Spinal Cord (2013) 51, 48–54

www.nature.com/sc

ORIGINAL ARTICLE

Determinants of in-hospital death after acute spinal cord injury: a population-based study

AW Selassie[1], A Varma[2], LL Saunders[3] and W Welldaregay[4]

Objectives: First, to evaluate the influence of comorbid diseases and concomitant injuries on the risk of in-hospital death after traumatic spinal cord injury (TSCI). Second, to identify the risk characteristics of TSCI patients with likelihood of death.
Study design: Population-based retrospective cohort study.
Setting: Sixty-two acute care hospitals in South Carolina, USA.
Methods: Records of 3389 TSCI patients hospitalized with acute TSCI were evaluated. Days elapsing from the date of injury to date of death established the survival time (*T*). Cox regression examined risk of in-hospital death as a function of counts of comorbid conditions and injuries along with their joint effects controlling for other covariates.
Results: Counts of comorbid conditions and injuries showed dose-dependent risk of death while in-hospital independent of demographical and clinical covariates. Hazard ratios (HR) for counts 3+, 2 and 1 comorbid conditions were 2.19 ($P<0.001$), 1.73 ($P=0.005$) and 1.20 ($P=0.322$), respectively. For counts of 4+, 3 and 2 other injuries were 1.85 ($P<0.001$), 1.81 ($P<0.001$) and 1.46 ($P=0.022$), respectively. The joint effect of the two was transadditive with statistically significant HR ranging from 1.72–3.14.
Conclusion: Counts of comorbid conditions and injured body regions strongly indicate risk of in-hospital death after TSCI and their joint effects elicited dose-dependent gradient independent of demographical and clinical covariates. Assessing risk of in-hospital death based on joint use of counts of comorbid diseases and injuries is highly informative to target TSCI patients at high risk of dying.
Spinal Cord (2013) **51,** 48–54; doi:10.1038/sc.2012.88; published online 31 July 2012

Keywords: traumatic spinal cord injury; comorbidity; concomitant injury; in-hospital death; hazard model

INTRODUCTION

The annual incidence of traumatic spinal cord injury (TSCI) in the United States is 40 per million population and there are ~262 000 persons living with TSCI.[1,2] The average age of TSCI is 40.2 years and there is a 3:1 male preponderance in the incidence of TSCI, while racial differences are minimal.[2] Published data on the proportion of deaths following TSCI differ widely from 4.1 to 10.8%.[3,4] Surveillance data in most states indicate in-hospital mortality rates of 7.5%.[5] However, there is uncertainty if all deaths are attributable to the TSCI and what risk factors indicate mortality.

Epidemiological studies of in-hospital mortality after TSCI have identified important risk factors that include advancing age,[6] lesion type and level of injury,[6] comorbidities[4,6] and complications such as venous thromboembolism,[7,8] traumatic brain injury[6] and polytrauma[3] with varying strength of association. While there is uniformity in most of the studies regarding the risk of death with advancing age and medical complications, there is discordant association on the effect of comorbid conditions due to different classification schemes. Most studies used the Charleson Comorbidity Index[9] to account for the confounding effect of pre-existing conditions. The Charleson Comorbidity Index was originally developed for prospectively predicting 1-year mortality risk among patients with breast cancer in clinical trials of new treatments. It defined weights for 19 specific comorbid diseases in a relatively small data set of 685 women that may differ from other clinical populations and did not include, for example, mental health disorders, drug and alcohol use, obesity or weight loss, fluid or electrolyte disturbances, anemia and blood loss. Validation in trauma patients indicate its limited usefulness[10] due to the small number of comorbid conditions it includes.[9] Another common approach is the more comprehensive Elixhauser Comorbidity Index. It was developed using a large data set with 1.8 million records, which includes 30 comorbid conditions.[11] Studies also accounted for polytrauma using the count of injuries in various body regions.[3,6]

We did not find any published study that evaluated TSCI mortality in large population with counts of comorbid conditions, injuries and their joint effects. The purpose of this study was to identify mutable risk factors of in-hospital death among TSCI patients accounted by the counts of comorbidities, injuries and their joint effects using time-to-event analyses. The ultimate goal is informing clinical practice to improve patient safety and survival. The study hypothesized that the risk of post-TSCI in-hospital death is incrementally elevated with more counts of comorbid conditions and concomitant injuries. It further hypothesized that joint effect of comorbidity and concomitant

[1]Department of Medicine, Division of Epidemiology and Biostatistics, Medical University of South Carolina, Charleston, SC, USA; [2]Department of Neuroscience, Division of Neurosurgery, Medical University of South Carolina, Charleston, SC, USA; [3]Department of Health Science and Research, College of Health Professions, Medical University of South Carolina, Charleston, SC, USA and [4]School of Public Health, Dillard University, New Orleans, LA, USA
Correspondence: Dr AW Selassie, Department of Medicine, Division of Epidemiology and Biostatistics, Medical University of South Carolina, 135 cannon Street, Suite 303, Charleston, SC 29425, USA.
E-mail: selassie@musc.edu
Received 7 October 2011; revised 29 June 2012; accepted 1 July 2012; published online 31 July 2012

injuries would elicit dose-response gradient independent of demographical and clinical covariables.

