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Acute traumatic quadriplegia: Predictors of in-hospital and six-month mortality

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Abstract

Background: Traumatic spinal cord injury is one of the most disastrous and devastating health burdens all over the world with a high mortality rate. The present study aimed to evaluate the predictors of in-hospital and six-month mortality in these patients.

Methods: The electronic medical records of 87 consecutive patients with acute complete traumatic quadriplegia were reviewed to extract clinical, radiological, and laboratory data. Simple and multiple logistic regression models were used to estimate crude and adjusted odds with 95% confidence interval (CI) ratios for the predictors of in-hospital mortality and six-month mortality.

Results: There were 48 males and the mean age was 38.67 ± 12.81; in-hospital and six-month mortality were 21.84% and 11.76%, respectively. Traffic road accidents (67.8%) and falls (12.6%) were the most common causes of injury. The univariate analysis demonstrated advanced age, level of injury, late surgery or no surgical intervention, the lack of methylprednisolone therapy, a higher Charlson comorbidity index, the Injury Severity Score, and the presence of respiratory failure or bradycardia on admission were predictors of in-hospital mortality ($p < 0.05$). In the final multiple logistic regression model, the level of injury (OR = 0.02 (0.001,0.35), $p = 0.008$) and the presence of respiratory failure (OR = 2.37 (0.03,13.88), $p = 0.024$) were the only predictors of in-hospital mortality. The univariate model showed that the level of injury, respiratory failure on admission, and the Injury Severity Score were the predictors of six-month mortality; however, the level of injury was the only predictor of the six-month mortality (OR = 1.12 (0.99, 1.27), $p = 0.028$) according to the multiple logistic regression model.

Conclusions: Several factors could affect in-hospital and six-month mortality in patients with traumatic spinal cord injury. Our findings demonstrated the level of injury and respiratory failure on admission as independent predictors of in-hospital mortality in these patients. Furthermore, the level of injury was the only independent predictor of six-month mortality in the present study.

Keywords

Traumatic spinal cord injury, in-hospital mortality, six-month mortality, Injury Severity Score

Introduction

Traumatic spinal cord injury (TSCI) is one of the most disastrous and pernicious injuries all over the world.[1,2] Although survival rates have increased significantly by improving medical management, the annual incidence is increasing especially in developing countries[3] with an incidence of 10.4–83.0 per million population per year.[4,5] TSCI has a high mortality rate; about 10–20% of patients do not survive to reach the hospital

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and 3–25% of patients die during hospitalization.[2,6] Early mortality can be affected by a number of factors and advanced age, a higher spinal level of injury, cause of injury (falling), late surgery against early surgery, and presence of respiratory failure on admission have been suggested as contributory factors.[7–9]

According to previous studies, the early stage of SCI is accompanied by a higher mortality rate than the later stages[1,10] with neurological dysfunction, respiratory failure, and concomitant injuries suggested as the leading causes.[11,12] Apart from a substantial rate of mortality, increasing numbers of patients will survive with a potentially catastrophic level of disability; due to the lack of effective treatment, SCI is a major health burden all over the world.[13,14]

The present study was designed to assess the early predictors of in-hospital and six-month mortality in patients with complete quadriplegia following TSCI in a single spinal injuries unit.

Methods

This study retrospectively investigated all consecutive patients with acute complete traumatic quadriplegia admitted to our hospital between May 2009 and April 2018. Their clinical, radiological and laboratory data were extracted from the electronic medical records. Included patients had acute complete traumatic quadriplegia (according to American Spinal Injury Association guidelines[15]) and were aged more than 18 on admission. Patients who died during the first 24 h from injury, those with incomplete spinal cord injury, and patients with concomitant brain injuries were excluded (Figure 1).

