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Increased risk of depression in patients with acquired sensory hearing loss
A 12-year follow-up study

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Abstract

Acquired sensory hearing loss (SHL) is suggested to be associated with depression. However, some studies have reported conflicting results. Our study investigated the relationship between the prevalence of SHL and the incidence of depression over 12 years of follow-up by using data from the Taiwan National Health Insurance Research Database (NHIRD). We sought to determine the association between SHL and subsequent development of depression and discuss the pathophysiological mechanism underlying the association.

Patients with SHL were identified from the NHIRD (SHL cohort). A non-SHL cohort, comprising patients without SHL frequency-matched with the SHL patients according to age group, sex, and the year of diagnosis of SHL at the ratio of 1:4, was constructed, and the incidence of depression was evaluated in both cohorts. A multivariable model was adjusted for age, sex, and comorbidity.

The SHL cohort and non-SHL cohort comprised 5043 patients with SHL and 20,172 patients without SHL, respectively. The incidences density rates were 9.50 and 4.78 per 1000 person-years in the SHL cohort and non-SHL cohort, respectively. After adjustment for age, sex, and comorbidities, the risk of depression was higher in the SHL cohort than in the non-SHL cohort (hazard ratio = 1.73, 95% confidence interval = 1.49–2.00).

Acquired SHL may increase the risk of subsequent depression. The results demonstrated that SHL was an independent risk factor regardless of sex, age, and comorbidities. Moreover, a strong association between hearing loss and subsequent depression among Taiwanese adults of all ages, particularly those aged ≤49 and >65 years and without using steroids for the treatment of SHL was observed. Prospective clinical and biomedical studies on the relationship between hearing loss and depression are warranted for determining the etiopathology.

Abbreviations: 5-HT = 5-hydroxytryptamine, ADLs = activities of daily living, CAD = coronary artery disease, CI = confidence intervals, CKD = chronic kidney disease, COPD = chronic obstructive pulmonary disease, HR = hazard ratios, LHID200 = Longitudinal Health Insurance Database of 2000, NHI = National Health Insurance, NHIRD = National Health Insurance Research Database, SHL = Sensory Hearing Loss, SSRIs = selective serotonin reuptake inhibitors, US = United States.

Keywords: depression, NHIRD, sensory hearing loss

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1. Introduction

Hearing impairment is a common ailment associated with ageing and the most common cause of disability worldwide. Approximately 1 in 4 adults aged ≥45 years experiences mild or greater hearing loss.[1] World Health Organization estimated 360 million persons, about 5.3% of the world's population, suffered from disabling hearing loss.[2] Depression is a common mental disorder, which affect 350 million people in the world.[3] Unipolar depressive disorders and adult-onset hearing loss, the most common neuropsychiatric conditions, and sense organ disorder, respectively, are the first and second leading nonfatal causes of year loss due to disability among adults in high-income countries.[1] Hearing loss may increase deterioration of health-related quality of life, and hearing impairment influences social behavior, making affected people prone to depression, anxiety, interpersonal sensitivity, and hostility.[4–6] Several cross-sectional studies have reported that hearing loss is independently associated with depression in the elderly population.[6–8] However, some studies have reported conflicting results.[9,10] A nationwide study reported a strong association between hearing impairment and depression among adults of all ages in the United States.[11] In this 12-year nationwide population-based cohort study, we explored the relationship between acquired sensory hearing loss (SHL) and the incidence of depression by comparing Taiwanese patients with and without hearing impairment.

2. Methods

2.1. Data source

Data from the Longitudinal Health Insurance Database of 2000 (LHID2000) released by the National Health Research Institutes of Taiwan were used. Briefly, the Taiwan National Health Insurance (NHI) program is a universal healthcare system that covers 99% of the country's population of 23 million.[12] The details of this program have been described previously.[13,14] The LHID2000 contains detailed records of each visit of each patient, including outpatient visits, emergency department visits, and hospital admission. The LHID2000 also includes principal and secondary diagnostic codes, prescription orders, and claimed expenses. The diagnoses and procedures are coded according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). The study protocol was approved by the Ethics Review Board of China Medical University (CMUH-104-REC2-115).