MATERIALS AND METHODS

Data sources

This study relied on the South Carolina hospital discharge data set. State law mandates that all 62 non-federal hospitals report uniform, abstracted billing data to the SC State Budget and Control Board. The contents of the data file are reported elsewhere.[6] The Central Nervous System injuries (CNS) Registry System augments and validates the data through medical chart review and interviewing a representative sample of patients. Data are reliable and valid. This study was approved by the Medical University of SC Institutional Review Board.

Study setting and population

Patients who sustained TSCI from 1 January 1998 to 31 December 2009 and were admitted to hospital were eligible for the study. TSCI refers to a lesion to the neural elements of the spinal cord resulting in a sudden, and depending on the level and extent of damage, variable loss of voluntary muscle strength, sensation and internal organ function below the level of spinal cord injury, including altered bladder and bowl control.[1] Patients were ascertained with ICD-9-CM diagnosis codes 806.0–806.9 and 952.0–952.9 consistent with the guideline of the Centers for Disease Control and Prevention (CDC).[1] We excluded patients coded as late effects of spinal cord injuries (907.2). About 99% of the patients had a hospital stay not exceeding 120 days, and this was used as the censoring point for the study.

Definitions

The main outcome of interest was death in an acute care facility within 120 days after acquiring TSCI. The number of days elapsing from the date of injury to date of death established the survival time (T). The main independent variable, comorbidity, relied on the count of diseases unrelated to TSCI based on the Elixhauser Comorbidity Index classification scheme.[11] All diagnosis fields were searched for these diseases and their counts were categorized as 0, 1, 2 or 3 or more (Table 1). Injury severity was determined by translating ICD-9-CM diagnosis codes into Abbreviated Injury Scale (AIS) using ICDMAP-90 software for each of the nine AIS body regions.[12] To account for the effect of multiple injuries, we counted the number of injuries from each body region other than the spine with an AIS of $\geqslant 2$, and were categorized as 1 (if only spine), 2, 3 and 4 or more. We classified neurological impairment of TSCI based on the categorization scheme of Jones *et al*.[8] as, (1) complete tetraplegia, (2) incomplete tetraplegia, and (3) complete and incomplete paraplegia including other types of impairments. Venous thromboembolism is a fatal complication of TSCI in acute care. It was identified based on secondary diagnosis ascertained with ICD-9-CM codes of 415.1, 451.1x, 451.2, 451.81, 451.9, 453.1, 453.2, 453.4, 453.8, 453.9 and V12.51. For the analysis, venous thromboembolism was split into pulmonary embolism and deep venous thrombosis. All 62 acute care non-federal hospitals in the state were categorized as Level I–III and Undesignated. The remaining variables were categorized as noted in Table 1.

Statistical analysis

Data analyses relied on SAS V.9.1.2 software package. Descriptive statistics—t-test for continuous variables and χ^2-tests for proportions—were used to compare group characteristics. The relationship between the dependent variable (in-hospital death after TSCI) and different risk factors was examined as a function of time using Cox-hazard regression. This model estimates the instantaneous relative risk of death averaged over the entire time of follow-up and assumes proportional hazard over time. This assumption was tested with the goodness-of-fit χ^2-test and graphically using log-log Kaplan–Meier curves.[13] Variables with bivariate association, P-value $\leqslant 0.20$, were included in the multivariable model. Multicollinearity among covariates was evaluated by assessing the deviations of the regression coefficients and their standard errors in the fitted univariate and multivariate models[14] and none was detected. Covariates were entered simultaneously into the model. Kaplan–Meier (K–M) survival curves graphically presented the relationship of the cumulative proportion of deaths and counts of comorbid diseases, as well as neurological impairment adjusting for a third variable. This was done in Proc Lifetest by including a 'Group' option in the 'Strata' statement. This SAS step compares the survival curves mentioned as the 'Strata' variable, while controlling the effect of a third variable mentioned as the 'Group' variable. A log-rank test was used to test the homogeneity of survival curves across comorbid counts.[15] Test statistics with P-values of <0.05 were considered significant.

