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ORIGINAL ARTICLE

Predictors of mortality in veterans with traumatic spinal cord injury

MH Rabadi[1,2], SK Mayanna[1] and AS Vincent[3]

Study design: Retrospective.
Objectives: To determine the predictors of mortality in veterans with traumatic spinal cord injury (tSCI).
Setting: Tertiary clinic in the state of Oklahoma.
Methods: One hundred and forty-seven patients with tSCI who were enrolled in our Spinal Cord Injury program from 1 January 2000 to 31 December 2011 were retrospectively studied. The study sample was divided into two groups, based on the survival status by 31 December 2011.
Results: In this sample of 147 patients with tSCI, survival at the end of the 12-year study period was 60%. There were three major causes of death: infection-related, such as pneumonia (21%), urinary infection (14%), and infection of the pressure ulcers (11%); cardiovascular-related, such as congestive heart failure (16%), coronary arterial disease (13%), and atrial fibrillation (2%); and cancer-related (16%). In veterans with complete SCI, deaths were mainly infection-related and occurred in the hospital (51%), while deaths in veterans with incomplete SCI were primarily cardiovascular and cancer-related and occurred in the community. A Cox regression analysis showed the age at the time of injury to be the main predictor of SCI-related mortality.
Conclusion: This study suggests that an older age at the time of injury is a significant predictor of mortality following tSCI with patients more likely to die from cardiovascular deaths than the general population. These findings support the need for preventative strategies, including a focus on cardiovascular risk factor management, in order to decrease long-term mortality.
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Keywords: mortality; veterans; traumatic; spinal cord injury; retrospective; observational

INTRODUCTION

According to the National Spinal Cord Injury Statistical Center, it is estimated that the annual incidence of traumatic spinal cord injury (tSCI), not including those who die at the scene of the accident, is $\sim$40 cases per million in the United States or 12 000 new cases each year. The number of people in the United States who were alive in 2009 with SCI was approximately 262 000 persons.[1] With recent medical advances, the survival rate for patients with tSCI has greatly improved, with life expectancy approaching that of the general population. There have also been historical changes in the leading cause of death following SCI. Although renal failure and urinary tract infections were once the leading causes of death among persons with tSCI,[2] advances in urological management have addressed this. Today, the leading causes of death are infection, respiratory, and cardiovascular diseases.[1,3–6] Nonetheless, the mortality rates remain significantly greater in the first 2 years following injury owing to increased medical and surgical complications. Prognostic factors for increased survival have been young age at the time of injury, incomplete and lower spinal injury level.[7]

The combination of these risk and prognostic factors has been examined in four large studies (Australia, Denmark, United Kingdom and the United States), which have looked at predictors of survival after tSCI over a time period greater than 10 years. However, these studies were undertaken in different time periods, within different medical care systems, and used different methods of assessing the severity of SCI, thus making a comprehensive comparison difficult. The study authors, Lidal *et al.*,[3] followed 387 patients from Denmark over a 20-year period. Predictors of mortality in this sample were increased age at the time of injury, higher injury level (cervical), depression, alcohol/substance abuse and pre-injury heart disease. The main causes of death were pneumonia (16%), coronary heart disease (13%) and urogenital causes (13%). The study authors concluded that their high mortality rate was due in part to preventable SCI-related complications and stressed the importance of addressing these treatable factors. The next study, by O'Connor[4], followed 2892 patients with tSCI in Australia over a 12-year period and found age at the time of injury (>45 years), level of injury, male gender and severity of injury to be the main predictors of mortality. Whitneck *et al.*[5] followed 834 patients with tSCI in the United Kingdom over a 40-year period and found that 24% of the deaths were due to genito-urinary, followed by cardiovascular (23%) and respiratory (14%), causes. Renal deaths were more common in paraplegics, and respiratory failure was more common in tetraplegics. Furthermore, they found that the cause of mortality in tSCI was more attributable to the aging process as these patients were living longer and closely approximated the general population. Finally, Samsa *et al.*[6] followed 5545 veterans over a 40-year period. They showed that older age at the time of injury was a strong predictor of poor long-term survival. The level of injury was a predictor of short-term mortality. Urogenital causes and infection were responsible for 10% of the deaths.

[1]Veterans Affairs Medical Center, Oklahoma City, OK, USA; [2]Department of Neurology at the Oklahoma Health Sciences Center, Oklahoma City, OK, USA and [3]Cognitive Science Research Center, University of Oklahoma at Norman (Statistician), Oklahoma City, OK, USA
Correspondence: Dr MH Rabadi, Veterans Affairs Medical Center, 921 NE 13th Street, Oklahoma City, OK 73104, USA.
E-mail: rabadimh@gmail.com
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Given these varied findings, further research would help provide insight into the factors associated with decreased survival, which we can then address to help decrease mortality. The primary aim of this study was to therefore explore predictors of mortality in a sample of veterans with tSCI who have been enrolled in and have regularly followed our SCI program since 2000.

