Long-term and delayed functional recovery in patients with severe cerebrovascular and traumatic brain injury requiring tracheostomy

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OBJECTIVE Data on long-term functional recovery (LFR) following severe brain injury are essential for counseling of surrogates and for appropriate timing of outcome assessment in clinical trials. Delayed functional recovery (DFR) beyond 3–6 months is well documented following severe traumatic brain injury (sTBI), but there are limited data on DFR following severe cerebrovascular brain injury. The objective of this study was to assess LFR and DFR in patients with sTBI and severe stroke dependent on tracheostomy and tube feeding at the time of discharge from the intensive care unit (ICU).

METHODS The authors identified patients entered into their tracheostomy database 2008–2013 with sTBI and severe stroke, encompassing SAH, intracerebral hemorrhage (ICH), and acute ischemic stroke (AIS). Eligibility criteria included disease-specific indicators of severity, Glasgow Coma Scale score < 9 at time of tracheostomy, and need for tracheostomy and tube feeding at ICU discharge. Assessment was at 1–3 months, 6–12 months, 12–24 months, and 24–36 months after initial injury for presence of tracheostomy, ability to walk, and ability to perform basic activities of daily living (B-ADLs). Long-term functional recovery (LFR) was defined as recovery of the ability to walk or perform B-ADLs by the 24- to 36-month follow-up. Delayed functional recovery (DFR) was defined as progression in functional milestones between any 2 time points beyond the 1- to 3-month follow-up.

RESULTS A total of 129 patients met the eligibility criteria. Functional outcomes were available for 129 (100%), 97 (75%), 83 (64%), and 80 (62%) patients, respectively, from assessments at 1–3, 6–12, 12–24 and 24–36 months; 33 (26%) died by 24–36 months. Fifty-nine (46%) regained the ability to walk and 48 (37%) performed B-ADLs at some point during their recovery. Among survivors who had not achieved the respective milestone at 1–3 months, 29/58 (50%) were able to walk and 28/74 (38%) performed B-ADLs at 6–12 months. Among survivors who had not achieved the respective milestone at 6–12 months, 5/16 (31%) were able to walk and 13/30 (43%) performed B-ADLs at 12–24 months. There was no significant difference in rates of LFR or DFR between patients with sTBI and those with severe stroke.

CONCLUSIONS Among patients with severe brain injury requiring tracheostomy and tube feeding at ICU discharge, 46% regained the ability to walk and 37% performed B-ADLs 2–3 years after injury. DFR beyond 1–3 and 6–12 months was seen in over 30% of survivors, with no significant difference between sTBI and severe stroke.

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KEYWORDS acute brain injury; traumatic brain injury; stroke; tracheostomy; activities of daily living; trauma; vascular disorders

BRAIN injury caused by cerebrovascular disease, encompassing acute ischemic stroke (AIS), intracerebral hemorrhage (ICH), and subarachnoid hemorrhage (SAH), is a leading cause of long-term disability in the United States, with an estimated prevalence

of about 6.8 million cases among adult Americans.⁹ Traumatic brain injury (TBI) is another important cause of functional impairment, with an estimated US prevalence of TBI-related long-term disability of about 3.32 million.³⁶ Over 40% of patients hospitalized with TBI in

ABBREVIATIONS AIS = acute ischemic stroke; B-ADL = basic activity of daily living; CI = confidence interval; DFR = delayed functional recovery; FIM = Functional Independence Measure; GCS = Glasgow Coma Scale; GOS = Glasgow Outcome Scale; ICH = intracerebral hemorrhage; ICU = intensive care unit; IQR = interquartile range; LFR = long-term functional recovery; mRS = modified Rankin Scale; NIHSS = National Institutes of Health Stroke Scale; OR = odds ratio; SAH = subarachnoid hemorrhage; sTBI = severe TBI; TBI = traumatic brain injury.