Suggested predictors of in-hospital mortality including age, sex, mechanism of injury, level of spinal cord injury, pre-injury comorbidity, bradycardia and hypotension on admission, the Injury Severity Score (ISS), and the presence of respiratory failure within the first 24 h of injury were evaluated. Based on surgical intervention, patients were divided into three groups: patients with early surgery (within the first 48 h from injury), patients with late surgery (after the first 48 h) and patients without any surgical procedures.

Our unit has a standard protocol for the use of methylprednisolone (MP) after spinal cord injury with the following exclusions: patients more than 8 h from injury, those with a gunshot wound to the spine, pregnant women or those with a history of continuous steroid consumption.

The Charlson medical co-morbidity score was used to quantify pre-injury comorbidity;[11] it comprises three scores from zero to two—a healthy individual scores zero and with increasing illness, the score rises. Hypotension was defined as a systolic blood pressure less than 90 mmHg and bradycardia as a heart rate less than 50 beats per minute; respiratory distress was defined as the presence of irregular breathing patterns and a PaO_2 value of <60 mmHg, or a $PaCO_2$ of >50 mmHg that required mechanical ventilation.[2]

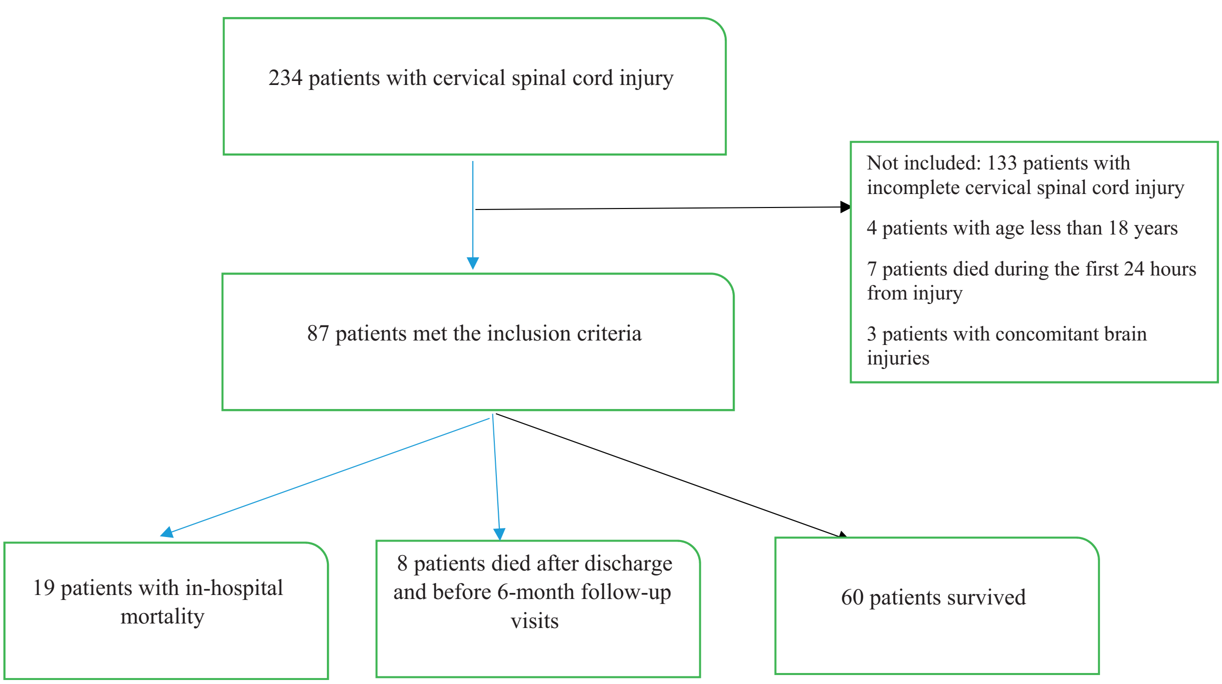

Figure 1. Flowchart of study population.

