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ORIGINAL ARTICLE

Risk factors for mortality after spinal cord injury in the USA

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Study design: Cohort study.
Objectives: First, to examine three sets of risk and protective factors for mortality after spinal cord injury (SCI), with an emphasis on health and secondary conditions. Second, to extend earlier work with several methodologic enhancements and addition of new predictors.
Setting: Twenty hospitals designated as SCI Model Systems (SCIMSs) of care in the United States.
Methods: Altogether, 8183 adults with traumatic SCI who received at least one follow-up evaluation between November 1995 and October 2006 from one of the SCIMSs were included in the study. There were 76 262 person–years and 1381 deaths at the end of June 2011. Mortality status determined by National Death Index and Social Security Death Index searches. Three successive sets of risk factors were evaluated with a logistic regression model on person–year observations to estimate the chance of dying in any given year.
Results: Several biographic and injury, socio-environmental and health factors were significantly related to the odds of mortality. A history of pneumonia or kidney calculus was associated with greater odds of mortality, whereas deep vein thrombosis was not. Poor general health, decline in health over the past year, hospitalization and a grade 3 or 4 pressure ulcer were also related to mortality. Consistent with a mediating effect, odds ratios declined with the addition of each successive set of factors.
Conclusion: The relationship of biographic and injury characteristics with mortality after SCI is mediated by socio-environmental and health factors. Assessment of these variables enhances our ability to identify individuals at risk for excess mortality.
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Keywords: spinal cord injury; mortality; risk; income; secondary health conditions

INTRODUCTION

Advances in medicine and injury management have helped to decrease the risk of mortality associated with spinal cord injury (SCI) in the first year post injury. However, mortality rates thereafter appear to have remained stable with long-term mortality estimated at around 1.3–2.5% annually.[1–3] If long-term mortality is to decrease, prevention strategies are needed, targeting individuals at risk for excess mortality. This study addresses this issue by identifying the risk and protective factors that may become targets for intervention.

In recent years, investigators have begun to focus on a wider array of risk and protective factors for mortality in addition to the biographic and injury characteristics that have been most widely investigated. Krause[4] developed a theoretical risk and prevention model (TRPM) to guide studies of mortality after traumatic neurologic injury, proposing a series of mediational relationships between the different sets of risk and protective factors, with health factors being most proximal and highly related to mortality. A series of analyses on data from the SCI Model Systems (SCIMSs) in the United States has been used to evaluate different sets of predictors.[5–7] Unlike studies using SCIMS data to monitor patterns of mortality over time primarily as a function of biographic and injury characteristics at injury onset,[1,8] this research has utilized follow-up data from a subset of participants. In the first study,[5] several sets of risk factors were structured *post-hoc* according to the theoretical risk model and evaluated among 5497 participants. Hospitalization in the previous year, grade 3 or 4 pressure ulcer, community integration, type of insurance and household income at or below the poverty level were all predictive of mortality and related to substantial variations in life expectancy.[5]

Several follow-up studies have been conducted using this data and addressing one or more aspects of the preliminary findings. Strauss *et al.*[6] replicated the original study[5] using updated data and a larger participant cohort ($n=7331$), only focusing on economics. They found a significant effect for economics, but smaller than obtained previously.[5] However, two recent subsequent analyses[7,9] focused on socioeconomic factors (income, education and employment), using a yet larger participant cohort ($n=8027$ and $n=7955$) and correcting for a limitation in the earlier studies, found prominent economic effects consistent or greater than that of by Krause *et al.*[5]

A series of studies using data from a clinical USA cohort[10–15] found general support for the TRPM and the importance of each type of predictor. In a simultaneous analysis of all predictors, four health factors were predictive of mortality (that is, hospitalizations, fractures/amputations, surgeries for pressure ulcers, probable major depression), whereas two types of health behaviors (prescription medication use, binge drinking) and one socio-environmental

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variable (income) were significant. Other studies have found respiratory disease and cardiovascular disease highly related to mortality after SCI.[16,17]

Taken together, these studies have identified several risk factors for excess mortality. Nevertheless, there are limitations in the scope of risk and protective factors, and study methodologies. Specifically, the last comprehensive report of the SCIMS data was 2004, and the sample size has been substantially augmented since that time, creating an opportunity for inclusion of additional predictors.