We assessed heterogeneity of the stratum-specific hazard ratios between counts of comorbidities (main exposure) and in-hospital death across the number of concomitant injuries as proposed by Breslow-Day for analysis of cohort data[16] and noted transadditivity as a function of the joint effect of the two factors.[17] To avoid sparseness of cell distributions as a cross-product of the two factors, we collapsed the categories from 4×4 to 3×3 and fitted a separate model that examined these relationships accounting for the major covariates. The adjusted hazard ratios and 95% confidence intervals are reported.

RESULTS

During the 12-year period of study, 3389 acutely injured TSCI patients were hospitalized, of which 272 (8.0%) died. The average annual incidence of TSCI was 67.2 per million. This rate was 68% higher than the national average of 40 per million population. While blacks represent 31% of the population in the state, they accounted for 40.4% of the TSCI, indicating the high incidence of TSCI among minorities. Mean age of the cohort was 45.5 years. The deceased were significantly older than survivors ($P<0.001$). There were significant differences between the deceased and the survivors in all covariates but gender and race (Table 1). Significantly increased death rate was noted with more counts of comorbidities and concomitant injuries, advancing age, and higher neurological level of impairment.

Table 2 summarizes the result of Cox proportional hazards regression model. Patients with two or more comorbid conditions showed a significantly elevated risk of dying (HR for $\geqslant 3 = 2.19$, $P<0.001$ and HR for $2 = 1.73$, $P = 0.005$). Similar gradient in the HR was observed with the number of concomitant injuries with 1.85, 1.81 and 1.46 for $\geqslant 4$, 3 and 2 injuries, respectively (all $P<0.05$). The external causes of injuries in the cohort analyzed were motor vehicle crashes (42.6%), falls (30.6%), struck by/caught (13.5%), firearms (6.0%), motor cycle (3.8%) and sports (3.5%). Patients who developed pulmonary embolism had nearly a twofold increased risk of in-hospital death ($P = 0.037$), while DVT did not ($P = 0.103$). There was a 2.5-fold increased risk of death with complete tetraplegia ($P<0.001$) and a 1.6-fold increase with incomplete tetraplegia ($P = 0.001$). Older age ($\geqslant 65$) was the most significant predictor of death (HR = 5.28; 95%, $P<0.001$). Other age groups also demonstrated an increased risk of death with advancing age but this result was not statistically significant. Blacks tended to have a 24% lower risk of death compared with whites ($P = 0.034$). Persons without health insurance had a 53% increased risk of dying ($P = 0.042$). There was also lower risk of death for patients managed in Level III trauma centers ($P = 0.005$).

Table 3 shows the distribution of the various body regions affected by the trauma and the comorbid conditions noted during acute care hospitalization. Most frequently involved body regions along with SCI were abdomen and pelvic content (20.3%), contents of the thoracic cavity and the bony structures (19%), the skin and subcutaneous tissues (17.4%), and the cranium and the brain (15.8%). The comorbid conditions most commonly noted were hypertensions (14.9%), neurological conditions such as seizures and movement disorders (9.4%), and heart problems (8.4%). The joint occurrence of

Table 1 Demographic and clinical characteristics of TSCI patients by survival status