METHODS

Participants

Following the local Institutional Review Board approval, a retrospective chart review of 147 veterans with tSCI, registered in our SCI program at the Oklahoma City VA Medical Center since 1 January 2000 and followed routinely (every 4 months and annually) until 31 December 2011 (end of the study period), was undertaken. This represents all the patients with tSCI seen in the clinic during this time frame. Veterans with tSCI are enrolled in our program within a year of their injury. During the clinic visit, patients were assessed for current medical conditions such as urinary tract infection, pneumonia, myocardial infarction, congestive heart failure and arrhythmias. Self-care strategies for managing neurogenic bowel and bladder complaints, pressure ulcer prevention and the control of modifiable vascular risk factors such as blood pressure, blood sugar, and lipids were also reviewed during their follow-up visits. Data collected for the chart review included the age of injury, gender, ethnicity, level and severity of injury (ASIA Impairment Scale (AIS) grade: A–E), modifiable vascular risk factors such as hypertension, diabetes mellitus, hyperlipidemia, body mass index and current smoking status.

Table 1 Baseline demographics of veterans with traumatic spinal cord injury whether they were alive or dead (mean ± s.d. or %)

Grouping variables	*Total population (*N = *147)*	*Alive (*n = *88)*	*Dead (*n = *59)*	P*-value*
Age, years	59.6 ± 13.5	56.2 ± 12.9	64.7 ± 12.8	**0.0001**[a]
Gender (M:F)	144:3	85:3	59:0	0.27[c]
Ethnicity (White/Black/American Indian/Hispanic)	121/19/4/2	72/11/3/1	49/8/1/1	0.97[c]
Age at the onset of SCI (years)	37.7 ± 14.4	34.6 ± 13.1	42.3 ± 15.1	**0.001**[a]
Duration since SCI (years)	24.0 ± 15.8	24.3 ± 15.9	23.5 ± 15.8	0.74[a]
Spinal injury level (%)				
Cervical	53.0	51.1	55.9	0.82[b]
Thoracic	33.3	35.2	30.5	
Lumbosacral	13.6	13.6	13.6	
Spinal injury severity—AIS grade (%)				
A	36.1	29.6	45.8	**0.03**[b]
B	17.0	12.5	23.7	
C	18.4	22.7	11.9	
D	23.1	28.4	15.3	
E	5.4	6.8	3.4	
Etiology of SCI (%)				
Motor vehicle accident	46.6	48.3	44.8	0.10[b]
Gunshot	13.1	10.3	17.2	
Fall	26.9	24.4	31.0	
Diving	4.1	3.5	5.2	
Other	9.0	13.8	7.7	
Risk factors (%)				
Hypertension ($n = 128$)	51.6	50.0	54.8	0.61[b]
Diabetes mellitus ($n = 136$)	22.8	22.7	22.9	0.98[b]
Hyperlipidemia ($n = 124$)	49.1	57.7	34.8	**0.01**[b]
Body mass index (BMI; $n = 132$)	26.8 ± 8.0	27.8 ± 7.2	25.0 ± 8.9	**0.05**[a]
Current smoker ($n = 137$)	43.1	42.5	44.0	0.87[b]
Vascular risk factors total[d]	2.0 ± 1.3	2.2 ± 1.3	1.6 ± 1.3	**0.006**[a]
Co-morbidities				
Myocardial infarction ($n = 143$)	16.1	9.2	26.8	**0.005**[b]
Congestive heart failure ($n = 137$)	5.1	4.6	6.0	0.71[c]
Depression ($n = 142$)	45.8	48.3	41.8	0.45[b]
Pressure ulcers ($n = 144$)	34.0	23.5	49.2	**0.001**[b]
Pressure ulcers Grade 3–4 (% of those with pressure ulcers)	42.9	55.0	34.5	0.15[b]
Osteomyelitis ($n = 110$)	16.4	12.7	20.0	0.30[b]
Neurogenic bowel ($n = 136$)	53.7	61.7	41.8	**0.02**[b]
Neurogenic bladder ($n = 142$)	85.2	82.6	89.3	0.27[b]

Abbreviations: AIS, ASIA Impairment Scale; F, female; M, male; SCI, spinal cord injury.
Bold highlights significance of the baseline demographics between the two groups.
[a]Student's *t*-test.
[b]χ^2-Test.
[c]Fisher's exact test.
[d]Calculated as the total number of vascular risk factors recorded.

