ORIGINAL ARTICLE

Mortality Over Four Decades After Traumatic Brain Injury Rehabilitation: A Retrospective Cohort Study

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ABSTRACT. Harrison-Felix CL, Whiteneck GG, Jha A, DeVivo MJ, Hammond FM, Hart DM. Mortality over four decades after traumatic brain injury rehabilitation: a retrospective cohort study. Arch Phys Med Rehabil 2009;90:1506-13.

Objective: To investigate mortality, life expectancy, risk factors for death, and causes of death in persons with traumatic brain injury (TBI).

Design: Retrospective cohort study.

Setting: Used data from an inpatient rehabilitation facility, the Social Security Death Index, death certificates, and the U.S. population age-race-sex–specific and cause-specific mortality rates.

Participants: Persons with TBI (N=1678) surviving to their first anniversary of injury admitted to rehabilitation from an acute care hospital within 1 year of injury between 1961 and 2002.

Interventions: Not applicable.

Main Outcome Measures: Vital status, standardized mortality ratio, life expectancy, cause of death.

Results: Persons with TBI were 1.5 times more likely to die than persons in the general population of similar age, sex, and race, resulting in an estimated average life expectancy reduction of 4 years. Within the TBI population, the strongest independent risk factors for death after 1 year postinjury were being older, being male, having less education, having a longer hospitalization, having an earlier year of injury, and being in a vegetative state at rehabilitation discharge. After 1 year postinjury, persons with TBI were 49 times more likely to die of aspiration pneumonia, 22 times more likely to die of seizures, 4 times more likely to die of pneumonia, 3 times more likely to commit suicide, and 2.5 times more likely to die of digestive conditions than persons in the general population of similar age, sex, and race.

Conclusions: This study demonstrated life expectancy after TBI rehabilitation is reduced and associated with specific risk factors and causes of death.

Key Words: Brain injuries; Cause of death; Life expectancy; Mortality; Rehabilitation.

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LiFE EXPECTANCY AFTER major traumatic events is of interest to a wide range of audiences, including those who survive the trauma, sometimes with lifelong disabilities, their family members, care providers, insurers, and legal systems. TBI is a leading cause of disability in the United States.¹ Of the 1.59 million Americans who sustain TBI annually,¹ 15% are admitted to acute hospitals,¹⁻³ and 20% of those hospitalized require inpatient rehabilitation.⁴⁻⁷ Several studies on mortality during the first months after injury have shown an association with the effects of the initial injury itself, concomitant trauma, and treatment received.⁸⁻²⁰ However, fewer studies on life expectancy after TBI have focused on longer-term follow-up, particularly those who are discharged from inpatient rehabilitation and survive through the first year postinjury.²¹

The studies of longer-term survival have tended to involve registries of military veterans.²²⁻²⁶ specific states or counties, ²⁷⁻³² or individual clinics.³³⁻³⁷ We previously reported on mortality risk factors, life expectancy, and causes of death in the TBI Model Systems.^{38,39} Studies comparing death rates of persons with TBI with the general population have found higher rates among those with TBI, though the reduction in life expectancy depends largely on the severity of residual disability.²¹ As in the general population, studies reporting the causes of death after TBI often find that diseases of the circulatory system account for the largest number of deaths, but that the rates are not significantly higher than expected for the general population.^{26,30,39} Similarly, persons with TBI have been reported to be at increased risk of death from seizure^{23,25,26,30,35,39,40} and pneumonia.^{30,36} While some studies have found TBI to increase the risk of suicide^{33,36,41} and meningitis,³³ others have not.^{23,24,30,34}

Risk factors for later mortality have also been suggested in the literature. As for the general population, older age and male sex are associated with increased mortality. A seizure disorder is one of the earliest factors to be identified as significantly associated with longer-term mortality after TBI^{22,26,42}; however, this has not been a universal finding.²³ More recently, several studies have emphasized functional status as being a major determinant of life expectancy after TBI.^{30,31} Other factors that have been studied include alcohol use, time since injury, year of injury, communication and cognitive functions, education, initial TBI severity (eg, Glasgow Coma Scale score, Abbreviated Injury Scale, duration of loss of consciousness, duration of posttraumatic amnesia), and

List of Abbreviations

CI	confidence interval
GOS	Glasgow Outcome Scale
ICD-9-CM	International Classification of Diseases–9th
	Revision–Clinical Modifications
SMR	standardized mortality ratio
SSDI	Social Security Death Index
TBI	traumatic brain injury

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maladaptive behaviors (eg drug use, criminal behavior).²¹ The causal relationships between these various factors can be complicated, and the strengths of the associations between individual factors can vary substantially depending on what other factors are considered in the analysis. Calendar year of injury has not been found to be a risk factor in 2 studies where it was reported.^{31,34}

The focus of this study was to investigate long-term mortality in a large cohort of persons who incurred a TBI over the last 40 years and received inpatient rehabilitation. The study hypotheses were the following: (1) TBI increases mortality in persons with TBI completing inpatient rehabilitation and surviving to 1 year postinjury over the last 40 years, relative to the general population, (2) the risk of death is greater in certain TBI subgroups—those who are less functional and older at injury, and (3) the causes of death do not match the causes in the general population. The unique contribution of this study is the 40-year follow-up period of persons with TBI who received rehabilitation and the ability to determine how the findings compare with prior studies and whether survival rates have improved in recent decades.

METHODS

The Institutional Review Board for Craig Hospital, HCA-HealthONE Institutional Review Board, approved this study.