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the United States in 2003 were left with long-term disability.³⁰ There are relatively limited data on long-term functional recovery (LFR) in survivors of severe brain injury of any cause who require intensive care unit (ICU) admission and remain dependent on an artificial airway and tube feeding at the time of discharge from the ICU. This is significant because of a common perception that these patients are unlikely to attain a meaningful long-term recovery.^{10,18} More recent studies of patients in the most severe strata of injury, including “poor-grade” SAH, suggest that a significant number may in fact attain a good LFR.^{11,17,24,35} A major potential confounder in some of these studies, however, is the influence of early reversible factors such as hydrocephalus, residual sedation following intubation, and seizures at onset, which may result in overestimation of the initial severity of injury.³⁴ Up to 30% of SAH patients classified as “poor grade” at admission may rapidly improve by at least 1 grade prior to surgery, following early ventricular drainage.²⁸ Contemporary data are essential for appropriate counseling of surrogate decision makers. Our primary aim, therefore, was to describe the trajectory of functional recovery over a 3-year period in a contemporary setting, in patients with severe brain injury, of both cerebrovascular and traumatic etiology, who did not demonstrate rapid neurological improvement following admission and required tracheostomy and artificial enteral nutrition at the time of ICU discharge.

The time period over which recovery may occur is also of critical importance. While most deaths following withdrawal of life-sustaining therapy occur in the ICU within 7 days of brain injury,^{22,32} it is not clear that an individual’s full potential for recovery can be reliably estimated during this time. The phenomenon of delayed functional recovery (DFR), with progression in functional recovery milestones beyond 3–6 months, is well documented following severe TBI (sTBI).^{1,11,13,17,19,21,25,29,31} There are, however, relatively limited published data on the incidence of DFR—and time taken to reach specific milestones of recovery—following severe stroke.^{17,23,24,35} Such information also guides the determination of appropriate time points for outcome assessment in clinical trials, which is typically performed 1–3 months after stroke,^{2,3,7,20,26} as against 6–12 months after sTBI, where DFR is expected.^{4,6,14} Delayed recovery beyond the time point of outcome assessment may not be captured, resulting in an incomplete assessment of the benefit of an intervention.^{11,35} An additional goal of this study was, therefore, to examine the incidence of DFR—the recovery of significant functional milestones beyond 3–12 months—in patients in the most severe strata of cerebrovascular injury and compare the findings to the incidence in sTBI.

Our specific objectives were to 1) describe rates, and the trajectory, of LFR to specific endpoints—tracheostomy decannulation, the ability to walk, and the ability to perform basic activities of daily living (B-ADLs)—over a period of 2–3 years, in patients in the most severe strata of brain injury requiring tracheostomy and tube feeding at ICU discharge; and 2) compare DFR beyond 3–12 months among patients with cerebrovascular brain injury (SAH, ICH, and AIS) and sTBI.

Methods

Approval for this study was obtained from the University of Michigan institutional review board.

Eligibility Criteria

We included patients with sTBI, SAH, ICH, and AIS entered into our neurointensive-care tracheostomy database over a 5-year period (2008–2013). Injury severity was established by: a) disease-specific indicator of severity the time of admission: Glasgow Coma Scale (GCS) score < 9 for sTBI, Hunt and Hess grade > 3 for SAH, National Institutes of Health Stroke Scale (NIHSS) score > 15 for AIS, and ICH score > 2 plus NIHSS score > 15 for ICH; b) need for tracheostomy; c) GCS score < 9 at the time of tracheostomy, and d) requirement for tracheostomy and artificial enteral nutrition at the time of ICU discharge. Patients who underwent tracheostomy were selected to avoid including patients whose initial severity may have been overestimated because of early reversible factors and to identify patients whose surrogates were likely committed to the provision of supportive care beyond the ICU stay. Patients were also required to have a GCS score < 9 off sedation at the time of tracheostomy; the purpose of this requirement was to select patients who required the procedure for their neurological disability and impaired consciousness rather than exclusively for respiratory reasons. The presence of significant respiratory failure was not an exclusion criterion, however, in patients with a GCS score < 9 off sedation at the time of the procedure. Patients with less than 1 month of follow-up were excluded. We included patients with 1 month of follow-up to capture subjects with unexpectedly rapid improvements in functional ability.

