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ORIGINAL ARTICLE

Serum Galectin-3 and Glial Fibrillary Acidic Protein Levels in Patients with Spinal Cord Injury in Relation to Injury Severity and Prognosis

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SUMMARY

Background: **This research aimed to assess the link between serum galectin-3 (Gal-3) and glial fibrillary acidic protein (GFAP) levels and the severity and prognosis of spinal cord injury (SCI) patients.**
Methods: **Serum Gal-3 and GFAP levels were measured in SCI patients. Serum Gal-3 and GFAP levels were analyzed in relation to SCI injury severity and prognosis. The prognostic value of serum Gal-3 and GFAP was assessed using ROC curve analysis.**
Results: **The American Spinal Injury Association Impairment Scale (AIS) categorized 59 patients into the severe SCI group (AIS A-B). Serum Gal-3 and GFAP levels were higher in patients with severe SCI than in patients with non-severe SCI. The 6-month follow-up AIS classified 60 patients as having a poor prognosis. Serum Gal-3 and GFAP levels were higher in poor-prognosis SCI patients than in good-prognosis SCI patients. A significant association between poor prognosis and serum Gal-3 and GFAP was demonstrated through multivariate logistic regression analysis. ROC curve analysis showed that the AUCs for serum Gal-3 and GFAP were 0.856 and 0.890, respectively.**
Conclusions: **Serum Gal-3 and GFAP levels are significantly associated with injury severity at admission and 6-month prognosis in SCI patients. Serum Gal-3 and GFAP levels can be used as clinical risk factors for predicting SCI injury severity and 6-month prognosis.**
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KEYWORDS

spinal cord injury, galectin-3, glial fibrillary acidic protein, injury severity, prognosis

INTRODUCTION

Acute traumatic spinal cord injury (SCI) has risen to be a critical global health issue, now seen as the second leading cause of morbidity and disability, following traumatic brain injury [1]. These injuries not only lead to health and disability issues for individuals and their families but also place a financial strain on the healthcare system and economy [2,3]. A worldwide study indicates that the number of traumatic SCI is rising annually, with over 27 million people globally anticipated to be impacted, primarily due to falls and road accidents

[4]. To determine the severity of SCI, the American Spinal Injury Association Impairment Scale (AIS) is employed and serves as the most frequent prognostic tool [5,6]. However, the unpredictability of spontaneous neurological recovery complicates forecasting long-term results [7]. Consequently, employing clinical biomarkers to anticipate prognosis is essential in designing treatment plans.

Fluid biomarkers are an affordable, accessible, and unbiased method for SCI research and treatment. Some protein biomarkers have been examined in SCI, showing some effectiveness in categorizing patients based on the severity of injury and forecasting outcomes [8,9]. Galectins, a class of proteins, are evolutionarily conserved and can be found in sponges, invertebrates, and mammals [10]. Within the galectin family, galectin-3 (Gal-3) stands out as a chimera type, recognized for its β-galactoside-binding lectin properties [11]. Involvement of Gal-3 is noted in pathophysiological conditions, including metastasis [12], inflammation [13], immune responses [14], and cancer [15]. It has been shown that Gal-3 levels are related to aneurysmal subarachnoid hemorrhage severity and prognosis [16]. There are currently no studies that established a connection between serum Gal-3 levels and the severity or outcome of SCI. In cases of neurotrauma, glial fibrillary acidic protein (GFAP) is associated with both the severity of the injury and the recovery of neurological functions [17-20]. This investigation aimed to explore whether serum Gal-3 and GFAP could potentially predict the severity of injury and 6-month outcomes in patients suffering from SCI.

MATERIALS AND METHODS

Patients

Individuals with acute traumatic SCI were included based on the following criteria: 1) aged 18 years or older; 2) within 12 hours post-injury; and 3) a Glasgow Coma Scale score of 15. Exclusion criteria encompassed the following: 1) pre-existing neurological impairments or conditions (such as ischemic stroke or brain hemorrhage); 2) medications of steroid-related drugs or diabetes; 3) kidney function damage or hematological system disorders; 4) data missing; and 5) traumatic body injury, excluding the spinal cord, with an abbreviated score of 3 or greater. This study was a clinical observational study and followed the STROBE guidelines. The study was approved by the Ethics Committee of West China Hospital of Sichuan University, and all patients provided written informed consent.

