Research article

Mortality and causes of death after traumatic spinal cord injury in Estonia

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Study design: Retrospective population-based study with mortality follow-up.

Objective: To study mortality, causes and risk factors for death in Estonian patients with traumatic spinal cord injury (TSCI).

Setting: All Estonian hospitals.

Methods: Medical records of patients with TSCI from all regional, central, general, and rehabilitation hospitals in Estonia from 1997 to 2007, were retrospectively reviewed. Mortality status was ascertained as of 31 December 2011. Causes of death were collected from the Estonian Causes of Death Registry. Standardized mortality ratios (SMRs) were calculated for the entire sample and for causes of death. A Cox proportional hazards modeling was used to identify the risk indicators for death.

Results: During the observation period (1997–2011) 162 patients of 595 died. Nearly half of the patients ($n = 76$) died during the first year after TSCI. The main causes of death were external causes (30%), cardiovascular disease (29%), and suicide (8%). The overall SMR was 2.81 (95% confidence interval 2.40–3.28) and SMR was higher for women than for men (3.80 vs. 2.70). Cause-specific SMRs were markedly elevated for sepsis and suicide. Mortality was significantly affected by the age at the time of injury, neurological level, and extent of the injury as well as the year of TSCI and complications.

Conclusion: Life expectancy is significantly decreased in patients with TSCI in Estonia compared with the general population. Deaths during the first year after the injury have an important impact on statistics. Treatment of cardiovascular diseases, infections, and prevention of suicide are useful for reducing mortality in patients with TSCI.

Keywords: Spinal cord injuries, Traumatic, Epidemiology, Paraplegia, Tetraplegia, Estonia, Mortality, Causes of death

Introduction

Traumatic spinal cord injury (TSCI) may cause physiological dysfunctions and a range of complications in different body systems.^{1,2} After incurring spinal cord injury (SCI), the individuals' longevity declines significantly.

Although medical care improves survival, TSCI remains a disease with high mortality rates.^{2,3} The risk of death is the highest during the first two years after the injury.^{4–7} Mortality rate has been approximately three times higher among patients with TSCI than in able-bodied individuals.² The death rate has been found to be higher among the elderly, with more

counts of comorbidities.⁸ Also, the predictors of survival are the neurological level and extent of injury.²

Country-specific, as well as cross-country studies are desirable to inform relevant health policy for improved primary and secondary prevention and care.⁹ The incidence of TSCI in Estonia is one of the highest in Europe,^{10,11} with a high number of deaths resulting from injury in general.¹² Therefore, it is crucial to investigate causes of increased mortality after TSCI in order to implement suitable prevention strategies promptly. Moreover, there is a lack of previous studies on mortality of TSCI in Eastern Europe, so our data would be integrated into the broader injury surveillance efforts.

We aimed to evaluate the causes of death and to explore the predictors of acute and long-term death among the people with TSCI.

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Methods

Study design

The study design was retrospective. Five hundred and ninety-five patients, with TSCI from 1997 to 2007, were included.

Study population

The data collection has been described elsewhere.¹⁰ In brief, medical records of the patients with the TSCI diagnoses or suspected TSCI were reviewed in all Estonian hospitals (22). The inclusion criteria were (1) TSCI or cauda equina injury with neurological deficit found at discharge, (2) permanent resident of Estonia at time of injury, and (3) neurological symptoms must have lasted ≥ 7 days. We excluded patients with non-traumatic spinal cord injuries. The patients who died before hospitalization were also excluded from the study.¹⁰

Information was obtained from Statistics Estonia¹³ and linked with the data from the Cause of Death Registry. Cases were matched by the identity codes.

The coding system used was the 10th version of the International Classification of Diseases (ICD). Information concerning the date of death and the immediate and underlying cause of death was registered.

The severity of injury was determined using the standardization as described by DeVivo *et al.*¹⁴ The patients were divided into five main groups: (1) C1–C4 and American Spinal Injury Association (ASIA) Impairment Scale (AIS) grade A, B, or C; (2) C5–C8 and AIS A, B, or C; (3) C1–C8 and AIS D; (4) T1–S5 and AIS A, B, or C; and (5) T1–S5 and AIS D. The ventilator-dependent patients were included in the first group.