Data Source

The purpose of the tracheostomy quality-control database, established in 2008, was to track short- and long-term complications of all tracheostomies performed in the neuro-ICU.²⁷ Information on demographics, baseline disease severity, timing and type of tracheostomy (surgical vs percutaneous), individual performing the tracheostomy, short- and long-term complications, and tracheostomy decannulation was prospectively entered.

Tracheostomy Timing and Follow-Up

Timing of tracheostomy was at the discretion of the attending physician. Although a specific protocol was not in use, clinical practice favored performance of tracheostomy toward the end of the 1st week in patients judged likely to require an artificial airway for more than 3 weeks. This time period was considered sufficient to clarify the effect of easily reversible factors such as hydrocephalus, seizure at onset, and drugs used to facilitate endotracheal intubation. Subsequent systematic assessment of readiness for weaning (based on improvement in mental status and suctioning requirements) and downsizing, capping, and decannulation of tracheostomy was performed by the procedural team for the duration of the inpatient stay, although a specific protocol was not used. Responsibility for tracheostomy management and removal was assumed by

the providers at the rehabilitation or nursing facility the patient was transferred to following discharge.

Timing of percutaneous endoscopic gastrostomy (PEG) was highly variable; it was sometimes performed in the ICU around the time of tracheostomy and often deferred until a later time point, following several weeks of nutrition using transnasal feeding tubes. Given the variability in PEG tube use, and limited data available on timing of PEG tube removal following discharge, we were unable to systematically analyze long-term PEG tube usage and removal.

Functional Outcome Assessment

Functional endpoints were assessed at 1–3 months, 6–12 months, 12–24 months, and 24–36 months following injury. Follow-up beyond 36 months was included in the last category. Functional outcome assessment at discharge was not considered useful (as opposed to assessment at specific time periods from injury), since patients were frequently discharged to long-term acute care facilities soon after tracheostomy in order to facilitate weaning off mechanical ventilation. Patients were then often brought back to our institution for inpatient rehabilitation or for follow-up in the ambulatory setting. Specific endpoints assessed included the need for mechanical ventilation, presence of tracheostomy, ability to walk independently (with or without assistive device), and the ability to perform B-ADLs. We also assessed the GCS score at 1–3 months. This information was not part of the database and was abstracted from inpatient and clinic notes of physical therapists, occupational therapists, and physical medicine and rehabilitation providers. Independence in ambulation was defined as a Functional Independence Measure (FIM) score of 5 or greater for locomotion/household ambulation in the physical therapist's note.^{5,8} Independence with respect to B-ADLs was defined as an FIM score of 5 or greater for the specific tasks of dressing, eating, ambulation, toileting, and bathing in the occupational therapist's note.^{5,8} For patients deemed ineligible for therapy, functional status was estimated from neurosurgery and vascular neurology clinic notes. Patients judged to have insufficient documentation of functional ability related to the milestones of interest during a follow-up visit were deemed to not have had follow-up at that time point for the purposes of this study, even if a clinic visit did occur. Modified Rankin Scale (mRS)³³ and Glasgow Outcome Scale (GOS)¹⁵ scores were estimated at the time of each follow-up. We selected the ability to walk and perform B-ADLs as primary outcome measures, rather than the mRS or GOS score, because of the difficulty with determination of the ability to “look after one's own affairs without assistance” (mRS score 2 vs 3) and “... help with daily living” (GOS score 3 vs 4). “Independence in daily living” in these assessment scales—which is distinct from independence in B-ADLs, which we assessed as described above—requires the ability to manage finances, procure food, and/or be employed, all of which are difficult to determine from a retrospective review of documentation. The ability to walk and the ability to perform B-ADLs were therefore selected as outcome measures that could more consistently and accurately be extracted from a review of documentation in the medical record. These outcomes,

which approximately correspond to an mRS score of 3 (independent ambulation) and “upper severe disability” on the extended GOS (E-GOS) scale (independence within the home), also frequently serve as thresholds for favorable outcome in clinical trials of severe brain injury.^{7,14,26} Long-term functional recovery (LFR) was defined as recovery of the ability to walk or perform B-ADLs by the 24- to 36-month follow-up. Delayed functional recovery (DFR) was defined as progression in functional milestones between any 2 time points beyond the 1- to 3-month follow-up.