SCI was diagnosed through MRI and physical examination at admission. The clinical severity of every patient was evaluated using AIS. Severe SCI was categorized as AIS grades A and B, while non-severe SCI was categorized as AIS grades C-E [21]. Clinical data were collected, encompassing gender, age, injury mechanism, injury location, AIS grade at admission, heart rate, SBP, DBP, and laboratory tests. To locate the SCI site, all patients underwent MRI examinations. The care and management of SCI patients adhered to the guidelines for SCI treatment [22].

Measurement of serum biochemical indicators

A sample of 10 mL of peripheral venous blood was taken from patients who were conclusively diagnosed with SCI upon their admission. The collected blood sample was left undisturbed for 10 minutes at 25°C to coagulate, followed by centrifugation at 3,000 revolutions per minute for 20 minutes. The serum specimens were isolated and preserved at -80°C. Gal-3 serum levels were measured using an enzyme-linked immunosorbent assay (Human Galectin-3 Quantikine ELISA Kits, R&D Systems). GFAP in serum was determined through the highly sensitive Simoa software on the Quanterix SR-X system (Quanterix).

Outcome assessment

The prognosis for SCI patients was determined by the ordinal change in AIS grade 6 months post-injury. The prognosis of patients with SCI was meticulously assessed at 6 months using outpatient follow-ups or telephone consultations after they were discharged. SCI patients who finished follow-up were assessed with a prognosis of either poor (AIS A-C) or good (AIS D-E) [6].

Statistical analysis

All statistical analyses were conducted using SPSS version 21.0. Categorical variables are displayed as percentages, and continuous variables are presented as the mean ± standard deviation or median and interquartile range. The Shapiro-Wilk test was employed to assess the normality of the data. In the case of variables with normal distribution, Student's *t*-test or ANOVA was employed for comparisons, while those with non-normal distribution utilized Kruskal-Wallis or Mann-Whitney U test. Univariate analysis was employed to examine the risk elements contributing to poor prognosis in SCI. Factors with a p-value less than 0.05 in the Univariate analysis were incorporated into the multivariate logistic regression model. The prognostic value of serum Gal-3 and GFAP was analyzed using receiver operating characteristic (ROC) curves. Statistical differences were considered to exist when $p < 0.05$.

RESULTS

Patient characteristics

Among the 120 patients with acute traumatic SCI who qualified for the study, there were 96 males and 24 females (Table 1), with ages spanning from 18 to 75 years, and a mean age of 50.8. The majority of injuries were due to falls (62, 51.7%), followed by motor vehicle accidents (40, 33.3%), being struck by objects (6, 5.0%), and other causes (12, 10.0%). Cervical SCI made up 79.2% of all instances, while thoracic and lum

Table 1. Patient characteristics.

Characteristics	Patients with acute traumatic SCI (n = 120)
Gender, n (%)	
Male	96 (80.0%)
Female	24 (20.0%)
Age (years), mean (range)	50.8 (18 - 75)
Injury mechanism, n (%)	
Fall	62 (51.7%)
Motor vehicle accident	40 (33.3%)
Hit by object	6 (5.0%)
Others	12 (10%)
Injury location, n (%)	
Cervical	95 (79.2%)
Thoracic	10 (8.3%)
Lumbar	11 (9.2%)
Others	4 (3.3%)
AIS grade at admission, n (%)	
A	46 (38.3%)
B	13 (10.8%)
C	22 (18.3%)
D	34 (28.3%)
E	5 (4.2%)
Surgical decompression, n (%)	
Yes	101 (84.2%)
No	19 (15.8%)
6-month follow-up AIS grade, n (%)	
A	27 (22.5%)
B	18 (15.0%)
C	15 (12.5%)
D	50 (41.7%)
E	10 (8.3%)

bar SCI represented 8.3% and 9.2%, respectively. The AIS grading system showed that the frequencies of impairments were 46 (38.3%) for grade A, 13 (10.8%) for grade B, 22 (18.3%) for grade C, 34 (28.3%) for grade D, and 5 (4.2%) for grade E.