Purpose and hypotheses

Our purpose was to utilize the TRPM to structure analysis of multiple risk and protective factors for excess mortality, including three health factors not previously investigated. There were several study enhancements including an increase in the sample size, use of repeated measured predictors, a refined measure of participants' economic status and the addition of the three secondary health condition predictors. Our key hypotheses were:

1. Three newly added secondary health conditions and the new economic status measure will relate to excess mortality.
2. Socio-environmental factors will mediate the association between mortality and injury severity.
3. Health and secondary conditions will mediate the association between mortality and socio-environmental factors.

MATERIALS AND METHODS

Participants and procedures

The National Spinal Cord Injury Statistical Center Database contains data reported from SCIMS rehabilitation hospitals since 1973. Institutional review board approval was obtained locally at each center prior to data collection. Eligibility criteria included: admission within 1 year of injury, traumatic SCI, residence within the catchment area and discharge with some neurologic deficit. We excluded those <18 years old, as socio-environmental variables (income) are not measured by SCIMS for this group. The subset of data was restricted to those years during which the socio-environmental and health predictors were assessed (1995–2006). Twenty SCIMS hospitals contributed data to this study. There were a total of 8183 participants, in contrast with 5947 in the original study[5] and 7331 utilized by Strauss *et al.*[6] Among 8183 participants, 4773 had only one follow-up and the remaining 3410 had two or more follow-ups.

Measures

Mortality status was determined by routine follow-up at each SCIMS and by Social Security Death Index, with the most recent searches conducted in June 2011. We also used NDI search to confirm 340 participants' mortality status. Participants not found deceased were presumed to be alive.

Predictors from the original 2004 study[5] include: sex, age, race, neurologic level of injury, ASIA Impairment Scale (AIS) grade, ventilator dependency, marital status, four participation subscales from the Craig Handicap Assessment and Reporting Technique (CHART; physical independence, mobility, occupation and social integration), worker compensation insurance, interaction term between age and worker compensation insurance, self-perceived health (original 5-point scale was combined into three categories: poor, fair and good/excellent), health status compared to 1 year ago (worse/much worse versus others), hospitalization in the past year and pressure ulcer grade. A more complete description of these variables may be found in the original manuscript.[5] The economic sufficiency scale was replaced by a single item on annual familial income using the following categories consistent with recent research:[7] $<$\$25 000, \$25 000–\$74 999 and $\geqslant$\$75 000. Three additional health variables were included based on a history of the following conditions within the 12 months prior to assessment: pneumonia, deep vein thrombosis (DVT) and kidney calculus.

Analysis

The data were analyzed by the logistic regression model on person–year observations.[18,19] We broke each individual's event history into a set of separate observations, one for each year until death or censoring (the last available date known to be alive). For example, a person who participated in our study in 2000 and died in 2008 would contribute eight observations (or eight person–years). For each of these observations, we coded the outcome variable as 1 if deceased during that time unit, otherwise 0. The predictors were either time-invariant or time-variant (repeated measurement available). In our model, gender, race, injury level, AIS grade and ventilator usage were time-invariant predictors, whose values remained the same until censoring or deceased. All other predictors were time-variant in the model. They took on whatever value occurred during the time of measurement, and remained the same until the next measurement. We pooled these observations and estimated a logistic regression model by maximum likelihood.

Based on the TRPM, three logistic regression models were analyzed hierarchically. The first model included basic demographic and injury severity predictors. Socio-environmental factors were added to the second model, and health and secondary conditions were added to the final model. The generalized rescaled R^2, a coefficient of determination, was used to measure how well we can predict mortality based on independent variables' values. We cannot interpret this R^2 as a proportion of variance explained, therefore it was used for comparison purpose only. As its upper bound is <1, it is possible its value is lower than the R^2 of the linear regression model.[20,21] We calculated the proportion of concordant, discordant and tied pairs for each model.

Statement of ethics

We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research.

RESULTS

Of the 8183 participants, 1381 deaths occurred during the 76 262 person–years of follow-up. The mean length of time between injury date and the date of entering the study was 7.7 years, and the average follow-up time was 9.3 years. Of the participants, 79.5% were male, 72.0% were white, 50.6% had a cervical injury and 49.4% were neurologically complete injuries.

