ORIGINAL ARTICLE

Mortality After Discharge From Acute Care Hospitalization With Traumatic Brain Injury: A Population-Based Study

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ABSTRACT. Ventura T, Harrison-Felix C, Carlson N, DiGuiseppi C, Gabella B, Brown A, DeVivo M, Whiteneck G. Mortality after discharge from acute care hospitalization with traumatic brain injury: a population-based study. Arch Phys Med Rehabil 2010;91:20-9.

Objective: To characterize mortality after acute hospitalization with traumatic brain injury (TBI) in a socioeconomically diverse population.

Design: Population-based retrospective cohort study.

Setting: Statewide TBI surveillance program.

Participants: Colorado residents with TBI discharged alive from acute hospitalization between 1998 and 2003 (N=18,998).

Interventions: Not applicable.

Main Outcome Measures: Vital status at the end of the study period (December 31, 2005) and statewide population mortality rates were used to calculate all-cause and cause-specific standardized mortality ratios (SMRs) and life expectancy compared with population mortality rates. The influence of demographics, injury severity, and comorbid conditions on time until death was investigated using age-stratified Cox proportional hazards modeling.

Results: Patients with TBI carried about 2.5 times the risk of death compared with the general population (SMR=2.47; 95% confidence interval [CI], 2.31–2.65). Life expectancy reduction averaged 6 years. SMRs were largest for deaths caused by mental/behavioral (SMR=3.84; 95% CI, 2.67–5.51) and neurologic conditions (SMR=2.79; 95% CI, 2.07–3.77) and were smaller but significantly higher than 1.0 for an array of other causes. Injury severity and older age increased mortality among young people (age <20y). However, risk factors for mortality among adults age 20 and older involved multiple domains of demographics (eg, metropolitan residence), injury-related measures (eg, falls versus vehicular incidents), and comorbidity (eg, ≥3 comorbid health conditions versus none).

Conclusions: TBI confers an increased risk of mortality in the months and years after hospital discharge. Although life expectancy is reduced across the population, the excess in mortality lessens as time since injury increases. Specific risk factors (eg, high injury severity, poor general health) pose an especially high threat to survival and should prompt an increased vigilance of health status, especially among younger patients.

Key Words: Brain injuries; Comorbidity; Mortality; Population surveillance; Rehabilitation.

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PERSONS WHO EXPERIENCE traumatic brain injury often face an array of health-related challenges, including a reduction in life expectancy for the most severely injured.[1,2] While fatality during the acute postinjury period is well characterized,[3-5] less is known about postacute mortality in the months and years after discharge from initial medical care. Researchers have made recent contributions to a small but growing body of literature on long-term survival after TBI.[1,6-13]

Factors predicting mortality in previous research have included older age, male sex, presence of comorbid health conditions, higher injury severity, Medicare versus commercial insurance, and treatment at trauma centers with lower level designations,[11] as well as unemployment and greater disability.[1] The risk of death after a TBI has been estimated to be 7 times that of the general population in the first year after

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List of Abbreviations

AIS	Abbreviated Injury Scale
CDC	Centers for Disease Control and Prevention
CDPHE	Colorado Department of Public Health and Environment
CI	confidence interval
CTBISS	Colorado Traumatic Brain Injury Surveillance System
GCS	Glasgow Coma Scale
HR	hazard ratio
ICD-9	*International Classification of Diseases–9th Revision*
ICD-9-CM	*International Classification of Diseases–9th Revision–Clinical Modifications*
ICD-10	*International Classification of Diseases–10th Revision*
MSA	metropolitan statistical area
PH	proportional hazard
SMR	standardized mortality ratio
TBI	traumatic brain injury

injury[11] and 5.3 times that of the population over an average of 7 years after injury.[7] In the years after discharge from inpatient TBI rehabilitation, mortality rates have been reported to be higher than the expected population estimates for deaths caused by seizures, sepsis, digestive conditions, pneumonia and other respiratory conditions, and external causes/unintentional injury.[10] Such results provide a valuable characterization of mortality in the postdischarge recovery period. However, the methodologies used have limitations, including follow-up limited to the first postinjury year,[1] low sociodemographic diversity in the study cohorts (high standard of living and ready access to health care; <5% of cohort of minority race or ethnicity),[7] and limited generalizability to nonrehabilitation populations.[10] Thus, there is room for similar examinations of long-term mortality in population-based cohorts that are relatively diverse sociodemographically.

The purpose of the current study was to characterize long-term mortality after TBI among persons from diverse races, ethnicities, and socioeconomic conditions (ie, income). Results were intended to expand on previous findings suggesting that TBI confers an elevated risk for both all-cause mortality (ie, a shortened life expectancy) and mortality from specific causes.[1,10] This study aimed to examine relative mortality and life expectancy compared with the general population as well as the causes of and risk factors for mortality. Study hypotheses were the following:

1. Compared with the population, persons with a history of TBI have a greater all-cause mortality rate and a shorter life expectancy.
2. Compared with the population, persons with a history of TBI have a greater mortality rate for selected causes of death, including seizures, sepsis, digestive conditions, pneumonia and other respiratory conditions, and external causes/unintentional injury.
3. Among those with a history of TBI, time to death is associated with specific risk factors, including older age, greater TBI severity, and presence of comorbid health conditions at the time of injury.

