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ORIGINAL ARTICLE

Factors predictive of survival and estimated years of life lost in the decade following nontraumatic and traumatic spinal cord injury

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Study Design: Retrospective chart review.
Objectives: To identify factors predictive of survival after spinal cord injury (SCI).
Setting: Tertiary care institution.
Methods: Multiple-variable Cox proportional hazards regression analysis for 759 patients with SCI (535 nontraumatic and 221 traumatic) included age, sex, completeness of injury, level of injury, functional independence measure (FIM) scores, rehabilitation length of stay and SCI cause. Estimated years of life lost in the decade after injury was calculated for patients vs uninjured controls.
Results: Median follow-up was 11.4 years. Population characteristics included paraplegia, 58%; complete injury, 11%; male sex, 64%; and median rehabilitation length of stay, 16 days. Factors independently predictive of decreased survival were increased age (+10 years; hazard ratio (HR (95% CI)), 1.6 (1.4–1.7)), male sex (1.3 (1.0–1.6)), lower dismissal FIM score (–10 points; 1.3 (1.2–1.3)) and all nontraumatic causes. Metastatic cancer had the largest decrease in survival (HR (95% CI), 13.3 (8.7–20.2)). Primary tumors (HR (95% CI), 2.5 (1.7–3.8)), vascular (2.5 (1.6–3.8)), musculoskeletal/stenosis (1.7 (1.2–2.5)) and other nontraumatic SCI (2.3 (1.5–3.6)) were associated with decreased survival. Ten-year survival was decreased in nontraumatic SCI (mean (s.d.), 1.8 (0.3) years lost), with largest decreases in survival for metastatic cancer and spinal cord ischemia.
Conclusions: Age, male sex and lower dismissal FIM score were associated with decreased survival, but neither injury severity nor level was associated with it. Survival after SCI varies depending on SCI cause, with survival better after traumatic SCI than after nontraumatic SCI. Metastatic cancer and vascular ischemia were associated with the greatest survival reduction.
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INTRODUCTION

Nontraumatic spinal cord injury (NTSCI) makes up a notable proportion of all causes of SCI and the majority of SCI cases at some medical centers.[1,2] NTSCI is defined as any SCI not caused by external traumatic force to the body. Common causes include spinal stenosis, cancer, infection, ischemia, transverse myelitis, inflammatory disease, radiation, syringomyelia and metabolic disorders.[3] No published estimates are available for the incidence or prevalence of NTSCI in the United States, but ~12 000 new traumatic SCIs (TSCIs) occur each year in the country.[4] International epidemiologic studies suggest that NTSCI could have a similar incidence.[5] Most of the currently available literature focuses on TSCI or includes small patient populations with NTSCI.

Age at injury, neurologic level of SCI, extent of lesion, ventilator dependence and year of injury are common predictors of survival in TSCI.[6] Survival in patients with NTSCI is significantly less than in those with TSCI because of increased average age and concurrent diseases, such as malignancy and vascular or inflammatory disorders.[6] With the increasing age of the general US population, NTSCI incidence is likely to expand as age-related causes, such as cancer and stenosis, increase. Limited data are available on factors associated with survival after NTSCI, making evidence-based clinical decisions, patient education, prognosis determination and resource allocation decisions difficult.

Most data analyses on survival after SCI were performed on populations with traumatic causes of SCI or with cancer that caused myelopathy.[7–15] Among patients with cancer that caused SCI, median survival has been reported as 11–26 months.[14,15] Survival rates have been increasing slowly in patients with TSCI, with previous studies finding that general improvements in health care significantly decreased the overall mortality rate.[16] Renal disease was the leading cause of death in 1970, but with improved bladder treatment in the past few decades, respiratory and cardiac diseases have become the leading cause of death among persons with TSCI, accounting for >50% of all deaths.[17–25]

The primary goals of this study were to identify factors predictive of survival after SCI of various etiologic causes and to compare expected survival in the 10 years after injury. To achieve these goals, we used

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Table 1 Population demographic characteristics