Out of all the patients, 84.2% received surgical operations like laminoplasty, internal fixation, fusion, and spinal decompression. At the 6-month follow-up, the distribution of patients was 27 (22.5%) in grade A, 18 (15.0%) in grade B, 15 (12.5%) in grade C, 50 (41.7%) in grade D, and 10 (8.3%) in grade E.

Relationship between serum Gal-3 and GFAP levels and injury severity

A total of 59 patients were classified under severe SCI (AIS A-B), whereas 61 patients were classified under non-severe SCI (AIS C-E). According to Table 2, the severe and non-severe SCI groups differed significantly in injury location, heart rate, SBP, DBP, and WBC count. In addition, all SCI patients were tested for serum Gal-3 and GFAP levels at admission, and the results showed that serum Gal-3 and GFAP levels were higher in patients with severe SCI than in patients with non-severe SCI (Figure 1).

Relationship between serum Gal-3 and GFAP levels and prognosis

There were 60 patients with poor prognosis (AIS A-C) and 60 patients with good prognosis (AIS D-E). Univariate analysis revealed a significant association between the 6-month prognosis and variables like injury severity, injury location, SBP, DBP, heart rate, and WBC

Table 2. The differences in clinical features and laboratory data between severe and non-severe SCI.

Characteristics	Severe SCI (n = 59)	Non-severe SCI (n = 61)	p-value
Gender, n			
Male	49	47	0.411
Female	10	14	
Age (years), median (IQR)	52 (43, 59)	53 (44, 60)	0.396
Injury mechanism, n			
Fall	33	29	0.811
Motor vehicle accident	18	22	
Hit by object	3	3	
Others	5	7	
Injury location, n			
Cervical	45	50	0.007
Thoracic	9	1	
Lumbar	2	9	
Others	3	1	
Heart rate (beats/minute), median (IQR)	71 (62, 80)	78 (70, 85)	< 0.001
SBP (mmHg), median (IQR)	114 (100, 125)	129 (118, 140)	< 0.001
DBP (mmHg), median (IQR)	67 (59, 75)	79 (71, 86)	< 0.001
WBC count (10^3/μL), median (IQR)	11.0 (9.3, 13.7)	9.6 (7.8, 12.2)	< 0.001

Table 3. Univariate analysis for risk factors of poor prognosis in SCI.

Characteristics	Poor prognosis (n = 60)	Good prognosis (n = 60)	p-value
Severity of injury, n			
Severe SCI	55	4	< 0.001
Non-severe SCI	5	56	
Gender, n			
Male	50	46	0.361
Female	10	14	
Age (years), median (IQR)	52 (44, 60)	53 (45, 60)	0.748
Injury mechanism, n			
Fall	33	29	0.739
Motor vehicle accident	20	20	
Hit by object	2	4	
Others	5	7	
Injury location, n			
Cervical	40	55	0.016
Thoracic	2	8	
Lumbar	9	2	
Others	3	1	
Heart rate (beats/min), median (IQR)	72 (64, 80)	77 (69, 84)	< 0.001
SBP (mmHg), median (IQR)	116 (100, 128)	127 (116, 138)	< 0.001
DBP (mmHg), median (IQR)	68 (59, 77)	78 (71, 86)	< 0.001
WBC count (10^3/μL), median (IQR)	10.9 (9.2, 13.8)	9.9 (7.9, 12.4)	< 0.001

Table 4. Multivariate logistic regression analysis for risk factors of poor prognosis in SCI.

