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ORIGINAL RESEARCH

Risk and Protective Factors for Cause-Specific Mortality After Spinal Cord Injury

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Abstract

Objective: To investigate the association of multiple sets of risk and protective factors (biographic and injury, socioeconomic, health) with cause-specific mortality after spinal cord injury (SCI).

Design: Retrospective analysis of a prospectively created cohort.

Setting: Spinal Cord Injury Model Systems facilities.

Participants: Adults (N=8157) with traumatic SCI who were enrolled in a model systems facility after 1973 and received follow-up evaluation that included all study covariates (between November 1, 1995 and October 31, 2006).

Interventions: Not applicable.

Main Outcome Measures: All-cause mortality was determined using the Social Security Death Index as of January 1, 2014. Causes of death were obtained from the National Death Index and classified as infective and parasitic diseases, neoplasms, respiratory system diseases, heart and blood vessel diseases, external causes, and other causes. Competing risk analysis, with time-dependent covariates, was performed with hazard ratios (HRs) for each cause of death.

Results: The HRs for injury severity indicators were highest for deaths due to respiratory system diseases (highest HR for injury level C1−4, 4.84) and infective and parasitic diseases (highest HR for American Spinal Injury Association Impairment Scale grade A, 5.70). In contrast, injury level and American Spinal Injury Association Impairment Scale grade were relatively unrelated to death due to neoplasms and external causes. Of the socioeconomic indicators, education and income were significantly predictive of a number of causes of death. Pressure ulcers were the only 1 of 4 secondary health condition indicators consistently related to cause of death.

Conclusions: Injury severity was related to mortality due to infective disease and respiratory complications, suggesting that those with the most severe SCI should be targeted for prevention of these causes. Socioeconomic and health factors were more broadly related to a number of causes of death. Intervention strategies that enhance socioeconomic status and health may also result in reduced mortality due to multiple causes.

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Survival within the 2 years after spinal cord injury (SCI) onset has improved significantly over the past few decades,[1-3] yet long-term mortality continues to exceed that of the general population.[4] This gap in mortality may be due, in part, to a wide array of social, psychological, and environmental factors.[5] In recent years, there has been an increase in studies of risk and protective factors for mortality that may ultimately become the focus of prevention strategies.[5-11] However, nearly all this research has focused on all-cause mortality. If we are to improve longevity, we need to better understand the risk factors for specific causes of death, particularly those for which the mortality rate is highly increased for those with SCI.

According to the 2014 National Spinal Cord Injury Statistical Center (NSCISC) annual report,[12] the leading causes of death for individuals with SCI in the United States were diseases of the respiratory system (21.6%), infective and parasitic diseases (11.9%), cancer (10.0%), hypertensive and ischemic heart disease (9.9%), and other heart diseases (8.6%). The 2 causes of death that appear to have the greatest effect on reduced life expectancy include pneumonia, which account for 67.4% of the cases of diseases of the respiratory system, and septicemia, which account

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for 82.9% of the cases of infective or parasitic diseases.[12-14] Compared to the general population, the standardized mortality ratio is 17.0 for pneumonia/influenza and 36.5 for septicemia.[15] Over the years, age-adjusted mortality rates in persons with SCI have increased for accidents, endocrine, metabolic, and nutritional diseases, nervous system diseases, musculoskeletal disorders, and mental disorders; mortality rates have decreased for cancer, cardiovascular disease, stroke, arterial diseases, pulmonary embolus, urinary tract diseases, digestive diseases, and suicide.[13,16]

Several types of risk and protective factors have been linked to all-cause mortality, providing a foundation for the selection of risk and protective factors for investigation in relation to cause-specific mortality. These include biographic and injury factors, psychological and socioenvironmental characteristics, behaviors, and health status and secondary health conditions.[2-9,17-21] The most well-established risk factors include older age, higher level of SCI, and more severe neurologic impairment, including more neurologically complete injuries.[2-4,9,22] Other investigations have identified a wider array of risk factors for mortality including psychological[10,11,19,20,23,24] and behavioral[18,23,25,26] factors as well as socioeconomic[26-30] and health[5,20,31-33] factors (the last 2 are the focus of the present investigation).