2.2. Sampled patients

Patients aged >20 years from 2000 to 2011 and newly diagnosed with SHL (ICD-9 codes 388.01 and 389.10-389.12) were identified (SHL cohort). The index date was the date of initial diagnosis of SHL. Patients without SHL were randomly selected from the LHID2000 for inclusion in a non-SHL cohort and were frequency-matched with the SHL patients according to age group (every 5-year span), sex, and the year of SHL diagnosis at the ratio of 1:4. The index date for the non-SHL patients was randomly assigned as a day and month in the index year of the matched SHL patient. Both cohorts excluded patients with a history of depression (ICD-9-CM codes 296.2, 296.3, 300.4, and 311) at the baseline and those with incomplete information on age or sex. All patients were followed from the index date until the diagnosis of depression, date of NHI withdrawal, or end of 2011.

2.3. Comorbidity

The following baseline comorbidities were considered covariates: cirrhosis (ICD-9-CM code 571), rheumatoid arthritis (ICD-9-CM code 714), hypertension (ICD-9-CM codes 401-405), hyperlipidemia (ICD-9-CM code 272), diabetes mellitus (ICD-9-CM code 250), asthma (ICD-9-CM code 493), chronic kidney disease (CKD, ICD-9-CM codes 580-589), coronary artery disease (CAD, ICD-9-CM codes 410-414), alcohol-related illness (ICD-9-CM codes 291, 303, 305, 571.0, 571.1, 571.2, 571.3, 790.3, A215, and V11.3), anxiety (ICD-9-CM code 300.00), chronic obstructive pulmonary disease (COPD, ICD-9-CM code 491, 492, 496), stroke (ICD-9-CM code 430-438). Steroids was known for treatment of SHL.[15] The ICD-9-CM code we used for anxiety was "unspecified anxiety disorder" rather than other specific diagnosis of anxiety disorder, such as generalized anxiety disorder or panic disorder.

2.4. Statistical analysis

The χ^2 test and t test were used for analyzing the differences between the cohorts in categorical and continuous variables, respectively. The cumulative incidence of depression between the 2 cohorts was plotted using the Kaplan–Meier method, and the difference was analyzed using a log-rank test. The incidence density rates of depression in both cohorts were calculated. Univariable and multivariable Cox proportional hazard regression analyses were conducted for estimating the relative hazard ratios (HRs) and 95% confidence intervals (CIs) of depression in the SHL cohort compared with the non-SHL cohort. The multivariable model was adjusted for age, sex, and comorbidity variables that had a significant difference according to Table 1. All data analyses were conducted using the SAS statistical package (version 9.3 for Windows; SAS institute Inc, Cary, NC). A 2-tailed P value <0.05 indicated statistical significance.

3. Results

Table 1 presents the demographic characteristics and comorbidities of the 5043 patients in the SHL cohort and 20,172 patients in the non-SHL cohort. Most patients in both cohorts were aged ≥65 years (50%) and men (61.9%). The mean ages of the patients in the SHL cohort and non-SHL cohort were 61.8±17.0 years and 61.2±17.0 years, respectively. Comorbidities, except for rheumatoid arthritis, were more prevalent in the SHL cohort than in the non-SHL cohort (P <0.05). The mean follow-up periods for the SHL cohort and non-SHL cohort were 5.70±3.14 years and 5.54±3.15 years, respectively. After 12 years of follow-up, the cumulative incidence of depression was higher in the SHL cohort than in the non-SHL cohort (P <0.001; Fig. 1).

The incidences density rates in the SHL cohort and non-SHL cohort were 9.50 (crude HR=1.99, 95% CI=1.72–2.31) and 4.78 per 1000 person-years, respectively (Table 2). After adjustment for age, sex, and comorbidities, the risk of depression was higher in the SHL cohort than in the non-SHL cohort (aHR=1.73, 95% CI=1.49–2.00). The incidence of depression increased with age and was higher in women than in men. The multivariable analysis revealed that the risk of depression was 1.35-fold higher in women than in man (95% CI=1.17–1.56). The risk of depression was higher in patients with the comorbidities of CAD (aHR=1.52, 95% CI=1.28–1.81), alcohol-related illness (aHR=1.61, 95% CI=1.12–2.29), anxiety (aHR=2.38, 95% CI=1.95–2.89), stroke (aHR=1.31, 95% CI=1.01–1.70).

Demographic characteristics and comorbidities in cohorts with and without sensory hearing loss.

