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A prospective study of health and risk of mortality after spinal cord injury

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Abstract

Objective—To test hypothesized relationships between multiple health parameters and mortality among persons with spinal cord injury (SCI) while controlling for variations in biographical and injury characteristics.

Design—Prospective cohort study with health data collected in late 1997 and early 1998 and mortality status ascertained in December 2005.

Setting—A large rehabilitation hospital in the Southeastern United States.

Participants—A total of 1389 adults with traumatic SCI, at least 1 year postinjury.

Interventions—Not applicable.

Main Outcome Measures—The primary outcome was time from survey to mortality (or time of censoring). Mortality status was determined using the National Death Index and the Social Security Death Index. There were 225 deaths (16.2%) by December 31, 2005.

Results—Cox proportional hazards modeling identified several significant health predictors of mortality status, while controlling for biographic and injury factors. Two sets of analyses were conducted—the first identifying the significance of a single variable of interest and the second analysis building a comprehensive model based on an optimal group of variables. Multiple types of health conditions were associated with mortality. The best set of health predictors included probable major depression, surgeries to repair pressure ulcers, fractures and/or amputations, symptoms of infections, and days hospitalized. Inclusion of these variables, along with a general health rating, improved prediction of survival compared with biographic and injury variables alone, as the pseudo R^2 increased from .12 to .18 and the concordance from .730 to .776.

Conclusions—In addition to secondary conditions that have been the traditional focus of prevention efforts (eg, pressure ulcers, urinary tract infections), amputations, fractures, and

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depressive symptoms were associated with higher risk for mortality; however, further research is needed to identify the association of specific conditions with causes of death and to determine if interventions can modify these conditions and ultimately improve survival.

Keywords

Mortality; Outcomes assessment (health care); Rehabilitation; Risk; Spinal cord injuries

Although there has been a trend toward substantial improvement in year-1 survival rates among persons with SCI, there has been no improvement beyond that in the past 25 years, and persons with SCI remain at high risk for premature death.^{1–3} Enhancing longevity is not solely dependent on new medical breakthroughs. It may also result from new knowledge from epidemiologic research that helps professionals better apply existing techniques by identifying and targeting people at highest risk and by a better understanding of the risks and protective factors leading to early mortality.

Our understanding of the epidemiology of mortality after SCI remains rather limited. We know that the chance of dying is greatest in the first year after injury.^{4–6} The risk is greatest for those with a more severe injury and multiple trauma at time of injury⁴ and for elderly persons who are likely to have compromised health and a greater number of comorbidities.⁶ Evidence from several studies, including a study spanning 50 years of 3179 participants, clearly indicates that a higher neurologic level and completeness of SCI and older age at injury are related to an elevated risk of mortality.^{6–12} Additional strong predictors of premature mortality include ventilator dependency,^{12,13} preinjury cardiovascular disease, alcohol or substance abuse, psychiatric diagnosis, and being female.⁹

Contrary to findings of Lidal et al,⁹ when compared by age and injury severity, the MSCIS found that women have slightly higher survival rates, yet the difference was not as great as between men and women in the general population.⁵ The MSCIS further reported that being white⁵ and being married¹⁴ were determinants of survival.

Causes of Death

Investigators attempting to identify health factors that may precipitate mortality have generally relied on retrospective studies or studies of causes of death, rather than prospective cohort studies collecting uniform data on health outcomes and assessing their later relationship with mortality. Whiteneck et al¹⁵ used life-table techniques to determine survival rate, causes of death, and psychosocial outcomes of persons with SCI in 2 British hospitals. The most prevalent causes of death were genitourinary problems (primarily renal failure), followed by cardiovascular and respiratory diseases. In a study of 195 persons experiencing new SCI between 1955 and 1994, Soden et al¹⁶ reported incidences of death from septicemia, pneumonia and influenza, diseases of the urinary system, and suicide were significantly greater than in the general population.

In an analysis of underlying and contributing causes of death, DeVivo and Stover¹⁷ classified a total of 1403 deaths recorded on death certificates into categories suggested by the National Center for Health Statistics. They noted that pneumonia and influenza were the primary cause of death (17.7%), followed by nonischemic heart disease (16.5%), and septicemia (12%). They calculated SMRs to compare causes of deaths of persons with SCI to the ratio of deaths expected in the general population for all causes. The highest SMRs were for septicemia (64.2 times the general population), disease of the pulmonary circulation (47.1), pneumonia and influenza (35.6), symptoms and ill-defined conditions (13.8), and diseases of the urinary system (10.9). It is noteworthy that almost all causes of death were higher among the SCI sample, with the exception of homicide, legal intervention, and cancer.

A study of 361 men with SCI ages 23 to 87, who had been injured 1 to 56.5 years, assessed the relationship between comorbid medical conditions and other health-related factors to mortality.¹⁸ The NDI provided cause-specific mortality over a median of 55.6 months (range, 0.33–74.4) through December 31, 2000. Mortality was elevated (SMR=1.47) compared with U.S. rates. Diabetes (RR=2.62), heart disease (RR=3.66), reduced pulmonary function, and smoking were major risk factors for death. The most common underlying and contributing causes of death were diseases of the circulatory system (40%) and of the respiratory system (24%).¹⁸ In a less-detailed follow-up, DeVivo et al² noted that respiratory-related cause of death occurring after the first anniversary of injury was the only cause for which the relative odds increased meaningfully during the latest time period (76% increase over 1988–1992 compared with all other causes).