Characteristics	*Total* N = *3389 (%)*	*Survival status*		P-*value*[a]
		Deceased n = *272 (%)*	*Alive* n = *3117 (%)*	
Elixhauser comorbidity count				0.002
⩾3	413 (12.2)	70 (25.7)	343 (11.0)	
2	624 (18.4)	73 (26.8)	551 (17.7)	
1	1054 (31.1)	79 (29.0)	975 (31.3)	
0	1298 (38.3)	50 (18.4)	1248 (40.0)	
Concomitant injury count				<0.001
⩾4 other body regions	504 (14.9)	47 (17.3)	457 (14.7)	
3 other body regions	605 (17.9)	66 (24.3)	539 (17.3)	
2 other body regions	680 (20.1)	61 (22.4)	619 (19.9)	
1 (TSCI only)	1600 (47.2)	98 (36.0)	1502 (48.2)	
Venous thromboembolism				<0.001
Pulmonary embolism	32 (0.9)	10 (3.7)	22 (0.7)	
Deep venous thrombosis	108 (3.2)	7 (2.6)	101 (3.2)	
None	3249 (95.9)	255 (93.8)	2994 (96.1)	
Neurologic impairment of TSCI				<0.001
Tetraplegia	239 (7.1)	52 (19.1)	187 (6.0)	
Incomplete tetraplegia	1767 (52.1)	156 (57.4)	1611 (51.7)	
Paraplegia/other	1383 (40.8)	64 (23.5)	1319 (42.3)	
Age group				<0.001
65 and older	668 (19.7)	140 (51.5)	528 (16.9)	
45–64	1039 (30.7)	62 (22.8)	977 (31.3)	
25–44	1051 (31.0)	46 (16.9)	1005 (32.2)	
24 and younger	631 (18.6)	24 (8.8)	607 (19.5)	
Age (mean, s.d.)	45.5 (20.2)	59.3 (21.9)	44.3 (19.6)	<0.001[b]
Gender				0.103
Male	2542 (75.0)	215 (79.0)	2327 (74.7)	
Female	847 (25.0)	57 (21.0)	790 (25.3)	
Race				0.308
Black[c]	1369 (40.4)	102 (37.5)	1267 (40.6)	
White	2020 (59.6)	170 (62.5)	1850 (59.4)	
Insurance status				<0.001
Uninsured	456 (13.5)	32 (11.8)	424 (13.6)	
Indigent Care/medicaid	752 (22.2)	38 (14.0)	714 (22.9)	
Medicare	774 (22.8)	121 (44.5)	653 (20.9)	
Commercial	1407 (41.5)	81 (29.8)	1326 (42.5)	
Trauma facility level				0.045
Level I	2069 (61.1)	182 (66.9)	1887 (60.5)	
Level III	888 (26.2)	48 (17.6)	840 (26.9)	
Level II	432 (12.7)	42 (15.4)	390 (12.5)	

[a]Log-likelihood ratio χ^2-test.
[b]Paired *t*-test for equality of means.
[c]Black includes 4.8% of other races.

counts of comorbid conditions and injuries indicated enhanced risk of in-hospital death (Table 4). In our data, all but 16.9% of the TSCI patients had one of the comorbid conditions and/or one concomitant injury. Generally, with more counts of comorbidities and injuries, the higher the risk of in-hospital death (trend test $P<0.001$). However, a much stronger effect of mortality was noted with two comorbid conditions and two injuries, HR = 3.73 (95% CI = 2.14, 6.51). The effect measure reflected in this joint analysis is transadditive. For instance, patients who had two comorbid conditions with three injuries had HR = 2.92 (95% CI = 1.49, 5.72) compared with 2.66 (95% CI = 1.50, 4.05), if it were the sum of the separate components.

The survival characteristic of TSCI patients by the counts of comorbid diseases and type of neurological impairment was depicted by the Kaplan–Meier curves (Figures 1 and 2). Figure 1 shows as the

Table 2 Multivariable adjusted hazard ratio of in-hospital death after TSCI

Characteristics	*Adjusted hazard ratio (95% confidence limit)*	P-*value*
Comorbidity count		
⩾3	2.19 (1.47, 3.25)	<0.001
2	1.73 (1.18, 2.54)	0.005
1	1.20 (0.84, 1.73)	0.322
0	Referent	
Concomitant injury count		
⩾4other body regions	1.85 (1.29, 2.66)	<0.001
3 other body regions	1.81 (1.32, 2.49)	<0.001
2 other body regions	1.46 (1.06, 2.02)	0.022
1 (TSCI only)	Referent	
Venous thromboembolism		
Pulmonary embolism	1.98 (1.04, 3.76)	0.037
Deep venous thrombosis	0.53 (0.25, 1.14)	0.103
None	Referent	
Neurologic impairment of TSCI		
Tetraplegia	2.54 (1.73, 3.73)	<0.001
Incomplete tetraplegia	1.63 (1.21, 2.21)	0.001
Paraplegia/other	Referent	
Age group		
65 and older	5.28 (3.12, 8.97)	<0.001
45–64	1.49 (0.92, 2.43)	0.108
25–44	1.17 (0.71, 1.92)	0.543
24 and younger	Referent	
Gender		
Male	1.22 (0.90 1.66	0.198
Female	Referent	
Race		
Black[a]	0.76 (0.58, 0.98)	0.034
White	Referent	
Insurance status		
Uninsured	1.53 (1.03, 2.32)	0.042
Indigent Care/medicaid	0.69 (0.45, 1.04)	0.076
Medicare	1.09 (0.77, 1.55)	0.643
Commercial	Referent	
Trauma facility level (acute care)		
Level I	0.93 (0.66, 1.31)	0.672
Level III	0.55 (0.36, 0.84)	0.005
Level II	Referent	

[a]Black includes 4.8% of other races.

