



Increased Risk of Anxiety or Depression After Traumatic Spinal Cord Injury in Patients with Preexisting Hyperlipidemia: A Population-Based Study

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■ **OBJECTIVE:** Anxiety or depression (AD) is a common complication after traumatic spinal cord injury (tSCI). This study sought to investigate the role of preexisting hyperlipidemia in new-onset AD after tSCI using a longitudinal population database.

■ **METHODS:** This retrospective cohort study used Longitudinal Health Insurance Database data from January 1997 to December 2011. The case and comparison groups were individuals who experienced tSCI and who did and did not have preexisting hyperlipidemia, respectively. Kaplan-Meier curves were plotted, and log-rank test was used to compare the differences between these 2 groups. A Cox regression model was used to estimate the relative risk of AD.

■ **RESULTS:** A total of 26,892 adult patients were enrolled in this study. After 1:3 matching with age and gender, it showed 1) tSCI patients with preexisting hyperlipidemia have a 1.32-fold adjusted hazard ratio (HR) compared with those without hyperlipidemia ($P < 0.05$); 2) The Kaplan-Meier plot in tSCI patients with hyperlipidemia were more likely to develop the new-onset AD than those without hyperlipidemia during the follow-up period ($P = 0.0003$); and 3) the stratified analysis showed the risk of AD among

patients with tSCI aged 18–34 years (HR, 3.2; 95% confidence interval (CI) 1.2–8.9), male patients (HR, 1.3; 95% CI 1.1–1.6), and higher Charlson's comorbidity index (CCI) score (CCI > 2; HR, 1.9; 95% CI 1.2–2.9), and those with a history of stroke (HR, 1.7; 95% CI 1.0–2.7).

■ **CONCLUSIONS:** Preexisting hyperlipidemia is an independent predictor of new-onset AD in patients with tSCI, especially in those who are younger, male, have a higher CCI score, and have stroke.

INTRODUCTION

Traumatic spinal cord injury (tSCI) greatly impacts quality of life and psychological well-being. In the United States, the estimated number of patients with tSCI in 2007 ranged from 227,080 to 300,938.¹ In Taiwan, there are approximately 23,000 patients with tSCI, most of whom are young and active in the work force. Therefore, further conditions in these young patients may lead to decreased productivity and increased costs of medical services.²

Anxiety or depression (AD) are both common psychiatric disorders. After tSCI, patients often experience AD^{3,4} because of their

Key words

- Anxiety
- Depression
- Hyperlipidemia
- Population database
- Spinal cord injury

Abbreviations and Acronyms

- AD:** Anxiety or depression
CAD: Cardiovascular disease
CCI: Charlson's comorbidity index
CI: Confidence interval
DM: Diabetes mellitus
HR: Hazard ratio
ICD-9-CM: International Classification of Diseases, 9th Revision, Clinically Modified
LHID2000: Longitudinal Health Insurance Database 2000
NHI: National Health Insurance
NHIRD: National Health Insurance Research Database
NHRI: National Health Research Institutes

SCI: Spinal cord injury

TBI: Traumatic brain injury

tSCI: Traumatic spinal cord injury

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symptoms of pain,⁵ erectile dysfunction,⁶ and adjustment impairment.⁷

In addition to tSCI, age,⁸ sex,⁹ hypertension,¹⁰ diabetes mellitus (DM),¹¹ cardiovascular disease (CAD),¹² renal disease,¹³ stroke,¹⁴ and hyperlipidemia are risk factors for AD.¹⁵ Among these risk factors, hyperlipidemia is common, with the prevalence ranging from 10.2%–13.4% in the general adult population in Taiwan.¹⁶ Therefore, whether hyperlipidemia is associated with AD, especially among patients after tSCI, is worthy of investigation.

In our previous study, we found preexisting hyperlipidemia to be an independent predictor of new-onset anxiety¹⁷ and depression¹⁸ in patients with traumatic brain injury (TBI), especially among female patients.¹⁷ Furthermore, we found that patients with tSCI have a higher incidence of new-onset AD and that the associated risk factors included higher injury severity score, older age, female sex, and lower economic status.¹⁹ Until the present, the association between preexisting hyperlipidemia and the risk of new-onset AD in patients with tSCI has not been investigated. Because tSCI and TBI are classified as neurotrauma, we hypothesized that preexisting hyperlipidemia may be a risk factor for new-onset AD in patients with tSCI.