METHODS

This retrospective cohort study used a population-based sample of patients who were hospitalized with TBI and discharged alive between January 1, 1998 and December 31, 2003. The outcome of interest was length of time between the date of discharge and date of death or end of study period (December 31, 2005). Case definition and analytical methods of this study, described here, are similar to work reported previously.[1,10]

Participants

Subjects were identified from the CTBISS, administered by CDPHE. The CTBISS, currently funded by the CDC, tracks fatal and nonfatal TBIs among Colorado residents based on detailed hospital discharge data collected from all of Colorado's nonfederal acute care hospitals (numbering between 64 and 71 during the years of data collection). Persons entering the CTBISS were Colorado residents discharged alive during the inception period with a TBI matching the CDC case definition[14] (ICD-9-CM codes 800.0–801.9 [skull fractures, vault and base], 803.0–804.9 [other skull fractures], 850.0–854.1 [intracranial injury], 950.1–950.3 [optic nerve injuries], 959.01 [head injury, unspecified], 995.55 [shaken infant syndrome]). For patients having multiple hospitalizations with TBI, only the most recent hospitalization was included. There were 20,523 patients who met the criteria. CDPHE personnel (including B.G.) reviewed the medical records of a subsample of CTBISS cases (approximately 1000 a year), comparing progress notes and physician discharge diagnoses, to validate the ICD-9-CM codes used to identify TBI. Analysis of the 959.01 diagnosis revealed a low predictive value positive for true TBI (<70%). In addition, the software program for assigning injury severity based on ICD-9-CM codes does not include the 959.01 diagnosis on its list of codes used in the determination of injury severity per methods described below (see section below: Injury severity and external cause of injury), which precludes the assignment of a TBI severity score for these cases. Therefore, cases carrying the ICD-9-CM diagnosis 959.01 (head injury, unspecified) as the sole TBI-related diagnosis were excluded (n=1525). The mortality rate among these cases was similar to that of the remaining 18,998 cases that comprised the analysis dataset (14% vs 13%, respectively).

Study Variables

Mortality and causes of death. Vital status during the study period was determined by linking cohort cases to death certificate data from the Colorado Death Master File, which captures all deaths occurring in Colorado and out-of-state deaths of Colorado residents. For persons identified as dead, death certificate data provided the date, manner, and up to 11 causes of death (ICD-9 codes for deaths occurring in 1998; ICD-10 codes for death after 1998), 1 of which was designated as the underlying cause. Prior to data analysis, ICD-9 codes were converted to ICD-10 codes using a crosswalk file provided by the National Center for Health Statistics.[15] A comprehensive list of ICD-10 codes from the World Health Organization is available elsewhere.[16] To avoid overestimation of deaths caused by external causes attributed to the TBI itself, cases with TBI as the only cause of death indicated were recoded to "unknown" cause of death. Where TBI was indicated as the primary cause of death among a list of several causes of death, the next available non-TBI cause of death was recoded to become the primary cause of death for the purposes of this analysis.

Demographics. The CTBISS data included age at injury (in years), sex, and race/ethnicity. The original dataset contained 5898 cases (27%) with unknown race. For these, race/ethnicity data were supplemented with linkage to demographic information from the Colorado Trauma Registry, which provided detailed data from Colorado's Level I, II, and III trauma centers, as reported to CDPHE. This linkage enabled the recoding of 66% of the unknown race/ethnicity cases to a known race or ethnicity and reduced the proportion of the "other/unknown" cases to 10% overall. Expected source of hospitalization payment was collapsed into 4 categories: private health insurance, liability insurance (automotive), government pay (ie, Medicare, Medicaid, Civilian Health and Medical Program of the Uniformed Services, Colorado Medically Indigent Program or other government payment source), and self-pay/no charge. Only the primary payor was included in the dataset. Also included was residence at the time of hospitalization, which was assigned an MSA classification per the U.S. Office of Management and Budget designations[17] and collapsed to metropolitan (ie, "Denver-Boulder 6-county consolidated MSA" and "other MSA") versus nonmetropolitan (ie, "non-MSA") for analysis. Additional community-level sociodemographic variables from the 2000 U.S. Census (including median income and population) were linked to individual cases by zip code of residence at the time of hospitalization.

Injury severity and external cause of injury. CTBISS data included up to 15 ICD-9-CM diagnoses associated with the acute hospitalization. External cause of injury was extracted

from ICD-9-CM external cause of injury codes (E-codes) provided among the available diagnoses. AIS scores[18] were computed using ICDMAP 90 software[a] and added to the CTBISS by CDPHE personnel. The AIS has the following values and ratings: 1 (minor), 2 (moderate), 3 (severe), 4 (serious), 5 (critical), and 6 (unsurvivable). The maximum AIS score assigned to the head region served as the indicator of TBI severity. For risk factor modeling, maximum head AIS was collapsed into 3 categories according to the distribution of cases in the dataset: minor/moderate (AIS=1 or 2), severe/serious (AIS=3 or 4), and critical (AIS=5). Cases coded as unsurvivable (AIS=6; n=8) were not included in severity analyses. There were also 270 cases with AIS rating of 9 (unknown) and 132 cases not assigned an AIS because of insufficient data, all of which were excluded from the severity analyses.

Acute care measures. Also included in CTBISS data were the length of acute hospital stay (in days) and discharge destination, which was collapsed into 4 levels: home with no follow-up care required; home with outpatient care; inpatient nursing/rehabilitation; and an "other" category consisting of swing beds, home intravenous care service, and other miscellaneous types of care.

Comorbid health conditions and associated injuries. Non-TBI diagnoses (per ICD-9-CM) were classified using an adaptation of the Elixhauser comorbidity framework, which delineated 31 types of comorbid health conditions. The coding algorithm, developed by researchers at University of Manitoba, has produced estimates of comorbidity prevalence in administrative data similar to other algorithms, but potentially outperforms the other algorithms in predicting mortality.[19,20] Variables were created to indicate overall comorbidity (ie, the number of comorbid health conditions present during hospitalization) and associated injuries to other body regions per AIS scores (ie, the number of injured regions other than the head). For analysis, comorbid health conditions and associated injuries were each collapsed into 4 levels: 0, 1, 2, or ≥3 conditions or injuries.

Human Subjects Protection

This research was approved by the institutional review boards of CDPHE and Craig Hospital (HCA-HealthONE).