CVD is the most common underlying cause of death noted on death certificates of persons with or without SCI. Long-term SCI or being nonambulatory is a risk factor for a greater prevalence of CVD, obesity, lipid disorders, metabolic syndrome, and diabetes—all factors related to increased mortality.¹⁹

Health Factors and Mortality

In the aforementioned studies, the health conditions leading to mortality were directly identified from causes of death mostly listed on death certificates. In contrast, there has been limited research that has independently and prospectively measured secondary conditions and other indicators of morbidity and linked them with eventual mortality. We therefore know very little about how the development of a specific health condition may increase the likelihood of mortality or how subtle indicators of change in health may also signal risk of early death. Nevertheless, the success of interventions to enhance longevity is dependent on an understanding of these factors.

Early studies of the association of multiple variables with mortality suggested the psychosocial and vocational outcomes were more highly correlated with mortality than were general health indicators.^{20,21} Because the time between collection of the prospective data and determination of mortality status was 11 years and 15 years, respectively, health status could have changed substantially in the years after data collection, as was suggested by a study that used a shorter follow-up interval (4y) but had only identified 22 deceased cases.²² A relatively recent report from the MSCIS in the United States¹⁴ found general health ratings were associated with an elevated risk of mortality, but the data on more specific conditions were limited.

Purpose

The purpose of this study was to identify which health outcomes are associated with elevated risk of mortality after SCI. By focusing on health factors and mortality, this study evaluated the primary component of a hierarchical empirical risk model for mortality²³ while controlling for the independent effects of biographical and injury factors.* There are 2 related objectives: (1) to evaluate the extent to which health outcomes, as measured by general indices, indicators of health impact, and secondary conditions, are associated with hazard of mortality after SCI; and (2) to evaluate the extent to which accounting for different sets of predictors enhances our prediction of mortality, moving progressively from injury severity to a comprehensive model that includes all the health factors available in the study.

*It was beyond our scope to address the other 3 components of the model: psychologic proxy variables, environmental factors, and risk and protective behaviors.

Our hypotheses were (1) when statistically controlling for biographical and injury characteristics, several types of health factors will be associated with hazard of mortality, including indices of general health, health impact, and secondary conditions; and (2) when building an optimal risk model for mortality, inclusion of health factors will enhance our prediction of hazard for mortality above and beyond that of biographical and injury factors alone.

METHODS

Participants

After obtaining approval from the institutional review board, participants were identified from 3 types of records of a specialty hospital in the Southeastern United States: (1) MSCIS patient database, (2) MSCIS registry, and (3) outpatient directory. To be included in the study, participants were adults with traumatic SCI occurring at least 1 year prior to the study that resulted in some residual impairment (those with no neurologic deficits were excluded). Of an original cohort of 1929 patients, 1389 participated (response rate, 72%).

Seventy-four percent were men, and 75% were white. The overall breakdown by sex and race and ethnicity was 54.7% white men, 19.3% white women, 20.2% minority men, and 5.8% minority women. Of the minority participants, 87.7% were African American. Average age at time of injury was 31.8 years (IQR, 20.6–39.8y). At time of prospective data collection, participants' mean age was 40.7 years (IQR, 30.3–48.9y). They had been injured a mean of 9.8 years (IQR, 3.5–12.2y), and the average education was 13.1 years. The primary etiology was vehicular crashes (50.9%), followed by falls or flying objects (17.3%), acts of violence (12.7%), sports (11.9%), and other (7.2%). Fifty-five percent reported cervical injuries. Just over a fifth (21.4%) reported functional movement below level of injury sufficient to assist ambulation.

Prospective Data Collection Procedures

Letters announcing the study were sent to all prospective participants followed by a mailed survey 4 to 5 weeks later. All introductory letters followed U.S. Postal Service standard guidelines to identify changes of address whenever possible. Two additional mail-out attempts and a follow-up phone call were made to nonresponders. Prospective data collection was initiated in July 1997 and ended in April 1998, although nearly all data had been collected by the end of December 1997. To elicit the highest possible response rates, participants were offered a \$20 stipend and were made eligible for drawings totaling \$1500.

Determination of Mortality Status

Mortality status was determined an average of 8 years after the primary data collection (December 2005). Persons not found to be deceased by December 31, 2005, were assumed alive. To ensure a comprehensive determination of mortality, we elected to use both the NDI of the National Center for Health Statistics²⁴ and the SSDI of the Social Security Administration.²⁵ Although neither data source is reported to be 100% inclusive,^{26–28} researchers often use the NDI and the SSDI to determine mortality. NDI provides access to information on decedents through a centralized computer index by searching death records provided by state offices. NDI provides information on the name of the state where death occurred, the death certificate number, and the date of death for each subject searched and identified. NDI death records are available approximately 16 months after the conclusion of a given year (ie, NDI records were not available for 2004–2005). Among persons in the MSCIS whose full name and social security number were known, sensitivity and specificity of using the SSDI were 92.4% and 99.5%, respectively.⁵ In a later study of 371 known decedents, SSDI correctly identified almost 87% of decedents ages 50 years and older, 69.8% of decedents ages

30 to 49 years, and only 34.6% of decedents younger than age 30. Factors that influenced sensitivity were older age, male sex, white race, married, and survival greater than 1 year after injury.²⁹

Measures

Several instruments were used to measure the health factors and secondary conditions, including subsets of items from the BRFSS³⁰ and LSQ-R.³¹ The OAHMQ³² was used to measure depressive symptoms. Selected items were also developed for the study.