Data Sources

Craig Hospital. A total of 1678 persons were identified for this study. These consisted of persons with TBI, admitted to Craig Hospital for inpatient rehabilitation from an acute care hospital, within 1 year of injury, between 1961 and 2002, who survived to their first anniversary of injury, and were 16 years of age or older at the time of injury. Craig Hospital is a freestanding private nonprofit adult rehabilitation hospital with 93 licensed beds that specializes exclusively in the treatment of patients with spinal cord injury or TBI. Since 1956, Craig has treated over 23,000 patients, and it treats approximately 126 new patients with TBI each year. Persons with TBI are generally admitted from regional (Colorado and surrounding states) acute care hospitals, and must be at a level of recovery to participate in an active inpatient rehabilitation program that includes a comprehensive range of physician-led interdisciplinary rehabilitation services.

TBI was defined as injury to brain tissue caused by an external mechanical force as evidenced by loss of consciousness caused by brain trauma, posttraumatic amnesia, or objective neurologic findings that can be reasonably attributed to TBI on physical or mental status examination.43 For case-finding purposes, the Craig Hospital Business Accounting System was used to identify all potential patients with a diagnosis of a brain injury/disorder or brain injury/ spinal cord injury dual diagnosis using ICD-9-CM diagnostic coding. There were 3172 potential cases identified, and each person's medical record was reviewed by a trained registered health information technologist to determine whether the person fit the study inclusion criteria. A total of 1678 persons were found to have met all the study criteria, and all demographic and injuryrelated information for the study was available and abstracted from the hospital medical record. Most of the cases that were excluded were found to be brain injury of nontraumatic origin (eg, stroke).

The Social Security Death Index. The Social Security Administration's Death Index⁴⁴ was used to determine the vital status of persons in the study as of December 31, 2003. The SSDI was available through the World Wide Web at http://www.ancestry.com.⁴⁴ The sensitivity and specificity of the

SSDI in determining vital status in various non-TBI adult populations range from 88% to 99%.⁴⁵⁻⁴⁷ In a study conducted using the TBI Model Systems National Database, the SSDI had a sensitivity of 89% and a specificity of 100%, indicating that the SSDI was a relatively good source of vital status information.³⁸ All persons who died were identified using the SSDI. Persons not found in the SSDI were assumed to be alive as of December 31, 2003.

Death certificates. Death certificates were used in this study to determine the cause of death of those who were identified as having died. All causes of death listed on each certificate were coded using the ICD-9-CM.⁴⁸ In addition, the primary cause of death for each case was assigned an ICD-9-CM code, using standardized guidelines established for this study adapted from DeVivo and used in previous survival studies.^{39,49} Of note, if the death certificate indicated the cause of death as the original event leading to the TBI, then the cause of death was coded as unknown, unless other information was available.

Follow-Up

For study hypothesis testing, survival was measured beginning at the 1-year postinjury anniversary; with follow-up of study subjects terminated on December 31, 2003. Only deaths occurring after the 1-year postinjury anniversary and before January 1, 2004, were included. The exclusion of early deaths in the first year was designed to focus the research on longerterm deaths rather than on deaths occurring during or soon after initial acute and rehabilitation hospitalization.

Statistical analysis. Descriptive statistics (means for continuous variables and proportions for categorical variables) were used to characterize the overall study population. An important use of mortality data is to compare 2 or more populations that differ in regard to a particular characteristic, such as TBI, while holding constant other characteristics, particularly age, which may account for observed differences in mortality. One approach used by epidemiologists is to compare the observed number of deaths to the expected number of deaths based on a reference population.⁵⁰ The expected number of deaths in the absence of TBI was calculated by applying mortality rates by age, sex, race, and cause of death published by the federal government^{51,52} for the calendar year 1992 (the median person-years of follow-up in the study) to each year of follow-up for each person in the study and summing the result. The SMR for this TBI population was then calculated as the ratio of actual to expected deaths. Statistical significance of the SMR was determined by calculating its 95% CI based on a normal distribution, which was considered significant if it did not contain 1.0.53

This same approach was used to calculate the SMRs for selected causes of death for the causes accounting for the greatest proportion of deaths in this study, or those identified in the literature as potentially being greater than expected for persons with TBI. Statistical significance of these cause-specific SMRs was determined by calculating their 95% CI on the basis of the Poisson distribution, which was considered significant if it did not contain 1.0.⁵⁴

Comparative life expectancy with and without TBI by age, sex, and race was also estimated by applying the overall SMR to the age-sex-race–specific mortality rates published by the federal government⁵⁵ for the most current year available at the end of the study (calendar year 2002) for those without TBI, using the methodology described by DeVivo and applied in previous survival studies.^{39,49}

Finally, Cox proportional hazards regression analysis was used to assess the impact of each potential risk factor on length of survival. Demographic factors assessed in the analyses were

 Table 1: Demographic Characteristics of Study Population

Characteristics	No.	Percent			
Mean age at injury, 32y					
Sex, male	1279	76			
Race/ethnicity, white	1482	88			
Occupations status at rehabilitation admission					
Employed	1216	73			
Student	306	18			
Other	150	9			
Education level at rehabilitation admission					
Less than high school	328	21			
High school/GED	536	34			
Greater than high school	721	45			
Cause of injury					
Vehicle	1221	73			
Falls	291	17			
Other	165	10			
Year of Injury					
1961–1979	220	13			
1980–1989	291	17			
1990–1999	815	49			
2000–2002	352	21			
Payor source					
No fault	596	36			
Commercial	494	29			
Worker's compensation	272	16			
Medicare/Medicaid	200	12			
HMO/self/other	116	7			
Discharge disposition					
Home	1264	75			
Nursing home	212	13			
Other	202	12			
Duration of unconsciousness					
None	129	8			
1d	495	32			
2–7d	360	23			
8–129d	568	37			
GOS at rehabilitation discharge					
Good recovery	25	2			
Moderate disability	405	24			
Severe disability	1212	72			
Vegetative	33	2			
Mean acute care length of stay=42d					
Mean rehabilitation length of stay=55d					