Characteristic	*Total SCI population*	*TSCI*	*NTSCI*	P-*value*[a]
Male sex, no (%)	485 (64)	166 (74)	319 (60)	<0.001
Tetraplegia, no (%)	318 (42)	117 (52)	201 (38)	<0.001
Complete myelopathy (AIS A), no (%)	83 (11)	65 (29)	18 (3)	<0.001
Married status, no (%)	503 (66)	129 (58)	374 (70)	0.001
Age at admission, mean (s.d.), years	58.3 (18.7)	46.7 (20.8)	63.1 (15.3)	<0.001
Admission FIM score, mean (s.d.)	68.8 (20.8)	56.2 (19.2)	74.0 (19.0)	<0.001
Dismissal FIM score, mean (s.d.)	92.6 (23.2)	81.0 (26.3)	97.5 (19.8)	<0.001
Length of stay, median, days	16	26	14	<0.001

Abbreviations: AIS, American Spinal Injury Association Impairment Scale; FIM, functional independence measure; NTSCI, nontraumatic spinal cord injury; SCI, spinal cord injury; TSCI, traumatic spinal cord injury.
[a]*P*-values from χ^2, 2-sample *t*, and Wilcoxon rank sum tests.

the traditional Cox proportional hazards regression model and visualization of survival with Kaplan–Meier curves, in addition to analysis of years of life lost, a newer statistical analysis that can provide data more easily applied to individual patients.

PATIENTS AND METHODS

This study included consecutive, consenting adult patients with documented newly diagnosed SCI or myelopathy who were dismissed from inpatient rehabilitation at Mayo Clinic Hospital—Rochester, Saint Marys Campus, in Rochester, Minnesota, between 1 January 1995, and 31 December 2003. Patients with a previous diagnosis of SCI or myelopathy were excluded.

All data were obtained by physicians through review of electronic and paper health records, Minnesota death records and the US Social Security Death Registry. Documentation had to have clinical characteristics, imaging, or other relevant investigations to support the diagnosis and cause of the SCI. Collected data included age, sex, mechanism of SCI (traumatic vs nontraumatic), level of injury (paraplegia vs tetraplegia), completeness of SCI (American Spinal Injury Association Impairment Scale (AIS) A (complete) vs AIS B-D (incomplete)), functional independence measure (FIM) scores, rehabilitation length of stay, discharge location (home vs skilled nursing facility vs acute hospital) and cause of SCI.[26,27] The primary outcome measure was duration of survival after dismissal from inpatient rehabilitation.

Statistical analysis

Patient demographic characteristics were compared with χ^2, 2-sample *t* and Wilcoxon rank sum tests. *P*-values $<.05$ were considered statistically significant. Two separate analyses, described below, were performed to assess survival after SCI.

Multiple-variable Cox proportional hazards regression models. Cox proportional hazards models were used to examine the effects of potential risk factors on survival. All statistical tests were 2-sided. A multiple-variable Cox proportional hazards model was constructed to determine survival rates after dismissal from inpatient rehabilitation. Survival curves were visualized with the Kaplan–Meier method. Death was the dependent measure; Table 1 lists the independent variables that were considered. The causes of SCI were aggregated into six groups: traumatic, metastatic cancer, primary central nervous system tumors, all-cause vascular, degeneration or stenosis and other nontraumatic. Hazard ratio (HR) and 95% confidence interval (CI) were calculated for survival. Data were split 60–40 to build training and test models for variable selection and assessment of concordance, and the final multiple-variable proportional hazards model was constructed with the selected variables and all data. Statistical software SAS version 9.3 (SAS Institute Inc) and R version 3.1 (R Core Team, 2014) were used for all analyses.