Statistical Analysis

Descriptive statistics included proportions with percentages for categorical data and medians with interquartile ranges (IQRs) for continuous data. We first described recovery to each major functional milestone—the ability to walk and to perform B-ADLs—at any time, as a proportion of the total initial cohort. All patients lost to follow-up were, therefore, assumed to have died or otherwise not attained the milestone for the purposes of this calculation, which yielded the *minimum* proportion of 1-month survivors who demonstrated recovery to that specific milestone at any subsequent time. We then also described the proportion of patients with follow-up (including patients known to have died in the denominator) who achieved each milestone at each time point of follow-up (Table 1). Delayed functional recovery was described as the proportion of patients who were alive but had not attained the functional outcome measure (walking or performance of B-ADLs) at a specific time point and had follow-up at the subsequent time period of follow-up, who had achieved the functional outcome measure at the subsequent time period of follow-up. The chi-square or Fisher exact test was used, as appropriate, to test the significance of association between categorical variables. The Mann-Whitney U-test was used to test for statistically significant differences in continuous variables between groups. A p value < 0.05 was the threshold for statistical significance. Multivariate analysis was performed to study predictors of LFR using binary logistic regression, with age, sex, diagnosis, and GCS score at time of tracheostomy as the explanatory variables. An odds ratio (OR) with 95% confidence interval (95% CI) was calculated for predictors. Multivariate analysis using the same explanatory variables was repeated for the response variable of DFR.

Results

A total of 144 patients met inclusion criteria. Fifteen were then excluded for having less than 1 month of follow-up. The remaining 129 patients were included in the analysis. The median age of these patients was 57 years (IQR 22 years), and 64 (50%) were women. The median GCS score at the time of tracheostomy was 7T (IQR 5–7). The median GCS score at 7 days after injury was 7T (IQR 5–9). The median number of days from injury to tracheostomy was 6 (IQR 4–8). The median APACHE-2 score was 19 (IQR 16–21). The diagnoses were as follows: SAH in 50 cases (39%), ICH in 33 (26%), sTBI in 27 (21%), and AIS in 19 (15%).

Information on follow-up, death, recovery to specific

TABLE 1. Milestones of functional recovery at different time periods of follow-up

Time Period & Diagnosis	Adequate Documentation of Functional Status*	Median No. of Days to Follow-Up (IQR)	Median mRS (IQR)	Median GOS (IQR)	Dead†	Mechanical Ventilation Required	Tracheostomy Present	Able to Walk Independently	Able to Perform B-ADLs
1–3 mos									
All diagnoses	129	44 (34–59)	4 (4–4)	3 (3–3)	20	5 (4%)	61 (47%)	23 (18%)	3 (2%)
sTBI	27	44 (38–59)	4 (3–4)	3 (3–3)	5	1 (4%)	12 (44%)	7 (26%)	2 (7%)
SAH	50	48 (34–62)	4 (3–4)	3 (3–3)	6	0 (0%)	20 (40%)	13 (26%)	1 (2%)
ICH	33	39 (33–56)	4 (4–4)	3 (3–3)	5	3 (9%)	20 (61%)	3 (9%)	0 (0%)
AIS	19	43 (34–65)	4 (4–4)	3 (3–3)	4	1 (5%)	9 (26%)	0 (0%)	0 (0%)
6–12 mos									
All diagnoses	97	226 (187–271)	3 (1–4)	3 (3–5)	31	0 (0%)	1 (1%)	47 (48%)	31 (32%)
sTBI	18	224 (212–264)	3 (1–4)	4 (3–5)	6	0 (0%)	1 (6%)	8 (44%)	5 (28%)
SAH	38	224 (177–257)	2 (1–3)	4 (3–5)	9	0 (0%)	0 (0%)	25 (66%)	19 (50%)
ICH	24	234 (175–326)	3 (2–4)	3 (3–4)	10	0 (0%)	0 (0%)	9 (38%)	5 (21%)
AIS	17	238 (208–320)	4 (3–4)	3 (3–3)	6	0 (0%)	0 (0%)	5 (29%)	2 (12%)
12–24 mos									
All diagnoses	83	472 (400–606)	2 (1–3)	4 (3–5)	32	0 (0%)	1 (1%)	41 (49%)	35 (42%)
sTBI	17	465 (412–604)	1 (1–2)	5 (3–5)	6	0 (0%)	1 (6%)	9 (53%)	9 (53%)
SAH	32	571 (407–658)	2 (1–3)	4 (3–5)	9	0 (0%)	0 (0%)	21 (66%)	17 (53%)
ICH	20	414 (394–533)	3 (2–4)	4 (3–4)	10	0 (0%)	0 (0%)	7 (35%)	6 (30%)
AIS	14	428 (371–568)	3 (2–4)	3 (3–5)	7	0 (0%)	0 (0%)	4 (29%)	3 (21%)
24–36 mos									
All diagnoses	80	992 (828–1078)	2 (1–3)	4 (3–5)	33	0 (0%)	1 (1%)	38 (48%)	34 (43%)
sTBI	17	845 (766–1204)	2 (1–2)	5 (3–5)	6	0 (0%)	1 (1%)	9 (53%)	9 (53%)
SAH	29	1009 (828–1075)	1 (1–2)	5 (4–5)	10	0 (0%)	0 (0%)	18 (62%)	17 (59%)
ICH	19	986 (828–1068)	3 (2–4)	3 (3–5)	10	0 (0%)	0 (0%)	7 (37%)	6 (32%)
AIS	15	1016 (839–1120)	4 (2–4)	3 (3–5)	7	0 (0%)	0 (0%)	4 (27%)	2 (13%)