Abbreviations: GED, General Education Development; HMO, Health Maintenance Organization.

age at injury, sex, race, and level of education and employment status at rehabilitation admission. Injury-related risk factors included calendar year and cause of injury, and duration of loss of consciousness. Other potential risk factors included state of residence at the time of rehabilitation admission, acute and rehabilitation hospital length of stay, third-party sponsor of care, place of discharge after rehabilitation, and the GOS⁴² score at rehabilitation discharge. The GOS is a system for classifying overall patient disability after a TBI. The original scale has 5 outcome categories: good recovery, moderate disability, severe disability, vegetative state, and dead. For the risk factor analyses, GOS was dichotomized into "vegetative state" and "all other" excluding dead, because all those in the study were alive at rehabilitation discharge.

Bivariate Cox models including age at injury (the strongest risk factor) with each remaining separate risk factor were used as a

screen for inclusion in the final analysis. Factors with *P* less than .10, suggesting age-independent association with mortality, were eligible for inclusion in the final multivariate analysis. Because our primary aim was a mortality prediction model, rather than focusing on the validity of a particular regression coefficient, a forward stepwise selection procedure was used to determine the final model, with *P* less than .05 required for inclusion of any factor.⁵⁶ In addition, the 95% CIs of the adjusted relative risk of each significant factor were calculated.

RESULTS

Table 1 contains the characteristics of the study sample. Among the 1678 persons included in the study, a total of 16,599 person-years of life with TBI data were accumulated for analysis, with the length of follow-up ranging from 16 days to 40 years beyond the first anniversary of injury. The average age was 32 years, with 76% male and 88% white. There were 73% employed at rehabilitation admission, with 79% having completed high school. Most were injured in a motor vehicle collision. The average length of acute and rehabilitation hospitalization combined was 97 days, with three quarters being discharged home. The average duration of unconsciousness after injury was 12 days, with almost three quarters having severe disability at rehabilitation discharge.

There were 130 deaths occurring after 1 year postinjury for a mortality rate of 7.7%. The length of time between injury and death ranged from 381 days to 35 years, with a median interval of 11 years. The expected number of deaths in the absence of TBI given the length of time each person was followed was 85.83 for all persons included in the study. Because 130 deaths were observed, the SMR was 1.51 (95% CI=1.25–1.78), indicating that persons with TBI were one and a half times more likely to die than persons of comparable age, sex, and race from the general population.

Table 2 contains the estimated life expectancy in years (calculated on the assumption of a constant SMR of 1.51 in persons with TBI), with and without TBI for selected age, sex, and race groupings. Assuming survival to at least the first anniversary of injury, life expectancy was shortened thereafter between 3 and 6 years depending on age at injury, race, and sex. On average, TBI appeared to reduce life expectancy in this cohort by about 4 years.

Results of the bivariate Cox regression analyses (controlling only for age at injury as the strongest predictor) indicated that being male, not being employed and having less education at rehabilitation admission, longer hospitalization, earlier year of injury, longer duration of unconsciousness, and being in a vegetative state at rehabilitation discharge (measured by the GOS) were associated with an increased risk of death, independent of age, after 1 year post-TBI.

All of these variables were then entered into a multivariate Cox regression analysis; older age, being male, having less education at rehabilitation admission, longer hospitalization, earlier year of injury, and being in a vegetative state at rehabilitation discharge remained in the model as significant risk factors once the effects of all other factors were controlled (table 3). Results indicated that there was an 8% increased risk of death for each additional year of age at injury, and a 3% lower risk of death for every later calendar year of injury (or a 30% improvement in mortality with each later decade of the study period). Men were 3 times more likely to die than women. Persons who had completed high school, trade school, or some college at the time of rehabilitation admission were at 26% lower risk of death than those who did not complete high school. There was a 0.5% increased risk of death for each additional day of hospitalization (or a 15% increased risk of

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Table 2: Estimated	rears of Life Expect	ancy by Selected Ag	ges, with and without I	raumatic Brain injury*

MCAL

	White			Black			Hispanic							
		Men		Women		Men		Women		Women		Men	v	Vomen
Age	TBI	Non-TBI	TBI	Non-TBI	ТВІ	Non-TBI	TBI	Non-TBI	TBI	Non-TBI	ТВІ	Non-TBI		
20	50	54	55	59	43	49	50	55	52	57	57	62		
30	40	45	45	49	35	40	41	46	43	48	48	52		
40	31	36	36	40	26	31	32	36	34	38	38	43		
50	23	27	27	30	19	23	24	28	25	29	29	33		
60	15	19	18	22	13	16	16	20	17	21	21	24		
70	9	12	11	14	8	11	10	13	11	14	13	16		

*Assuming a constant standardized mortality ratio of 1.51 among persons with TBI.

death with each additional month of hospitalization). Finally, those in a vegetative state at rehabilitation discharge were 3 times more likely to die than those with better overall outcomes. The overall log likelihood chi-square test statistic for the final model is 187 with 7 df and significant at P less than .001.