Univariate analysis

The mortality rates of those with each of the health conditions were higher than those who did not have the condition (Table 1). For instance, the mortality rate of those with pneumonia in the previous year was 46.1 compared with 17.3 for those who did not report pneumonia (per 1000 person–years).

Multivariate logistic regression

There was a modest increase in the percentage of concordant pairs and the generalized rescaled R^2 with each stage in the analysis (Table 2). The percentage of concordant pairs increased from 71.4% for model 1 to 76% for model 3. A generalized rescaled R^2 increased from.085 to 118, indicating a greater model fit at each stage.

All predictors were significant in the first stage (Table 3). Participants who were male, older and Black had a higher level of injury, a more severe injury or were ventilator-dependent at discharge, were more likely to be deceased at follow-up.

In the second stage, several new variables were significant including each of the four scales from the CHART, family income and marital status (Table 3). Worker's compensation insurance and the interaction term between age and worker's compensation insurance were not

Table 1 Characteristics of participants by mortality status

Participants' characteristic	N (Total)	N (Deceased)	Total person–years	Mortality rate[a]
Sex				
Female	1676	242	15839	15.28
Male	6507	1139	60423	18.85
Race				
Black	1477	255	12199	20.90
White	5889	1029	56701	18.15
Others	817	97	7362	13.18
Ventilator dependency				
Yes	89	44	663	66.37
No	8094	1337	75599	17.69
Injury level				
Noncervical	4042	530	38570	13.74
C1–4	1420	315	12558	25.08
C5–8	2721	536	25134	21.33
AIS grade				
A	4042	769	37963	20.26
B	976	176	9343	18.84
C	997	170	9038	18.81
D	2168	266	19918	13.35
Marital status				
Married	2844	488	28762	16.97
Unmarried	5339	893	47500	18.80
CHART physical independence[b]				
>75	5786	815	58497	13.93
⩽75	2397	566	17765	31.86
CHART mobility				
>75	4952	616	52182	11.80
⩽75	3231	765	24080	31.77
CHART occupation				
>75	3318	380	38212	9.94
⩽75	4865	1001	38050	26.31
CHART social integration				
>75	6247	969	62648	15.47
⩽75	1936	412	13614	30.26
Income				
<$25 K	4482	826	37280	22.16
$25–75 K	3400	441	27613	15.97
>$75 K	1416	114	11369	10.03
Workers' compensation				
No	7479	1261	70254	17.95
Yes	704	120	6008	19.97
Self-perceived health				
Poor	422	105	2618	40.11
Fair	1758	307	12103	25.37
Good/excellent	6629	969	61541	15.75
Hospitalization				
No	5308	776	56892	13.64
Yes	2875	605	19370	31.23
Worse health than last year				
No	6824	1141	67503	16.90
Yes	1359	240	8759	27.40
Grade 3 or 4 pressure ulcer				
No	7942	1305	74916	17.42
Yes	241	76	1346	56.46
Pneumonia				
No	7741	1262	73678	17.13
Yes	442	119	2584	46.05
Deep vein thrombosis				
No	7961	1342	75016	17.89
Yes	222	39	1246	31.30
Kidney calculus				
No	7863	1320	74342	17.76
Yes	320	61	1920	31.77

[a]Per 1000 person–years.
[b]To be consistent with the original work, all CHART scales have used a score of 75 as the cutoff point for comparison purpose.

Table 2 Predictive power of each logistic regression model

Measure	Model 1	Model 2	Model 3
Concordant pairs (%)	71.4	74.6	76
Discordant pairs (%)	24.4	22.1	20.9
Tied pairs (%)	4.2	3.3	3.1
Generalized rescaled R^2	0.085	0.106	0.118

statistically significant, and were eliminated from the analysis, as was race. The odds ratios for several indicators of injury severity decreased after the inclusion of the new set of predictors. For instance, the odds ratio of ventilator dependency decreased from 2.73 to 2.39, a 13% change (that is, $((2.39-2.73)/2.73)\times 100$). The odds ratios of C1–4 level injury, C5–8 level injury, AIS A injury, AIS B injury and AIS C injury declined by 27, 15, 21, 18 and 14%, respectively.