Analysis

Standardized mortality ratios and life expectancy. Relative mortality among TBI survivors compared with the general population was estimated using the ratio of observed to expected deaths: the SMR.[21] CDPHE provided year 2000 rates for all-cause and cause-specific mortality for the Colorado population, stratified by age, race/ethnicity, and sex. Expected mortality was calculated by applying the Colorado mortality rate to each year of follow-up for each person in the study matched by age, race/ethnicity, and sex, and then summing the result. For estimates of mortality prior to 1 year, the monthly expected mortality rate computed as one twelfth of the yearly expected rate. All-cause SMR was calculated for the entire cohort and for separate subgroups based on stratifications of postdischarge period, age, sex, race/ethnicity, injury severity, and underlying cause of death, respectively. Underlying causes selected for this analysis were those that accounted for at least 5% of deaths in the cohort, as well as those identified in previous literature as elevated among persons with TBI.[10] A 95% CI based on the chi-square statistic was calculated for each SMR.

Life expectancy reduction among the TBI cohort, stratified by age group, race/ethnicity, and sex, was estimated with a

method developed for the spinal cord injury population, used in previous research.[1,22] In brief, this method uses the most recently reported population mortality rates (for this study, Colorado residents in 2005) and the estimated all-cause SMR to compute cumulative probabilities of survival for selected demographic strata (eg, probability of 20-year-old Hispanic men surviving 1 year, 2 years, 3 years, and so on up to age 100 years). The individual cumulative probabilities of survival are then summed to obtain life expectancy for the selected stratum.

Supplemental analyses (early deaths, associated injuries). To characterize early deaths after hospitalization with TBI, supplemental chi-square analyses were performed to examine differences in injury severity before and after 1 month postdischarge. Risk factor modeling prompted additional chi-square analyses to characterize external causes of injury in relation to the presence of non-TBI associated injuries.

Risk factor modeling. Cox PH models[23,24] were used to identify risk factors for mortality among the TBI cohort. The outcome of interest was number of days from hospital discharge to death. Those still alive as of December 31, 2005, were censored for data analysis. The PH models were stratified by age group to minimize violations of proportionality caused by differences in cause and severity of TBI across age[3,4] as well as disease comorbidity. Six age groups were delineated by examination of Kaplan-Meier hazard curves: infants (0–3y); children/adolescents (4-19y); and young (20-39y), middle-age (40-59y), older (60-79y), and elderly (≥80y) adults. Modeling was not performed for infants with TBI because mortality was very low: of the 791 infants in the cohort, only 9 (1.1%) died during the study period. Hence, models for the remaining 5 age groups were developed.

To reduce confounding and create a more parsimonious model, each covariate was grouped into 1 of 3 domains for preliminary model building: (1) demographics, (2) injury-related/acute care measures, or (3) comorbidities. Within each domain, a Cox PH model was estimated for each of the covariates, controlling for age. Age was included in construction of all models because of its importance as a predictor of mortality.[7,9,10] Covariates with a *P* value of .20 or smaller in the above univariate models were then included in a domain-specific multivariable Cox PH model. Thus, at this stage of analysis, there were 3 Cox PH models of interest, 1 for each domain. To arrive at a more parsimonious model for each domain, backward elimination was performed where the covariate with the highest *P* value greater than .10 was removed until only covariates with *P* values less than .10 remained in the domain-specific models.[21,24] Finally, to assess the influence of the domains on each other, the reduced multivariable domain-specific models were then combined into a full, adjusted model for each age group. All statistical analyses were performed using SAS 9.1 for Windows.[b] HRs and 95% CIs are reported for the reduced domain-specific models (demographics, injury-related/acute care measures, comorbidities) and for full, adjusted models incorporating all significant predictive factors from each of the 3 individual domains. Interpretations of the results are based on the full models.

RESULTS

The 18,998 patients in the cohort contributed 83,268 person-years, and median time of follow-up on each subject was 4.4 years (range, <1–8y). Nearly 20% of cohort members were of a racial or ethnic minority, including Hispanic (14%), black (3%), Asian (1%), and Native American subjects (<1%) (table 1). Community-level median annual income among the represented zip codes in 2000 ranged between $15,000 and $150,000, with 50% of cases residing in areas with median income ranging between $35,000 and $56,000. With 2494

Table 1: Demographics, Injury-Related Measures, and Comorbidities Among the TBI Cohort

Characteristic	Frequency*	%[†]
Total person-years	83,268	
Study time (d)		
Mean (range, 0–2921)	*1601*	
Median	*1584*	
Sex		
Male	12,259	65
Female	6739	35
Age at admission (y)		
Mean (range, 0–100)	*40*	
Median	*36*	
Less than 1	406	2
1–19	4156	22
20–39	5803	31
40–59	4267	22
60–79	2518	13
80 or more	1848	10
Race		
White	13,408	71
Black	603	3
Asian	226	1
Native American	43	<1
Hispanic	2754	14
Other/unknown	1964	10
Residence at admission		
Metropolitan	15,101	80
Nonmetropolitan	3881	20
Expected payment source		
Private health insurance	9520	50
Liability insurance (automotive)	1922	10
Government pay	4367	23
Self-pay/no charge	3184	17
Median annual income (zip code of residence)		
<$10,000	675	4
$10,000–$19,999	23	<1
$20,000–$29,999	1875	10
$30,000–$39,999	5330	28
$40,000–$49,999	4569	24
$50,000–$59,999	2949	16
$60,000–$69,999	1554	8
$70,000–$79,999	1126	6
≥$80,000	897	5
External cause of injury		
Vehicular	9548	50
Falls	6277	33
Violence	1676	9
Other	1497	8
Maximum AIS of the head		
1=Minor	820	4
2=Moderate	6703	36
3=Serious	3011	16
4=Severe	7152	38
5=Critical	902	5
6=Unsurvivable	8	<1
Length of hospital stay (d)		
Mean (range, 1–168)	6	
Median	3	
Discharge destination		
Routine home	12,766	67
Outpatient/home care	863	5
Nursing/rehabilitation facility	5282	28
Other (including hospice)	87	<1