Statistical analysis

All statistical analyses were performed using Stata version 14.2 (StataCorp, College Station, TX). Descriptive analysis was conducted on demographic and clinical characteristics, including age, sex, cause of injury, level of injury, surgery intervention, MP therapy, the Charlson comorbidity index, hypotension, bradycardia, respiratory failure, and ISS. Simple and multiple logistic regression models were applied to estimate crude (results of the univariate model) and adjusted (the results of the multivariate model) odds ratio with 95% confidence interval (CI) ratios for the predictors of mortality in order to eliminate the potential confounding effect. A p value <0.05 was considered as statistically significant.

Results

A total of 87 patients (48 males, 55.2%) with complete traumatic quadriplegia were analyzed; the mean age was 38.67 ± 12.81 [Table 1]; 69 patients (79.31%) received a bolus intravenous infusion of 30 mg/kg bodyweight of MP followed by infusion at 5.4 mg/kg/h for 23 h according to unit protocol.

In-hospital and six-month mortality were 21.84% (19/87) and 11.76% (11/68), respectively. The most common causes of injury were traffic road accidents (67.8%) and falls (12.6%; Table 1). Advanced age, level of injury, late surgery or no surgical intervention,

Table 1. Demographic and clinical characteristics of patients.

	Frequency (%)
Gender	
Male	48 (55.2)
Female	39 (44.8)
Cause of injury	
Road traffic crashes	59 (67.8)
Violence	8 (9.2
Fall	11 (12.6)
Sport	4 (4.6)
Struck by objects	5 (5.7)
Level of injury	
C2	1 (1.2)
C3	6 (6.9)
C4	11 (12.6)
C5	16 (18.4)
C6	28 (32.2)
C7	25 (28.7)
Cause of in-hospital mortality	
Ventilator dependent	9 (47.4)
Sepsis	4 (21.1)
Multiple organ failure	2 (10.5)
Bradycardia/ cardiovascular arrest	3 (15.8)
Unknown	1 (5.3)
Surgical intervention	
Early surgery	34 (39.1)
Late surgery	45 (51.7)
No surgical intervention	8 (9.2)
Methylprednisolone therapy	
No	18 (20.7)
Yes	69 (79.3)
Charlson co-morbidity score	
0	62 (71.3)
1	20 (23.0)
2	5 (5.7)
Hypotension on admission	
No	35 (40.2)
Yes	52 (59.8)
Bradycardia on admission	
No	69 (79.3)
Yes	18 (20.7)
Respiratory failure	
No	65 (74.7)
yes	22 (25.3)
Cause of death after discharge	
Ventilator dependent	1 (14.3)
Sepsis	2 (28.6)
Multiple organ failure	2 (28.6)
Unknown	2 (28.6)
ISS	
Mean ± SD	43.80 ± 14.12
Age	
Mean ± SD	38.67 ± 12.81
Length of stay (for patients with death before discharge)	
Mean ± SD	28.19 ± 27.57

the lack of MP therapy, a higher Charlson comorbidity index, the ISS, the presence of respiratory failure, and bradycardia on admission were the predictors of in-hospital mortality on univariate analysis ($p < 0.05$; Table 2). There was no significant difference in mortality between males and females ($p = 0.430$).

Early surgery was performed in 34 cases (39.1%) and 45 patients underwent late surgery (51.7%), with surgical intervention not performed in eight cases (9.2%); the odds of death were 4.19 and 6.2 times higher in patients with late surgery and those without surgical intervention compared to patients with early surgery ($p = 0.037$ and $p = 0.054$). With each unit increase in the Charlson comorbidity index score, the probability of in-hospital mortality was increased 5.43 times. Most patients received high-dose MP during the first 8 h after injury and the odds of in-hospital mortality in victims without MP therapy was 15.32 times more than those receiving it.

