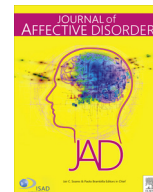




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Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Risk of depressive disorders following sudden sensorineural hearing loss: A nationwide population-based retrospective cohort study

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ARTICLE INFO

Article history:

Received 11 November 2015

Received in revised form

15 February 2016

Accepted 7 March 2016

Available online 9 March 2016

ABSTRACT

Background: Sudden sensorineural hearing loss (SSNHL) occurs as an unexplained, rapid loss of hearing that can cause significant stress in the affected individual. This study aims to assess the risk of depressive disorders in SSNHL patients.

Methods: From the National Health Insurance Research Database (NHIRD) in Taiwan, we identified new SSNHL patients diagnosed by an otolaryngologist between January 01, 2000, and December 31, 2008. A control group was composed of individuals who had never suffered from SSNHL. A total of 1717 SSNHL patients and 6868 individuals without SSNHL who were matched by sex, age and index date were followed until December 31, 2009, unless otherwise diagnosed with depressive disorders by a psychiatrist or deceased.

Results: The results found that after adjusting for patients' age, sex, comorbidities, urbanization, and monthly income, SSNHL patients are 2.17 times more at risk (95% confidence interval [CI], 1.51–3.08, $p < .001$) for depressive disorders than control patients, especially in younger age groups (< 60 years old).

Conclusions: Our study indicated an increased risk of developing depressive disorders in patients with SSNHL, particularly for younger patients. Symptoms of depression should be regularly evaluated in patients with SSNHL.

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1. Introduction

Sudden sensorineural hearing loss (SSNHL) is hearing loss of at least 30 dB at three different frequencies for three days or less (Hughes et al., 1996; Schreiber et al., 2010; Stokroos et al., 1998). In Taiwan, SSNHL has an incidence rate of 8.85 per 100,000 men and 7.79 per 100,000 women (Wu et al., 2006). SSNHL is one of the few acute disorders in otolaryngology; while some people may recover within several days or weeks, 75% of the patients only partially

recover or do not improve at all. For these patients, loss of an organ essential for communication with the outside world is a terrifying experience and a stressor (Carlsson et al., 2011; Lazarini and Camargo, 2006).

Depressive disorders have been referred to as a 21st century disorder that imposes an incredible burden, with a lifetime prevalence of 17.1%. One-fourth of women and one-sixth of men will suffer from depressive disorders at some point in their lives (Kessler et al., 2010, 1994; Organization, 2004). Depressive disorder patients require a large amount of medical resources and cause large economic losses for the society (Katon and Sullivan, 1990). Depressive disorders also cause a severe decline in the patient's quality of life (De Graaf et al., 2002). Several studies have found that early intervention and treatment have positive effects on depressive disorders (Arnarson and Craighead, 2009; Garber et al., 2009; Young et al., 2006). However, universal screening for depressive disorders would be an unnecessary drain on resources and would have ethical problems. Therefore, determining the risk

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factors for depressive disorders and screening in high-risk populations are critical.

A recent study demonstrated that patients with depressive symptoms are at a higher risk for developing SSNHL (Lin et al., 2015). Incidence of SSNHL was 1.45 times higher in the depressive disorders group compared to the non-depressive disorders group ($p=0.0041$). On the other hand, stresses from physical illness have been associated with susceptibility of depressive disorders (Cattaneo and Riva, 2015; Perng et al., 2014). The previous study had demonstrated that severe depressive symptoms were more common in patients who did not recover from SSNHL, which may be associated with greater emotional distress (Chen et al., 2013). Therefore, it can be assumed that stresses caused by SSNHL may be associated with the following of the risk of depressive disorders. In addition, immune system and inflammatory response dysfunctions had been identified as depressive disorder risk factors (Berk et al., 2013). The inflammatory response is also an important part of SSNHL pathogenic mechanisms (Fujioka et al., 2006; Maruyoshi et al., 2005; Masuda et al., 2012). Therefore, the SSNHL-related inflammatory response may be also associated with the following of the risk of depressive disorders. For reasons outlined above, bidirectional temporal association between SSNHL and depressive disorders may be considered. Unfortunately, there had not been any studies utilizing large databases to analyze the association between SSNHL and the subsequent risk of depressive disorders. Therefore, we used the Taiwan National Health Insurance Research Database (NHIRD) to assess whether SSNHL patients are at a higher risk for developing depressive disorders. We also performed a Cox proportional-hazards regression model to identify risk factors that predicted depressive disorders in the SSNHL patients.