Table 1: (Cont'd) Demographics, Injury-Related Measures, and Comorbidities Among the TBI Cohort

Characteristic	Frequency*	%[†]
Comorbid conditions (count)		
0	8633	45
1	5040	27
2	2561	13
≥3	2764	15
Associated injuries (count)		
0	10,787	57
1	4725	25
2	2085	11
≥3	1401	7

*Reported numbers are frequencies, except where indicated: numbers in italics are means and medians for continuous time variables.
[†]Because of rounding, sum of percentages may not be 100.

deaths among the TBI cohort, the mortality rate was 3.0 deaths per 100 person-years of follow-up. Demographic and clinical characteristics of the cohort are shown in table 1.

Standardized Mortality Ratios

All-cause standardized mortality ratio. Over the entire study period, the observed risk of death among patients with TBI was almost 2.5 times the expected risk of those in the general population of similar age, sex, and race/ethnicity (SMR=2.47; 95% CI, 2.31–2.65) (table 2). The risk of dying within the first month after discharge was much higher than expected (SMR=25.20; 95% CI, 16.13–39.38). As survival time increased after the first postdischarge month (3, 6, 12mo), the excess in mortality dropped markedly and continued to diminish to less than twice the expected risk (SMR=1.71; 95% CI, 1.57–1.86) for those surviving at least 1 year.

Age-stratified, all-cause SMR was largest among those 40 to 59 years (SMR=4.72; 95% CI, 3.74–5.96) and decreased with successively older age groups. Whether stratified by sex, race/ethnicity, or injury severity, SMRs were similar in magnitude to the unstratified all-cause cohort SMR, with the exception of patients with critical injury (SMR=5.55; 95% CI, 3.78–8.15) (see table 2).

Causes of death and cause-specific standardized mortality ratio. Deaths among the TBI cohort were significantly greater than expected for almost all specific causes of death examined (table 3). The data suggested a substantially elevated risk of death caused by seizures relative to the expected rate, but the estimated SMR of 15.0 is based on only a few observed events and only 1 expected death. There were notable elevations in death caused by mental/behavioral disorders (SMR=4.70; 95% CI, 3.30–6.70), which include dementia as well as death caused by nervous system diseases (SMR=3.33; 95% CI, 2.48–4.46), which include some types of seizures and Alzheimer disease. Of similar magnitude to the estimated all-cause SMR of 2.5 were deaths caused by sepsis, digestive system diseases, and stroke. Smaller but significant SMRs were estimated for deaths caused by circulatory system diseases, respiratory diseases, malignant neoplasms, and external causes, including suicide, which had 2.4 times the expected rate (see table 3).

For the 504 deaths occurring within the first postdischarge month, supplementary analyses identified circulatory system diseases as the most prevalent underlying cause of death category (n=182; 36%). After this was the category for "unknown" underlying cause of death (n=105; 21%), among

Table 2: SMRs* by Postdischarge Period, Patient Characteristics, and Injury Severity

Characteristic	Observed Deaths	Expected Deaths	SMR	95% CI
Overall	**2494**	**1008**	**2.47**	**2.31–2.65**
Postdischarge period				
0–1mo	**504**	**20**	**25.20**	**16.13–39.38**
1–3mo	**225**	**40**	**5.63**	**4.02–7.87**
3–6mo	**209**	**59**	**3.54**	**2.66–4.73**
6–12mo	**241**	**119**	**2.03**	**1.63–2.52**
After 12mo	**1315**	**770**	**1.71**	**1.57–1.86**
Age at admission (y)				
<1	6	3	2.00	0.50–7.94
1–19	**41**	**11**	**3.73**	**1.92–7.24**
20–39	**135**	**35**	**3.86**	**2.66–5.58**
40–59	**392**	**83**	**4.72**	**3.74–5.96**
60–79	**777**	**299**	**2.60**	**2.30–2.93**
≥80	**1143**	**576**	**1.98**	**1.84–2.14**
Sex				
Male	**1345**	**509**	**2.64**	**2.39–2.92**
Female	**1149**	**499**	**2.30**	**2.09–2.54**
Race/ethnicity				
White	**1865**	**769**	**2.43**	**2.24–2.63**
Black	**67**	**24**	**2.79**	**1.78–4.39**
Asian	**16**	**6**	**2.67**	**1.06–6.69**
Native American	3	1	3.00	0.33–27.72
Hispanic	**179**	**72**	**2.49**	**1.90–3.25**
Injury severity (maximum AIS of the head region)				
1=Minor	**113**	**52**	**2.17**	**1.59–2.97**
2=Moderate	**470**	**262**	**1.79**	**1.55–2.08**
3=Serious	**336**	**140**	**2.40**	**1.98–2.90**
4=Severe	**1360**	**504**	**2.70**	**2.45–2.97**
5=Critical	**161**	**29**	**5.55**	**3.78–8.15**

*Boldface data reflect SMRs that are significantly greater than 1.0.

which 86% were accompanied by TBI diagnosis codes on the death certificate. Additionally, early deaths were associated with a higher prevalence of severe/serious TBIs (77% vs 42%; $P<.001$) and a lower prevalence of minor/moderate TBIs (11% vs 41%; $P<.001$) compared with later deaths.