Table 3 Distribution of concomitant injuries and comorbid conditions among TSCI patients

ICD-9-CM-based listing of concomitant injuries and comorbidity	*Count*	*Percent*
I. Concomitant injuries based on the abbreviated injury scale		
Body region 1. Cranium and brain	535	15.8
Body region 2. Face—including ear and eye	319	9.4
Body region 3. Neck—mainly trachea, pharynx and vessels	133	3.9
Body region 4. Thorax—mainly ribs, sternum, lungs and heart	645	19.0
Body region 5. Abdomen and pelvic content	687	20.3
Body region 6. Spine (C1-S5)	3389	100.0
Body region 7. Upper extremity	328	9.7
Body region 8. Lower extremity	354	10.4
Body region 9. Skin and subcutaneous tissues	591	17.4
II. Major comorbid conditions clustered per Elixhauser et al.[11] *grouping*		
Hypertensions—complicated and uncomplicated	506	14.9
Neurological conditions—seizures, movement disorders, Parkinson's	317	9.4
Heart problems—CHF, valvular lesions, MI	285	8.4
Nutritional and metabolic disorders—deficiencies without diabetes m.	227	6.7
Mental health problems—including depression and anxiety disorders	216	6.4
Diabetes mellitus—complicated and uncomplicated	155	4.6
COPD, asthma, and other chronic lung diseases	118	3.5
Blood dyscrasias and coagulopathies	77	2.3
Other illnesses	70	2.1
Malignancies	38	1.1
Liver and digestive problems	30	0.9
Renal diseases	19	0.6
Stroke	17	0.5
Arthritis	13	0.4
No comorbid illness noted	1298	38.3

Abbreviations: CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction.

number of comorbid conditions increased, survivorship decreased, with steep decline noted for ⩾3 conditions (log-rank $P<0.001$), after adjusting for neurological impairment. At the sixtieth day mark, survival fell to 62% for TSCI patients with ⩾3 conditions, 78% for those with 2, and 84% for those with 1 comorbid condition, while survivorship was 90% for those with no comorbid condition. Figure 2 shows faster decline in survivorship with tetraplegia, complete or incomplete, than paraplegia of any type and other lesions of the spinal cord and cauda equina combined. The stratified test of equality of the curves indicate statistically significant difference (log-rank $P<0.001$).

DISCUSSION

This large, population-based cohort of persons hospitalized with acute TSCI experienced significant death rate within 120 days of hospital stay. Results from this study indicated that several factors were associated with in-hospital death. These included comorbid conditions, concomitant injuries, age, venous thromboembolism, neurological impairment of TSCI, insurance status and the trauma level of the hospital that provided acute care. Our finding uniquely highlighted the importance of joint assessment of the number of injuries and counts of comorbid conditions.

Our result showed greater death risk with more comorbid conditions and polytrauma. As noted in other studies,[4] having a single comorbidity did not show a significant effect on mortality. Overall, studies that used counts showed better risk estimates of mortality[3,6] than studies that assigned weights to selected diseases.[10] Despite prolific use, the Charleson Comorbidity Index showed little or limited predictive power on trauma mortality.[18] The incremental risk of death with more comorbid diseases and polytrauma is mainly explained by allostatic load, a dose-dependent physiological stress resulting from chronic 'wear and tear'.[19] Studies that incorporated concomitant injuries on mortality prediction mostly relied on the Injury Severity Score (ISS) with demonstrable effectiveness.[20] Our

Table 4 Adjusted[a] joint hazard ratios of in-hospital death with TSCI by joint exposure level

Total count	*Levels of joint exposure*		*Frequency (N = 3389)*	*Hazard ratio[b] (95% CL)*	P-*value*
	Count of comorbidity	*Count of injured body regions*			
6	⩾3, comorbidities	3 or more body regions	84	3.14 (1.76, 5.59)	<0.001
5	2 comorbidities	3 or more body regions	77	2.92 (1.49, 5.72)	0.002
5	⩾3, comorbidities	2 body regions	173	2.75 (1.57, 4.82)	<0.001
4	2 comorbidities	2 body regions	135	3.73 (2.14, 6.51)	<0.001
4	⩾3, comorbidities	1 body region (spine only)	852	2.87 (1.86, 4.41)	<0.001
4	1 or no comorbidity	3 or more body regions	252	2.78 (1.71, 4.53)	<0.001
3	1 or no comorbidity	2 body regions	316	1.83 (1.10, 3.05)	0.019
3	2 comorbidities	1 body region (spine only)	468	1.72 (1.02, 2.90)	0.042
2/1	1 or no comorbidity	1 body region (spine only)	1032	Referent	

[a]Adjusted for age and neurological impairment of TSCI.
[b]Linear trend of hazard ratios *P*-value <0.001.