Values represent numbers of patients unless otherwise indicated.

* Including death.

† Number of patients who were dead at the follow-up time specified (cumulative).

milestones, and median mRS and GOS scores at different time points is shown in Table 1.

Death and Follow-Up

Of 129 patients, 20 (16%) had died at 1–3 months of follow-up. Of the remaining 109, by 6–12 months, 32 (29%) were lost to follow-up and 11 (10%) had died. Of the remaining 66, at 12–24 months, a further 15 (23%) were lost to follow-up and 1 (2%) had died. Finally, at 24–36 months, of the remaining 50, 7 (14%) were lost to follow-up, and 1 (2%) had died.

Mechanical Ventilation and Need for Tracheostomy

Five (4%) patients were dependent on mechanical ventilation and 61 (47%) had a tracheostomy at the 1–3 month follow-up assessment. There was no significant difference between diagnoses in the need for mechanical ventilation ($p = 0.4$) or tracheostomy ($p = 0.34$) at this time point. At all subsequent time points, no patient was dependent on mechanical ventilation and only a single patient with sTBI required tracheostomy, present at 3 years. The median duration from tracheostomy to decannulation was 34 days (IQR 21–53 days).

mRS and GOS Scores

There was no statistically significant difference in either score at any time point between patients with sTBI and those with stroke. There was also no difference in median scores between pairings of individual diagnoses at any time point with the following exceptions. Compared to ICH patients, those with SAH had a significantly lower median mRS score at 6–12 months ($p = 0.031$) and 24–36 months ($p = 0.015$). Also, compared to AIS patients, those with SAH had a significantly lower median mRS score at 6–12 months ($p = 0.001$) and 24–36 months ($p = 0.008$), and a lower median GOS score at 6–12 months ($p = 0.016$) and 24–36 months ($p = 0.021$).

Ability to Walk Unassisted

Overall, 59 (46%) of the original cohort of 129 patients regained the ability to walk (at any time). There was no significant difference between sTBI and stroke at any time point. In multivariate analysis, younger age ($p = 0.000013$, OR 0.93, 95% CI 0.91–0.96), male sex ($p = 0.02$, OR 3.07, 95% CI 1.20–7.89), higher GCS score at time of tracheostomy ($p = 0.016$, OR 1.50, 95% CI 1.08–2.08), and a diagnosis of SAH ($p = 0.019$, OR 4.63, 95% CI 1.29–16.56).

