ARTICLE

Post-discharge mortality in patients with traumatic spinal cord injury in a Brazilian hospital: a retrospective cohort

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Received: 24 February 2018 / Revised: 24 June 2018 / Accepted: 3 July 2018 / Published online: 8 August 2018
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Abstract

Study design Retrospective cohort.

Objective To evaluate the survival outcomes in patients with traumatic spinal cord injury (TSCI).

Setting A teaching hospital in Brazil.

Methods A total of 434 patients diagnosed with TSCI (2004–2014) were included. Overall survival, standardized mortality ratios (SMR), and causes of death were assessed by Student's *t*-test, χ^2 test, Kaplan–Meier analysis, and Cox proportional-hazards regression.

Results The mean follow-up was 4.8 years (± 3.3 years). Individuals with tetraplegia had a median survival of 11 years, with participants in the paraplegia group not reaching median survival. The overall mortality rate was 37 per 1000 person-years. Age-adjusted SMR was 28.8 (95% CI: 22.8–36). There were 77 deaths with 56 defined causes, of which pneumonia was the most frequent (35.7%). Combined infectious etiologies caused 55.3% of deaths. Multivariate analysis revealed higher mortality among individuals with tetraplegia vs. paraplegia in the first 2 years post injury (HR = 8.28, 95% CI: 2.76–24.80), after 2 years post injury (HR = 2.35, 95% CI: 1.31–4.24), and in all years combined (HR = 3.36, 95% CI: 2.04–5.52).

Conclusion Mortality among patients with TSCI was 28.8 times higher than in the reference population. In more than half of the cases, the cause of death was linked to infectious diseases. Pneumonia caused two times more deaths in individuals with tetraplegia than in individuals with paraplegia, with a higher impact in the first 2 years post injury. Reported findings indicate the need for a surveillance and prevention program with emphasis on vaccination and respiratory rehabilitation.

Introduction

In low-income and middle-income countries (LMIC) [1], which account for ~80% of the global population, epidemiological data on spinal cord injury (SCI) are particularly limited. Socioeconomic circumstances in LMIC often correlate with a higher incidence of traumatic SCI

(TSCI), such as high rates of violence, road traffic injuries, and work-related accidents [1–6]. Current in-hospital survival estimates suggest that mortality in acute TSCI is approximately three times higher in LMIC than in high-income countries [7]. Post-discharge survival data in LMIC are scarce and heterogeneous. Although the data from South India show a 1–2-year mortality rate of <5%, the data from Bangladesh, Nepal, and Sierra Leone show rates of 13%, 25%, and 61%, respectively [8–11]. The most frequent causes of death, such as infections and pressure ulcers, were preventable [8, 10, 11]. When comparing individuals with TSCI in LMIC and high-income countries, there are many possible contributory factors for the disparity in mortality rates and etiologies, including limited access to healthcare for individuals with SCI, higher complication rates, and decreased social participation [1, 3, 4, 12]. To the best of our knowledge, only two prior studies have investigated post-discharge mortality in large LMIC populations; both were conducted in Southern Asia [9, 10].

Electronic supplementary material The online version of this article (<https://doi.org/10.1038/s41393-018-0183-y>) contains supplementary material, which is available to authorized users.

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The metropolitan area of São Paulo, Brazil, has an estimated population of 20 million and unique socioeconomic characteristics. Obtaining the data on local mortality rates, risk factors, and causes of death for individuals with SCI would enable the development of preventive programs, and allow cost estimates and appropriate resource allocation by both local government and foreign aid organizations. Our study aimed to assess mortality rates and causes of death for people with TSCI who were admitted to a teaching hospital in São Paulo, Brazil between 2004 and 2014.

Methods

This article follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) initiative [13]. This retrospective hospital cohort study was approved by the Ethics Committee for Analysis of Research Projects (CAPPesq) of the Hospital das Clínicas at the University of São Paulo's Medical School, São Paulo, Brazil (CAPPesq CAEE:64907617.2.0000.0068).

Study design: Retrospective cohort.

Setting: Institute of Orthopedics and Traumatology (IOT), Clinical Hospital of the Faculty of Medicine, and University of São Paulo. The hospital is a quaternary public teaching facility with 2400 beds.