Life Expectancy Reduction

Among the demographic strata selected for the life expectancy table (table 4), the overall reduction in life expectancy associated with TBI was an average of 6 years (range,

Table 3: SMRs* for ICD-10 Underlying Causes of Death

Cause of Death	Observed Deaths	Expected Deaths	SMR	95% CI
All causes	**2494**	**1008**	**2.47**	**2.31–2.65**
Mental/behavioral disorders (F00–F79)	**174**	**37**	**4.70**	**3.30–6.70**
Dementia (F00–F03)	**95**	**30**	**3.17**	**2.10–4.77**
Nervous system diseases (G00-G99, R56.8)	**193**	**58**	**3.33**	**2.48–4.46**
Alzheimer disease (G30.9)	**106**	**37**	**2.87**	**1.97–4.16**
Seizures (G40-G41, R56.8)	**15**	**1**	**15.00**	**1.98–113.54**
Sepsis (A40-A41)	**30**	**10**	**3.00**	**1.47–6.14**
Digestive system diseases (K00-K93)	**119**	**42**	**2.83**	**1.99–4.03**
Stroke (I64)	**120**	**52**	**2.31**	**1.67–3.19**
Circulatory system diseases (I00-I99)	**864**	**377**	**2.29**	**2.03–2.58**
External causes (V01–Y98)	**174**	**75**	**2.32**	**1.77–3.04**
Unintentional injury (V01–X59)	**113**	**51**	**2.22**	**1.59–3.08**
Assault (X85.0–Y09.9)	10	4	2.50	0.78–7.97
Suicide (X60–X84)	**38**	**16**	**2.38**	**1.33–4.26**
Respiratory system diseases (J00–J99)	**242**	**118**	**2.05**	**1.65–2.55**
Pneumonia (J12–J18)	**91**	**28**	**3.25**	**2.13–4.96**
Aspiration pneumonia (J69)	**37**	**11**	**3.36**	**1.72–6.59**
Malignant neoplasms (C00–D48)	**259**	**184**	**1.41**	**1.17–1.70**

*Boldface data reflect SMRs that are significantly greater than 1.0.

Table 4: Estimated Years of Life Expectancy for TBI Cohort at Selected Ages, and Difference From Non-TBI Population,* by Race/Ethnicity[†] and Sex

| Age at Admission (y) | White | | | | Black | | | | Hispanic | | | | All Races | |
| | Male | | Female | | Male | | Female | | Male | | Female | | Both Sexes | |
	TBI	Difference	TBI	Difference	TBI	Difference	TBI	Difference	TBI	Difference	TBI	Difference	TBI	Difference
1	65	−10	71	−9	60	−13	67	−11	62	−11	69	−9	63	−10
10	57	−10	62	−9	52	−12	58	−11	54	−11	61	−9	55	−9
20	47	−10	52	−9	42	−12	48	−10	44	−10	51	−9	47	−9
30	38	−9	43	−8	35	−11	39	−10	36	−9	42	−9	38	−9
40	30	−9	33	−8	26	−10	30	−10	27	−9	32	−8	30	−9
50	22	−8	25	−8	18	−9	22	−9	19	−8	24	−8	22	−8
60	14	−7	16	−7	12	−8	15	−8	12	−7	16	−7	15	−7
70	8	−5	9	−6	7	−6	8	−6	7	−5	9	−5	9	−6
80	3	−4	4	−4	4	−5	4	−5	2	−3	4	−4	5	−4
90	1	−3	2	−3	2	−3	2	−3	1	−3	1	−3	3	−3

*Life expectancy for non-TBI population was based on 2005 Colorado death rates.
[†]Estimates for Asians, Native Americans, and Other are not reported because of small sample sizes.

3–13y). Presented in table 4 are estimated years of life expectancy for the TBI cohort and respective differences from population life expectancy for those of the same age, sex, and race/ethnicity. Reductions in life expectancy declined with increasing age among all sex and race/ethnicity strata examined.

Risk Factors for Death Among Patients With Traumatic Brain Injury

A specific example of the domain-specific risk-factor modeling can be found in the legend of table 5. The patterns of findings across the subdomains and age groups are summarized.

Demographics. Older age was a consistent predictor of death for all of the adult age groups (see table 5). Increasing age was the only significant demographic predictor of death among those 4 to 19 years old. Among the other specific age groups, younger adults (20–39y) were also more likely to die if they lived in a lower income neighborhood. The same was true for those 40 to 59 years old, for whom metropolitan residence and hospitalization payment source also predicted mortality, with government payor (versus private health insurance) associated with greater risk of death. For older adults (age 60–79y) and elderly adults (age 80y and older), the significant demographic risk factors for death were older age, male sex, and metropolitan residence (see table 5).

Injury-related/acute care measures. For all age groups except the oldest (80y and older), injury severity was the strongest injury-related predictor of mortality (see table 5). Critical injuries (vs minor/moderate) conferred significant elevations in mortality. For all adult age groups, external cause of injury predicted mortality, with falls (versus vehicular causes) conferring significant elevations in risk. Discharge destination predicted mortality for the oldest 3 age groups (ie, 40y and older), with destinations other than home without follow-up care associated with greater risk of mortality.

Comorbidities. The presence of comorbid health conditions at the time of injury predicted death among adults over 20 years old (see table 5), with 3 or more health conditions (vs none) associated with a significantly higher risk of death. Number of associated injuries was generally not predictive of mortality. However, the direction of the parameter estimates suggests that the greatest risk of death is associated with having no associated injuries (ie, no injuries other than TBI), notably among older and elderly adults. Supplemental chi-square analysis demonstrated that among those with no associated injuries, there was a higher proportion of injuries with fall-related TBI and a lower prevalence of vehicular-related TBIs.

Age effects. Although not formally tested, modification of effects by age were demonstrated across the risk factor modeling strata. Among the 3 oldest age groups, the strength of the association between death and government payor demonstrated an overall decrease with older age and was significant only for the youngest of the 3 age groups (age 40–59y). A more striking pattern over the age strata was that the importance of comorbid conditions on the risk of death decreased with increasing age, notably for those with 3 or more comorbid health conditions, versus none.