Several types of health outcomes were measured that fall into the following broad categories: (1) general health indicators, (2) treatment variables, and (3) secondary conditions. The secondary conditions variables fell into 3 general classes: symptoms of SCI complications, (particularly symptoms of infections, eg, urinary tract complications, sweats, chills), irreversible conditions (eg, amputations), and reoccurring conditions (eg, pressure ulcers, injuries, depression). To minimize the potential for an inflated type I error rate, the biologic plausibility of each health variable was considered prior to analysis. Whereas the first 2 classes of variables, general health indicators and treatment variables, are indicators of overall health, secondary condition variables are more viable targets for intervention.

Table 1 summarizes the variables to be used in the study. The first variable (self-health rating) may be best conceptualized as the summation of health, not linked to any specific secondary condition, event, or health variable. It was measured by a single BRFSS item—self-rating current health. Two other health impact variables were measured by 2 additional BRFSS items—days in poor physical health and days in poor mental health, each of which required participants to indicate the number of days out of the past 30 for which their physical or mental health was not good. The CDC has used these items extensively and has existing data available for normative purposes. Three treatment variables were used from the LSQ-R. Each of the 3 LSQ-R items require participants to indicate over the previous 12 months the (1) number of nonroutine physician office visits, (2) number of hospitalizations, and (3) number of days hospitalized.³¹

Several types of secondary conditions were assessed. Symptoms of secondary conditions were measured by items reflecting complications of SCI. These included fevers, sweats and chills, and UTIs (self-report based on diagnoses by physician). Participants were asked to indicate the number of occurrences of each of these in the past year using ordinal rankings (0, 1–2, 3–6, 7–12, ≥13). A summary measure (summated score) was created. Irreversible secondary conditions reflect either historical events that cannot be reversed (eg, upper- or lower-limb amputation); events that led to a major nonrecurrent complication (upper- or lower-extremity fracture, DVT); or the accumulation of conditions that, although in theory reversible, in practice rarely occur (eg, upper- or lower-limb contractures, curvature of the spine). There were 8 items, each of which asked participants whether the condition had ever occurred. The items included: (1) blood clots (DVT), (2) amputation of a lower extremity (leg, foot), (3) amputation of an upper extremity (hand, arm), (4) curvature of the spine (more difficulty sitting up straight), (5) broken bone in a lower extremity (leg, foot), (6) broken bone in an upper extremity (hand, arm), (7) contracture in hip, knee, or ankle, and (8) contracture in elbow or shoulder.*

In contrast, recurrent secondary conditions may have repeated cycles. We assessed 3 types of conditions: pressure ulcers, subsequent injuries, and depressive symptoms. Pressure ulcers were defined as “*open sores* in pressure areas, such as your tailbone, ischium, heel, elbows. They are usually caused by pressure but may also be caused by friction or shearing (rubbing),

*DVT is technically reversible (the condition is corrected over time) but is not likely to be recurrent.

moisture, burns, or falls.”^{33(p1259)} Participants were to indicate: (1) the number of pressure ulcers they have had in the past year, (2) the number of days they were forced to reduce their sitting time as the result of a pressure ulcer over the past year (they were presented 8 multiple-choice categories), (3) whether they had a pressure ulcer at time of the study, (4) the number of surgeries since the onset of their SCI to heal pressure ulcers, and (5) indicate which of 5 categories best described their pressure ulcer history (categories were described along a continuum from nonrecurrent to recurrent).

Developed in collaboration with the National Center for Injury Prevention of the CDC, subsequent injuries were defined in the following manner: “The following questions relate to INJURIES, including broken bones, burns, or lacerations (cuts). Injuries happen as the result of some type of mishap or event, such as a fall, collision, motor vehicle wreck, or act of violence.”^{34(p1504)} Participants were asked the number of times in the past year they had been injured seriously enough to receive medical care in a clinic, emergency department, or hospital and if any of these injuries had been serious enough to require treatment in a hospital for at least 1 night. Subsequent injuries were reported in 19% of participants over a 12-month period, with 27% of participants who reported at least 1 injury also reporting 1 or more injury-related hospitalizations.³⁴

The 22-item OAHMQ³² was used to measure depressive symptoms. The OAHMQ was developed to measure depression in older adults and among people with physical disabilities by including few items that reflect physical or vegetative symptomatology, as these types of items often invalidate commonly used measures of depression and other clinical syndromes. Scores that were 11 or higher were considered as probable major depression. Kemp and Adams³² reported test-retest correlations were found to be .87 ($P<.001$) and alphas were .93 ($P<.001$). In terms of validity, sensitivity, and specificity were reported to be .93 and .87, respectively. The OAHMQ was also compared to 2 other depression scales with established validity and reliability, the Geriatric Depression Scale and the Symptom Checklist—90—Revised. Correlation for the OAHMQ and both measures was .70 ($P<.001$). This instrument has been used in previous research with SCI.³⁵

Data Analyses

A 3-stage hierarchical strategy to model building was employed in order to identify the association of each health variable with mortality and to define an optimal set of health predictors of mortality. Cox proportional hazards modeling was used with the number of days between the survey and event (ie, mortality) as the dependent variable. The censoring date was December 31, 2005, the date up to which mortality status could be verified.

During the first stage of analysis, a base model consisting of biographic and injury characteristics, including sex, race (white-minority), age, years lived since injury, and injury severity, was specified (table 1 summarizes the variables and their coding). Injury severity was defined by a combination of 2 items that were used to generate 5 categories that were similar, but not equivalent, to those frequently reported in the SCI mortality literature.* The groups were defined as a combination of injury level and neurologic completeness of injury, with injury level broken down into 3 categories (C1-4, C5-8, T1-S5) among those who did not report motor functional recovery sufficient for ambulation. Among those who had recovery sufficient for ambulation, we further broke this group into those with cervical injuries and those with noncervical injuries. Table 2 summarizes the breakdown of participants according to this categorization.