Study population: All cases of individuals with acute TSCI discharged alive are routinely included in the IOT data registry. Individuals discharged between January 2004 and December 2014 without age restriction were considered for inclusion ($n = 454$). Those with incomplete clinical data and/or unknown SCI date were excluded ($n = 20$). A total of 434 participants were included in the final analysis.

Data collection: Clinical history, demographic information, and outcomes were extracted from the hospital medical records. Data from all clinical encounters in our SCI clinic have been collected using the same standardized form since 2003. Enrolled participants were followed up until December 2016. Vital status updates were obtained from:

- Medical records from our hospital, including recent exams, and visits to other clinics;
- Telephone contacts with individuals and their families;
- City and State electronic databases for death certificates [14], which are managed by the City and by the State Health Department. After providing a list of identifiers for each individual, researchers obtained the corresponding death certificates.

Brazilian death certificates register the underlying cause of death, its consequent conditions, and the immediate cause of death, all coded by ICD-10. In this study, we defined the cause of death as the “underlying cause of

death” noted in the death certificates. If chronic SCI was noted in death certificates as the underlying cause of death, we defined its first consequent condition as the cause of death for the purpose of this study.

Individuals with no hospital visit after 1 year and unknown vital status were considered lost to follow-up and were censored at the date of the last contact.

Statistical analysis

We conducted a survival analysis and analyzed the following parameters:

- Person-year incidence and median time to death;
- Standardized mortality ratios (SMR);
- Causes of mortality;
- Multivariate survival analysis.

Baseline demographics were analyzed by Student's t -test or χ^2 test. The difference in survival between individuals with paraplegia and tetraplegia was assessed by Kaplan–Meier with log-rank statistics. Multivariate adjustment for confounding variables was performed using a Cox proportional hazards model. All covariates were established a priori: age, gender, time from injury to hospital admission, level of injury, American Spinal Injury Association Impairment Scale (AIS), spine surgery during admission, intra-hospital complications (deep vein thrombosis, orotracheal intubation, admission to the ICU, and pneumonia), time from injury to discharge, and mechanical ventilation at discharge. Covariate selection was made using a stepwise approach guided by the Bayesian information criterion with cumulative martingale residual plots and a Kolmogorov-type supremum test to evaluate the proportionality of hazards. There was no violation of the proportional hazards assumption. The standardized mortality ratio (SMR) was obtained relative to the reported mortality rates of the metropolitan city of São Paulo from 2004 to 2014 [14], using indirect standardization for age-specific rates. Cause-specific SMRs were obtained relative to mortality rates by ICD-10 chapters. Confidence intervals of SMR were estimated using Fisher's exact test.

All analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC, USA), and a nominal significance level of 0.05 was used in all testing.

Results

Baseline data and follow-up time are presented in Table 1. Overall mortality rate per 1000 person-years was 37; 35.8 in the first 2 years post injury and 25.4 for those that survived more than 2 years. Median survival for people with

Table 1 Demographics, neurological data, and follow-up time

	Tetraplegia (n = 186)	Paraplegia (n = 248)	Total (n = 434)
Age at injury, in years [†]			
Median (IQR)	37 (25–50)	32 (22–44)	33 (24–46)
Mean (SD)	38.9 (16.5)	33.3 (15.1)	35.7 (15.9)
Gender			
Male	86.6% (161)	83.1% (206)	84.6% (367)
Female	13.4% (25)	16.9% (42)	15.4% (67)
Neurologic level			
C1–C4	33.9% (63)	—	14.5% (63)
AIS A	20.9% (39)	—	9% (39)
AIS B	5.4% (10)	—	2.3% (10)
AIS C	3.7% (7)	—	1.6% (7)
AIS D	3.2% (6)	—	1.4% (6)
Missing	0.5% (1)	—	0.2% (1)
C5–C8	66.1% (123)	—	28.3% (123)
AIS A	26.3% (49)	—	11.2% (49)
AIS B	17.7% (33)	—	7.6% (33)
AIS C	10.7% (20)	—	4.6% (20)
AIS D	9.1% (17)	—	3.9% (17)
Missing	2.2% (4)	—	0.9% (4)
T1–S5	—	100% (248)	57.1% (248)
AIS A	—	61.3% (152)	35% (152)
AIS B	—	13.7% (34)	7.8% (34)
AIS C	—	11.3% (28)	6.4% (28)
AIS D	—	6.5% (16)	3.7% (16)
Missing	—	6.8% (17)	3.9% (17)
Mechanical ventilation at discharge	1.1% (2)	2% (5)	1.6% (7)
Cause of TSCI [†]			
Falls	40.3% (75)	43.6% (108)	42.2% (183)
Traffic injuries	38.2% (71)	35.1% (87)	36.4% (158)
Assault	7.5% (14)	13.3% (33)	10.8% (47)
Sports/leisure	11.8% (22)	0.8% (2)	5.5% (24)
Fall of object	2.2% (4)	6% (15)	4.4% (19)
Others	—	1.2% (3)	0.7% (3)
Length of hospital stay, days			
Median (IQR)	45 (26–80)	41.5 (29–65)	43 (28–72)
Mean (SD)	65.1 (64.1)	55.4 (47.4)	59.6 (55.3)
Follow-up time, years			
Mean (SD)	4.4 (3.2)	5.1 (3.4)	4.8 (3.3)
Median (IQR)	3.8 (1.5–7.1)	4.3 (2.2–8.3)	4.1 (1.8–7.8)