Characteristics	OR (95% CI)	p-value
Severity of injury	0.010 (0.005 - 0.022)	< 0.001
Injury location	0.964 (0.916 - 1.014)	0.23
Heart rate	1.002 (0.972 - 1.032)	0.961
SBP	1.010 (0.979 - 1.043)	0.613
DBP	0.981 (0.934 - 1.032)	0.282
WBC count	1.025 (0.921 - 1.140)	0.635
Serum galectin-3	0.153 (0.076 - 0.305)	0.027
Serum GFAP	0.057 (0.024 - 0.118)	0.016

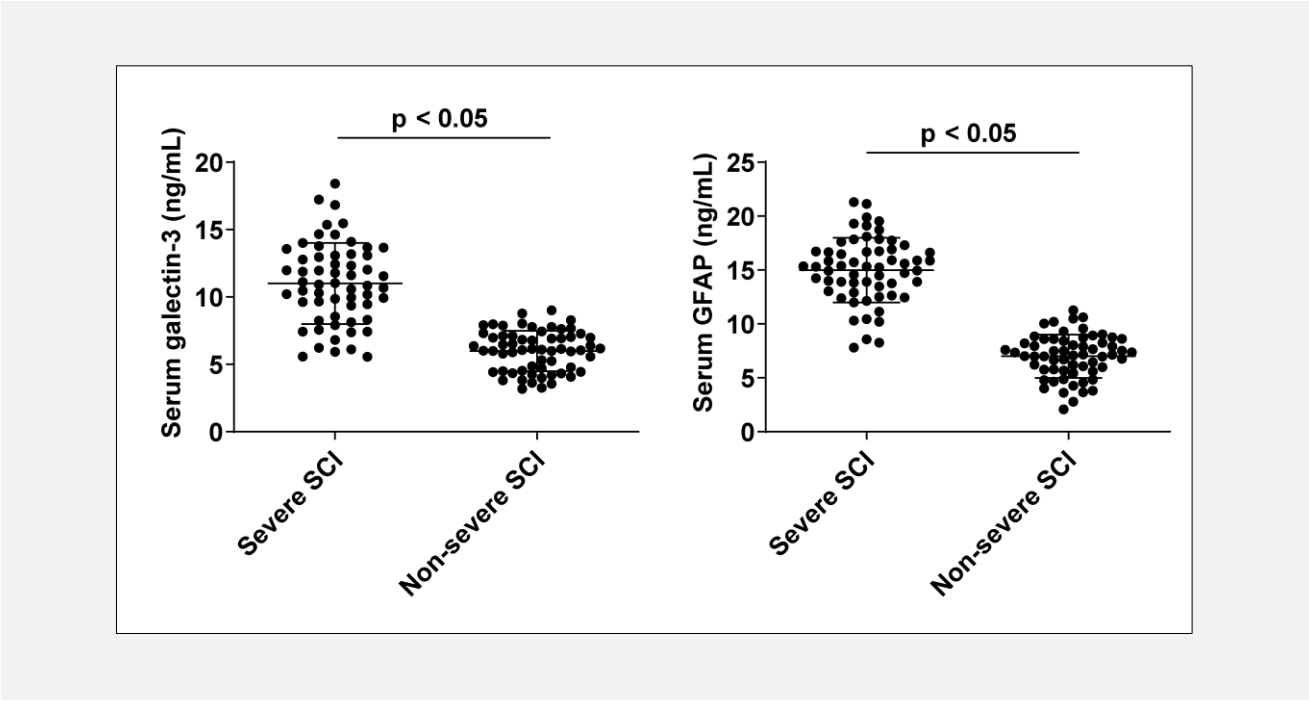

Figure 1. Serum galectin-3 and GFAP levels in severe SCI patients and non-severe SCI patients.

count (Table 3). Serum Gal-3 and GFAP levels were higher in SCI patients with poor prognosis than in SCI patients with good prognosis (Figure 2). Multivariate logistic regression analysis found that injury severity, serum Gal-3, and GFAP levels were independent factors affecting the 6-month prognosis of SCI patients (Table 4).