The largest proportion of deaths was secondary to circulatory conditions (25%). The next largest proportion of deaths occurred secondary to respiratory conditions (22%), with 9% of all deaths a result of aspiration pneumonia and 8% a result of other types of pneumonia. The next largest proportion of deaths was attributable to external causes of injury (18%), with half a result of unintentional injuries and half secondary to suicide. In addition, 14% of all deaths were caused by neoplasms, 8% of deaths resulted from digestive system conditions, and 5% of all deaths were seizure-related. Twelve of the 130 deaths identified had an unknown cause of death because there was no death certificate, or the cause of death was attributed to the original injury leading to the TBI.

Table 4 contains the cause-of-death-specific SMRs, indicating that the number of deaths secondary to suicide, aspiration pneumonia, other pneumonias, digestive conditions, and seizures among persons with TBI was greater than expected

Table 3: Risk Factors for Death After Traumatic Brain Injury From Cox Regression Multivariate Analysis

Characteristics (n=1581)	Relative Risk	95% CI
Age at injury for each additional year of		
age	1.084	1.068–1.099
Year of injury for each additional		
calendar year	0.968	0.944–0.992
Male sex	3.136	1.661–5.923
Education at rehabilitation admission		
 Less than high school (reference 		
group)	1	NA
 High school/trade school/some 		
college	0.739	0.471–1.160
 College degree 	0.334	0.169–0.661
Days of acute and rehabilitation		
hospitalization for each additional		
day of hospitalization	1.005	1.003–1.008
GOS		
 Good recovery, moderate disability, and severe disability (reference 		
group)	1	NA
Vegetative state	2.903	1.274–6.612

Abbreviation: NA, not applicable.

compared with the number of deaths in the general population of similar age, sex, and race, and these differences were statistically significant. Persons with TBI were about 49 times more likely to die of aspiration pneumonia, 22 times more likely to die of seizures, 4 times more likely to die of pneumonia, about 3 times more likely to commit suicide, and 2.5 times more likely to die of digestive conditions than persons in the general population of similar age, sex, and race.

DISCUSSION

Risk of Mortality and Life Expectancy After Traumatic Brain Injury

This study found that persons with TBI were 1.5 times more likely to die than persons of comparable age, sex, and race from the general population. This finding is lower than that reported in previous studies, which found SMRs among persons with TBI ranging from 2.0 to 7.1 depending on the population and study timeframe.^{24,27-29,31,34,37,38} Most of these higher SMRs may be explained by the inclusion of persons with the most severe TBI and/or the inclusion of early deaths. In studies of mortality restricted to persons with TBI who received inpatient rehabilitation, the SMRs ranged from 2 to 4,^{34,37,38} with the TBI Model System Study³⁸ that also excluded deaths in the first year and began follow-up at 1 year postinjury (as in the present study) reporting an SMR of 2.

The discrepancy between the TBI Model System Study (SMR 2.0) and the present study (SMR 1.5) warrants further discussion. Although both studies used the same inclusion criteria, the present study included most persons rehabilitated

Table 4: Deaths by Cause in the Traumatic Brain Injury Cohort
After 1 Year Postinjury Compared With the General Population

Cause of Death (ICD-9-CM Codes)	Number of Actual Deaths	Number of Expected Deaths	SMR	SMR 95% Limits
Circulatory (390–459)	30	30.16	0.99	0.67–1.42
Aspiration pneumonia				
(507)	10	0.21	48.64*	23.32-89.44
Pneumonia (480–486)	9	2.08	4.33*	1.98-8.22
Suicide (E950–E959)	10	3.39	2.95*	1.42–5.43
Unintentional injuries				
(E800–E949)	11	6.82	1.61	0.80-2.88
Cancer (140–208)	16	21.13	0.76	0.43–1.23
Digestive (520–579)	9	3.61	2.49*	1.14–4.73
Seizure (780.3,				
345–345.9)	6	0.27	22.48*	8.25–48.93

*Statistically significant SMR.

between 1961 and 1998, before the center was designated as a TBI Model System. In contrast, most persons included in the TBI Model System cohort were rehabilitated after 1998 when the TBI Model Systems expanded from 5 to 17 centers. Because it is not likely that an earlier era of care would account for a better survival rate, this was further investigated. When expected deaths were analyzed by age, 40% of the expected deaths were in the cohort over age 65 years. However, only 25% of the actual deaths occurred over age 65 years, and therefore the SMR in this cohort over age 65 years was substantially less (SMR=0.97; 95% CI=0.64-1.30) than the overall study sample. This would suggest that the SMR decreases as people with TBI age, resulting in the overall lower SMR in this study than in the TBI Model System cohort. This may be similar to the healthy worker effect seen in environmental exposure studies, or the effects of TBI on risk of mortality may decrease over time, particularly for healthy persons with a longer life expectancy.

TBI reduced life expectancy an average of 4 years in this study population, which was consistent with previous studies (ie, 3–5y).^{22,23,25,30-33,35} However, Harrison-Felix et al³⁸ reported a somewhat higher average life expectancy reduction of 7 years in the TBI Model Systems cohort. It should be noted that using a constant SMR with advancing age often results in a slight underestimation of long-term survival probabilities and life expectancy.⁵³ As such, the life expectancies reported in table 2 may be slightly shorter than would be expected.