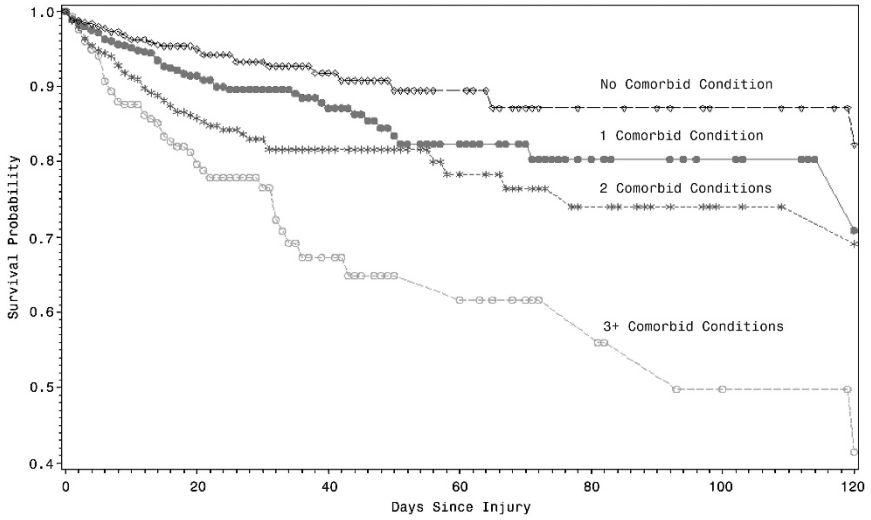

Figure 1 Kaplan–Meier plot of survival probability of TSCI patients by number of comorbid conditions. A full color version of this figure is available at the *Spinal Cord* journal online.

approach of counting all major injuries (AIS⩾2) from the nine body regions provides intuitive clarity and better predictive ability. The gradient in the risk of death noted in our study with more counts of injuries suggests the robustness of this approach. A similar effect has been observed in other studies.[3]

Age ⩾65 was strongly associated with increased risk of dying after TSCI. The influence of advanced age on risk of death after trauma is not surprising, as older patients have a higher number of pre-existing comorbid conditions that increase complications,[4] diminished number of functional cells for tissue repair, cardiac reserve and altered homeostasis.[21] Although the inherent risk potential associated with advancing age is immutable, our data suggest that aggressive treatment of comorbid diseases could reduce in-hospital mortality in older patients.

As noted in Table 4, the joint use of counts of comorbid conditions and injuries provided stronger predictive ability of in-hospital mortality after controlling for the effect the neurological level of impairment of TSCI and age. Although the joint effects of the two factors are manifested in the effect measure modification due to transadditive interaction,[17] our finding provided intuitive clarity by eliciting a dose-dependent hazard ratio of in-hospital death corresponding to higher counts of comorbid conditions and injuries. The possible biological explanation for this enhanced joint effect could be the result of allostatic load of chronic exposure from pre-existing disease stressor(s) that reduced physiological tolerance to trauma. Response to allostatic load from chronic insult (physical or emotional) and the decline in physiological tolerance had been reported to be dose dependent.[19]

The increased risk of death noted among TSCI patients without health insurance was surprising but not unexpected. A trauma outcome study in Massachusetts noted that the uninsured received less trauma-related care and experienced higher mortality rate,[22] while another large population-based study from New York[23] indicated that the uninsured were 2.35 (95% CI = 1.40–3.95) times likely to have received substandard care that increased adverse outcomes. It is therefore possible that the uninsured TSCI patients in our cohort might have not received the needed resources for appropriate care due to cost containment practices. The lower risk of death observed among blacks stood contrary to other studies. Comparable population-based studies found either slightly increased risk[3] or null effect.[8] The lower risk of death noted in Level III trauma facilities was intriguing. A likely explanation for this could be a