Estimated years of life lost analysis. An estimated years of life lost (EYOLL) survival analysis was performed as described in the study by Miller[28] and the study by Therneau and Grambsch.[29] Survival of the enrolled patients was compared against Minnesota death rates for a set of controls without SCI, matched on age, sex and dates of follow-up.[27] For this analysis, SCI causes were divided into 17 categories: 5 TSCI categories (all-cause traumatic, motor vehicle crash, fall, sports-related and other traumatic) and 12 NTSCI categories (all-cause nontraumatic, metastatic cancer to spine or spinal cord, intramedullary primary tumors, extramedullary primary tumors, spinal cord ischemia, arteriovenous malformation or fistula, other vascular, spinal stenosis or spondylosis, cervical instability due to rheumatoid arthritis, inflammatory disease, infection and other nontraumatic). To compare survival of primary tumors by location within the spinal canal, the intramedullary and extramedullary primary tumor groups contained all primary tumor types within the specified locations, including both 'benign' and 'malignant' tumor types. The broad intramedullary and extramedullary primary spinal cord tumor classification was used because it generally correlates with lesion behavior. Intramedullary tumors such as gliomas and ependymomas often result in very different long-term ramifications for patients than extramedullary lesions such as meningiomas. In addition, this classification can be confirmed by imaging and surgery, which may facilitate confirmation by other investigators. Certainly, tumor grade has a tremendous impact on survival as well; unfortunately, sorting tumors by grade would have resulted in small, difficult-to-use group sizes.

For each cause of SCI, the EYOLL in the period from discharge to 10 years post discharge was calculated, accounting for censoring.[29] Patients who survived the full 10 years lost 0, whereas someone who died at 6.5 years lost 3.5; this value was then compared with the age- and sex-matched expected value for the population. EYOLL values were considered clinically relevant when they were >1 year; we included 2-sided *P*-values for the test of >1 year difference.

RESULTS

In total, 759 participants were enrolled—535 with NTSCI and 224 with TSCI. Table 1 shows the patient demographic characteristics. Mean (s.d.) age at injury was 58.3 (18.7) years; median (range) age was 62 (18–90) years. Median (range) follow-up duration (until death or last known date alive) was 11.4 years (1 day–19.3 years). Only 7% of patients died or had their last follow-up in the first year.

Causes of SCI in the 'other traumatic' category included bicycle accidents, farming equipment accidents, violence and medical and surgical events. For example, a spinal cord deficit that developed as a complication of a medical or surgical procedure such as an aortic aneurysm surgery was included in the 'other traumatic' category. 'Other vascular' causes of NTSCI included vasculitis, epidural hematomas and intramedullary hematomas. 'Other nontraumatic and idiopathic' causes included syringomyelia, subacute combined degeneration, idiopathic causes and multifactorial myelopathy.

Independent factors

The final multiple-variable Cox model identified four independent factors as significantly predictive of decreased survival (Table 2):

Table 2 Results of analysis with multiple-variable Cox proportional hazards model

Characteristic	*Patients, no (%; N = 759)*	*Deaths, no (%; n = 355, 46.8%)*	*Hazard ratio (95% CI)*
Cause of SCI			
Traumatic	224 (29.5)	70 (31.3)	1.0
Nontraumatic	535 (70.5)	285 (53.3)	2.6 (2.0–3.3)[a]
Metastatic cancer	57 (7.5)	53 (93.0)	13.3 (8.7–20.2)[a]
Primary CNS tumor	111 (14.6)	51 (6.7)	2.5 (1.7–3.8)[a]
All-cause vascular	68 (9.0)	40 (58.8)	2.5 (1.6–3.8)[a]
Musculoskeletal/ stenosis	211 (27.8)	100 (47.4)	1.7 (1.2–2.5)[a]
Other nontraumatic	88 (11.6)	41 (46.6)	2.3 (1.5–3.6)[a]
Severity of SCI			
Incomplete (AIS B-D)	675 (88.9)	323 (47.9)	1.0
Complete (AIS A)	83 (10.9)	31 (37.3)	0.8 (0.5–1.3)
Tetraplegia spinal cord injury	318 (41.9)	144 (45.3)	0.9 (0.7–1.2)
Sex			
Female	276 (36.4)	119 (43.1)	1.0
Male	483 (63.6)	236 (48.9)	1.3 (1.0–1.6)[a]
Age, years			1.6 (1.4–1.7)[a,b]
16–30 (min, 18)	78 (10.3)	6 (7.7)	
31–45	120 (15.8)	30 (25.0)	
46–60	158 (20.8)	56 (35.4)	
61–75	251 (33.1)	145 (57.8)	
⩾76	152 (20.0)	118 (77.6)	
Discharge FIM score			1.3 (1.2–1.4)[a,c]
⩽79	185	108 (58.4)	
80–99	197	109 (55.3)	
100–109	154	63 (40.9)	
⩾110	211	65 (30.8)	