2. Materials and methods

2.1. Data sources

Instituted in 1995, the National Health Insurance (NHI) program is a mandatory health insurance program which offers comprehensive medical care coverage, including outpatient, inpatient, emergency, and traditional Chinese medicine, to all residents of Taiwan; the coverage rate is as high as 99% (Wu et al., 2012). The NHI research database (NHIRD) contains comprehensive information regarding clinical visits, including prescription details and diagnostic codes based on the International Classification of Diseases, ninth revision, Clinical Modification (ICD-9-CM). The NHIRD was managed by the National Health Research Institutes (NHRI), and confidentiality was maintained according to the directives of the Bureau of the NHI. The data source for our study was the Longitudinal Health Insurance Database 2005 (LHID 2005), which is a dataset of the NHIRD. Data for the LHID were collected by systematic and random sampling from the NHIRD; the database included data from one million individuals. The NHRI of Taiwan reported that there were no significant differences in gender distribution, age distribution, or average insured payroll-related amount between the patients in the LHID and those in the original NHIRD (Database).

2.2. Ethics statement

The Institutional Review Board of the Taipei Veterans General Hospital approved this study. Written consents from study patients were not obtained because the NHI dataset consisted of de-identified secondary data for research purposes, and the Institutional Review Board of Taipei Veterans General Hospital issued a formal written waiver for the need for consent.

2.3. Study population

Using data extracted from the LHID 2005, we conducted a retrospective cohort study of patients aged 20 years and older who were newly diagnosed with SSNHL between January 1st, 2000, and December 31st, 2008. SSNHL was defined as ICD-9-CM code: 388.2. To ensure diagnostic validity and patient homogeneity, we included only patients who were diagnosed by certificated otorhinolaryngologists based on the audiological criteria of 30 dB hearing reduction, over at least three contiguous frequencies, occurring over a period of 72 h or less. In addition, only patients who were diagnosed with SSNHL by otorhinolaryngologists repeatedly during two consecutive visits were included. We excluded patients who were diagnosed with depressive disorders (ICD-9-CM code: 296.2X–296.3X, 300.4, and 311.X) before enrollment. Insurance premiums, which were calculated according to the beneficiary's total income, were used to estimate monthly income. Monthly income was grouped into low income (monthly income < 20,000 New Taiwan Dollar [NTD]), medium income (20,000 NTD \leq monthly income < 40,000 NTD), and high income (monthly income \geq 40,000 NTD). Urbanization was divided into three groups: urban, suburban, and rural. Urbanization and monthly income levels were used to represent socioeconomic status. For each SSNHL patient included in the final cohort, four age-, sex-, and enrollment-date-matched control patients who were not diagnosed with SSNHL or depressive disorders were randomly selected from the LHID 2005. All SSNHL and control patients were observed until diagnosed with depressive disorders (first depressive episode) by a psychiatrist based on the criteria of ICD-9-CM through clinical interview, death, or December 31, 2009. The primary clinical outcome assessed was psychiatrist-diagnosed depressive disorders. The study design and the criteria had been used in similar studies (Cheng et al., 2015; Shen et al., 2015; Wang et al., 2014).

2.4. Statistical analyses

The incidence of newly diagnosed depressive disorders in the SSNHL and control patients, stratified by gender and age (equal or older than 60 years old or younger than 60 years old), was calculated. Independent *t*-tests and chi-squared tests were used to examine the differences in the demographic characteristics between the SSNHL and control patients.

A Cox proportional-hazards regression model was used to identify variables that predicted depressive disorders in the SSNHL and control patients and in SSNHL patients only. Control variables, such as age, sex, common comorbidities (including hypertension, diabetes mellitus, dyslipidemia, coronary artery disease, congestive heart failure, hyperthyroidism, hypothyroidism, cerebrovascular disease, and malignancy), urbanization and monthly income, were included as covariates in the univariate model. The reason why urbanization and monthly income were included in the analysis was that previous studies demonstrated that different socioeconomic statuses were associated with depression. (Christiani et al., 2015; Cifuentes et al., 2008; Messias et al., 2011). Because several physical comorbidities had been observed to correlate with depressive disorders (Bunevicius et al., 2012; Göthe et al., 2012; Meng et al., 2012; Nouwen et al., 2010; Scherrer et al., 2015), common comorbidities such as coronary artery disease, cerebrovascular disease, hypertension, diabetes, and hyperlipidemia were also adjusted in our analysis. Furthermore, previous studies demonstrated that older SSNHL patients have had worse prognoses (Dass et al., 2015; Kuhn et al., 2011). Therefore, we divided subjects into two groups (young age and older age) to evaluate if these two groups had different incidences of depressive disorders. Factors which demonstrated a moderately significant statistical

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