[†] $p < 0.05$ comparing tetraplegia and paraplegia

tetraplegia was 11 years. Median survival for people with paraplegia and for the overall cohort was not reached. Individuals with tetraplegia had higher mortality than those with paraplegia (Fig. 1).

Fig. 1 Survival after spinal cord injury by injury level

There were 77 deaths (Table 2), of which 29 occurred in the first 2 years post injury. Considering all causes of death, multivariate analysis showed that people with tetraplegia had higher mortality than those with paraplegia (Table 3). Cox regression according to time post injury showed that the effect of tetraplegia on mortality was higher when analyzing only the first 2 years post injury (HR = 8.28, 95% CI: 2.76–24.80, $p = 0.0002$), compared with the analysis of more than 2 years post injury (HR = 2.35, 95% CI: 1.31–4.24, $p = 0.0042$). Further details of the Cox regression by time post injury can be found in Table S1.

Compared to the population of São Paulo, our cohort presented a SMR = 28.8 (Table 4). Defined causes of death were available in 56 cases (Table 5). Pneumonia was the most frequent cause (35.7%), and combined infectious etiologies caused 55.3% of deaths. Cancer, which was the cause of death in four individuals, occurred in the following primary sites: colorectal, testicular, head/neck, and unknown primary. A comprehensive list of the causes of death stratified by time post injury (<2 vs. ≥2 years) can be found in Table S2.

Discussion

To the best of our knowledge, this is the first study evaluating post-discharge mortality of people with SCI in Brazil. Our cohort exhibited a high mortality rate, which was more pronounced in the first 2 years post injury. Higher mortality in the acute period after SCI also has been observed in several other studies [14–18].

Pneumonia caused high number of deaths, namely 35.7% of total defined cases, with a higher impact in the group

with tetraplegia. Although this is not uncommon for individuals with SCI [19–25], the proportion of deaths attributed to pneumonia was higher in this cohort than in other populations [18–20, 26, 27]. Here, we present several

Table 2 Deceased status, in percentage (frequency), by different characteristics

	Deceased		
	Yes (<i>n</i> = 77)	No (<i>n</i> = 226)	Unknown (<i>n</i> = 131)
Gender			
Male	89.6% (69)	84.1% (190)	82.5% (108)
Female	10.4% (8)	15.9% (36)	17.6% (23)
Age at end of study			
<15	0% (0)	3.5% (8)	3.1% (4)
15–29	14.3% (11)	23.5% (53)	37.4% (49)
30–44	31.2% (24)	35.4% (80)	32.8% (43)
45–59	27.3% (21)	27.9% (63)	20.6% (27)
60–74	19.5% (15)	8.9% (20)	4.6% (6)
>75	7.8% (6)	0.9% (2)	1.5% (2)
Neurological level			
C1–C4	32.5% (25)	9.3% (21)	13% (17)
Complete	22.1% (17)	5.8% (13)	6.9% (9)
Incomplete	10.4% (8)	3.5% (8)	5.3% (7)
C5–C8	35.1% (27)	26.1% (59)	28.2% (37)
Complete	22% (17)	8.4% (19)	9.9% (13)
Incomplete	9.1% (7)	17.7% (40)	17.6% (23)
T1–S5	32.5% (25)	64.6% (146)	58.8% (77)
Complete	23.4% (18)	42.5% (96)	29% (38)
Incomplete	9.1% (7)	16.8% (38)	26% (34)