Data on co-morbidities such as the presence of cardiovascular diseases (for example, coronary artery disease and cardiac failure) and tSCI-related complications (for example, presence of depression, pressure ulcer with or without osteomyelitis and neurogenic bowel and bladder) were also collected during their initial evaluation and subsequent follow-up visits by a certified physician at the VA Medical Center. Survival was recorded up to 31 December 2011. The cause(s) and location of death (home, long-term care facility or during acute hospitalization) were obtained from the patient's death certificate.

Statistical analysis

Differences between baseline and clinical characteristics were examined based on the survival status (alive/deceased) at the end of the study period. Time since the injury was calculated as the difference between the date of injury and the end-of-study date or the death date for deceased patients. Three groups were created among the deceased patients based on the year of death (2000–2003, 2004–2007 and 2008–2011) to examine whether the mortality rate and cause changed over the 12-year study period. Interval data were compared between groups using a two-tailed Student's *t*-test. Categorical data were compared using a χ^2 or Fisher's exact test, as appropriate. The overall survival was estimated using the Kaplan–Meier method.[8] The survival duration was calculated from the date of the injury to the date of death or the end of the study period. The association of age at the time of injury, severity of injury (AIS grade), vascular risk factor score, pressure ulcers (presence/absence) and neurogenic bladder and bowel (presence/absence) with survival was evaluated using Cox proportional hazards regression models and summarized using hazard ratios and 95% confidence intervals. A multivariate model using the stepwise selection with the *P*-value for a variable to enter or leave the model set at 0.05 was used for the survival rate and survival analysis. The standard mortality ratio was calculated to compare the risk of death in our veteran tSCI population with that in the general population stratified by age and gender over the duration of the follow-up. Data analyses were conducted using the SAS software (SAS System for Windows, ver. 9.2, SAS Institute Inc., Cary, NC, USA). The significance level was set at $P<0.05$ for all the analyses.

RESULTS

Table 1 presents the baseline characteristics of our study sample ($N=147$). White men comprised 82% of the study population, with a mean age during the clinic visit (±s.d.) of 59.6±13.5 years (range: 26–90 years). The mean age at the time of injury was 38±14.4 years (range: 18–82 years), and the duration of time that had passed since the injury was 24±16 years (range: 1–67 years), with AIS A and B occurring in 53% of the total sample. The cervical part of the spinal cord was involved in 53% of the cases, and the primary cause of the tSCI was motor vehicle accidents (47%).

Patient mortality at the end of the 12-year study period was 40% (59 deaths). Patients with tSCI AIS Grade A and B mainly died in the hospital, while patients with tSCI AIS Grade C, D and E mainly died in the community ($P=0.26$; Table 2a and 2b). There was no difference between the frequencies of deaths across each of the year bands ($\chi^2=1.25$, $P=0.53$). Similarly, there were no significant differences in the distribution of the cause of death according to the year of death ($P=0.068$; Fisher's exact test). However, there was a trend toward an increase in the number of cardiovascular deaths ($P=0.06$) and a trend toward a decrease in the number of infection deaths ($P=0.08$) from 2004 onward (Table 3). For those with a known cause of death, the three main causes of death were infection (46%), cardiovascular (23%) and cancer (16%). There were more infection-related deaths in veterans with AIS Grade A and B and more cardiovascular- and cancer-related in those with AIS Grade C, D and E ($P=0.045$).

Based on the Kaplan–Meier analysis, the overall estimated survival since the time of injury for the SCI patients was 39.3±2.3 years (mean±s.e.m.). The 10- and 20-year survival rates after injury were 87% and 78%, respectively. When the Cox proportional hazards analysis adjusted for the covariates (Table 4), only age at the time of injury was significantly associated with survival in this multivariate

Table 2a Causes and locations of death in veterans with traumatic spinal cord injury

Cause of death[a] (n(%); n=56)	
Infection	
Urinary tract infection	8 (14)
Pneumonia	12 (21)
Pressure ulcer	6 (11)
Cardiovascular	
Myocardial infarction	7 (13)
Stroke	2 (4)
Arrhythmia	1 (2)
Cardiac arrest	1 (2)
Congestive heart failure	2 (4)
Cancer	9 (16)
Other	
Respiratory failure	5 (9)
End-stage renal disease	1 (2)
Alcoholic cirrhosis	1 (2)
Pulmonary embolism	1 (2)
Deceased at (n(%); n=57)	
Home	26 (46)
Hospital	26 (46)
Nursing home	5 (9)

Place of death was unavailable for two subjects.
[a]Cause of death was unavailable for three subjects.