Therefore, the main aim of the current study was to investigate the incidence and risk ratio of new-onset AD in patients with tSCI and preexisting hyperlipidemia using data from the nationwide database of the National Health Insurance (NHI) Program in Taiwan (1997–2011).

METHODS

Database

Taiwan's National Health Insurance Research Database (NHIRD) was used in this retrospective cohort study. The NHIRD is provided by the Bureau of NHI in Taiwan and is managed by the National Health Research Institutes (NHRI). The NHIRD contains 99% of inpatient and outpatient medical benefit participants from the Taiwanese population, and the NHRI randomly selected 1 million beneficiaries from the NHIRD for research purposes; this sample is the Longitudinal Health Insurance Database 2000 (LHID2000). This retrospective cohort study used LHID2000 data from January 1997 to December 2011. The encrypted personal identifications were retained according to data regulations of the Bureau of NHI, which uses them in the event of ethical violations, and this study was exempt from institutional review board approval by the Chi Mei Medical Center.

Ethics Statement

To protect patient privacy and to avoid the possibility of ethical violations, personal identifications were encrypted according to regulations of the Bureau of National Health Insurance in Taiwan. The study was approved by the institutional review board of Chi Mei Medical Center.

Definition of Individuals with Spinal Cord Injury and Hyperlipidemia

Patients were identified as having spinal cord injuries based on the International Classification of Diseases, 9th Revision, Clinically Modified (ICD-9-CM) codes 806 (fracture of vertebral column with spinal cord injury) and 952 (spinal cord lesion without evidence of

spinal bone injury).^{19–21} In addition, patients with hyperlipidemia (ICD-9-CM codes: 272.0, 272.1, 272.2, 272.4) were defined as those with at least 3 outpatient visits within 1 year or with 1 inpatient admission for the disorder.

Study Population

The study subjects were selected from outpatient or inpatient claims in the LHID2000 from January 1, 1999 to December 31, 2008. The case group consisted of individuals with both spinal cord injury and preexisting hyperlipidemia, and the comparison group consisted of individuals with spinal cord injury but without hyperlipidemia. The study group and the comparison control cohort were matched 1:3 on age and gender, and all study subjects were followed for at least 3 years until the end of follow-up, death, or new-onset AD. Individuals with a history of AD before SCI and those who developed hyperlipidemia after tSCI were excluded.

Definition of Outcome

New-onset AD patients were those with at least 3 outpatient claims within 1 year or at least 1 inpatient hospitalization claimed during 1997–2011. To identify the new-onset AD, the individuals with SCI had an AD history before SCI diagnosis date. They were excluded from this study. Patients were identified using codes for AD: dissociative and somatoform disorders (300, including the depression category of 300.4); predominant disturbance of other emotions (309.2); adjustment disorder with disturbance of conduct (309.3); and adjustment disorder with mixed disturbance of emotions and conduct (309.4). Then, the depression was coded as follows: major depressive disorder, single episode (296.2); major depressive disorder, recurrent episode (296.3); bipolar I disorder, most recent episode of (or current) depression (296.5); depressive disorder, not elsewhere classified (311); dysthymic disorder (300.4); atypical depressive disorder (296.82); adjustment disorder with depressed mood (309.0); and prolonged depressive reaction (309.1).

Definition of Covariates

The baseline covariates included age, sex, Charlson's comorbidity index (CCI), and hyperlipidemia-related comorbidities. Age was grouped into the following 5 categories: <18 years, 18–34, 35–49, 50–64, and older than 65 years. CCI was used to summarize important concomitant diseases based on the ICD-9-CM codes,²² and the CCI score was used to estimate each individual's disease severity level. Hyperlipidemia-related comorbidities were hypertension (ICD-9-CM codes: 401–405, 437.2, and 362.11), CAD (ICD-9-CM codes: 410–414), DM (ICD-9-CM codes: 250, 357.2, 362.0, and 366.41), renal disease (ICD-9-CM codes: 582, 583, 585, 586, and 588), and stroke (ICD-9-CM codes: 430–438). The comorbidities of CCI and hyperlipidemia-related comorbidities were defined as at least 3 outpatient visits or 1 inpatient admission in the year before the first TBI diagnosis for a given illness.

Statistical Analysis

The Pearson's χ^2 test was used to analyze the differences in categorical variables, including age group, gender, economic status, comorbidity, and outcomes, between tSCI patients with preexisting hyperlipidemia and those without. Student's t-test and the Wilcoxon rank sum test were used to compare age at first diagnosis during the study period and time to AD, respectively. The

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