Risk Factors for Death After Traumatic Brain Injury

The strongest risk factors for death after 1 year postinjury were older age at injury, being male, having less education at rehabilitation admission, earlier year of injury, longer hospitalization, and being in a vegetative state at rehabilitation discharge. Age, which is associated with comorbidities such as heart disease and diabetes, was found to be a risk factor in some previous studies^{28,33,35,38,57-59} but, surprisingly, not in others.^{22,31,37} Male sex being a risk factor for death after TBI has been identified in some studies^{28,31,57} but not in others.^{34,38} Corkin et al²² is the only previous study that identified less education as a risk factor for death after TBI, while Ratcliff et al³⁷ and Harrison-Felix³⁸ reported education not to be a risk factor. It is possible that education represents a proxy for socioeconomic status, which has been shown to be negatively associated with mortality.⁶⁰

Year of injury was found to be a risk factor, which has not been consistently reported by other studies. There was a 30% lower risk of death for every later decade of injury, which could be attributed to advances in medicine improving longerterm survival after TBI. Flaada et al⁵⁸ also found year of injury to be a significant risk factor in their study, but only for survival within the first 6 months postinjury timeframe.

The finding of longer hospitalization as a risk factor is unique to this study, having not been previously identified. Given the span of 4 decades covered by this study, there would have been a much greater range on lengths of stay represented in this study, and possibly a proxy for earlier eras of care when lengths of stay were longer. It is also likely that this could be a proxy for overall injury severity.

Interestingly, severity of TBI as indicated by various measures in previous studies was found to be a significant risk factor in studies that did not include a measure of functional outcome.^{27,28,57,58} However, for those studies that did include both,^{37,38} functional status was a significant risk factor, while severity of TBI was not. This study corroborates the findings of previous studies that revealed shortened life expectancy when severe disability is present.^{29-31,34,37,38}

Causes of Death After Traumatic Brain Injury

In this study, persons with TBI were almost 50 times more likely to die of aspiration pneumonia. It is not known whether these persons were on modified diets, adhered to diet recommendations, or experienced worsening of their swallowing ability for some reason over time. These persons were, however, an average of 18 years postinjury at the time of death. Of the 10 persons who died of aspiration pneumonia, 1 was categorized as being in a vegetative state and 9 as having severe disability at the time of rehabilitation discharge.

Persons with TBI were about 4 times more likely to die of pneumonia. These findings substantiate previous studies.^{30,33,38} Roberts³³ reported that patients with TBI were twice as likely to die of respiratory-related conditions, Shavelle et al³⁰ reported that clients with TBI were 10 times more likely to die of respiratory conditions, and Harrison-Felix³⁸ reported that persons with TBI were 4 times more likely to die of pneumonia.

In this study, persons with TBI were 22 times more likely to die of seizures. This finding is consistent with other studies. Roberts³³ reported a 40 times greater risk of death as a result of epilepsy after TBI, Shavelle³⁰ reported a 24 times greater risk of death as a result of seizures, and Harrison-Felix et al³⁹ reported that persons with TBI were 37 times more likely to die of seizures.

It is known that persons with TBI are at risk of developing posttraumatic epilepsy.⁶¹ Unfortunately, it is not known whether these persons had experienced any prior seizures or were on anticonvulsant medications (and if it was at therapeutic level) at the time of death. Herman,⁶² Chang and Lowenstein,⁶³ and Temkin et al,⁶⁴ among others, have reported that administration of anticonvulsant drugs after acute brain insults failed to prevent late epilepsy. Thus, it is unlikely that prophylactic use of anticonvulsants would have prevented these deaths. This is further highlighted by the fact that most of these persons were an average of 16 years postinjury at the time of death. Rehabilitation professionals should monitor the growing literature on sudden unexpected death in epilepsy,⁶⁵⁻⁶⁹ because these findings may eventually shed light on ideas to prevent death as a result of seizure after TBI.⁷⁰⁻⁷⁴

Persons with TBI in the study were almost 3 times more likely to commit suicide. Age at the time of injury for these persons averaged 23.5 years. Three previous studies have reported an increased risk of suicide after TBI.^{33,36,41} However, 3 other studies did not.^{24,30,38} Therefore, given the uncertainty of the suicide findings relative to other findings in this study, and the report by Simpson and Tate⁷⁵ that suicidality is a common psychological reaction to TBI among outpatient populations, prudent management should involve careful history taking of suicidal behavior, assessment of postinjury adjustment to TBI, and close monitoring of those persons with high levels of hopelessness and suicide ideation.

Persons with TBI were 2.5 times more likely to die of digestive conditions. Harrison-Felix³⁸ reported that persons with TBI were 3 times more likely to die of digestive conditions, with most secondary to liver disease with underlying chronic alcoholism. However, in the current study, 5 of the 9 deaths were secondary to nonalcoholic liver disease. Two of the deaths in this study were caused by ulcer, 1 by intestinal obstruction, and 1 by vascular insufficiency of the intestines. Of the 9 persons who died of digestive causes, 8 were classified as having severe disability at the time of rehabilitation discharge.

Even though the greatest proportion of deaths in this study (25%) resulted from circulatory conditions, this number of deaths was not significantly greater than would be expected in the general population. Previous studies have also found this to

be true^{33,38}; however, Shavelle³⁰ and Selassie et al²⁸ found that persons with TBI were more likely to die of circulatory conditions. Thus, it appears that the question of excess deaths caused by circulatory conditions after TBI is still equivocal. Given the findings of this study, close longitudinal follow-up of medical conditions in the years after TBI remains important.