TABLE 2. Delayed functional recovery: ability to walk

Description	All Diagnoses	sTBI	SAH	ICH	AIS
Alive but unable to walk unassisted at 1–3 mos, follow-up available at 6–12 mos	58	7	21	17	13
Unable to walk unassisted at 1–3 mos but able to walk by 6–12 mos' follow-up (% of survivors w/ follow-up)	29 (50%)	3 (43%)	14 (67%)	7 (41%)	5 (38%)
Alive but unable to walk unassisted at 6–12 mos, follow-up available at 12–24 mos	16	4	4	3	5
Unable to walk unassisted at 6–12 mos but able to walk by 12–24 mos' follow-up (% of survivors w/ follow-up)	5 (31%)	2 (50%)	2 (50%)	0 (0%)	1 (20%)
Alive but unable to walk unassisted at 12–24 mos, follow-up available at 24–36 mos	9	1	2	3	3
Unable to walk unassisted at 12–24 mos but able to walk by 24–36 mos' follow-up (% of survivors w/ follow-up)	1 (11%)	0 (0%)	0 (0%)	1 (33%)	0 (0%)

were independent predictors of the ability to walk at any time. Three (33%) of 9 patients with a GCS score of 3T off all sedation at the time of tracheostomy recovered the ability to walk at any time. Four of 8 patients with a GCS motor score < 4 at 1–3 months' follow-up had subsequent follow-up. All but one of these had died. The last patient, who had sTBI, was in a minimally conscious state 3 years following injury.

Ability to Perform B-ADLs

Overall, 48 (37%) of the original cohort of 129 patients regained the ability to perform B-ADLs at any time point. Patients with sTBI were more likely to perform B-ADLs than those with stroke at 1–3 months ($p = 0.049$), but there was no statistically significant difference at any other time point. In multivariate analysis, younger age ($p = 0.000048$, OR 0.94, 95% CI 0.92–0.97) and higher GCS at time of tracheostomy ($p = 0.019$, OR 1.49, 95% CI 1.07–2.07) were independent predictors of the ability to perform B-ADLs at any time. Two (22%) of 9 patients with a GCS score of 3T off all sedation at the time of tracheostomy recovered the ability to perform B-ADLs at any time.

Delayed Functional Recovery

Overall, DFR of the ability to walk occurred in 35 (27%) of the original cohort of 129 patients and ability to perform B-ADLs in 43 (33%). The proportion of survivors with follow-up in each diagnosis category who demonstrated DFR in the ability to walk between specific time periods is shown in Table 2, and the proportion

who demonstrated DFR in ability to perform B-ADLs is shown in Table 3. There was no significant difference in rates of DFR between the broad categories of sTBI and stroke at any time point. In multivariate analysis, younger age ($p = 0.003$, OR 0.96, 95% CI 0.93–0.99) and a diagnosis of SAH ($p = 0.03$, OR 4.47, 95% CI 1.15–17.41) were independent predictors of DFR of the ability to walk at any time, while younger age ($p = 0.001$, OR 95% CI 0.96, 0.93–0.98) and a diagnosis of SAH ($p = 0.03$, OR 3.97, 95% CI 1.16–13.60) were independent predictors of DFR of the ability to perform B-ADLs at any time.

Discussion

In this retrospective longitudinal study of patients with acute severe brain injury who were dependent on an artificial airway and artificial nutrition at the time of transfer out of the ICU, 46% of the original cohort regained the ability to walk by 24–36 months after the initial injury, while 37% regained the ability to perform B-ADLs. There was no significant difference in rates of LFR between patients with cerebrovascular injury and those with traumatic injury. Among survivors, delayed functional recovery beyond 1–3 months (50% and 38%, respectively, for the ability to walk and perform B-ADLs)—and beyond even 6–12 months (31% and 43%, respectively, for the ability to walk and perform B-ADLs)—was common, with rates that did not differ significantly between patients with traumatic and cerebrovascular injury. Patients with SAH were overall more likely to demonstrate both LFR and DFR, compared to patients with ICH or AIS. Other predictors