Table 2b Causes and locations of death in veterans with traumatic spinal cord injury according to the severity of injury based on American Spinal Injury Association (ASIA) Impairment Scale (AIS) grade

AIS grade	*Severity*			P
	Severe A/B (n=41)	*Moderate C/D* (n=7)	*Mild E* (n=9)	
Age of injury (mean (s.d.))	40.1 (13.7)	43.7 (16.4)	49.1 (15.3)	0.25
Cause of death[a] (n(% of severity); n=56)				
Infection	22 (56)	3 (43)	1 (13)	**0.045**[b]
Cardiovascular	6 (15)	2 (29)	5 (63)	
Cancer	4 (10)	2 (29)	1 (13)	
Other	7 (18)	0 (0)	1 (13)	
Deceased at (n(%); n=57)				
Home	16 (39)	6 (86)	3 (43)	0.26[b]
Hospital	21 (51)	1 (14)	4 (57)	
Nursing home	4 (100)	0 (0)	0 (0)	

Abbreviation: AIS: ASIA Impairment Scale.
Bold highlights significance of the baseline demographics between the two groups.
Place of death was unavailable for two subjects.
[a]Cause of death was unavailable for three subjects.
[b]Fisher's exact test.

Table 3 Cause of death (frequency (%)) according to each of the year bands; $P = 0.068$ (Fisher's exact test)

Year bands	*2000–2003*	*2004–2007*	*2008–2011*
Numbers (%)	19 (34)	23 (39)	16 (27)
Cancer	1 (5)	5 (22)	3 (21)
Cardiovascular	1 (5)	8 (35)	4 (29)
Infection	14 (74)	7 (30)	5 (36)
Other	3 (16)	3 (13)	2 (14)

Year bands	*2000–2003*	*2004–2007*	*2008–2011*	P
Numbers (%)	20 (34)	23 (39)	16 (27)	0.53
Cancer	1 (5)	5 (22)	3 (21)	0.26
Cardiovascular	1 (5)	8 (35)	4 (29)	0.06
Infection	14 (74)	7 (30)	5 (36)	0.08
Other	3 (16)	3 (13)	2 (14)	0.88
Unknown	1 (5)	0 (0)	2 (12.5)	0.56

Table 4 Cox regression analysis of variables known to predict survival of veterans with traumatic spinal cord injury

Variable	*Hazard ratio*	*95% CI*	P
Age at injury	1.097	(1.069, 1.126)	<0.0001
Severity of injury (AIS Grade)	1.262	(0.900, 1.769)	0.18
Vascular risk factors composite	1.007	(0.774, 1.310)	0.96
Pressure ulcers	1.397	(0.749, 2.605)	0.29
Neurogenic bladder	1.000	(0.312, 3.205)	0.99
Neurogenic bowel	0.915	(0.477, 1.756)	0.79

Abbreviations: AIS, ASIA Impairment Scale; CI, confidence interval.

model. Each additional year of age at the time of injury was associated with a 9.7 percent increase in the hazard of death. Injury severity, vascular risk factors, pressure ulcers and neurogenic bladder and bowel were not significant predictors. The univariate associations of the predictor variables with survival indicated that age at the time of injury ($P < 0.0001$) was significantly associated with survival time, with a trend toward significance for pressure ulcers ($P = 0.06$). However, only age at the time of injury contributed significantly to the model ($\chi^2 = 54.7$, $P < 0.0001$) when the effects of the remaining covariates were controlled.

A second Kaplan–Meier analysis was conducted assessing group differences in survival curves stratified by groups defined by age at the time of injury: 45+ versus <45 years. Figure 1 shows the survival curve for these data. The unadjusted hazard ratio for the risk of death in the older group (45+ years), as compared with the younger group (<45 years), was 6.84 (95% CI: 3.66–12.78), meaning that the risk of death is higher in the 45+ group compared with the <45 group. The difference between the survival probabilities of the two groups was statistically significant ($P < 0.0001$, using the log-rank test). When the severity of injury, vascular risk factors, pressure ulcers and neurogenic bowel and bladder were taken into account, the adjusted hazard ratio for death decreased slightly (5.91 (95%: CI = 2.96–11.81)), confirming that the decrease in survival for patients injured after the age of 45 depends mostly on age and not on the other risk factors examined. None of the covariates examined were significantly related to survival in the two groups.