Statistical analysis

Standardized mortality ratios (SMRs), survival rates, and life expectancy were calculated. SMR is expressed as the ratio of observed deaths of persons with TSCI to expected deaths in the general Estonian population using Estonian Life Tables (obtained from Statistics

Estonia,¹³ years from 1997 to 2011), adjusted for age and gender distribution of TSCI sample. Kaplan–Meier curves were used to visualize survival by age at death or censoring the SCI population compared with the general population. A Cox proportional hazards regression model was used to identify the probability of death in the presence of specific risk factors. We used the log–log plot to test the proportional hazard assumption that the ratio of the hazard is constant over time. The risk factors were estimated for the patients who died within the first 2 years of injury and those who survived beyond the cut-off point of 2 years. This distribution was chosen since it has been reported that the risk of death is disproportionately higher among the patients with high cervical TSCI during the first two years post injury.^{6,7,15}

The independent variables (age, sex, year of the injury, cause of trauma, preinjury alcohol consumption, concomitant injury, head injury, extent of injury, vertebral fracture, need for mechanical ventilation, operation within 6 weeks, methylprednisolone in acute phase, complications in acute phase) that were included in the model were obtained from the medical records earlier.¹⁰ Pre-existing conditions or co-morbidities were not included into the model because the information gained from the medical records was frequently not available.

This study was approved by the Research Ethics Committee of the University of Tartu, Estonia, and by the Data Projection Inspectorate of Estonia.

Results

The analysis was based on 595 patients with TSCI, 162 of whom (139 men and 24 women) were dead by 31 December 2011. The mean age at injury was 51.0 ± 17.5 years (range 16–93) in men and 49.9 ± 19.3 years (range 5–87) in women. Among the patients who survived, the mean age at injury was 34.8 ± 14.6 years (range 1–76). During the first year after TSCI, there were 46.9% ($n = 76$) deaths. Table 1 presents the division of deaths in different impairment groups.

Table 1 Distribution of deaths in patients with traumatic spinal cord injury in Estonia from 1997 to 2011

Impairment (neurol. group and AIS grade)	N	Deaths (<12 months)		Deaths (12 months–2 years)		Deaths (>2 years)	
		N	%	N	%	N	%
C1–C4 ABC	59	19	32.2	1	1.7	6	10.2
C5–C8 ABC	172	35	20.3	4	2.3	23	13.4
C1–C8 D	96	5	5.2	4	4.2	12	12.5
Th1–S5 ABC	159	12	7.5	2	1.3	26	16.4
Th1–S5 D	46	0	0	1	2.2	3	6.5
Unknown	63	1	1.6	4	6.3	4	6.3

AIS, American Spinal Injury Impairment Scale.

The predominant cause of injury was falls (41.0%), followed by traffic accidents (29.4%).

During the first year, the leading underlying causes of death were external causes (52.6%) and cardiovascular diseases (21.1%). Later, the cardiovascular diseases became predominant (35.6%), followed by suicides (13.8%). All the patients who committed suicide were males, and all but one attempt happened after the first year of TSCI. The survival of the patients, whose cause of death was suicide, was 1951 ± 1342 days (range 0–4282). Seven of the patients had tetraplegia, six had paraplegia.

The overall SMR was 2.81 (95% confidence interval 2.40–3.28). SMRs were higher for women (Tables 2 and 3). Males with TSCI younger than 76 years and women younger than age 61 years had increased mortality compared with the general population. Fig. 1A and B illustrates the survival in the study population among men and women.

During the study period, SMR decreased 11% per year from 7.99 to 2.13 ($P < 0.001$). The mortality rate in the first year of injury did not show any change ($P = 0.29$).

Cause-specific SMR was the highest for sepsis (Table 4). Cause-specific SMR for suicide was 8.7 among men, none of the women committed suicide during the study period in Estonia. The sole cause of death with decreased SMR compared with the general population was cancer (Table 4).