The presence of bradycardia and respiratory failure on admission increased the odds of mortality 4.22 and 3.81 times, respectively. According to the multiple logistic regression, the level of injury and respiratory failure on admission were the only independent predictors of in-hospital mortality ($p < 0.05$; Table 2). Eight patients of those who survived to discharge (11.76%) died after discharge and before a six-month follow-up visit; according to the univariate model, the level of injury, respiratory failure on admission, and ISS were predictors of six-month mortality. However, multivariate analysis showed that the level of injury was the only predictor of six-month mortality (OR = 1.12 (0.99, 1.27), $p = 0.028$; Table 3).

Discussion

In this present study, in-hospital and six-month mortality were 21.84% and 11.76%, respectively, compared to reported mortalities for patients with cervical cord injuries of 4.0–28%.[6,13] Advanced age, a higher level of injury, cause of SCI, late surgery against early surgery, and presence of respiratory failure on admission have been suggested as contributing factors[6,16] whereas in this study multivariate analysis showed the level of injury and respiratory failure as the only independent predictors of in-hospital mortality.[4,13] There are some explanations about the impact of a higher level of injury on mortality—patients with a higher level of cervical cord injury are generally accompanied by a higher rate of respiratory failure, more severe neurological dysfunction, and a higher risk of pulmonary complications such as pneumonia.[17,18]

The diaphragm, innervated by the phrenic nerve, as the main respiratory muscle provides a driving force for respiratory movements and provides 65% of tidal volume; the phrenic nucleus is placed at the anterior horn of the C4 cervical cord and is susceptible to injury in patients with a higher cervical cord injury.[10,17] Respiratory complications secondary to diaphragm dysfunction are reduced respiratory force and as a result, retained respiratory secretions, and a higher rate of infection.[2,17] Furthermore, patients with a cord injury

Table 2. Predictors of in-hospital mortality.

Variables	Crude odds ratio (CI 95%) (univariate analyses)	*p* value	Adjusted odds ratio (CI 95%) (multivariate analyses)	*p* value
Age	1.07 (1.03, 1.11)	0.001	0.99 (0.89, 1.11)	0.903
Gender, Ref: female	1.52 (0.53, 4.34)	0.430		
Level of injury	0.06 (0.02, 0.23)	<0.0001	0.02 (0.001, 0.35)	0.008
Surgical intervention, Ref: early surgery				
Late surgery	4.19 (1.09, 16.78)	0.037	0.5.82 (0.30, 112.19)	0.243
No surgical intervention	6.2 (0.97, 39.76)	0.044	0.32 (0.003, 33.57)	0.630
No methylprednisolone therapy	15.23 (2.76, 83.98)	0.002	11.85 (0.01, 15,986.52)	0.501
Charlson co-morbidity score	5.43 (2.17, 13.53)	<0.0001	8.37 (0.84, 83.63)	0.070
Hypotension on admission	2.21 (0.72, 6.83)	0.168	0.22 (0.01, 10.37)	0.442
Bradycardia	4.22 (1.36, 13.07)	0.013	11.16 (0.26, 485.86)	0.210
Respiratory failure	3.81 (1.29, 11.26)	0.016	2.37 (0.03, 13.88)	0.024
ISS	1.13 (1.07, 1.19)	<0.0001	0.98 (0.87, 1.11)	0.777

Table 3. Predictors of six-month mortality.

Variables	Crude odds ratio (CI 95%) (univariate analyses)	*p* value	Adjusted odds ratio (CI 95%) (multivariate analyses)	*p* value
Age	1.06 (0.99, 1.13)	0.063	0.91 (0.78, 1.05)	0.183
Gender, Ref: female	1.55 (0.34, 7.12)	0.566	–	
Level of injury	0.09 (0.02, 0.41)	0.001	0.04 (0.01, 0.71)	0.028
Surgical intervention, Ref: early surgery				
Late surgery	5.56 (0.61, 50.59)	0.128	91.81 (0.83, 10,143.65)	0.060
No surgical intervention	20 (1.37, 269.07)	0.028	11.16 (0.03, 3924.30)	0.420
No methylprednisolone therapy	–		–	
Charlson co-morbidity score	1.27 (0.27, 6.05)	0.763	–	
Hypotension on admission	2.62 (0.49, 14.07)	0.260	–	
Bradycardia	2.17 (0.37, 12.65)	0.391	–	
Respiratory failure	5.67 (1.19, 26.87)	0.029	9.30 (0.61, 142.25)	0.109
ISS	1.14 (1.05, 1.24)	0.002	1.12 (0.99, 1.27)	0.065