potential explanations for this outcome, although more studies would be needed to draw firm conclusions. First, since no death certificate reported an influenza-related death, it is likely that some influenza cases were miscoded as pneumonia. Miscoding other pulmonary infections as pneumonia is, unfortunately, a common mistake in death certificates in Brazil [28, 29]. Second, respiratory rehabilitation was not part of the standard treatment for individuals with SCI in the outpatient setting. It is possible that our participants had a sub-optimal respiratory capacity and, therefore, had an increased risk for pneumonia [23–25, 30, 31].

Urogenital diseases caused 10.7% of defined deaths, all due to urinary tract infections. They presented the second highest cause-specific SMR in this cohort. Management of neurogenic bladder in our population has several limitations, such as: obtaining proper equipment/material for catheterization, difficulty in obtaining anticholinergic medication, and deviations in the catheterization technique [32].

All deaths attributed to skin diseases were due to pressure ulcers. They caused 7.1% of defined deaths and the highest cause-specific SMR. Preventing pressure ulcers can be very challenging in our population, since there is a high prevalence of poor social and family, which hinders the compliance to frequent postural shift. Since those individuals usually live in regions with poor accessibility and low availability of wound care centers, treatment is also a challenge.

Cancer was the most common cause of mortality in individuals with paraplegia, followed by pneumonia. However, due to the small number of these cases, it is difficult to establish an association between paraplegia and cancer-related deaths. Only one out of four cancer cases was

Table 3 Univariable and multivariable regression for mortality risk

Variables	Univariable analysis			Multivariable analysis		
	HR	95% CI	<i>P</i>	HR	95% CI	<i>P</i>
Age at injury (years) = 1	1.04	1.03–1.16	<0.001	1.05	1.03–1.06	<0.001
Age at injury (>65) = 1	4.07	2.21–7.49	<0.001			
Complete injury	2.15	1.30–3.57	0.003	2.71	1.61–4.54	<0.001
DVT (yes) = 1	0.62	0.23–1.71	0.359			
ICU admission (yes) = 1	2.41	1.48–3.92	<0.001			
Intubation during acute period (yes) = 1	2.43	1.49–3.96	<0.001			
Male (yes) = 1	1.44	0.69–3.01	0.335			
Mechanical ventilation at discharge (yes) = 1	0.89	0.12–6.45	0.911			
Pneumonia (yes) = 1	1.21	0.73–2.03	0.453			
Spasticity (yes) = 1	0.89	0.53–1.51	0.671			
Tetraplegia (yes) = 1	3.25	2.01–5.24	<0.001	3.36	2.04–5.52	<0.001
Time from injury to discharge (days)	1.00	1.00–1.00	0.220			
Tracheostomy at discharge (yes) = 1	1.12	0.50–2.82	0.802			
UTI during acute period (yes) = 1	1.93	1.09–3.42	0.024			

DVT deep vein thrombosis, ICU intensive care unit, UTI urinary tract infection

Bold values highlight the statistically significant results

Table 4 Standardized mortality ratios (SMR), per age

Age	Deaths	Expected deaths	Years of exposure	SMR (95% CI)
<2 years after injury				
<15	0	0.01	20.7	—
15–29	3	0.13	194.5	22.9 (4.8–67.4)
30–44	8	0.30	261.3	26.5 (11.5–52.6)
45–59	10	0.70	192.2	14.2 (6.9–26.3)
60–74	6	0.77	67.5	7.8 (2.9–17)
>75	2	0.77	17.7	2.6 (0.3–9.4)
Total	29	2.67	754.1	10.8 (7.3–15.6)
≥2 years after injury				
<15	0	0.01	23.2	—
15–29	8	0.09	254.2	89.6 (38.4–175.1)
30–44	16	0.24	550.5	67.2 (38.1–108.3)
45–59	11	0.53	359.8	20.6 (10.4–37.1)
60–74	9	0.53	110.5	17.1 (7.8–32.2)
>75	4	0.54	28.7	7.5 (2–19)
Total	48	1.98	1327	24.2 (17.9–32.1)
All years				
<15	0	0.01	44	—
15–29	11	0.13	448.7	76.3 (42.2–151.4)
30–44	24	0.30	811.9	83 (51.3–119)
45–59	21	0.70	552	29.8 (18.6–45.9)
60–74	15	0.77	178.1	19.5 (10.9–32.1)
>75	6	0.77	46.4	7.8 (2.9–17)
Total	77	2.67	2081.1	28.8 (22.8–36)

diagnosed in a primary site that has a well-established screening protocol.