Cox proportional hazards modeling revealed several predictors of mortality (Table 5). During the first two years, the significant risk factors of death were higher age at injury, cervical spinal cord injury, completeness of injury, and concomitant trauma, including head injury. During the first year post injury, the patients with C1–C4 (AIS A–C) neurological impairment had 6.25 times higher risk of dying compared with the patients with injury below cervical level. They had also seven times higher risk of dying than those with

Table 3 Standardized mortality ratios for age-groups among females with traumatic spinal cord injury in Estonia from 1997 to 2011

Age-group	Observed	Expected	SMR	95% CI
0–15	1	0.004	214.2	5.4–1193.6
16–30	2	0.1	17.4	2.1–63.0
31–45	8	0.3	23.4	10.1–46.2
46–60	6	0.6	10.3	3.8–22.3
61–75	4	1.4	2.8	0.8–7.2
>75	2	3.6	0.6	0.1–2.0
Total	23	6.1	3.8	2.4–5.7

CI, confidence interval.

C1–C8 AIS D impairment (Table 1). After the first year, the risks levelled off. Fig. 2 illustrates survival probability in the study population for different levels of neurological impairment. Two years after the injury only age and completeness of lesion remained significant risk factors for death, the cause of injury also became significant.

Discussion

This is the first research study to examine mortality after TSCI in Eastern Europe. As expected, life expectancy of patients with TSCI was found to be significantly reduced in comparison to the general population. Almost half of the patients died during the first year after TSCI. The risk of death was higher in the group with C1–C4 AIS A–C lesions. SMRs are higher among women and the cause-specific SMRs in Estonia were noted to be extremely high for sepsis and skin-related causes, as well as significantly increased for other causes including genitourinary disease and suicide. In fact, there is a large discrepancy due to some methodological differences between the survival studies. Most of them have excluded the patients who die at the scene of the accident, on arrival at the hospital, or during the first days. Many studies have focused on patients in the rehabilitative phase and excluded deaths occurring in the acute or sub-acute phase of injury.^{2,16} Therefore, the mortality rates are considerably variable.

Our results have a number of similarities with Hagen *et al.*'s¹ findings, which showed that women and patients younger than 40 years of age at the time of injury, have particularly decreased life expectancy. It is noteworthy that so far, only Scandinavian countries have reported higher female mortality.^{1,17–19} In our study, gender was not statistically significant in the Cox proportional hazard modeling. This could be explained in Estonia by the fact that mortality among men in the general population is high, reducing the differences between sexes.²⁰

Table 2 Standardized mortality ratios for age-groups among males with traumatic spinal cord injury in Estonia from 1997 to 2011

Age-group	Observed	Expected	SMR	95% CI
0–15	0	0.01	0	0–435.2
16–30	16	2.7	5.9	3.4–9.7
31–45	32	6.3	5.1	3.5–7.2
46–60	43	14.4	3.0	2.2–4.0
61–75	36	18.7	1.9	1.3–2.7
>75	12	9.4	1.3	0.7–2.2
Total	139	51.5	2.7	2.3–3.2

CI, confidence interval.

Figure 1 Survival probability of patients with traumatic spinal cord injury (with 95% confidence interval), injured from 1997 to 2007, compared with the Estonian population. (A) Male. (B) Female.