Prognostic value of serum Gal-3 and GFAP

An ROC curve was constructed, and the AUC was calculated to assess the prediction performance of serum Gal-3 and GFAP. The AUCs of serum Gal-3 and GFAP were 0.856 and 0.890, respectively (Figure 3).

DISCUSSION

This study investigated for the first time the association of serum Gal-3 and GFAP levels with injury severity at admission and 6-month prognosis in SCI patients. In this study, serum Gal-3 and GFAP levels were significantly associated with injury severity at admission and 6-month prognosis in SCI patients. Therefore, serum Gal-3 and GFAP have the potential to be used as biomarkers of SCI severity and to predict patient prognosis.

There are ongoing attempts to discover easy-to-use prognostic predictors for SCI to improve therapeutic

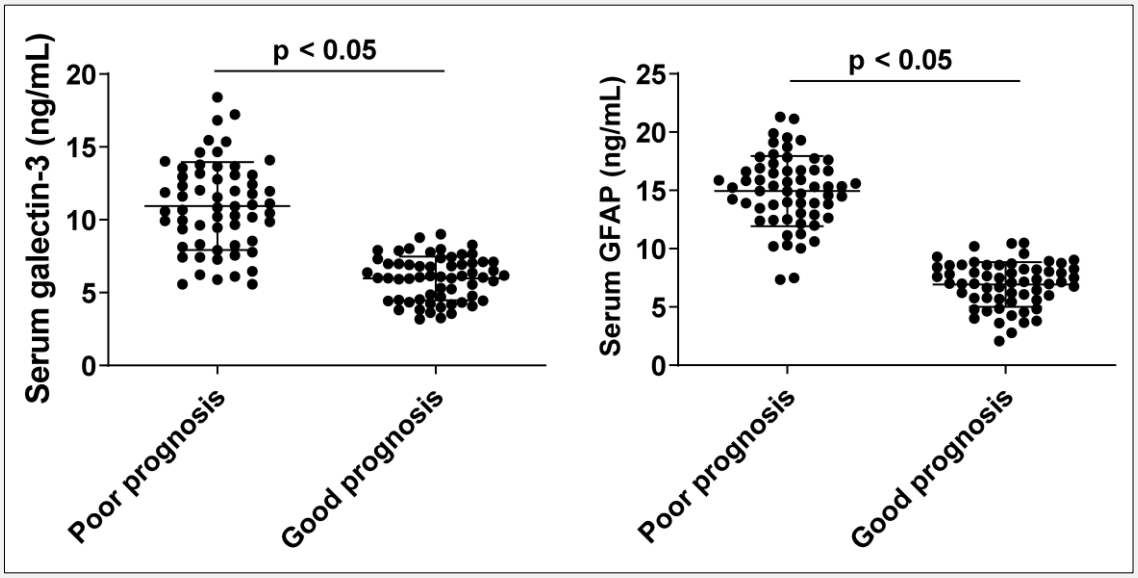

Figure 2. Serum galectin-3 and GFAP levels in SCI patients with poor prognosis and SCI patients with good prognosis.