Several global and secondary health variables have been associated with an increased risk of mortality after SCI, including hospitalizations,[6,20,34] comorbidities and secondary health conditions (eg, pressure ulcers, cardiovascular disease, renal disease, psychiatric disease, and depressive symptoms),[6,18,20,24,32,33,35-37] and poor health status.[34] In a prospective assessment of male patients with SCI, health factors including diabetes, heart disease, and lower levels of pulmonary function were associated with a higher risk of mortality.[36] However, in a smaller sample of veterans with SCI, health factors including vascular risk factors, pressure ulcers, and neurogenic bladder and bowel were not found to be significant predictors of survival.[38]

The purpose of this study was to develop a competing risk model of causes of death using multiple sets of predictors including biographic, injury, socioeconomic, and health variables using reanalysis of previously analyzed data. We used 6 categories of causes of death, including infective and parasitic diseases, neoplasms (cancer), respiratory system diseases, heart and blood vessel diseases, external causes, and all other causes. Our working hypothesis was that the predictors would differ as a function of cause of death.

Methods

Participants

We used data from the Spinal Cord Injury Model Systems (SCIMS) national database. Participants were recruited during acute care or inpatient rehabilitation at 1 of 20 SCIMS hospitals since 1973 after receiving institutional review board approval at each institution. At the end of March 2016, a total of 28,815 participants completed at least 1 follow-up assessment in the SCIMS database. We selected our study sample from 13,517 who had been followed between November 1, 1995 and October 31, 2006, because 4 of our secondary health condition covariates—pressure ulcer, atelectasis and/or pneumonia, deep vein thrombosis, and kidney calculus—were collected during this time frame. Of these 13,517 participants, 8216 (61%) met the following eligibility criteria: traumatic SCI, admission within 1 year of injury, discharged alive with American Spinal Injury Association Impairment Scale (AIS) or Frankel grades A to D, minimum of 18 years of age at follow-up, and having data on household income collected at least once postdischarge. We removed 59 participants who did not have valid time indicators for the survival analysis with time-dependent covariates. Therefore, our final study cohort of 8157 participants included those who had usable data out of the 13,517 individuals who completed at least 1 follow-up assessment during the study time frame (ie, November 1, 1995−October 31, 2006). This cohort has been used in previous studies of economic factors and all-cause mortality.[6,27,30]

List of abbreviations:

AIS	**American Spinal Injury Association Impairment Scale**
CI	**confidence interval**
HR	**hazard ratio**
NSCISC	**National Spinal Cord Injury Statistical Center**
SCI	**spinal cord injury**
SCIMS	**Spinal Cord Injury Model Systems**
SSDI	**Social Security Death Index**

Procedures

All-cause mortality was assessed annually using the Social Security Death Index (SSDI), an online mortality database. SSDI data now have a 3-year lag, so we have completed analyses using data that previously were the focus of all-cause mortality. This time frame also corresponds with the most recent analyses of socioeconomic data and all-cause mortality.[27] The SSDI has 92.4% sensitivity and 99.5% specificity in identifying mortality in persons in the NSCISC database.[10] Participants who were not found deceased were presumed to be alive, and their censoring date was either the most recent date of contact or January 1, 2014.

Data on cause of death were obtained from the National Death Index and classified according to the NSCISC syllabus by using procedures identical to previous studies using the SCIMS data. One of the coauthors has >30 years of experience classifying all causes, with physician clarification when necessary. The *underlying cause of death* is defined as the cause that initiated the sequence of events directly leading to the person's death. This was used for the analysis. For example, if a person's cause of death is septicemia due to (or as a consequence of) pneumonia, then septicemia is the immediate cause of death but pneumonia is the underlying cause of death. When the underlying cause of death was listed as either "SCI" or the original event that caused the SCI (such as a car crash 20y ago), a different cause was selected from the other listed causes based on clinical judgment. Causes of death were classified into 6 categories (inclusive *International Classification of Diseases, Ninth Revision, Clinical Modification* codes in parentheses): infective and parasitic diseases (001−139), neoplasms (cancer) (140−239), respiratory system diseases (460−519), heart and blood vessel diseases (390−448), external causes (E800−E999), and other causes.

Measures

Injury level was categorized as cervical 1 through 4 (C1−4), cervical 5 through 8 (C5−8), and noncervical. Neurologic completeness of injury was measured by either Frankel grade (used until 1993)[11] or AIS grade.[12] Each Frankel grade was