Table 4 Causes of death of deceased TSCI patients in Estonia from 1997 to 2011

Causes of death	No. of deaths			
	Observed	Expected	SMR	(95% CI)
Sepsis				
Total	12	0.04	339.5	175.5–593.1
Male	9	0.03	296.3	135.5–562.4
Female	3	0.01	604.3	124.6–1765.9
Cancer				
Total	7	13.9	0.5	0.2–1.0
Male	5	12.3	0.4	0.1–1.0
Female	2	1.6	1.2	0.2–1.0
Cardiovascular disease				
Total	46	30.9	1.5	1.1–2.0
Male	41	25.7	1.6	1.1–2.2
Female	5	5.2	1	0.3–2.3
Respiratory disease				
Total	13	2.4	5.5	2.9–9.4
Male	11	2.2	2.5	2.5–8.9
Female	2	0.2	13.1	1.6–47.2
Digestive system disease				
Total	5	2.6	1.9	0.6–4.4
Male	5	2.4	2.1	0.7–4.9
Female	0	0.3	0	0–13.1
Skin disease				
Total	5	0.05	105.4	34.2–246.0
Male	5	0.04	128.4	41.6–298.9
Female	0	0.01	0	0–439.0
Musculoskeletal disease				
Total	2	0.13	14.6	1.8–52.6
Male	2	0.1	19.9	2.4–71.8
Female	0	0.03	0	0–100.8
Genitourinary disease				
Total	9	0.5	18	8.2–34.2
Male	8	0.42	18.9	8.2–37.2
Female	1	0.08	13.2	0.3–73.7
External causes				
Total	48	8.4	5.7	4.2–7.6
Male	38	8	4.7	3.3–6.5
Female	10	0.4	28.3	13.6–52.1
Suicide				
Total	13	1.6	8.3	4.4–14.3
Male	13	1.5	8.7	4.6–14.8
Female	0	0.05	0	0–65.8

*TSCI, traumatic spinal cord injury; SMR, standardized mortality ratio; CI, confidence interval.

Physical changes after TSCI affect the patient emotionally, socially, and psychologically. Krause *et al.*^{21,22} have pointed out that important predictors of mortality are social support, income, psychology and behavioral factors. It is worthwhile noting the results from Pentland *et al.*²³ claiming that women with TSCI feel isolated and have the perception of being forgotten. Factors such as these may have impact on the observed high risk of death in women. Consistent with earlier studies, the incidence of death in patients with TSCI from septicemia, respiratory disease, urinary system disease, and suicide is significantly higher than in the general population.^{1,16} Soden *et al.*¹⁶ suggest that TSCI places patients at considerable risk of suicide. Suicide in the general population is also a

major issue in Estonia.²⁴ After the first year, the incidence of suicides increased to 13.8% among patients with TSCI in Estonia. In contrast to the Finnish study,¹⁷ in Estonia, the patients who committed suicide were men, and half of them had tetraplegia.

Survival is considered to be strongly related to neurological level and the degree of impairment.^{2,5,15} Although in recent years there has been a trend toward improvement in acute phase survival rates, the longer-term mortality has remained constant.²⁵ As might have been expected, we also found a strong relationship between the neurological level and completeness of injury. During the first year, the mortality risk was significantly higher among the patients with C1–C4 injury level, AIS A, B, C; afterwards it stabilized.

Table 5 Risk factors for death of patients with TSCI in Estonia from 1997 to 2011

Factors	≤2 years after TSCI			>2 years after TSCI		
	RR	95% CI	P value	RR	95% CI	P value
Age at injury	1.05	1.04–1.06	<0.001	1.04	1.03–1.05	<0.001
Gender						
Male	1.00	–	–	1.00	–	–
Female	0.96	0.54–1.74	0.91	0.84	0.44–1.67	0.65
Year	0.97	0.91–1.03	0.29	0.92	0.85–1.00	0.06
Cause of trauma						
Sport (ref.)	1.00	–	–	1.00	–	–
Assault	1.35	0.45–4.04	0.59	1.04	0.20–5.36	0.96
Traffic accident	1.02	0.46–2.23	0.97	1.52	0.56–4.15	0.41
Falls	1.70	0.83–3.48	0.14	3.90	1.56–9.83	0.004
Other	1.24	0.48–3.21	0.66	0.79	0.19–3.32	0.75
Preinjury alcohol consumption						
No (ref.)	1.00	–	–	1.00	–	–
Yes	1.29	0.75–2.24	0.40	1.39	0.76–2.54	0.29
Concomitant injury						
No (ref.)	1.00	–	–	1.00	–	–
Yes	1.34	0.87–2.06	0.18	0.93	0.55–1.58	0.80
Head injury						
No (ref.)	1.00	–	–	1.00	–	–
Yes	1.84	1.20–2.83	0.005	0.96	0.57–1.61	0.87
Neurological level						
C1–4	5.00	2.64–9.48	<0.001	1.19	0.54–2.59	0.67
C5–8	2.88	1.64–5.06	<0.001	0.98	0.60–1.60	0.93
T1–S5	1.00	–	–	1.00	–	–
Completeness of injury						
Complete (ref.)	1.00	–	–	1.00	–	–
Incomplete	0.29	0.19–0.45	<0.001	0.80	0.50–1.30	0.37
Vertebral fracture						
No (ref.)	1.00	–	–	1.00	–	–
Yes	0.75	0.48–1.87	0.23	0.67	0.42–1.09	0.12
Mechanical ventilation**						
No (ref.)	1.00*	–	–	1.00	–	–
Yes	*	*	0	0.89	0.39–2.06	0.78
Operation in 6 weeks						
No (ref.)	1.00	–	–	1.00	–	–
Yes	0.30	0.19–0.47	<0.001	0.80	0.51–1.25	0.33
Methylprednisolone in acute phase***						
No (ref.)	1.00	–	–	1.00	–	–
Yes	1.26	0.80–1.98	0.32	0.97	0.60–1.59	0.92
Complication in acute phase***						
No (ref.)	1.00	–	–	1.00	–	–
Yes	2.00	1.25–3.16	0.004	1.48	0.93–2.35	0.1