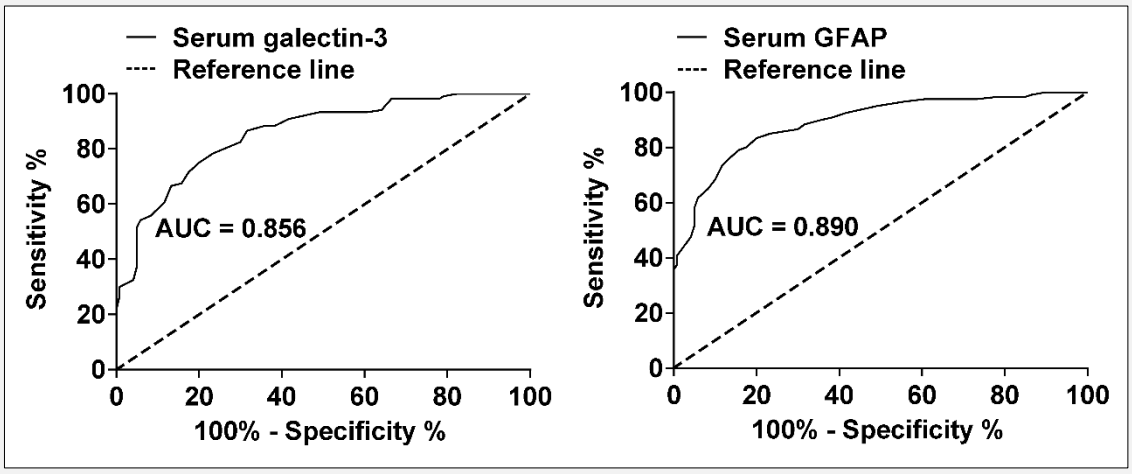

Figure 3. Prognostic value of serum galectin-3 and GFAP analyzed by ROC curves.

choices. The AIS grade is widely recognized as the most accepted predictor of prognosis after SCI [23,24]. The study demonstrated that the AIS system, which measures SCI severity at admission, is a significant independent predictor of patient prognosis. However, there are certain drawbacks to its application in clinical settings [25]. To begin with, patients with spinal shock face a lot of uncertainty, since it is generally acknowledged that some spontaneous recovery may take place within several hours post-injury. Furthermore, the variability among patients with SCI deserves more focus, as it can greatly affect the findings and is not adequately

represented in existing clinical studies. Hence, further studies are essential to develop models for diagnosing and predicting acute traumatic SCI, along with a framework for pinpointing key biomarkers to improve the precision of prognostic prediction.

The risk of death or major disability in ischemic stroke is higher with increased Gal-3 serum levels during the 3-month follow-up [26]. Patients with ischemic stroke and hyperglycemia show a correlation between high serum Gal-3 levels and a greater risk of poor functional outcomes [27]. Gal-3 deficiency significantly influences the inflammatory response initiated by SCI, promoting faster recovery of motor functions [28]. In this study, serum Gal-3 levels were higher in patients with severe SCI than in patients with non-severe SCI. In addition, serum Gal-3 levels were higher in SCI patients with poor prognosis than in SCI patients with good prognosis. Multivariate logistic regression analysis showed that serum Gal-3 level was an independent factor affecting the 6-month prognosis of SCI patients. ROC curve analysis showed that serum Gal-3 was a good predictor of the prognosis of SCI patients.

Biomarkers such as total tau, S100B, GFAP, and neuron-specific enolase found in circulating blood and cerebrospinal fluid have gained interest for evaluating the prognosis and severity of SCI [29-31]. In the present study, serum GFAP levels were significantly associated with injury severity at admission and 6-month prognosis in patients with SCI. A previous study reported that higher serum levels of neurofilament light and GFAP are associated with worse neurological outcomes after acute SCI [32]. Our findings further support the prognostic relevance of serum GFAP in patients with SCI.

There are limitations to this study. Initially, the study gathered serum samples from SCI patients only upon admission, making it impossible to ascertain the timing and duration of changes in serum Gal-3 and GFAP levels in these patients. Future large-scale multicenter studies are needed to confirm the findings from this single-center small sample study.

CONCLUSION

For the first time, this study highlights a strong connection between serum Gal-3, GFAP, and both the severity of injury at admission and the 6-month prognosis in SCI patients. Serum Gal-3 and GFAP can be used as clinical risk factors for predicting the severity and prognosis of SCI.

Data Availability Statement:
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Consent to Participate:
Written informed consent was obtained from each subject.

Consent to Publish:
Written informed consent for publication was obtained from all participants.

Ethical Approval Statement:
The present study was approved by the Ethics Committee of West China Hospital of Sichuan University (No. 202206CD-21), and written informed consent was provided by all patients prior to the study start. All procedures were performed in accordance with the ethical standards of the Institutional Review Board and the Declaration of Helsinki and its later amendments or comparable ethical standards.

Declaration of Interest:
The authors have no conflicts of interest to declare.

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