DISCUSSION

We observed high excess mortality within the first month after hospital discharge (SMR=25.20; 95% CI, 16.13–39.38). Our supplemental examination of deaths within the first postdischarge month revealed a high number of accompanying TBI diagnoses and greater injury severity compared with later deaths. For those surviving past the first month to at least 1 year postdischarge, there remained a significantly elevated mortality, emphasizing the importance of continued monitoring and care in the first year after TBI. A persisting increase in long-term mortality was also demonstrated in the TBI Model Systems rehabilitation research,[1,25] but not in the population-based Olmsted County studies.[7,9] This discrepancy most likely reflects the difference in cohorts, because the Olmsted County studies included both hospitalized and nonhospitalized cases. Another difference is the relative socioeconomic diversity of our cohort, in which lower income and lack of insurance were associated with mortality.

To our knowledge, relative mortality caused by mental/behavioral disorders and nonseizure neurologic disorders has not been examined in previous reports. While anatomical damage conferred by TBI may contribute directly to the etiology of these deaths, our study design does not allow for inferences about causality. Furthermore, mechanisms by which TBI might exacerbate deaths caused by existing mental/behavioral and neurologic disorders—be they physiologic, behavioral, or related to quality of life—could not be determined in this analysis. Future investigations should examine the possible role of TBI as an effect modifier in deaths caused by mental, behavioral, and neurologic disorders.

Table 5: Domain-Specific and Full, Adjusted Cox PH Models* for Mortality as a Function of Demographics, Injury-Related Measures, and Comorbidities

Age Group (y)	4–19 (n=3313)		20–39 (n=5506)		40–59 (n=4137)		60–79 (n=2355)		80+ (n=1848)	
	Domain Submodel†	Full Model‡	Domain Submodel†	Full Model‡	Domain Submodel†	Full Model‡	Domain Submodel†	Full Model‡	Domain Submodel†	Full Model‡
Demographics										
Age (1-year increments)	**1.21 (1.06–1.38)**	**1.23 (1.08–1.42)**	**1.10 (1.07–1.14)**	**1.07 (1.04–1.11)**	**1.05 (1.03–1.07)**	**1.03 (1.01–1.05)**	**1.07 (1.05–1.09)**	**1.05 (1.03–1.06)**	**1.06 (1.05–1.08)**	**1.06 (1.05–1.07)**
Male sex	—	—	1.47 (0.94–2.31)	1.35 (0.83–2.19)	—	—	**1.23 (1.05–1.43)**	**1.24 (1.06–1.46)**	**1.40 (1.24–1.58)**	**1.45 (1.28–1.64)**
White race/ethnicity	—	—	1.48 (0.99–2.22)	1.52 (0.99–2.33)	—	—	—	—	—	—
Metropolitan residence (vs nonmetropolitan residence)	—	—	**1.86 (1.07–3.22)**	1.69 (0.95–2.99)	**1.73 (1.20–2.47)**	**1.46 (1.01–2.11)**	**1.60 (1.29–1.98)**	**1.41 (1.14–1.76)**	**1.37 (1.17–1.60)**	**1.25 (1.06–1.47)**
Median income for zip code ($10,000 decrements)	—	—	**1.26 (1.10–1.44)**	**1.20 (1.04–1.39)**	**1.15 (1.07–1.25)**	**1.11 (1.03–1.20)**	—	—	—	—
Population for ZIP code (1000-person increments)	0.98 (0.96–1.00)	0.98 (0.96–1.00)	—	—	1.01 (1.00–1.02)	1.01 (1.00–1.02)	—	—	—	—
Expected payment source (vs private health insurance)										
Self-pay	—	—	—	—	**1.43 (1.07–1.92)**	1.16 (0.86–1.57)	0.81 (0.50–1.33)	1.01 (0.60–1.69)	**0.47 (0.24–0.91)**	0.85 (0.43–1.67)
Liability insurance	—	—	—	—	**0.62 (0.40–0.95)**	0.69 (0.44–1.10)	**0.60 (0.38–0.93)**	0.77 (0.48–1.23)	0.88 (0.52–1.48)	1.51 (0.87–2.61)
Government pay	—	—	—	—	**3.05 (2.33–3.98)**	1.68 (1.27–2.23)	**1.28 (1.09–1.50)**	1.03 (0.86–1.22)	**1.31 (1.14–1.51)**	1.10 (0.95–1.28)
Injury-related/acute care measures										
External cause of injury (vs vehicular)										
Falls	—	—	**1.98 (1.25–3.14)**	**1.63 (1.02–2.62)**	**2.82 (2.21–3.59)**	**1.58 (1.18–2.11)**	**2.01 (1.64–2.47)**	**1.38 (1.09–1.75)**	**1.83 (1.48–2.27)**	**1.65 (1.27–2.14)**
Violence	—	—	1.49 (0.85–2.62)	1.12 (0.63–1.98)	**2.63 (1.89–3.67)**	1.34 (0.91–1.96)	**1.89 (1.12–3.19)**	1.56 (0.91–2.66)	0.69 (0.22–2.20)	0.81 (0.25–2.61)
Other	—	—	1.54 (0.76–3.14)	1.54 (0.75–3.14)	**2.06 (1.41–3.00)**	1.43 (0.95–2.17)	**1.69 (1.19–2.38)**	1.20 (0.84–1.73)	**1.57 (1.13–2.18)**	1.30 (0.9–1.86)
Maximum AIS of the head (vs minor/moderate)										
Severe/serious	0.81 (0.34–1.93)	0.82 (0.34–1.95)	**1.79 (1.13–2.85)**	1.53 (0.95–2.45)	**1.51 (1.17–1.95)**	1.17 (0.89–1.53)	**1.22 (1.01–1.47)**	1.13 (0.93–1.36)	—	—
Critical	**3.40 (1.15–10.08)**	3.62 (1.24–10.58)	4.28 (2.27–8.04)	3.52 (1.85–6.70)	2.05 (1.36–3.10)	1.61 (1.04–2.51)	2.03 (1.43–2.89)	1.86 (1.29–2.66)	—	—
Discharge destination (vs routine home)										
Outpatient care	—	—	1.99 (0.86–4.63)	1.77 (0.76–4.16)	**2.80 (1.93–4.06)**	**2.32 (1.57–3.42)**	**2.02 (1.52–2.68)**	**1.87 (1.40–2.50)**	**1.30 (1.02–1.66)**	1.28 (1.00–1.64)
Inpatient nursing/rehabilitation	—	—	**1.95 (1.28–2.98)**	1.44 (0.92–2.25)	**1.86 (1.46–2.38)**	**1.58 (1.23–2.04)**	2.81 (2.35–3.35)	2.58 (2.14–3.10)	1.78 (1.51–2.09)	1.76 (1.49–2.08)
Length of acute hospital stay (1-day increments)	**1.03 (1.01–1.05)**	**1.03 (1.01–1.05)**	—	—	1.02 (1.00–1.03)	1.01 (1.00–1.02)	—	—	1.02 (1.01–1.03)	1.01 (1.00–1.02)
Comorbidities										
Associated injuries of AIS ≥2 (vs only TBI)										
1	—	—	—	—	**0.74 (0.57–0.96)**	0.88 (0.66–1.17)	0.84 (0.69–1.02)	0.83 (0.67–1.02)	**0.79 (0.68–0.93)**	**0.79 (0.67–0.93)**
2	—	—	—	—	0.74 (0.52–1.07)	0.92 (0.61–1.38)	0.73 (0.53–1.00)	**0.71 (0.50–0.99)**	0.97 (0.71–1.34)	1.03 (0.74–1.45)
3 or more	—	—	—	—	0.85 (0.57–1.28)	1.07 (0.67–1.70)	0.61 (0.35–1.06)	0.57 (0.32–1.02)	0.90 (0.51–1.60)	1.06 (0.57–1.96)
Comorbid health conditions (vs none)										
1	—	—	**1.68 (1.02–2.76)**	1.49 (0.89–2.48)	**3.47 (2.37–5.07)**	**2.62 (1.75–3.93)**	1.10 (0.82–1.48)	0.90 (0.66–1.21)	1.12 (0.87–1.44)	1.00 (0.77–1.30)
2	—	—	**4.01 (2.39–6.73)**	2.93 (1.69–5.09)	5.62 (3.82–8.26)	3.55 (2.34–5.4)	**1.73 (1.30–2.31)**	1.33 (0.99–1.79)	**1.50 (1.18–1.90)**	**1.32 (1.03–1.69)**
3 or more	—	—	**9.31 (5.49–15.77)**	5.51 (3.05–9.93)	11.94 (8.30–17.19)	6.93 (4.63–10.37)	3.18 (2.46–4.12)	2.12 (1.62–2.77)	2.05 (1.64–2.56)	1.68 (1.33–2.13)