at or above C3 level may die suddenly secondary to phrenic and intercostal nerves dysfunction.[19]

There is controversy about the impact of older age on in-hospital mortality in SCI patients with some studies showing that older age is a significant predictor for mortality while some do not.[20,21] Kumamaru et al. in an animal study showed that older mice had worse functional recovery and higher pro-inflammatory cytokines during the early stage of complete SCI. They focused on age-related differences in inflammatory responses of microglia after spinal cord injury.[22] Interestingly, our results showed that the probability of in-hospital mortality in patients that did not receive MP therapy was 15.32 times higher than those receiving it. The effectiveness of MP therapy in spinal cord injury patients has been clearly demonstrated.[23–25] Spinal cord injury can be divided into primary and secondary injuries—primary injury denotes the damage caused by external forces at the moment of insult[18] and secondary spinal cord injury denotes a cascade of damage after the primary injury including edema, ischemia, microcirculatory dysfunction, and severe inflammatory response; secondary injuries are usually more serious.[9] High-dose MP therapy can mitigate the secondary injuries by inhibition of inflammatory and pre-oxidative responses; although, high-dose MP therapy may carry a high risk for side effects including poor wound healing and/or gastrointestinal bleeding, the risk of such side-effects is not usually significant,[25] hence, high dose MP therapy carries a significant role in preventing further cord injury.

There is a controversy about the role of the timing of surgical decompression, reduction, and reconstruction in patients with TSCI.[26–28] Some authors have emphasized early surgical interventions[27,29] believing that early surgery can decompress the spinal cord and stabilize the injured level, to prevent further damage to the spinal cord from repeated motion of unstable cervical segments. Furthermore, some studies have demonstrated early surgical intervention can improve the clinical outcomes of these patients. However, other studies showed that early surgery can increase the risk of spinal cord injury and there was no significant difference between patients with early surgery and those with late surgery.[30] In this study, the probability of death was significantly lower in patients with early surgery compared to those who had late surgery and those without surgical intervention. However, the feasibility of early surgery in spinal cord injury patients is dependent on multiple conditions including pre-operative hemodynamic stability and possible concomitant injuries. Considering all these factors, as well as the results of a recent international survey of spine surgeons, early surgical decompression and reconstruction should be considered whenever possible.

Limitations

The present study had several limitations. It was retrospective and so some confounding variables may not have been measured or collected; furthermore, the sample size is relatively small and the single-center study could have limited the generalizability of the results. The establishment of a multicenter TSCI registry should be considered to completely investigate the probable predictors of mortality in these patients.

Conclusions

Several factors can affect in-hospital and six-month mortality in patients with TSCI. Our findings demonstrate that the level of injury and respiratory failure on admission are independent predictors of in-hospital mortality in these patients. Furthermore, the level of injury was the only independent predictor of six-month mortality in the present study.

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Contributorship

EA and SRB had the idea for this study. EA and CR participated in outlining the concept and design. PA and MJ did the data acquisition. EA and RS did the statistical analysis and wrote the first draft of the manuscript. EA, SRB, PA, and MJ revised the final manuscript. All authors have read and approved the manuscript.

Declaration of conflicting interests

The author(s) declare that there is no conflict of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

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Guarantor

EA.

Informed consent

Informed consent was not sought for the present study because it is a retrospective review of de-identified data.

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