*Convention has been to use 4 groups based on the breakdown according to the 3 levels for ASIA grades A to C, with a single group denoting ASIA grade D regardless of injury level. We have used ambulatory status in lieu of ASIA grades which are not available and have broken this down according to cervical and noncervical injuries.

The second stage of the analysis focused on adding single, biologically plausible health outcome variables to the base model thereby “screening” each of these potential predictors for inclusion in the final stage model. All variables significant at the α equal to .10 level of significance were considered for subsequent modeling.³⁶ Once variables had been screened within a biologic domain (eg, recurrent secondary conditions), those identified were then assessed for multicollinearity within a biologic domain, and backward selection was used to identify the key predictor variables for each biologic domain. The variables identified by using this process are summarized in table 3.

The final stage of the analysis formulated a Cox proportional hazards model that consisted of the base model in addition to the variables identified in stage 2 of the analysis. After assessment for multicollinearity, backward elimination was used to identify the final fitted model. The general health indicators domain was not considered for the backward elimination; however, the general health rating and physical health rating from the BRFSS were included in alternative (exploratory) models. We chose to focus on secondary conditions as they have more direct implications for prevention.

The proportional hazards assumption was assessed using the Schoenfeld residuals³⁷ and found to be tenable. The fit of the model was assessed using the likelihood ratio test and the c statistic.³⁸ The likelihood ratio test was used to calculate the Nagelkerke pseudo R^2 .³⁹ The value of the c statistic is closely related to the area under a receiver operating characteristic curve and is interpretable as the probability that the cases (ie, deaths) have higher risks as measured by the linear component of the regression model. Accordingly, a value of 0.5 is for chance prediction and the discrimination of the model is improved as the c value approaches 1.0.^{40, 41} Once the final model was determined, all pairwise interaction terms of the secondary conditions were included in a new model to further assess goodness of fit. A Wald linear contrast indicated these interaction terms were not needed in the model ($P>.50$), and, accordingly, these interaction terms were removed. All model building was conducted using the SAS.^a The validation of the proportional hazards assumption and the estimation of the c statistic were performed using Stata.^b

RESULTS

Of the 1389 participants originally studied, missing data related to the health indicators, to the uncertainty of the injury severity, and to an unknown time of SCI onset reduced the sample size for statistical modeling. The final statistical model consisted of 1265 observations and 188 observed deaths. Of the variables listed in table 1, many were found to be independent predictors of mortality after adjustment for general biographic and injury variables (table 3). Complications related to SCI were among the predictors identified for further modeling. In particular, an increased number of UTIs, sweats and chills, and fevers were all associated with an increased risk of mortality. The summated rating of these symptoms (mean $\pm$ SD, 10 $\pm$ 10) remained highly statistically significant, and for a 1 SD increase, the adjusted hazard of mortality increased by 34% (HR=1.34, $P<.01$). This finding persisted in the final model with negligible attenuation of the magnitude of the hazard ratio for the 1 SD change (HR=1.33, $P=.03$) when all other variables were held constant in the final model.

Two classifications (or biologic domains) consisting of treatment-related variables were studied. The first classification consisted of nonspecific measures of physician and hospitalization utilization. The second classification focused on subsequent injury-related

^aSuppliers

Version 9.1.3; SAS Institute Inc, 100 SAS Campus Dr, Cary, NC 27513.

^bVersion 9.2; StataCorp, 4905 Lakeway Dr, College Station, TX 77845.

physician and hospitalization utilization. While all 3 variables contained in the subsequent injury classification were significant predictors at stage 2 of the analysis, none persisted to the final model. The more general classification did yield a predictor that remained in the final model. In particular, the number of hospital bed days a participant had over the past year (mean, 4.4 ± 8.7) was a significant predictor in both stages 2 and 3 of the analysis. For each SD increase in the number of hospital bed days (and when all other variables were held constant), the adjusted hazard for mortality increased by 15% ($HR=1.13$, $P=.03$).

A participant's pressure ulcer history, recent and since time of injury, was an important prognostic class of variables. Variables representing the frequency of pressure ulcers as well as the severity of the pressure ulcers were identified for further modeling. In addition, people who classified themselves as "Always seem to have sores, often requiring surgery or hospitalization" were at a much greater risk ($HR=2.5$, $P<.01$) of mortality when compared with the other 4 classifications of pressure ulcer history; however, this variable was eliminated from consideration by the backward selection within biological domain that was included during stage 2 of the analysis. The number of surgeries to repair pressure ulcers was a statistically significant predictor during both stages 2 and 3 of the analysis. The final model estimated that for every additional ulcer that required surgery, the risk for mortality increased by 10% ($HR=1.16$, $P<.01$) when adjusted for all other variables in the model.

There was mixed evidence for the importance of irreversible symptoms. A history of an amputation or fracture since injury predicted mortality, yet a history of other irreversible symptoms (eg, DVT, curvatures of the spine, contractures) was not predictive of mortality. While a history of an amputation alone had the largest hazard ratio in stage 2, only 2% of the sample had an amputation at the time of the study. It was for this reason that a derived indicator representing injury to the extremities (either amputation or fracture to an extremity) was considered for the final stage of modeling. This approach attenuated the magnitude of the association of amputations alone, but since 18% of the sample had either an amputation or a fracture, the variable was conducive to regression modeling strategies. In particular, the hazard for mortality was 78% higher ($HR=1.78$, $P<.01$) in those participants that reported having either a fracture or amputation in the final model.