Abbreviations: AIS, American Spinal Injury Association Impairment Scale; CI, confidence interval; CNS, central nervous system; FIM, functional independence measure; SCI, spinal cord injury.
[a]Statistically significant.
[b]Per 10-year increase in age.
[c]Per 10-point decrease in discharge FIM score.

increased age, male sex, lower dismissal FIM score, and all subgroups of NTSCI (that is, metastatic cancer, primary tumors, musculoskeletal disease or spinal stenosis (musculoskeletal/stenosis), vascular and other NTSCI) vs TSCI. Level of injury, completeness of injury, length of stay, admission FIM score and change in FIM score during inpatient rehabilitation were not independently associated with survival. The corresponding univariate Kaplan–Meier curves are shown in Figures 1 through 3.

Estimated years of life lost

Mean (95% CI) 10-year survival with SCI etiologic subtype are listed in Table 3. As a broad group, NTSCI was associated with a mean (s.d.) loss of 1.8 (0.3) years in the decade after injury compared with the reference community population. This finding is in contrast to traumatic SCI as a broad group, which was associated with <1 EYOLL (mean (s.d.), 0.7 (0.4) years) compared with the same reference population. Compared with matched controls, nontraumatic causes of SCI that were associated with the greatest EYOLL in the first decade after injury were metastatic cancer and ischemia. Intramedullary tumors, extramedullary tumors and infection caused small decreases in mean survival after SCI.

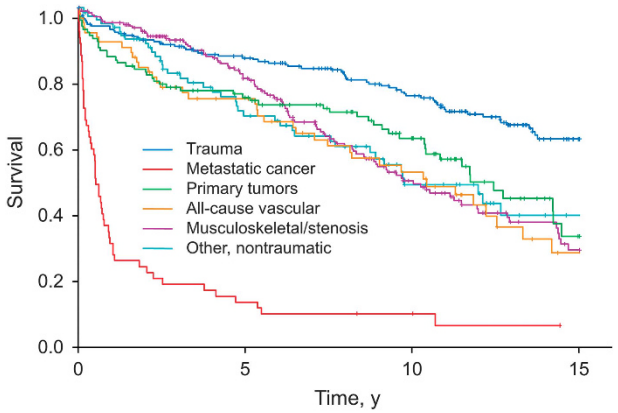

Figure 1 Kaplan–Meier survival curve for spinal cord injury diagnosis/ etiology group.

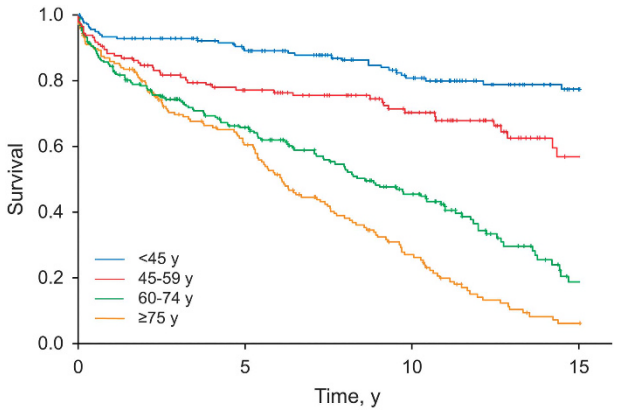

Figure 2 Kaplan–Meier survival curve for age-group.