	Sensory hearing loss		
	No	Yes	
Variable	N=20,172	N=5043	P value
Age, y			0.99
≤34	1796 (8.90)	449 (8.90)	
35–49	3132 (15.5)	783 (15.5)	
50–64	5168 (25.6)	1292 (25.6)	
65+	10,076 (50.0)	2519 (50.0)	
Mean±SD*	61.2 (17.0)	61.8 (17.0)	0.03
Sex			0.99
Women	7688 (38.1)	1922 (38.1)	
Men	12,484 (61.9)	3121 (61.9)	
Comorbidity			
Cirrhosis	3613 (17.9)	1275 (25.3)	<0.001
Rheumatoid arthritis	44 (0.22)	17 (0.34)	0.12
Hypertension	8726 (43.3)	2520 (50.0)	<0.001
Hyperlipidemia	4379 (21.7)	1442 (28.6)	<0.001
Diabetes mellitus	2515 (12.5)	692 (13.7)	0.02
Asthma	1731 (8.58)	555 (11.0)	<0.001
Chronic kidney disease	438 (2.17)	157 (3.11)	<0.001
Coronary artery disease	4345 (21.5)	1504 (29.8)	<0.001
Alcohol-related illness	564 (2.80)	183 (3.63)	0.002
Anxiety	1098 (5.44)	557 (11.1)	<0.001
COPD	3308 (16.4)	1218 (24.2)	<0.001
Stroke	284 (5.63)	1366 (6.77)	0.003
Medication			
Steroid	2209 (11.0)	732 (14.5)	<0.001

χ^2 test.
* T test.

The age-specific relative risk of depression for the SHL cohort compared with the non-SHL cohort was significant in all age groups, except in the age group of 50 to 64 years (Table 3). The sex-specific relative risk of depression for the SHL cohort compared with the non-SHL cohort was significant in both women (aHR=1.55, 95% CI=1.24–1.95) and men (aHR= 1.88, 95% CI=1.54–2.29). After stratification for comorbidity, the relative risk of depression was higher in the SHL cohort than in the non-SHL cohort for patients without comorbidity (aHR= 1.83, 95% CI=1.31–2.55) and those with comorbidity (aHR= 1.87, 95% CI=1.58–2.20).

Steroids were known for treatment of SHL.[15] In order to investigate whether SHL patients treated with steroids could lower the risk of subsequent depression, we further added the analysis of steroids treatment of SHL patients. As shown in Table 3, SHL patients without steroids treatment significantly increase the risk of subsequent depression (aHR=1.78, 95% CI=1.51–2.08). The relative risk of depression was significantly higher in the SHL cohort without steroids treatment (aHR=1.78, 95% CI=1.51–2.08) than in the SHL cohort with steroids treatment (aHR=1.40, 95% CI=0.94–2.09). Taken together, our study demonstrated no increased risk of subsequent depression among patients with steroids treatment. On the other hand, those without steroids treatment were noted having increased risk of subsequent depression.

4. Discussion

This is a population-based study in Taiwan to investigate SHL as a risk factor for depression by using a matched cohort and a 12-year follow-up period. Our data demonstrated that SHL may increase the risk of subsequent depression.

Despite a strong association between depression and SHL, the etiologic mechanisms underlying the relationship between hearing loss and depression have not been well established. Hearing impairment elicits a strong feeling of isolation and frustration in patients, particularly when they fail to communicate with others.[16,17] It can also impose a heavy social and economic burden on the patient and family.[18] Patients with moderate to severe hearing loss were more likely to have impaired activities of daily living (ADLs) and instrumental ADLs.[19] The declined quality of life and social isolation may lead to depression. On the other hand, serotonin (5-hydroxytryptamine, 5-HT) is a neurotransmitter associated with depression. Selective serotonin reuptake inhibitors (SSRIs) are used for treating depression by modulating the serotonin pathway.[20,21] An animal study reported that sertraline, an SSRI used widely in depression, has a protective effect on cisplatin ototoxicity, which leads to SHL.[22] Another study on rats demonstrated that early hearing loss affects the ability of 5-HT receptor activation to modulate primary auditory cortex excitability.[23] Acoustic trauma in an animal model induced substantial hearing loss and caused selective upregulation of serotonin receptor genes in the inferior colliculus.[24] These 3 studies have demonstrated that hearing loss may induce plasticity in the excitatory and inhibitory neurotransmitter systems in the central auditory brain regions. However, information on networks and etiologic mechanisms between auditory damage and depression via the serotonin pathway is scant. Clinical and experimental studies should clarify these networks and mechanisms in the future.