Several health variables were significant in the third stage, including each of those used in previous analyses. Those who had pneumonia during the past year had 1.33 times greater odds of dying. Kidney calculus was marginally significant ($P=0.05$), as the odds of dying were 1.30 times greater among those reporting the condition. However, DVT was not statistically significant and was eliminated from the final model. The odds ratios of several variables dropped further after the addition of the health measures. For instance, the odds ratios of ventilator dependency and AIS A injury declined by 5 and 6%, respectively. Odds ratios decreased for physical independence by 7%, for mobility by 10%, and for low income by 7%.

DISCUSSION

This study systematically builds upon earlier research using data from the SCIMS to predict excessive mortality by evaluating several predictors in relation to mortality. After using repeated measured variables, our results reaffirm and expand upon findings from

Table 3 Three-stage multivariate logistic regression models

Variables	*Stage I* *OR (95% CI)*	*Stage II* *OR (95% CI)*	*Stage III* *OR (95% CI)*
Sex (versus female)			
Male	1.25(1.09–1.44)	1.38(1.19–1.6)	1.38(1.2–1.6)
Race (versus all others)			
Black	1.32(1.15–1.52)	NA	NA
Age (versus 18–34[a])			
35–39	1.47(1.13–1.92)	1.53(1.17–1.99)	1.51(1.16–1.97)
40–44	2.09(1.65–2.65)	2.18(1.72–2.78)	2.16(1.7–2.75)
45–49	2.73(2.17–3.44)	2.84(2.25–3.58)	2.81(2.22–3.55)
50–54	3.72(2.94–4.69)	3.82(3.02–4.84)	3.77(2.97–4.77)
55–59	4.85(3.79–6.21)	4.95(3.85–6.35)	4.81(3.74–6.19)
60–64	6.19(4.76–8.07)	6.21(4.74–8.14)	6.05(4.61–7.94)
65–69	8.74(6.66–11.47)	8.82(6.66–11.66)	8.59(6.48–11.39)
70–74	13.4(10.13–17.73)	12.99(9.72–17.35)	12.46(9.31–16.68)
75–79	21.1(15.54–28.65)	19.69(14.35–27)	19.12(13.91–26.29)
80–84	27.27(18.5–40.2)	22.93(15.41–34.12)	23.12(15.5–34.49)
85–99	46.53(30.05–72.06)	38.43(24.56–60.11)	42.07(26.88–65.85)
Ventilator dependency (versus no)			
Yes	2.73(1.94–3.84)	2.39(1.7–3.35)	2.26(1.59–3.16)
Injury level (versus non-cervical)			
C1–4	1.9(1.63–2.22)	1.4(1.19–1.64)	1.41(1.2–1.66)
C5–8	1.8(1.58–2.04)	1.53(1.35–1.75)	1.55(1.36–1.77)
AIS grade (versus D)			
A	2.87(2.46–3.35)	2.27(1.94–2.66)	2.14(1.82–2.52)
B	2.2(1.8–2.69)	1.81(1.48–2.22)	1.82(1.48–2.24)
C	1.78(1.46–2.16)	1.52(1.24–1.86)	1.51(1.24–1.85)
Marital Status (versus married)			
Unmarried		1.37(1.21–1.56)	1.38(1.21–1.57)
CHART physical independence (versus >75)			
⩽75		1.43(1.26–1.62)	1.33(1.17–1.51)
CHART mobility (versus >75)			
⩽75		1.38(1.22–1.57)	1.25(1.1–1.42)
CHART occupation (versus >75)			
⩽75		1.23(1.07–1.41)	1.18(1.03–1.36)
CHART social integration (versus >75)			
⩽75		1.26(1.11–1.43)	1.22(1.07–1.39)
Income (versus >$75 000)			
<$25 000		1.70(1.37–2.11)	1.59(1.28–1.97)
$25 000–75 000		1.46(1.18–1.81)	1.41(1.14–1.74)
Self-perceived health (versus good/excellent)			
Fair			1.21(1.05–1.39)
Poor			1.50(1.2–1.88)
Hospitalization (versus no)			
Yes			1.51(1.35–1.7)
Worse health than last year (versus no)			
Yes			1.17(1.01–1.36)
Grade 3 or 4 pressure ulcer (versus no)			
Yes			2.32(1.8–2.98)
Pneumonia (versus no)			
Yes			1.33(1.08–1.64)
Kidney calculus (versus no)			
Yes			1.30(1–1.7)

Abbreviations: AIS, ASIA Impairment Scale; CI, confidence interval; NA, not available; OR, odds ratio.
[a]Because of relatively small sample sizes below age 35, we combined them as the reference group.

previous studies.[5,6] There was evidence to at least partially support each of the three study hypotheses.

