI Study. *Neurorehabil Neural Repair*. 2013;27:35–44.
8. Hoffman JM, Donoso Brown E, Chan L, Dikmen S, Temkin N, Bell KR. Change in inpatient rehabilitation admissions for individuals with traumatic brain injury after implementation of the Medicare inpatient rehabilitation facility prospective payment system. *Arch Phys Med Rehabil*. 2012;93:1305–1312.
9. Andelic N, Bautz-Holter E, Ronning P, et al. Does an early onset and continuous chain of rehabilitation improve the long-term functional outcome of patients with severe traumatic brain injury? *J Neurotrauma*. 2012;29:66–74.
10. Engberg AW, Liebach A, Nordenbo A. Centralized rehabilitation after severe traumatic brain injury–a population-based study. *Acta Neurol Scand*. 2006;113:178–184.
11. Socialstyrelsen. Rehabilitering för personer med traumatisk hjärnskada [Rehabilitation for people with traumatic brain injury]–Landstingens rehabiliteringsinsatser. http://www.socialstyrelsen.se/publikationer2012/2012-12-27. Accessed May 30, 2013.
12. Starmark JE, Stalhammar D, Holmgren E. The Reaction Level Scale (RLS85). Manual and guidelines. *Acta Neurochir (Wien)*. 1988;91:12–20.
13. Starmark JE, Stalhammar D, Holmgren E, Rosander B. A comparison of the Glasgow Coma Scale and the Reaction Level Scale (RLS85). *J Neurosurg*. 1988;69:699–706.
14. Walther SM, Jonasson U, Gill H. Comparison of the Glasgow Coma Scale and the Reaction Level Scale for assessment of cerebral responsiveness in the critically ill. *Intensive Care Med*. 2003;29:933–938.
15. Tesseris J, Pantazidis N, Routsi C, Fragoulakis D. A comparative study of the Reaction Level Scale (RLS85) with Glasgow Coma Scale (GCS) and Edinburgh-2 Coma Scale (modified) (E2CS(M)). *Acta Neurochir (Wien)*. 1991;110:65–76.
16. Wilson JT, Pettigrew LE, Teasdale GM. Structured interviews for the Glasgow Outcome Scale and the extended Glasgow Outcome Scale: guidelines for their use. *J Neurotrauma*. 1998;15:573–585.
17. Levin HS, Boake C, Song J, et al. Validity and sensitivity to change of the extended Glasgow Outcome Scale in mild to moderate traumatic brain injury. *J Neurotrauma*. 2001;18:575–584.
18. Craig P. Developing and evaluating complex interventions: new guidance developed on behalf of the Medical Research Council. General. Published 2008. http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC004871. Accessed February 2, 2014.
19. Turner-Stokes L. Evidence for the effectiveness of multidisciplinary rehabilitation following acquired brain injury: a synthesis of two systematic approaches. *J Rehabil Med*. 2008;40:691–701.
20. Krakau K, Hansson A, Karlsson T, de Boussard CN, Tengvar C, Borg J. Nutritional treatment of patients with severe traumatic brain injury during the first six months after injury. *Nutrition*. 2007;23:308–317.
21. Jourdan C, Bosserelle V, Azerad S, et al. Predictive factors for 1-year outcome of a cohort of patients with severe traumatic brain injury (TBI): results from the PariS-TBI study. *Brain Inj*. 2013;27(9):1000–1007.
22. Katz DI, Polyak M, Coughlan D, Nichols M, Roche A. Natural history of recovery from brain injury after prolonged disorders of consciousness: outcome of patients admitted to inpatient rehabilitation with 1–4 year follow-up. *Prog Brain Res*. 2009;177:73–88.
23. Olivecrona M, Olivecrona Z. Use of the CRASH study prognosis calculator in patients with severe traumatic brain injury treated with an intracranial pressure-targeted therapy. *J Clin Neurosci*. 2013;20:996–1001.
24. Grande PO. The Lund concept for the treatment of patients with severe traumatic brain injury. *J Neurosurg Anesthesiol*. 2011;23:358–362.