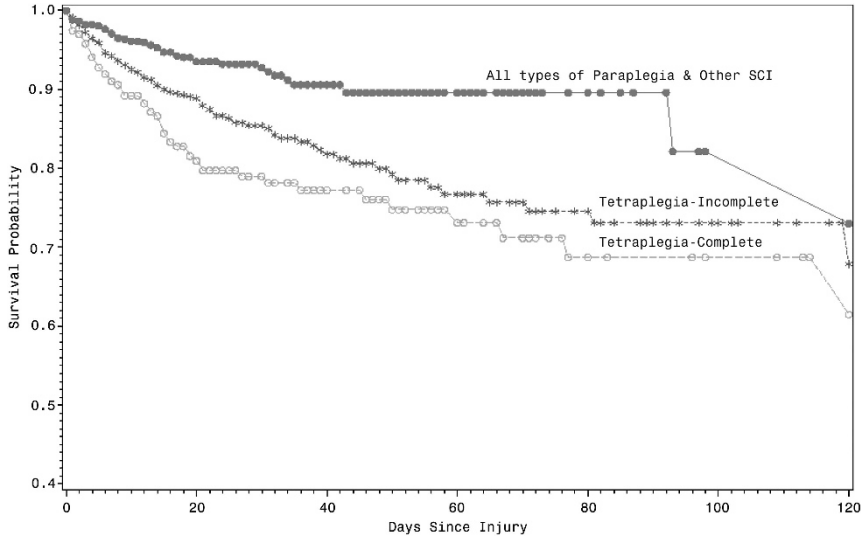

Figure 2 Kaplan–Meier plot of survival probability of TSCI patients by neurological impairment level. A full color version of this figure is available at the *Spinal Cord* journal online.

function of referral patterns where most seriously injured patients were transferred directly from site of trauma to higher level trauma facilities, leaving the less likely to die in smaller Level III facilities.

In summary, our study had several strengths. Risk of in-hospital death was quantified using a measurement approach that was not used earlier. We demonstrated that the counts of comorbid diseases and injured body regions, when used jointly or independently, elicited increased risk of in-hospital death. The use of a time-to-event analysis that incorporated clinical and demographical confounders on a large cohort of TSCI patients was another strength. Furthermore, data came from a well-validated population-based registry that received case-level information from all non-federal hospitals through legal mandate and spanning 12 years from a state that had 70% higher TSCI incidence rate than the United States.

Despite these strengths, our study had several limitations. First, although data were validated through chart review, the foundation of case ascertainment was based on administrative data primarily designed for billing purposes. In a prospective payment system, administrative data were likely to be influenced by diagnosis codes that maximize reimbursement.[24] It is, therefore, possible that the comorbid conditions and concomitant injuries listed might have been those with higher reimbursement values perhaps distorting the true estimate. Further, it is not possible to extract detailed clinical information, or to ascertain chronicity or impact of comorbid conditions, using an administrative data set. Additional clinical information from clinical examination, vital signs and specific test results may improve prediction of mortality risk. Second, there is wide variability in skillset and diagnostic resources among the hospitals increasing the possibility that the accuracy of the fourth and fifth digits of the diagnosis codes may be questionable from under-resourced hospitals. Third, there could be residual confounders that were unavailable in the data set analyzed. It is, therefore, possible that our estimate could have erred in either direction from the null. Nonetheless, the result reported in our study is consistent with the literature.

In conclusion, both counts of comorbidities and injuries strongly predicted in-hospital death after TSCI and their joint effects elicited a dose-response gradient independent of demographical and clinical covariates, thereby supporting our hypothesis. Important risk factors that could be integrated into clinical decision making include advancing age and meticulous attention to patients with comorbid conditions and multiple injuries.

DATA ARCHIVING

There were no data to deposit.

CONFLICT OF INTEREST

This manuscript has not been submitted to, nor is under review at, another journal or other publishing venue. The authors have no affiliation with any organization with a direct or indirect financial interest in the subject matter discussed in the manuscript.

ACKNOWLEDGEMENTS

This study is supported by a grant from the Department of Education, NIDRR grant number H133B090005 (PI: James Krause, PhD). The contents do not necessarily represent the policy of the Department of Education, and should not be assumed as endorsement by the Federal Government. We recognize Dr Linda Veldheer, Director of the Head and Spinal Cord Injury Division, South Carolina Department of Disabilities and Special Needs, for their data oversight and financial support to maintain the surveillance system, and Ms Georgette Demian and Ms Nicole Spivey from the South Carolina Department of Health and Environmental Control for their coordination of the abstraction process and for validating the accuracy of the medical record review report.

Author contributions: All authors have participated in (a) conception and design, or analysis and interpretation of the data; (b) drafting the article or revising it critically for important intellectual content; and (c) approval of the final version.