Study Limitations

Strengths of this study were that it included a large sample size, had a long follow-up period of up to 40 years post-TBI, and had a high rate of complete vital status follow-up. This study did have several limitations. Even though the follow-up was over a 40-year period, most persons were injured in the most recent 10 years. However, the number of person-years is more evenly distributed. It included only persons treated in 1 freestanding inpatient rehabilitation facility. Compared with those seen more recently in the TBI Model Systems, persons included in this study tended to be better educated, employed, and nonminority, with a longer length of rehabilitation stay, and thus may have had better support systems and access to care, resulting in better outcomes. Persons receiving inpatient rehabilitation also tend to represent those with more moderate to severe TBI, not those so severely injured that they are not considered for active rehabilitation or those more mildly injured who do not require inpatient rehabilitation. Thus, this is a very select sample with findings that may not generalize to other persons with TBI.

This study was based on a retrospective cohort identified by inpatient rehabilitation medical records from the past 40 years. However, the authors are confident that the rigor of the casefinding methods led to the identification of persons meeting inclusion criteria across all study years. It is the case, however, that the only risk factors examined in this study were those documented in records of events typically occurring several years prior to death. Furthermore, neither comorbid conditions nor their interaction with risk factors was examined.

An inherent limitation in using U.S. general population mortality rates as a comparison is that other important factors such as socioeconomic status and other existing health conditions are not taken into account. In addition, national death rates (as opposed to state rates) were used to provide a broader representation of the general population; however, they may have been too broad a comparison group. If national death rates by cause differ significantly from state rates, this could lead to an underestimation or overestimation of the SMRs.

The use of death certificate data to determine cause of death is also a limitation. Studies evaluating the accuracy of death certificates report problems with misclassification, errors, and incomplete information.^{76,77} These problems were minimized in this study by adhering to specific guidelines in coding and assigning the cause of death.

CONCLUSIONS

This TBI mortality study is the first in recent years to span 4 decades and provides important new information regarding mortality, life expectancy, risk factors for death, and causes of death in persons with TBI receiving inpatient rehabilitation and surviving past 1 year postinjury. These findings need to be considered with caution given the limitations noted with this type of investigation using a relatively select sample of persons receiving inpatient rehabilitation at a single facility. Future research should focus on why some causes of death are greater than expected in persons with TBI and study whether medical and lifestyle interventions can help prevent some of these deaths and prolong life expectancy after TBI. It is recommended to target persons at greater risk for later mortality for closer follow-up after inpatient rehabilitation to provide patient and family education regarding the risk of death.

References

- Thurman DJ, Alverson C, Dunn KA, Guerrero J, Sniezek JE. Traumatic brain injury in the United States: a public health perspective. J Head Trauma Rehabil 1999;14:602-15.
- Thurman D. The epidemiology and economics of head trauma. New York: Wiley and Sons; 2001.
- Thurman D, Guerrero J. Trends in hospitalization associated with traumatic brain injury. JAMA 1999;282:954-7.
- Chan L, Doctor J, Temkin N, et al. Discharge disposition from acute care after traumatic brain injury: the effect of insurance type. Arch Phys Med Rehabil 2001;82:1151-4.
- Mellick D, Gerhart KA, Whiteneck GG. Understanding outcomes based on the post-acute hospitalization pathways followed by persons with traumatic brain injury. Brain Inj 2003;17:55-71.
- Sorenson SB, Kraus JF. Occurrence, severity, and outcomes of brain injury. J Head Trauma Rehabil 1991;6:1-10.
- Wagner AK, Hammond FM, Grigsby JH, Norton HJ. The value of trauma scores: predicting discharge after traumatic brain injury. Am J Phys Med Rehabil 2000;79:235-42.
- Conroy C, Kraus JF. Survival after brain injury: cause of death, length of survival, and prognostic variables in a cohort of braininjured people. Neuroepidemiology 1988;7:13-22.
- Fiedler RC, Granger CV, Russell CF. UDS(MR)SM: follow-up data on patients discharged in 1994-1996. Uniform Data System for Medical Rehabilitation. Am J Phys Med Rehabil 2000; 79:184-92.
- Fabbri A, Servadel F, Marchesini G, Stein SC, Vendelli A. Early predictors of unfavourable outcome in subjects with moderate head injury in the emergency department. J Neurol Neurosurg Psychiatr 2008 May;79:567-73.
- Jiang JY, Gao GY, Li WP, Yu MK, Zhu C. Early indicators of prognosis in 846 cases of severe traumatic brain injury. J Neurotrauma 2002;19:869-74.
- Klauber MR, Marshall LF, Luerssen TG, Frankowski R, Tabaddor K, Eisenberg HM. Determinants of head injury mortality: importance of the low risk patient. Neurosurgery 1989;24:31-6.
- Lang EW, Pitts LH, Damron SL, Rutledge R. Outcome after severe head injury: an analysis of prediction based upon comparison of neural network versus logistic regression analysis. Neurol Res 1997;19:274-80.
- Lannoo E, Van Rietvelde F, Colardyn F, et al. Early predictors of mortality and morbidity after severe closed head injury. J Neurotrauma 2000;17:403-14.
- Luerssen TG, Klauber MR, Marshall LF. Outcome from head injury related to patient's age: a longitudinal prospective study of adult and pediatric head injury. J Neurosurg 1988;68:409-16.
- Marshall L, Gautille T, Klauber M, et al. The outcome of severe closed head injury. J Neurosurg 1991;75:S28-36.
- Mosenthal AC, Lavery RF, Addis M, et al. Isolated traumatic brain injury: age is an independent predictor of mortality and early outcome. J Trauma 2002;52:907-11.
- Peek-Asa C, McArthur D, Hovda D, Kraus J. Early predictors of mortality in penetrating compared with closed brain injury. Brain Inj 2001;15:801-10.
- Schreiber MA, Aoki N, Scott BG, Beck JR. Determinants of mortality in patients with severe blunt head injury. Arch Surg 2002;137:285-90.
- Signorini DF, Andrews PJ, Jones PA, Wardlaw JM, Miller JD. Predicting survival using simple clinical variables: a case study in traumatic brain injury. J Neurol Neurosurg Psychiatry 1999;66:20-5.