Considering the frequency of each cause of death, their respective SMRs, and potential impact of interventions, we should aim in reducing the incidence of respiratory infections. The emphasis on adherence to pneumonia and influenza vaccination during follow-up appointments, both of which are covered by the Brazilian government for individuals with SCI, represents a readily implementable change that may be highly beneficial. In Brazil, *Streptococcus pneumoniae* and influenza viruses are the most frequent causes of bacterial and viral pneumonia, respectively [33–35]. We also suggest the development of respiratory rehabilitation guidelines focused on prevention of respiratory complications [30, 36]. New research should be conducted on the impact of such activities on patient mortality.

Prevention of pressure ulcers can be challenging in settings with low resources, but the evidence to support the efficacy of specific strategies is lacking. Data from Bangladesh and Pakistan suggest that education and regular phone contact are feasible strategies for its prevention, although with unclear efficacy [37, 38].

Table 5 Number of deaths and cause-specific SMR for defined causes of death

Causes	Tetraplegia (n = 36)		SMR (95% CI)		Paraplegia (n = 20)		SMR (95% CI)		Total (n = 56)		SMR (95% CI)		Expected deaths/1000 people	
Respiratory	47.2% (17)		211.3 (123.1–338.3)		20% (4)		37.3 (10.2–95.5)		37.5% (21)		111.9 (69.2–171)		0.4326	
Circulatory	16.7% (6)		27.8 (10.2–60.5)		5% (1)		3.5 (0.1–19.4)		12.5% (7)		13.9 (5.6–28.6)		1.1610	
Cancer	0% (0)		0% (NA)		20% (4)		22.9 (6.2–58.7)		7.1% (4)		13.1 (3.6–33.5)		0.7035	
Urogenital	11.1% (4)		246.9 (67.3–632.2)		10% (2)		92.6 (11.2–334.5)		10.7% (6)		158.7 (58.2–345.5)		0.0871	
Skin	5.6% (2)		374.7 (45.3–1353.4)		10% (2)		281 (34–1015)		7.1% (4)		321.1 (87.5–822.2)		0.0287	
Bone	0% (0)		0% (NA)		5% (1)		103.4 (2.6–576.1)		1.8% (1)		59.1 (1.5–329.2)		0.0390	
Digestive	2.8% (1)		27.5 (0.7–153.1)		15% (3)		61.8 (12.7–180.6)		7.1% (4)		47.1 (12.8–120.6)		0.1957	
External	11.1% (4)		66.1 (18–169.2)		15% (3)		37.2 (7.7–108.6)		12.5% (7)		49.6 (19.9–102.1)		0.3255	
Other	5.6% (2)		N/A		0% (0)		N/A		3.6% (2)		N/A		N/A	

N/A not applicable

Study limitations

The present study has several limitations. First, 30.2% of the cohort had unknown deceased status. Even though the data were extracted from a metropolitan mortality database, this database only provides information on instances when the individual is deceased; if the person is alive, the database is defined as unknown. Secondly, 27.3% of mortality causes were unknown, primarily due to poorly reported death certificates, an unfortunately common problem in Brazil [39–41]. Hence, it is possible that the ranking of causes presented is inaccurate. Thirdly, the generalizability of our results might be limited, since our study was conducted in a national reference center for SCI located in the largest city in Brazil. It is likely that patients treated in centers with less experience, resources, and training will have different outcomes.

Conclusion

Our cohort presented high rates of death by preventable causes. The care of individuals with SCI in our center should emphasize the prevention of such causes. Focusing on vaccination and respiratory rehabilitation seems a readily implementable way to improve SCI outcomes in this population.

Author contributions VFL was responsible for the study design, data collection, data interpretation, manuscript writing, and manuscript editing. DRS was responsible for data collection, data interpretation, and manuscript editing. MI was responsible for study design and manuscript editing. LRB was responsible for the study design, data interpretation, and manuscript editing.

Compliance with ethical standards

Conflict of Interest The authors declare that they have no conflict of interest.

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