The first study hypothesis was partially confirmed, as two of the three new secondary condition predictors (pneumonia and kidney calculus) were significant risk. The presence of either condition should therefore be taken as a serious risk factor for future mortality. However, a history of DVT was not significantly related to *future* mortality. This apparent inconsistency with the well-established literature[22] no doubt relates to the type of analysis. Without question, DVT causes excess mortality in SCI. However, the current findings suggest that this relationship may be acute and that, once successfully treated, having a history of DVT does not necessarily indicate risk of excess future mortality. Alternatively, there were only 222 DVT recorded, therefore the number of deaths was limited.

The decrease in odds ratios with the addition of socio-environmental and health predictors provides confirmation for a mediating effect of each set of variables, consistent with the TRPM and hypotheses 2 and 3. The decrease in odds ratios for injury severity variables after introduction of socio-environmental factors was particularly striking, although this no doubt reflects, to some degree, the nature of two of the participation scales (independence and mobility) and their relationship with injury severity. Smaller, yet notable, additional decreases in odds ratios were observed after introducing health and secondary conditions, which also is consistent with the TRPM. In essence, this indicates that more sophisticated and more immediate predictors of mortality take on greater importance and help to explain the observed relationships between injury severity and mortality.

There are several important clinical implications of the findings related to both socio-environmental and health factors. Many of the health conditions that related to mortality are preventable, to varying degrees, with good health care and appropriate health maintenance behaviors. Clinicians should attempt to identify and prevent these conditions using multiple prevention approaches including, but not limited to, medical, educational and behavioral strategies. Furthermore, socio-environmental factors, such as low family income, may also become the focus of interventions. Owing to the well-documented association between unemployment and elevated risk of mortality, we need to be cautious about the possible unintended consequence led by policies providing health and financial disincentives to return to work and obtaining earned income. From a clinical perspective, enhancing participation may have the added benefit of enhancing longevity. Our results indicate the protective effect of marriage. However, marriage rates are low and divorce rates high among the spinal cord injured.[23] This suggests the importance of interventions that enhance opportunities to develop interpersonal relationships and enhance overall participation.

Methodological considerations

First, we included more participants than the original studies using the subsample of SCIMS data and included more years of follow-up.[5,6] Second, we used repeated measures predictors (that is, time-dependent covariates). Third, we evaluated several new variables. Lastly, we used the more accurate NDI search to confirm mortality status for a group of participants.[24,25]

There are also several study limitations. First, as all participants were enrolled at follow-up, there may be systematic differences between those who were and were not enrolled in the study. Second, the findings apply only to those who survived the first year. Third, time-dependent covariates were only available for 42% of the participants. Fourth, as SCIMS hospitals only record secondary health conditions occurring 12 months prior to assessment, we cannot assess complications happening outside of this window. Lastly, our data did not have psychological and behaviors factors available to test the mediational effects of behavioral factors suggested by the TRPM.

Future research

Additional research should address a wider array of predictive factors including more refined socio-environmental predictors, such as access to health care, and yet more diverse health factors. It should also include health behaviors, while maintaining the focus on modifiable risk and protective factors that may become the focus of intervention strategies. Lastly, there is a need to link risk and protective factors to specific causes of death, particularly those with elevated risk after SCI including septicemia, influenza and pneumonia.

Conclusion

Besides demographic and injury severity predictors, risk of mortality is related to social participation, income, general health and several secondary health conditions. A history of pressure ulcers, pneumonia and kidney calculus represents significant risk for excess mortality. Socio-environmental factors and health factors mediate the effect of demographic and injury severity on mortality.

DATA ARCHIVING

There were no data to deposit.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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