*Reported numbers are HRs with 95% CIs.

†Variables appearing in the "Domain Submodel" columns indicate P values less than .10 in the reduced, multivariable domain-specific model. Boldface covariates reached statistical significance with $P<.05$. For subjects 4 to 19 years old, for example, age and population size are the only variables in the Demographics domain associated with death with $P<.10$. Similarly, AIS and length of hospital stay are the only variables in the Injury-Related/Acute Care Measures domain associated with death with $P<.10$. No variables in the Comorbidities domain were associated with death in this age group.

‡The "Full Model" columns show the full, adjusted models for subjects 4 to 19 years old and describe the Cox PH model with all variables shown in the column included simultaneously. Covariates in boldface reached statistical significance with $P<.05$ and imply that the covariate is independently associated with time to death after adjusting for other covariates and possible confounders. For example, the full model for subjects 4 to 19 years old shows effect estimates when age, population size, AIS, and length of stay are all included in the model.

The rise in all-cause SMR from infancy to age 60 years supports a relationship between advancing age and an increased likelihood of mortality after TBI. However, we also observed a drop in SMR from age 60 years onward. The aging-related rise of competing risks of death among older and elderly adults, regardless of TBI history, likely contributes to this effect. Flaada et al[9] also report that differences between age groups in long-term mortality after TBI were accounted for by the increased mortality associated with aging itself, regardless of TBI status.

An aging-related increase in mortality may also have played a role in risk factor modeling. Although present in other age groups, there was no observed association between government payor and greater risk of death among adults age 60 years and older. This lack of effect was not accounted for by a putative high enrollment in Medicare among older and elderly adults in the cohort: government payor (including Medicare) was the expected payment source for only 58% of adults over age 60 years. Rather, the attenuation is likely in part a result of the higher mortality associated with falls observed in our cohort, with falls more prevalent among the elderly,[26] as well as an aging-related increase in mortality. The observed percentage of government payors among older and elderly adults in our cohort was lower than the estimated 83% enrollment in Medicare Parts A and B among Coloradans in this age group.[27] High enrollment in Medicare may not be accurately reflected in the expected hospitalization payment variable, as measured in our study. The CTBISS dataset included only a single payment source for each case; Medicare as a secondary payor would not have been reflected.

The lack of effect of hospitalization payment among older adults contrasts with the significant effect of government payor on mortality among those 40 to 59 years old. Among patients who had a government payor in this age group, almost one third had Medicare and would have had preexisting disability per Medicare's eligibility criteria. The remaining two thirds were largely enrolled in programs for low-income families (either Medicaid or a state indigent care program). Each of these characteristics may contribute to an increased risk of death for younger Medicare users.