1 Thurman DJ, Sniezek JE, Johnson D. *Guidelines for Surveillance of Central Nervous System Injury*, 1995. Centers for Disease Control and Prevention: Atlanta, GA.
2 National Spinal Cord Injury Statistical Center. Spinal cord injury. Facts and figures at a glance. *J Spinal Cord Med* 2005; **28**: 379–380.
3 Saunders LL, Selassie AW, Hill EG, Nicholas JS, Varma AK, Lackland DT *et al.* Traumatic spinal cord injury mortality, 1981–1998. *J Trauma* 2009; **66**: 184–190.
4 Shoko T, Shiraishi A, Kaji M, Otomo Y. Effect of pre-existing medical conditions on in-hospital mortality: analysis of 20,257 trauma patients in Japan. *J Am Coll Surg* 2010; **211**: 338–346.
5 Macias CA, Rosengart MR, Puyana JC, Linde-Zwirble WT, Smith W, Peitzman AB *et al.* The effects of trauma center care, admission volume, and surgical volume on paralysis after traumatic spinal cord injury. *Ann Surg* 2009; **249**: 10–17.

6 Varma A, Hill EG, Nicholas J, Selassie A. Predictors of early mortality after traumatic spinal cord injury: a population-based study. *Spine (Phila Pa 1976)* 2010; **35**: 778–783.
7 Selassie AW, Varma A, Saunders LL. Current trends in venous thromboembolism among persons hospitalized with acute traumatic spinal cord injury: does early access to rehabilitation matter? *Arch Phys Med Rehabil* 2011; **92**: 1534–1541.
8 Jones T, Ugalde V, Franks P, Zhou H, White RH. Venous thromboembolism after spinal cord injury: incidence, time course, and associated risk factors in 16,240 adults and children. *Arch Phys Med Rehabil* 2005; **86**: 2240–2247.
9 Charlson ME, Pompei P, Ales KL, Mackenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; **40**: 373–383.
10 Thompson HJ, Rivara FP, Nathens A, Wang J, Jurkovich GJ, MacKenzie EJ. Development and validation of the mortality risk for trauma comorbidity index. *Ann Surg* 2010; **252**: 370–375.
11 Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* 1998; **36**: 8–27.
12 Baker SP, O'Neill B, Haddon Jr W, Long WB. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. *J Trauma* 1974; **14**: 187–196.
13 Kleinbaum DG. Evaluating the proportional hazards assumption. In: *Survival Analysis—A Self-Learning Text*. Springer-Verlag: New York, NY, 2010, pp 130–166.
14 Darlington GA. Collinearity. In: Armtage P and Colton T (eds). *Encyclopedia of Biostatistics*. John Wiley & Sons: Chichester, West Sussex, UK, 1998, pp 788–789.
15 Allison PD. Estimating and comparing survival curves with proc lifetest. In: The SAS Institute Inc (ed.) *Survival Analysis Using the SAS System: A Practical Guide*. SAS Institute, Inc: Cary, NC, 1995, pp. 29–59.
16 Breslow NE, Day NE. Modelling the relaionship between risk, dose, and time. In: International Agency for Research on Cancer (ed.) *Statistical Method in Cancer Research: The Design and Analysis of Cohort Data*. Oxford University Press: Lyon, France, 1987, pp. 232–270.
17 Greenland S, Lash TL, Rothman KJ. Concepts of interaction, applications of stratified analysis. In: Rothman KJ, Greenland S and Lash TL (eds) *Modern Epidemiology*. Lippincott Williams & Wilkins, 2008, pp. 71, 283–286, 302.
18 Gabbe BJ, Magtengaard K, Hannaford AP, Cameron PA. Is the Charlson Comorbidity Index useful for predicting trauma outcomes? *Acad Emerg Med* 2005; **12**: 318–321.
19 Vanitallie TB. Stress: a risk factor for serious illness. *Metabolism* 2002; **51**: 40–45.
20 McGwin Jr G, MacLennan PA, Fife JB, Davis GG, Rue III LW. Preexisting conditions and mortality in older trauma patients. *J Trauma.* 2004; **56**: 1291–1296.
21 Kuhne CA, Ruchholtz S, Kaiser GM, Nast-Kolb D. Mortality in severely injured elderly trauma patients–when does age become a risk factor? *World J Surg* 2005; **29**: 1476–1482.
22 Haas JS, Goldman L. Acutely injured patients with trauma in Massachusetts: differences in care and mortality, by insurance status. *Am J Public Health* 1994; **84**: 1605–1608.
23 Burstin HR, Lipsitz SR, Brennan TA. Socioeconomic status and risk for substandard medical care. *JAMA* 1992; **268**: 2383–2387.
24 Thurman D, Guerrero J. Trends in hospitalization associated with traumatic brain injury. *JAMA* 1999; **282**: 954–957.