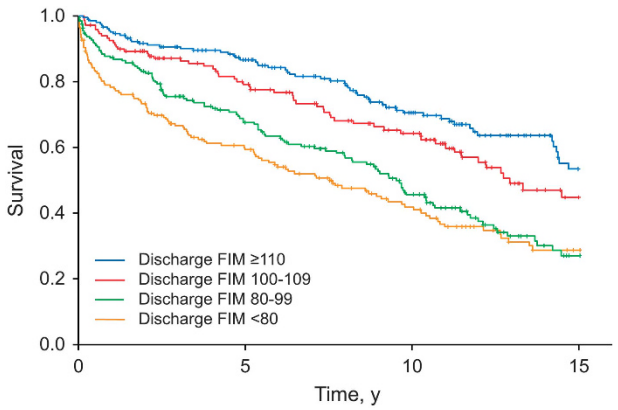

Figure 3 Kaplan–Meier survival curve for discharge FIM score. FIM indicates functional independence measure.

DISCUSSION

This is the first study to publish data on factors associated with survival in patients with NTSCI in the United States. It provides useful information for prognosis, patient education, dismissal planning and goals of care. Analysis in this study, including both TSCI and NTSCI or myelopathy, identified independent risk factors associated with decreased survival after SCI from any cause. These factors were increased age, male sex and lower dismissal FIM score. An additional

Table 3 EYOLL in the decade following spinal cord injury

Cause of myelopathy	*Patients, no*	*Survival, mean ± 95% CI, years*	*Control mean survival, years*	*EYOLL, mean ± 95% CI, years*
All-traumatic	224	8.5 ± 0.4	9.2	0.7 ± 0.4
Motor vehicle crash	115	9.0 ± 0.5	9.5	0.5 ± 0.5
Fall	52	7.4 ± 1.0	8.6	1.1 ± 1.0
Sports-related	12	9.8 ± 0.4	9.9	0.1 ± 0.4
Other traumatic	45	8.1 ± 1.0	9.0	0.9 ± 1.0
All nontraumatic	535	6.8 ± 0.3	8.6	1.8 ± 0.3[a]
Metastatic cancer to spine/spinal cord	57	1.6 ± 0.7	8.8	7.3 ± 0.7[a]
Spinal cord ischemia	25	5.5 ± 1.6	8.4	2.9 ± 1.6[a]
Intramedullary primary tumor	58	8.0 ± 0.9	9.5	1.5 ± 0.9
Extramedullary primary tumor	53	6.7 ± 1.1	8.6	1.9 ± 1.1
Infection	28	6.9 ± 1.3	8.7	1.8 ± 1.3
Arteriovenous malformation/fistula	31	8.0 ± 1.1	8.3	0.3 ± 1.1
Other vascular	12	7.7 ± 2.3	8.7	1.1 ± 2.3
Spinal stenosis, spondylosis, synovial cysts	211	7.6 ± 0.5	8.2	0.6 ± 0.5
Spinal instability/spondylolisthesis	9	6.9 ± 2.5	8.7	1.8 ± 2.5
Inflammatory disease	16	8.3 ± 1.5	9.2	0.9 ± 1.5
Other nontraumatic	35	7.0 ± 1.3	8.8	1.7 ± 1.3

Abbreviations: CI, confidence interval; EYOLL, estimated years of life lost.
[a]Statistically significant.

decade of age at discharge from inpatient rehabilitation was associated with a 55% decreased survival. Neither the duration of inpatient rehabilitation nor the changes in FIM scores during rehabilitation were independent predictors of survival. NTSCI as a broad category was associated with increased mortality risk, even after controlling for age.

Metastatic cancer had the highest association with decreased survival (median survival, 1.6 years; range, 0.9–2.3 years) after discharge from inpatient rehabilitation. This survival information was in the range of other studies, with previously reported median survival of 11.0 months to 2.2 years after SCI.[14,15] Nonetheless, with survival of 1.5 years after inpatient rehabilitation, resource utilization for inpatient rehabilitation appears to be justified. A 10-point increase in dismissal FIM score increased survival by 27%, and discharge FIM scores <100 were associated with a 10-year survival rate $<50\%$.