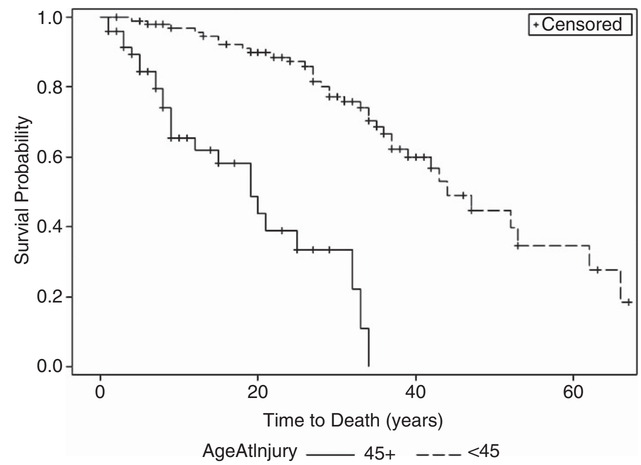

Figure 1 Estimated overall survival based on the duration of time that passed from the time of injury to death for patients with traumatic spinal cord injury (tSCI) stratified by age at injury (<45 or 45+).

The standard mortality ratio for our tSCI population was 3.1 of the peer Oklahoman white male population from which our veterans are drawn.

DISCUSSION

In this retrospective study of mortality after tSCI, there were 59 deaths (40%) at the end of the 12-year study period. The main causes of mortality were infection, cardiovascular disease and cancer. Patients with complete injury (AIS Grade A and B) had more infection-related mortality, while patients with incomplete injury (AIS grade C–E) had more cardiovascular and cancer-related deaths. Likewise, patients with complete injury were more likely to die in hospital while patients with incomplete injury were more likely to die in the community.

These results are consistent with the findings of Thietje *et al.*[9] in their analysis of 62 deceased subjects with tSCI. They found that paraplegics had a higher life expectancy (34 years) compared with tetraplegics (25 years) ($P = 0.008$). Septicemia, influenza/pneumonia and suicide were the leading causes of death in tetraplegics, whereas ischemic heart disease, neoplasms and septicemia were the leading causes of death in paraplegics.[9] Older studies of mortality due to chronic tSCI identified genito-urinary disorders to be the leading cause of death in 24–30% cases,[7,9,10] the other being septicemia in 38% cases.[11] Lately, patients with tSCI who survive the initial 2 years post-injury have been at an increased risk of pre-mature coronary arterial disease than the general population due to a sedentary lifestyle, glucose tolerance, insulin resistance and increased body mass index.[12] We found similar results when our subjects were divided according to the year of death: there was a trend toward a decline in the percentage of deaths due to infection from 2004 onward and a trend toward an increase in the number of deaths due to cardiovascular causes. However, this difference in the cause of mortality did not reach statistical significance. Importantly, when effective prevention of SCI-related complications and better control of modifiable vascular risk factors such as hypertension, hyperlipidemia, diabetes mellitus, obesity and smoking cessation were undertaken by us, between 2008 and 2011, the survival of tSCI patients improved from an average of 63% between 2000 and 2007 to 72% (Table 3).

Of the variables known to influence tSCI mortality, such as age at the time of injury, the level of tSCI, etiology of injury, pressure ulcers, or vascular risk factors, that were considered, only age at the time of injury had a significant association with the hazard of death. Each additional year of age at the time of injury was associated with a 9.7 percent increase in the hazard of death. A similar hazard ratio of 1.08 for each 1-year increase in a patient's age at the time of injury for death was found in the 499 patients enrolled in the Third National Spinal Cord Injury Study.[13] Notably, the death rate in this study was three times higher in the tSCI population or 310% of the general Oklahoman population from which our veterans are drawn.

The present study has several limitations. First, this study is limited primarily to the male veteran population; thus, it is difficult to generalize for the general population of tSCI patients. Second, the sample size is small and may preclude detecting important differences between groups. Third, it is a retrospective analysis of the computerized data of veterans with tSCI. Despite these limitations, the completeness of the data captured by the standardized SCI registry over a 12-year period and its similarity of basic demography to other tSCI data[13,14] provides a relevant rich data set to better understand predictors of mortality in the veteran population with tSCI. Future research is needed to understand the predictors of mortality after tSCI and how best to decrease them by overcoming the methodological limitations of this study.

CONCLUSION

Our study suggests that SCI-related mortality is mainly influenced by the person's age at the time of injury. The tSCI-related complications had no effect on mortality. This study suggests the need to not only incorporate strategies to prevent cardiovascular mortality in those who survive later on in life, but also educate people older than 45 years of age about the inherent increased mortality risk associated with tSCI-related complications.

DATA ARCHIVING

There were no data to deposit.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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