The subsequent injuries domain did not yield a predictor for the final model; however, all 3 variables were associated with mortality in stage 2 of the modeling. After backward elimination with domain, only the number of injuries since the time of SCI was considered for stage 3. This predictor was the last variable eliminated during stage 3.

The importance of probable major depression persisted in the final model. The hazard for mortality was 86% higher ($HR=1.86$, $P<.01$) for those meeting the definition of probable major depression (scores of ≥ 11) when compared with those not meeting the definition. While not considered for the final model, the stage 2 results for the number of poor mental health days over the past 30 days (mean, $6.2 \pm 8.6d$) supported this finding. In particular, for each SD increase in the number of poor mental health days, the hazard increased by a factor of 23% when controlled only for the core adjustment variables. In addition, as a participant's perception of his/her general health decreased (lower score) or as the number of poor health days increased, the risk of mortality increased (table 3, stage 2 results). While only the diagnosis of probable major depression was considered for stage 3 of the analysis, the other general physical health variables were evaluated further in sensitivity analyses.

Table 4 presents 5 models developed through model building exercises. The first model includes only the injury severity variable broken down into 5 categories related to neurologic level of injury to neurologic completeness of injury. This is the best single indicator of the SCI per se with mortality. The pseudo R^2 was only .02 and the c statistic was only .578. The addition

of biographic variables and age at injury onset substantially increased both indicators ($R^2=.121$, $c=.730$). Model 3 is the final model determined during stage 3 of the analysis. The model provided a high degree of discrimination ($c=.771$), which was substantially higher than the first model with injury severity alone (increase of .193 in the c statistic), but only modestly higher than the full biographic injury model alone (increase of .041 in the c statistic). The pseudo R^2 value ($R^2=.167$) represented a more substantial increase when compared with the biographic injury model (increase of .046). The fourth model, adding the 2 general health variables (overall rating of health and number of poor health days), slightly further improved the pseudo R^2 value (from .167 to .178), but with a negligible increase in discrimination (c increased from .771 to .776).

Figure 1 and Figure 2 graphically illustrate the estimated survival curves for the final model. As is illustrated in figure 1, the rate of mortality in the C1-4, nonfunctional injury classification was substantially higher than the other 4 injury classifications.

Figure 2 illustrates the impact of the health indicators on survival for 2 general classes of people. The first class presented is a “good health” class in which people were free of health complications (ie, not depressed, no ulcers, etc). The second class was defined to represent people who had a complication value of 1 SD above the mean for each respective health indicator.

DISCUSSION

The unique contribution of this study is the identification of the association of multiple health risk factors for mortality after SCI using prospective data rather than causes of death. This allowed us to test 2 study hypotheses relating health factors for mortality and the additional contributions of health factors to the overall efficacy of prediction of mortality.

The first hypothesis was confirmed as multiple health factors were found to be associated with mortality. The final model included 4 primary types of secondary conditions including symptoms of secondary conditions (particularly infections), irreversible conditions (amputations and fractures), surgeries for pressure ulcers, and the presence of probable major depression. A treatment variable, number of days hospitalized, was also included in the final model. The diversity of these factors speaks to the importance of overall health promotion in multiple areas of life. It must be noted that, although these were the factors that were included in the final model, many other conditions were significantly related to mortality. The final model simply incorporates those that predict the greatest amount of unique variance. Other factors, including subsequent injuries, were also related to increased risk for mortality but shared variance with other predictors of the equation. Similarly, although we selected 1 predictor from each secondary condition, other parameters were also important. For instance, although we ultimately retained the number of surgeries for pressure ulcers in the final equation, recurrent pressure ulcers and pressure ulcers within the past year were also related to early mortality during preliminary analyses. In sum, diverse secondary conditions should serve as markers for increased risk of early mortality.

The second hypothesis, that inclusion of health factors would enhance prediction of hazard for mortality above and beyond that of biographic and injury factors alone, was also supported, although the increase in prediction varied between indicators. The pseudo R^2 estimate was enhanced by the addition of the health predictors, increasing from .121 to .167 a 38% increase. However, the discrimination only increased from .730 to .771. Inclusion of general health ratings further increased the pseudo R^2 estimate to .178 and the discrimination to .776.

The overall magnitude of the pseudo R^2 suggests there is a great deal that one needs to learn about prediction of mortality; however, until more mortality events are observed, this

prediction is not likely to improve dramatically. The modest improvement in discrimination also suggests substantial limitations of our ability to enhance classification or prediction above and beyond that of the biographic and injury predictors using current methodologies that use snapshot measures of predictors (ie, a single point in time) when those predictors change over time. This is consistent with other research from the MSCIS where 4 different models were tested and the highest generalized R^2 was only .131.²²

One particularly interesting finding is that the simplest model based in functional status alone accounted for minimal variation in mortality (pseudo R^2 =.016, c =.578) and the true enhancement and prediction came from inclusion of the biographic variables that included age at injury onset. When we utilized an alternative model that was restricted to significant health variables (hospitalizations, secondary conditions) and compared this with the base model from injury severity alone, the alternative model accounted for a greater amount of variance (the pseudo R^2 for functional status alone was .016 compared with a pseudo R^2 of .075 for the alternative model, which included hospitalizations and secondary conditions). Similarly, the alternative model had a higher discrimination (c =.676) than the model with functional status alone (c =.578). Therefore, even though functional status (ie, injury severity) is the most commonly used parameter in tables related to life expectancy after SCI other than chronologic age, by itself, it is not as strong a predictor of mortality as is overall health.