Among all adults older than 40 years, living with TBI in a metropolitan area was associated with greater mortality. Although it has been suggested that TBIs for rural residents should have worse outcomes, some studies demonstrate better outcome in rural areas, possibly attributed to more openness to informal, social supports.[28] The metropolitan versus nonmetropolitan variable in our analysis depicted residence at the time of hospitalization and not necessarily residence at the time of death. The effect of changes in residence between hospital discharge and death (affecting metropolitan status and zip code–level variables) could not be accounted for in this analysis.

The presence of additional comorbid health conditions at the time of hospitalization strongly predicted mortality in risk factor modeling among adults in the TBI cohort, a finding consistent with previous research.[8,11] However, we further demonstrated that the size of the comorbidity effect is diminished among older age groups in both domain-specific and full, adjusted models. Two factors may contribute to this effect. First, there is a higher prevalence of comorbid health conditions among older and elderly patients; with all comorbidities treated equally in the analysis, this would attenuate their association with death among older age groups. Second, unmeasured aging-related factors, such as limited ability for self-care or reduced psychosocial resources, may also diminish the effect of comorbid health conditions.

Study Strengths and Limitations

This analysis provides a characterization of long-term survival after TBI in a large, sociodemographically diverse, population-based cohort. It includes the identification of deaths over an 8-year period, a disease comorbidity measure that is predictive of mortality, and risk factor modeling stratified by age group. Some limitations of this study pertain to the nature of the available datasets. Cases in the CTBISS originated from hospital discharge data, which excluded emergency departments and federal hospitals. Conclusions about mortality, life expectancy, and risk factors drawn from our work may not apply to those who are not hospitalized after TBI, those treated and released from emergency departments, and those treated in Veterans Affairs Medical Centers. Our results may have been biased by omitting these populations because nonhospitalized persons and patients released from emergency departments represent less severe TBIs (inflating the SMRs and HRs we calculated) and Veterans Affairs Medical Centers patients potentially represent more severe TBIs (leading to our underestimating SMRs and HRs). Additionally, the available data do not include levels of current functional ability or quality of life, nor do they contain health and behavioral risk factors for injury or mortality (eg, seat belt and helmet use). Thus, the effects of these factors on survival after TBI cannot be accounted for as they have in other reports. In our dataset, 0-day and 1-day stays made up one third of the cohort (4% and 29%, respectively). Such patients received inpatient services and stayed in inpatient wards on inpatient floors, and the hospitals received inpatient reimbursement (rather than reimbursement for observation or outpatient services). Inclusion of these short-stay patients may result in an overrepresentation of milder TBI.

A potential methodologic limitation of our study pertains to the exclusion of patients with 959.01 (unspecified head injury) as the sole TBI-related diagnosis code, representing approximately 7% of the cases originally meeting the CDC case definition. If such cases were of milder severity, excluding them could lead to underrepresentation of less severe TBIs, thereby inflating the overall SMR. However, separate examination of these cases demonstrated a mortality rate of 14%, which is similar to the 13% all-cause mortality observed in the analysis cohort of 18,998 patients.

Other methodologic limitations include those pertaining to coding. In our analysis, patients in a medically indigent care program were categorized into the government pay category (which included Medicare) and comprised roughly 12% of those with a government payor. Our conclusions about government pay (notably Medicare) may be limited by possible differences in mortality between the indigent care population and other government pay populations. Potential errors in coding ICD diagnoses for the hospital discharge record and causes of death would present systematic and nonsystematic biases that could not be quantified in this analysis. The AIS, as our index of TBI severity, is limited because it is solely an anatomical measure. Foreman et al[29] demonstrate that, while AIS is a better predictor of 12-month outcome than is the GCS used in clinical settings, a combination of AIS and GCS better predicts 12-month outcome than does any single index alone. However, the assessment of physiologic indicators of injury severity, such as the GCS, are not routinely captured in hospital discharge data sets. The use of ICD codes to compute AIS is itself a limitation, inasmuch as assignment of AIS is intended to be done based on direct observation of injuries or review of objective anatomical findings. Because this study included deaths from 1998, the 113 deaths occurring in that year had cause of death originally coded using ICD-9 codes, whereas

ICD-10 was used for all other study years. Comparability ratios for ICD-9 and ICD-10 suggest that the ICD-9 system codes for fewer external causes of injury and fewer falls than does the ICD-10,[30] which may lead to an underestimation of HRs for death from external causes in general and falls, specifically. No studies have been reported on the validity or reliability of causes of death on Colorado death certificates. While inaccuracies in the cause of death variable are possible, the extent to which they bias our results cannot be estimated at present.

Our methodologic approach presented other limitations unrelated to coding. The estimates of life expectancy were computed using the cohort all-cause SMR rather than age-specific SMRs. It is noted that this approach can slightly underestimate probabilities of survival at older ages.[22] Also not accounted for in our SMR estimates is the month-to-month variability in mortality. Our method of using one twelfth of the year 2000 expected rate could lead to inaccurate estimates of SMR for periods less than 1 year. In addition, the socioeconomic variable income, linked to our CTBISS data by zip code, is a community-level measure from the U.S. Census. Any conclusions about mortality and life expectancy based on income can only suggest an association that should be further explored. In terms of our risk factor analysis, it is not possible to eliminate all confounding between variables in the model. Thus, results should be interpreted within the context that unmeasured confounding could still be present.

CONCLUSIONS

This research provides support for previous reporting that TBI confers a reduced life expectancy and increased risk of death in the months and years after discharge from acute hospital care. Persons with TBI and their health care support systems should engage in regular and continuous evaluation of health status in the years after injury. Despite cross-sectional estimates of reduced life expectancy attributed to TBI, the excess risk of death after TBI decreases as survival time increases. Moreover, some specific risk factors pose a greater threat to survival than others. Those with the most critical injuries face an especially high elevation in mortality. Poorer general health at the time of injury should cue caregivers to an increased risk of early mortality, especially for those injured in their early adulthood. For older and elderly persons, the effects of aging itself appear to present competing risks to the excess risk of death posed by TBI.

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