- Shavelle R, Strauss D, Day S, Ojdana K. Life expectancy. In Brain injury medicine: principles and practice. Zasler ND, Katz DI, Zafonte RD, editors. New York: Demos; 2007. pp 247-61.
- Corkin S, Sullivan EV, Carr FA. Prognostic factors for life expectancy after penetrating head injury. Arch Neurol 1984;41:975-7.
- Rish BL, Dillon JD, Weiss GH. Mortality following penetrating craniocerebral injuries: an analysis of the deaths in the Vietnam Head Injury Registry population. J Neurosurg 1983;59:775-80.
- Walker AE, Blumer D. The fate of World War II veterans with posttraumatic seizures. Arch Neurol 1989;46:23-6.
- Walker AE, Leuchs HK, Lechtape-Gruter H, Caveness WF, Kretschman C. Life expectancy of head injured men with and without epilepsy. Arch Neurol 1971;24:95-100.
- Weiss GH, Caveness WF, Einsiedel-Lechtape H, McNeel ML. Life expectancy and causes of death in a group of head-injured veterans of World War I. Arch Neurol 1982;39:741-3.
- Brown AW, Leibson CL, Malec JF, Perkins PK, Diehl NN, Larson DR. Long-term survival after traumatic brain injury: a population-based analysis. NeuroRehabilitation 2004;19:37-43.
- Selassie AW, McCarthy ML, Ferguson PL, Tian J, Langlois JA. Risk of posthospitalization mortality among persons with traumatic brain injury, South Carolina 1999–2001. J Head Trauma Rehabil 2005;20:257-69.
- 29. Shavelle R, Strauss D. Comparative mortality of adults with traumatic brain injury in California, 1988–97. J Insur Med 2000; 32:163-6.
- Shavelle RM, Strauss D, Whyte J, Day SM, Yu YL. Long-term causes of death after traumatic brain injury. Am J Phys Med Rehabil 2001;80:510-6; quiz 7-9.
- Strauss DJ, Shavelle RM, Anderson TW. Long-term survival of children and adolescents after traumatic brain injury. Arch Phys Med Rehabil 1998;79:1095-100.
- Strauss DJ, Shavelle RM, Ashwal S. Life expectancy and median survival time in the permanent vegetative state. Pediatr Neurol 1999;21:626-31.
- Roberts A. Severe accidental head injury: an assessment of longterm prognostics. London: Macmillan; 1979. p 140-79.
- Baguley I, Slewa-Younan S, Lazarus R, Green A. Long-term mortality trends in patients with traumatic brain injury. Brain Inj 2000;14:505-12.
- Lewin W, Marshall TF, Roberts AH. Long-term outcome after severe head injury. Br Med J 1979;2:1533-8.
- Pentland B, Hutton LS, Jones PA. Late mortality after head injury. J Neurol Neurosurg Psychiatry 2005;76:395-400.
- Ratcliff G, Colantonio A, Escobar M, Chase S, Vernich L. Longterm survival following traumatic brain injury. Disabil Rehabil 2005;27:305-14.
- Harrison-Felix C, Whiteneck G, DeVivo M, Hammond FM, Jha A. Mortality following rehabilitation in the Traumatic Brain Injury Model Systems of Care. NeuroRehabilitation 2004;19:45-54.
- Harrison-Felix C, Whiteneck G, Devivo MJ, Hammond FM, Jha A. Causes of death following 1 year postinjury among individuals with traumatic brain injury. J Head Trauma Rehabil 2006:21:22-33.
- Walker AE, Erculei F. Post-traumatic epilepsy 15 years later. Epilepsia 1970;11:17-26.
- Teasdale TW, Engberg AW. Suicide after traumatic brain injury: a population study. J Neurol Neurosurg Psychiatry 2001; 71:436-40.
- 42. Jennett B, Bond M. Assessment of outcome after severe brain damage. Lancet 1975;1:480-4.
- 43. Traumatic Brain Injury Model Systems National Database. Traumatic Brain Injury Model Systems National Data and Statistical Center. Englewood: Craig Hospital. 2009. Available at: http://www.tbindsc.org. Accessed February 25, 2009.