TSCI, traumatic spinal cord injury; RR, relative risk; CI, confidence interval.

*Assumptions for the proportional hazards analysis were not fulfilled.

**Use of ventilatory assistance during hospital stay in the acute phase of injury.

***Acute phase is defined as the first hospitalization after the injury.

No significant reduction in the first-year mortality was detected during the follow-up period from 1997 to 2011 in Estonia. This may be the result of socio-economic disruption as a post-Soviet state, with Estonia having experienced financially hard times and crises.

Surprisingly, the level of alcohol consumption before the trauma did not have an effect on early or late mortality in our research. It is plausible that data about regular alcohol drinking, not available in our study, could have influenced the results obtained. Alcohol-attributable mortality in the Baltic countries is more

than four times higher for men and more than three times higher for women.²⁶ Krause *et al.*²⁷ showed that alcohol drinking, especially binge-drinking, is a type of behavior related to early mortality. According to this risk factor, and the findings that Estonians engage in binge drinking,²⁸ we would suggest that alcohol drinking be considered as an important risk factor in Estonia for mortality after TSCI.

Limitations of this study include insufficient information on the patients' death certificates regarding the causes of death. This has also been a noted problem in other studies.¹⁵ Some SMRs have been calculated on

Figure 2 Survival probability of patients with traumatic spinal cord injury with different level and extent of neurological impairment, injured from 1997 to 2007 in Estonia.

the basis of few deaths and should therefore be interpreted with caution. The risk factors were collected during the first hospitalization and were not assessed later. Chronic diseases, as potential risk factor for death, were not included in the analysis because the data were recorded inconsistently. Our study was retrospective and identification of patients took place according to the diagnostic codes. Patients who died before arrival at the hospital were excluded, which may induce underestimation of the mortality rates.

Despite the above-mentioned limitations, it is a unique study focused on all age groups in the Estonian population. Patients with TSCI were retrospectively sought from every Estonian hospital, and ICD-10 codes suggesting a TSCI was expanded to include spinal fractures at every level in order to screen more suspected cases.¹⁰ The overall SMR confirms that mortality is high among patients with TSCI in Estonia, although it decreased during the study period. Decline in mortality rates has been found in earlier studies, too. But unlike our study, a trend toward improvements in 1-year survival rates has been described earlier.^{5,15} Improvements in health care may explain the marked decline in mortality.

In this study, we identified that age at the time of injury, C1–C4 neurological level, and completeness of

injury, as well as concomitant injuries, were the risk factors for death during the first two years after the injury. Later, only age, completeness of and cause of TSCI were significant risk factors for mortality.

Conclusion

In conclusion, the main causes of death among the patients with TSCI were cardiovascular disease, pneumonia, genitourinary tract infection and infections related to pressure ulcers, and suicide. The overall life expectancy of the patients is significantly decreased compared with general population. The assertion by Hitzig *et al.*²⁹ that TSCI represents a model of premature aging affecting multiple body structures and functions should lead us to a holistic focus on multi-system management addressing all modifiable risk factors and their potential interactions.

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