TABLE 3. Delayed functional recovery: ability to perform B-ADLs

Description	All Diagnoses	sTBI	SAH	ICH	AIS
Alive but unable to perform B-ADLs at 1–3 mos, follow-up available at 6–12 mos	74	11	31	19	13
Unable to perform B-ADLs at 1–3 mos but able to perform B-ADLs by 6–12 mos' follow-up (% of survivors w/ follow-up)	28 (38%)	3 (27%)	18 (58%)	5 (26%)	2 (15%)
Alive but unable to perform B-ADLs at 6–12 mos, follow-up available at 12–24 mos	30	6	10	6	8
Unable to perform B-ADLs at 6–12 mos but able to perform B-ADLs by 12–24 mos' follow-up (% of survivors w/ follow-up)	13 (43%)	4 (67%)	4 (40%)	2 (33%)	3 (38%)
Alive but unable to perform B-ADLs at 12–24 mos, follow-up available at 24–36 mos	13	1	4	4	4
Unable to perform B-ADLs at 12–24 mos but able to perform B-ADLs by 24–36 mos' follow-up (% of survivors w/ follow-up)	2 (15%)	0 (0%)	1 (25%)	1 (25%)	0 (0%)

of LFR were, as may be expected, younger age and higher GCS score at the time of tracheostomy. Younger age was also a predictor of DFR. Strengths of our study include the length of follow-up (2–3 years) and the eligibility criteria. These criteria were designed to minimize overestimation of severity of injury as a result of early reversible factors and to select patients whose surrogates were likely committed to the delivery of supportive care for a significant period of time. This addresses a concern about early reversible factors leading to an overestimation of disease severity in prior studies, particularly in patients with poor-grade SAH.³⁴ In up to 30% of SAH cases initially classified as poor grade, the patients' condition may rapidly improve by at least 1 grade with early ventricular drainage, prior to clipping or coiling.²⁸

Our findings are significant for several reasons. First, they reinforce the evidence that therapeutic nihilism in the context of severe brain injury may not be justified,^{10,18} provided the ability to perform B-ADLs and ambulate independently are valued as meaningful outcomes by patients, families, and society as a whole.¹² Our data are potentially valuable for physicians who routinely counsel surrogates of such patients. Since these discussions typically lead to decisions on the continuation or withdrawal of life support measures, the importance of objective, data-driven counseling cannot be overstated. In our experience, families value estimates of both the likelihood and timeline of recovery to the specific milestones evaluated in our study. It is useful, for example, to inform families that most patients who survive their severe brain injury undergo tracheostomy decannulation within 6 months, and generally sooner (median 34 days in our study), when a systematic approach to weaning is used. It is essential to acknowledge the uncertainty involved and the wide range of possible outcomes for an individual patient. It is also important to ascertain, to the best extent possible, the degree of functional recovery an individual patient may consider meaningful while discussing these possible outcomes. Patients' surrogates should be counseled that functional recovery may proceed very slowly in patients with all forms of severe brain injury, sometimes extending beyond a year from injury. The high incidence of DFR following severe stroke also has implications for outcome assessment in clinical trials. Since DFR after sTBI is well described,^{1,11,13,17,19,21,29,31} outcome assessments in clinical trials involving patients with sTBI are routinely performed at 6 months or a year,^{4,6,14} in contrast to clinical trials for stroke, where outcome assessments are typically performed at 3 months.^{2,3,7,20} Our findings, and the findings of other investigators,^{23,24,35} suggest that routine outcome assessment at 6–12 months should be considered in clinical trials of interventions, such as decompressive craniectomy and tracheostomy, performed in patients with severe stroke. The investigators of the ongoing SETPOINT-2 clinical trial of early vs late tracheostomy in stroke have, for this reason, chosen a 6-month primary outcome measure (NCT02377167; clinicaltrials.gov).