Given its population size and follow-up period, our study confirms the previous work regarding the demographic characteristics of NTSCI and factors affecting survival.[2,3,13,30–34] People with NTSCI are older, more likely to have paraplegia, more likely to have an incomplete injury, and more likely to be married than people with TSCI. Neither injury severity nor injury level is independently associated with decreased survival in NTSCI. The NTSCI cause and male sex are predictive of decreased survival. Our study extends the previously published findings by also noting that the dismissal functional status was correlated with survival, with every 10-point increase in discharge FIM score being associated with a 27% improvement in survival.

In the Kaplan–Meier survival curves from the Cox proportional hazards model, all NTSCI groups had decreased survival compared with the TSCI group (Figure 1). The musculoskeletal/stenosis group and traumatic group had similar survival for the first 4 years after injury, with the other NTSCI subgroups having significantly decreased survival. However, after the first 4 years, survival in the musculoskeletal/stenosis group decreased quickly to equal that seen in the primary tumors, vascular and other NTSCI groups. The reason for this survival trend in the musculoskeletal/stenosis group is unclear because age and other variables were factored into the analysis. However, the analysis did not control for medical comorbidities, so these may have contributed to the trend.

New and McFarlane[35] reported 3.8 years of survival after spinal cord infarction. Similarly, we found that patients with spinal cord ischemia lost several years of life in the EYOLL analysis (mean (s.d.) EYOLL, 2.9 (1.6) years). We found a slightly longer mean survival of 5.5 years after ischemic myelopathy. In the Kaplan–Meier survival curves from the Cox proportional hazards model, vascular myelopathy as a broad group had a median survival of 10.3 years. This population included arteriovenous malformations and fistulas and other vascular causes, likely accounting for the favorable survival of the group overall.

None of the traumatic etiologic groups in the EYOLL analysis were associated with decreased survival in the decade after discharge from inpatient rehabilitation. From the results of this study, it was apparent that the pathology and etiology of the injury had higher correlation with survival than the degree of paralysis. Prior studies looking at survival after TSCI have found that violent causes of SCI showed mildly better survival vs nonviolent causes.[36,37] The results from the EYOLL analysis found no significant decrease in survival in the 10 years following SCI for any of the TSCI groups. Falls and 'other traumatic causes' showed a tendency for decreased 10-year survival vs injuries from sports and motor vehicle crashes.

The EYOLL analysis used in this study is novel in the field of SCI. It estimates survival in a way that can be easier to apply to an individual patient than to the traditional Kaplan–Meier survival curves. It was developed for use with categorical variables, but at present, its ability to be used for analysis of continuous variables is still under debate, making a similar analysis for such data as discharge FIM scores difficult to perform.

Study limitations

Limitations of this study include the retrospective design, which allows analysis for only associations between outcome and the variables analyzed. In addition, the patient population was gathered from admissions to an inpatient rehabilitation center at a US academic institution, so the data may not apply to other patient populations. Lastly, the EYOLL analysis is a distinctive evaluation not used in other studies, so its findings may not be directly comparable to other survival analyses.

CONCLUSION

People with NTSCI are older and are more likely to have paraplegia, to have incomplete injury and to be married than people with TSCI. Neither injury severity nor injury level was independently associated with survival in NTSCI. Survival after SCI differs depending on the cause of the SCI. In general, survival is better for traumatic causes of SCI than for nontraumatic causes. Survival after NTSCI differs greatly because of the etiologic factors, with metastatic cancer and ischemia having the greatest reduction in survival compared with the matched local control population. The good news is that myelopathy due to arteriovenous malformations, musculoskeletal/stenosis causes and inflammatory disease was not associated with significant increases in EYOLL in the decade after myelopathy onset. Factors that independently predicted decreased survival after SCI included increased age, male sex and lower dismissal FIM scores.

DATA ARCHIVING

There were no data to deposit.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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