Implications

Diminished life expectancy after SCI is one of the most well established findings in SCI research. Yet, how often does increased risk of mortality enter into routine outpatient assessments, patient conferences, or physician or health provider discussions with people with SCI? The current study does not address this question, yet it certainly indicates that this is a question that needs to be addressed. How can we intervene to reduce the risk of mortality if it is not even a topic discussed with our SCI clients?

We have sufficient research to direct interventions toward early identification of risk based on the presence of multiple health indicators. Pressure ulcers, UTIs, amputations or fractures, and the development of a depressive disorder are all predictive of early mortality, and the presence of these conditions should serve as a red flag for intervention. Some interventions can and should be incorporated into routine assessments, the minimum of which is to regularly inform SCI clients of the association between their health status and early mortality so they have heightened awareness of risk.

Although we have not demonstrated a causative relationship (only an association) between these factors and mortality, secondary conditions with the strongest associations with early mortality are logical targets for intervention. One type of screening that appears to be particularly important is that of depressive symptoms and the possibility of a major depressive disorder. Because the majority of people who find their way to outpatient clinics present with problems, health care providers and outpatient clinics may assume that depressive symptoms are a natural comorbidity of health complications. A minimum of brief screening is required, sometimes followed up by a full assessment by a licensed psychologist, in order to rule out more dangerous depressive diagnoses. Because the final model suggests that a broad constellation of risk factors, reflective of diverse underlying constructs, are predictive of mortality, a more "holistic" approach to promote better health may be needed to reduce mortality.

Study Limitations

This study had several limitations that limit the generalizability of the findings. First, we have only established an association of health outcomes with mortality, not causality. Second, the

data were heavily left censored. Participants entered into the analysis an average of just under 10 years after SCI onset, so a substantial number of potential participants may have died prior to initiation of the data collection. Similar to the most recent MSCIS analysis,²² there were no data in the first postinjury year when many factors such as ventilator-dependency, injury severity, and age exert their greatest influence on the likelihood of mortality. Third, NDI data was not available from January 1 to December 31, 2005, so there may be a small number of deaths that were not detected due to the 92.4% sensitivity of the SSDI among deceased persons.¹⁴ Fourth, we did not collect data on ventilator status which is highly correlated with probability of mortality, particular during the first few years after SCI onset.²² However, we do not anticipate a significant number of these cases given the left censoring (ie, because they have the shortest longevity, and many would have died before enrollment).

There were additional factors that limit the extent to which our design had the power to fully evaluate the relationships between health factors in mortality. First, the sample size was smaller in scope than that used with studies from the model SCI systems in the United States (these studies have focused primarily on biographic and injury characteristics). Although this limitation is balanced with the more detailed data on risk and protective health factors, larger sample sizes would have greater power to identify significant predictors of mortality. Second, recall bias may have influenced the accuracy of certain reports of health conditions during the perspective data collection. Inaccuracy in self-reported health would be an error in measurement and weaken our ability to identify relationships between health and mortality. Last, risk and protective factors were only collected once with as much as an 8-year lag between collection and determination to mortality status. If data on these variables were collected more recently, they would serve as more precise predictors of mortality. For instance, probable major depression was a prominent predictor of mortality, yet these symptoms may represent chronic dysphoria consistent with a major depressive disorder (highly stable) or transient symptoms more related to situational circumstances. Similarly, the absence of these at one point in time does not preclude their later development (ie, a portion of participants reporting no symptoms would have developed symptoms at a later point in time). Therefore, it may be best to consider the current estimates as conservative.

Future Research

Three types of research are suggested by the current findings. First, given that this study was based on a multistage model of prediction of mortality and health and secondary conditions are only 1 step of factors from the model, future research should investigate additional risk and protective factors including behaviors, psychologic characteristics, and environmental factors. Investigation of these factors is particularly important since identification of risk *prior to the development of complications* will enhance prevention strategies. Second, we need to identify risk and protective predictors for the health factors that related to early mortality. This essentially speaks to the same issue—identification of risk and protective factors early in the chain of events leading to early mortality. The third recommendation for future research is both the most important and most challenging—development and evaluation of interventions to increase longevity after SCI. Our findings clearly may serve as at least a partial foundation for the development of interventions in that they identify people at high risk for early mortality and the health conditions that lead to the elevated risk of mortality. It is only through continued epidemiologic and clinical intervention research that long-term survival will likely be enhanced.

Conclusions

Using a prospective design, we identified several types of secondary health conditions that were associated with hazard for mortality after SCI including surgeries for pressure ulcers,

infection symptoms, UTIs, irreversible conditions (amputations and fractures), and the presence of probable major depression. Consideration of these factors led to substantial enhancements in prediction and classification beyond injury severity alone but only modest enhancements in prediction above a base model that included additional biographic and injury factors including age at injury. Although not demonstrating causation, the results suggest the need for prevention strategies that target people who present with multiple secondary conditions, including such basic intervention strategies as providing SCI clients with concrete information of the association of their health with the likelihood of early mortality.