- 44. Social Security Administration. Social Security Death Master File, 2009. Available at: http://www.ancestry.com/search/db.aspx? dbid=3693. Accessed February 25, 2009.
- DeVivo MJ, Black KJ, Stover SL. Causes of death during the first 12 years after spinal cord injury. Arch Phys Med Rehabil 1993; 74:248-54.
- Sesso HD, Paffenbarger RS, Lee IM. Comparison of National Death Index and World Wide Web death searches. Am J Epidemiol 2000;152:107-11.
- 47. Wentworth DN, Neaton JD, Rasmussen WL. An evaluation of the Social Security Administration master beneficiary record file and the National Death Index in the ascertainment of vital status. Am J Public Health 1983;73:1270-4.
- ICD-9-CM: International Classification of Diseases, 9th Revision, Clinical Modification, 6th edition 2006; Los Angeles: Practice Management Information Corporation.
- 49. DeVivo MJ, Ivie CSr. Life expectancy of ventilator-dependent persons with spinal cord injuries. Chest 1995;108:226-32.
- Gordis L, editor. Epidemiology. 2nd edition. Philadelphia: Saunders Co; 2000.
- 51. Gardner P, Rosenberg HM, Wilson RW. Leading causes of death by age, sex, race and Hispanic origin: United States, 1992. Vital and Health Statistics. National Center for Health Statistics. 1996. Series 20, no. 29. Available at: http://www.cdc.gov/nchs/data/ series/sr_20/sr20_029.pdf. Accessed January 25, 2009.
- Kochanek KD, Hudson BL. Advance report of final mortality statistics, 1992: monthly vital statistics report. National Center for Health Statistics. March 2, 1995;43(6 Suppl). Available at: http:// www.cdc.gov/nchs/data/mvsr/supp/mv43_06s.pdf. Accessed February 25, 2009.
- DeVivo MJ. Estimating life expectancy for use in determining lifetime costs of care. Top Spinal Cord Inj Rehabil 2002;7: 49-58.
- Breslow NE, Day NE, editors. Statistical methods in cancer research: volume II—the design and analysis of cohort studies. New York: Oxford University Press; 1987.
- 55. Kochanek KD, Murphy SL, Anderson RN, Scott C. Deaths: final data for 2002 National Vital Statistics Reports. National Center for Health Statistics. October 12, 2004;53. Available at: http:// www.cdc.gov/nchs/data/nvsr/nvsr53/nvsr53_05.pdf. Accessed February 25, 2009.
- 56. Rosner B, editor. Fundamentals of biostatistics. 5th ed. Pacific Grove: Duxburry; 2000.
- Donohue JT, Clark DE, DeLorenzo MA. Long-term survival of Medicare patients with head injury. J Trauma 2007;62:419-23.
- Flaada JT, Leibson CL, Mandrekar JN, et al. Relative risk of mortality after traumatic brain injury: a population-based study of the role of age and injury severity. J Neurotrauma 2007;24: 435-45.
- Hammond F, Wiercisiewski DR, Gratton KD, Norton J, Yablon S. Mortality following traumatic brain injury: who dies and when. [abstract] Arch Phys Med Rehabil 2000;81:1260.
- Adler NE, Boyce WT, Chesney MA, Folkman S, Syme SL. Socioeconomic inequalities in health: no easy solution. JAMA 1993;269:3140-5.
- 61. Annegers JF, Coan SP. The risks of epilepsy after traumatic brain injury. Seizure 2000;9:453-7.
- 62. Herman ST. Epilepsy after brain insult: targeting epileptogenesis. Neurology 2002;59(9 Suppl 5):S21-6.
- 63. Chang BS, Lowenstein DH. Practice parameter: antiepileptic drug prophylaxis in severe traumatic brain injury: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2003;60:10-6.

- 64. Temkin NR, Dikmen SS, Wilensky AJ, Keihm J, Chabal S, Winn HR. A randomized, double-blind study of phenytoin for the prevention of post-traumatic seizures. N Engl J Med 1990;323:497-502.
- Ficker DM, So EL, Shen WK, et al. Population-based study of the incidence of sudden unexplained death in epilepsy. Neurology 1985;51:1270-4.
- 66. Lhatoo SD, Johnson AL, Goodridge DM, MacDonald BK, Sander JW, Shorvon SD. Mortality in epilepsy in the first 11 to 14 years after diagnosis: multivariate analysis of a long-term, prospective, population-based cohort. Ann Neurol 2001;49:336-44.
- 67. Morgan CL, Kerr MP. Epilepsy and mortality: a record linkage study in a U.K. population. Epilepsia 2002;43:1251-5.
- Sperling MR, Feldman H, Kinman J, Liporace JD, O'Connor MJ. Seizure control and mortality in epilepsy. Ann Neurol 1999;46: 45-50.
- Strauss DJ, Day SM, Shavelle RM, Wu YW. Remote symptomatic epilepsy: does seizure severity increase mortality? Neurology 2003;60:395-9.
- Nashef L, Hindocha N, Makoff A. Risk factors in sudden death in epilepsy (SUDEP): the quest for mechanisms. Epilepsia 2007;48: 859-71.

- Opeskin K, Berkovic SF. Risk factors for sudden unexpected death in epilepsy: a controlled prospective study based on coroners cases. Seizure 2003;12:456-64.
- Ryvlin P, Montavont A, Kahane P. Sudden unexpected death in epilepsy: from mechanisms to prevention. Curr Opin Neurol 2006; 19:194-9.
- Tomson T, Walczak T, Sillanpaa M, Sander JW. Sudden unexpected death in epilepsy: a review of incidence and risk factors. Epilepsia 2005;46(Suppl 11):54-61.
- Englander J, Bushnik T, Duong TT, et al. Analyzing risk factors for late posttraumatic seizures: a prospective, multicenter investigation. Arch Phys Med Rehabil 2003;84:365-73.
- 75. Simpson G, Tate R. Suicidality after traumatic brain injury: demographic, injury and clinical correlates. Psychol Med 2002;32: 687-97.
- Lloyd-Jones DM, Martin DO, Larson MG, Levy D. Accuracy of death certificates for coding coronary heart disease as the cause of death. Ann Intern Med 1998;129:1020-6.
- Messite J, Stellman SD. Accuracy of death certificate completion: the need for formalized physician training. JAMA 1996; 275:794-6.