Other investigators have reported findings consistent with ours. In a study of 36 patients in a vegetative or minimally conscious state who were admitted to a special rehabilitation center, over 40% regained the ability perform B-ADLs at 1 year.¹⁷ In one study of patients with sTBI who

required decompressive craniectomy, 48% demonstrated improvement in the GOS score between 6 and 18 months.¹¹ In the Copenhagen Stroke Study, AIS and ICH patients with mild or moderate injury demonstrated a plateau in functional recovery within 8.5 and 13 weeks, respectively, whereas patients with severe AIS/ICH continued to demonstrate functional recovery by 20 weeks.¹⁶ Studies of patients with poor-grade SAH enrolled in the Barrow Ruptured Aneurysm Trial (BRAT)³⁵ and from the University of California, San Francisco,²⁴ have shown rates of functional recovery of 61% and 57%, respectively, between discharge and 6 months. In BRAT, 18% demonstrated DFR between 6 and 12 months, and 19% demonstrated DFR between 12 and 36 months. Another study of poor-grade SAH from Columbia University found improvements in multiple domains between 3 and 12 months after injury.²³ While these studies, like ours, demonstrated the potential for LFR and DFR in poor-grade SAH, a key distinction is that all patients judged to have a poor grade at admission were included in these studies, while patients in our cohort had both a severe initial grade of injury and also did not show rapid improvement following resolution of rapidly reversible factors in the first few days.

Our study has several limitations. The assessments of functional outcome were retrospective and restricted to relatively crude measures—the ability to walk and perform B-ADLs. We could not assess measures of cognitive outcome or quality of life. Our findings are, therefore, most relevant to patients and surrogates who consider the ability to perform B-ADLs and ambulate to represent an acceptable quality of life. There was significant loss to follow-up, as might be expected in a retrospective study. Assuming the most pessimistic outcome for all patients who were lost to follow-up (death or failure to attain the specific functional milestone), however, 46% of the original cohort of 129 patients regained the ability to walk and 37% regained the ability to perform B-ADLs at some point in a 3-year period following injury. Similarly, assuming every patient lost to follow-up had a bad outcome, DFR was seen in 27% of the original cohort of 129 for the ability to walk, and 33% for the ability to perform B-ADLs. Some patients with severe brain injury may have undergone early withdrawal of life-sustaining therapy and would therefore not have been included in our study. Nevertheless, our focus was on patients whose surrogates had committed to the provision of supportive care beyond the ICU stay. Tracheostomy was performed a median of 6 days after injury. Patients were required to have a GCS score < 9 at the time of tracheostomy to be included in the study, however, and the median duration from tracheostomy to decannulation, with a systematic approach to weaning assessment, was 34 days, suggesting that in general tracheostomy was not performed prematurely and disease severity was not overestimated. We included patients with 4 different types of severe brain injury in our study; therefore the applicability of our findings to individual diseases—particularly AIS, which was relatively underrepresented—is limited. While our study does demonstrate that both LFR and DFR occur commonly among severely injured patients requiring tracheostomy in all 4 disease states, larger cohorts with prospective evaluation of outcomes are necessary to more

accurately establish specific rates of recovery in individual diseases. Ongoing clinical trials of tracheostomy in severe brain injury may prove useful in this regard (NCT02377167; clinicaltrials.gov). Our data may be most applicable to SAH, as an individual disease state, since we had a plurality of patients with this condition in our study ($n = 50$). Since SAH patients overall were more likely to demonstrate both LFR and DFR compared to patients with ICH or AIS, and SAH accounted for most cases of cerebrovascular disease (49%) in our study, much of the equivalence in LFR and DFR between sTBI and stroke may have been driven by this population. It is nevertheless noteworthy that a substantial proportion of AIS and ICH patients also demonstrated LFR and DFR (Tables 1–3). Finally, documentation was insufficient for us to estimate time to removal of feeding tubes.

In conclusion, among patients with severe brain injury requiring tracheostomy and tube feeding at the time of ICU discharge, about 46% had regained the ability to walk and 37% had regained the ability to perform B-ADLs 2–3 years after injury. Delayed functional recovery beyond 1–3 months as well as beyond 6–12 months was common, with no significant difference between traumatic and cerebrovascular etiologies.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Rajajee. Acquisition of data: Rajajee, Wabl, Williamson. Analysis and interpretation of data: Rajajee, Wabl, Pandey. Drafting the article: Rajajee, Wabl. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Rajajee. Statistical analysis: Rajajee, Wabl. Administrative/technical/material support: Rajajee. Study supervision: Rajajee, Pandey.

Supplemental Information

Previous Presentations

Early results from this study were presented at the Neurocritical Care Society 11th annual meeting, October 2013, Philadelphia, PA.

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