List of Abbreviations

ASIA, American Spinal Injury Association
 BRFSS, Behavioral Risk Factor Surveillance System
 CDC, Center for Disease Control and Prevention
 CVD, cardiovascular disease
 DVT, deep vein thrombosis
 HR, hazard ratio
 IQR, interquartile range
 LSQ-R, Life Situation Questionnaire–Revised
 MSCIS, Model Spinal Cord Injury Systems
 NDI, National Death Index
 OAHMQ, Older Adult Health and Mood Questionnaire
 RR, relative risk
 SCI, spinal cord injury
 SMR, standardized mortality ratio
 SSDI, Social Security Death Index
 UTI, urinary tract infection

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Fig 1.
Estimated survival curves for the 5 functional injury classifications at the mean level of all other variables included in the final model.

Fig 2.

Estimated survival curves for persons free of health complications (Good Health) relative to persons with numerous complications (Poor Health). Good Health is defined as nondepressed, zero days hospitalized over the past year, free of symptoms of infections, no broken bones or amputations, and no surgical repairs of ulcers. Poor Health was defined as probable major depression, with $13.1+1$ SD days hospitalized, $20.0+1$ SD occurrences of infection-like symptoms, a broken bone or amputation, and $2.1+1$ SD surgeries to repair pressure ulcers. All other variables included in the model were assumed to be at the mean level.

Table 1
Variables Used in the Data Analysis, Type of Variable, and the Instrument From Which They Were Selected

Biologic Domain	Variable	Type of Variable *	Instrument
A. General health indicators			
	General health rating	Ordinal: scale A	BRFSS
	No. days poor health over past 30 days	Continuous	BRFSS
	No. days poor mental health over past 30 days	Continuous	BRFSS
B. Treatments			
	Nonroutine physician visits over past year	Ordinal: scale B	LSQ-R
	Hospitalizations (any reason) over past year	Ordinal: scale B	LSQ-R
	Days spent hospitalized over past year	Ordinal: scale C	LSQ-R
C. Secondary conditions			
	C1. Symptoms of SCI		
	Complications (in past year)		
	Stomach pain and distention (bloating)	Ordinal: scale D	SCI health survey
	Bowel accidents	Ordinal: scale D	SCI health survey
	Rectal bleeding	Ordinal: scale D	SCI health survey
	Urine leaking or accidents	Ordinal: scale D	SCI health survey
	Fevers	Ordinal: scale D	SCI health survey
	Sweats and chills	Ordinal: scale D	SCI health survey
	UTIs (must be diagnosed by a doctor)	Ordinal: scale D	SCI health survey
	No. of UTI-like symptoms	Continuous	Derived as sum of fevers, sweats/chills, and diagnosed UTIs
C2. Irreversible conditions			
	Report fractures to lower or upper extremities since injury	Binary	SCI health survey
	Report amputations to lower or upper extremities since injury	Binary	SCI health survey
	Fracture or amputation since injury	Binary	Derived indicator of any fracture or amputation since injury
	Reported blood clots, curvature of the spine, or contracture since injury	Binary	Derived from items on SCI health survey
C3. Recurrent conditions			
	Pressure ulcers		
	Since injury, how many pressure ulcers were severe enough to require medical attention	Ordinal: scale B	SCI health survey
	Pressure ulcer that required attention	Binary	Derived as having at least 1 pressure ulcer
	Since injury, how many surgeries to repair pressure sores	Ordinal: scale B	SCI health survey
	Since injury, what best describes pressure ulcer history	Categorical: scale E	SCI health survey

Biologic Domain	Variable	Type of Variable *	Instrument
	History of frequent pressure ulcers	Binary	Derived indicator representing people who always seem to have ulcers, often requiring surgery or hospitalization
Subsequent injuries			
	In past year, no. of injuries that required medical care	Ordinal: scale B	SCI health survey
	Since injury, no. of injuries that required medical care	Ordinal: scale B	SCI health survey
	Since injury, no. of times hospitalized due to injuries	Ordinal: scale B	SCI health survey
Depressive symptoms			
	Probable major depression	Binary: scale F	OAHRM

* For each of the following scales, the value provided in parentheses is the ordinal score used for the analysis. If no score is given (and the type of variable is categorical), the corresponding indicator (ie, dummy variables) were constructed.

Scale A: poor (1), fair (2), good (3), very good (4), excellent (5).

Scale B: 0 (0), 1 (1), ..., 9 (9), 10+ (10).

Scale C: 0 (0), 1 (1), ..., 29 (29), 30+ (30).

Scale D: How many times did you have the following problems? 0, 1–2 (1.5), 3–6 (4.5), 7–12 (9.5), 13+ (14).

Scale E: A. Have never had any pressure ulcers; B. Had pressure ulcers immediately after injury, but rarely, if at all, since initial rehabilitation hospitalization; C. Get pressure ulcers about every couple years; D. Get at least 1 pressure ulcer a year; and E. Always seem to have ulcers, often requiring surgery or hospitalization.

Scale F: OAHRM scores: normal depressive symptomatology (OAHRM scores <6); clinically significant symptomatology (OAHRM score range, 6 to <11); and probable major depression (OAHRM score range, 11–22). Binary depression variable of OAHRM scores ≥ 11 .

Table 2

Breakdown as a Function of Injury Level and Neurologic Completeness and Ability to Ambulate

Category	n	% [*]
C1-4, nonfunctional	176	13.2
C5-8, nonfunctional	407	30.5
Noncervical, nonfunctional	469	35.2
Cervical, ambulatory	142	10.7
Noncervical, ambulatory	139	10.4
Unclassified (not used in analysis)	56	

* Percentages exclude the 56 observations not classified.

Table 3
Cox Proportional Hazards Analysis for the Preliminary and Full Models

Biologic Domain	Stage 2 Results				Stage 3 Results			
	Variable	HR [*]	95% CI	P	Selected for Stage 3	HR [†]	95% CI	P
Core adjustment variables [‡]								
Functional status	C1-4, nonfunctional	NA	NA	NA	Yes	4.25	1.88–9.64	<.01
	C5-8, nonfunctional	NA	NA	NA	Yes	2.87	1.30–6.34	<.01
	Noncervical, nonfunctional	NA	NA	NA	Yes	2.58	1.17–5.68	.02
	Cervical, ambulatory	NA	NA	NA	Yes	1.29	0.50–3.33	.60
	Noncervical, ambulatory (referent)	NA	NA	NA	Yes	1.00	ND	ND
	Caucasian vs non-Caucasian	NA	NA	NA	Yes	1.14	0.82–1.60	.43
	Sex	NA	NA	NA	Yes	1.22	0.87–1.73	.25
	Age at Injury	NA	NA	NA	Yes	1.06	1.05–1.07	<.01
	Years since injury	NA	NA	NA	Yes	1.04	1.02–1.06	<.01
	A. General health indicators							
	General health rating	0.62	0.53–0.72	<.01	No [§]	ND	ND	ND
	Poor health days	1.02	1.01–1.04	<.01	No [§]	ND	ND	ND
	Poor mental health days	1.03	1.01–1.04	<.01	No [§]	ND	ND	ND
B. Treatments								
	Nonroutine doctor visits	1.08	1.04–1.12	<.01	Yes	NS	ND	ND
	Hospitalizations	1.16	1.09–1.23	<.01	No	ND	ND	ND
	Days spent in hospital	1.03	1.02–1.05	<.01	Yes	1.02	1.00–1.03	.03
C1. Symptoms for SCI complications								
	Stomach pain/distention	1.02	1.00–1.05	.05	No	ND	ND	ND
	Bowel accidents	0.99	0.96–1.03	.71	No	ND	ND	ND
	Rectal bleeding	0.99	0.96–1.03	.59	No	ND	ND	ND
	Urine leaking or accidents	0.99	0.97–1.02	.61	No	ND	ND	ND
	Fevers	1.05	1.02–1.08	<.01	No	ND	ND	ND

Biologic Domain	Stage 2 Results				Stage 3 Results		
	Variable	HR [*]	95% CI	P	Selected for Stage 3	HR [†]	95% CI
C2. Irreversible conditions	Sweats and chills	1.05	1.02–1.08	<.01	No	ND	ND
	UTIs	1.07	1.03–1.10	<.01	No	ND	ND
	No. of infection symptoms	1.03	1.02–1.04	<.01	Yes	1.02	1.00–1.03
Fractures to extremities		1.50	1.05–2.15	.03	No	ND	ND
	Amputations to extremities	3.69	2.14–6.37	<.01	No	ND	ND
	Fracture or amputation since injury	1.81	1.31–2.52	<.01	Yes	1.78	1.27–2.51
	Other irreversible secondary conditions	1.24	0.94–1.64	.13	No	ND	ND
Pressure ulcers							
No. of ulcers needing medical care since injury		1.15	1.09–1.21	<.01	No	ND	ND
	At least 1 ulcer needing care	1.92	1.43–2.62	<.01	Yes	NS	ND
	Surgeries to repair ulcers	1.20	1.13–1.27	<.01	Yes	1.16	1.08–1.23
Subsequent injuries	History of frequent ulcers	3.68	2.18–6.19	<.01	No	ND	ND
Injuries in the past year needing medical care		1.13	1.00–1.26	.04	No	ND	ND
	Injuries since injury needing medical care	1.18	1.10–1.26	<.01	Yes	NS	ND
	Hospitalized for injury since injury	1.16	1.09–1.25	<.01	No	ND	ND
Depression							
	Probable major depression	2.21	1.66–2.94	<.01	Yes	1.86	1.36–2.53

Abbreviations: ND, no data to enter into cell; NS, variable was eliminated from the stage 3 model using backward selection.

* HRs from a Cox model predicting the time, measured in days, from survey to either mortality or censoring (12/31/05) and adjusted for core (biographic and injury) variables listed in the first biologic domain.

[†] HRs for the stage 3 final model are adjusted for all other variables in which an estimate is provided. Dashes indicate that the variable was not considered for stage 3 analysis.

[#] HRs for core adjustment variables not shown for stage 2 results because there is variability of the estimates depending on which of the candidate variables is used in the analysis.

[§]General health indicators, while significant predictors in stage 2, were not considered for stage 3 of the analysis. They were used, however, for sensitivity analyses and alternative model specifications.

Summary of the Pseudo R^2 , R Change, c Statistic, and Change in the c Statistic for Each of 4 Stages of Model Building and an Alternative Model

Model	Description	R^2	change	c Statistic	Change
1	Injury severity only	.016	ND	.578	ND
2	Core biographic and injury variables	.121	.105	.730	.152
3	Full final stage 3 model	.167	.046	.771	.041
4	Alternative model that includes the general health ratings	.178	.011	.776	.005
A	Treatment and secondary conditions	.075	.059	.676	.098

Abbreviation: ND, no data to enter into cell.

1. Five category breakdown (C1-4, C5-8, noncervical, etc).
2. Add core biographic variables includes white race, male sex, and age at injury.
3. Final model. Exclusive of general health indicators.
4. Alternative model that includes general health ratings.
- A. Alternative model that included only treatments and secondary conditions, but not biographic or injured variables. The change figures for this model are compared first model.