Risk factors for hearing loss include race, age, the male sex, diabetes mellitus, exposure to noise, and heavy smoking.[25] A study reported that CAD and exposure to noise have a synergistic effect on elevating hearing thresholds.[26] Another study
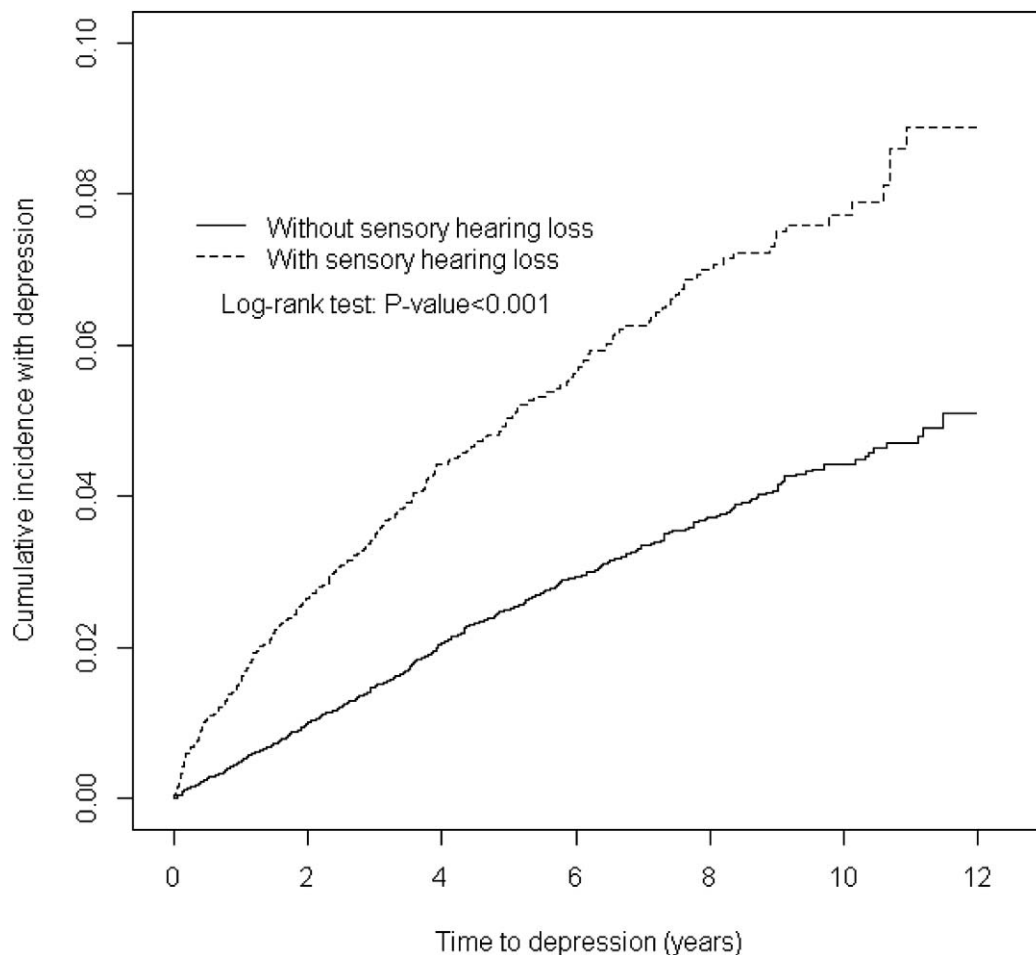
Figure 1. Cummulative incidence comparison of depression for patients with (dashed line) or without (solid line) sensory hearing loss.

suggested that hypertension and diabetes mellitus have a synergistic effect on hearing impairment.[27] Previous studies have reported that patients with hyperlipidemia have a greater risk of noise-induced hearing loss.[28,29] Moderate CKD was associated independently with hearing loss.[30] Smoking and heavy alcohol consumption were related to high-frequency hearing loss in the Korean population.[31] In our study, comorbidities of hypertension, hyperlipidemia, diabetes mellitus, CKD, CAD, and alcohol-related illness were more prevalent in the SHL cohort (Table 1). This observation is consistent with the results of previous studies.

Depression is associated with several comorbidities, such as CKD, CAD, alcohol-related illness, and generalized anxiety disorder, and the association has been clearly illustrated in previous studies.[32–34] Our study revealed that the risk of depression was higher in patients with comorbid CAD, alcohol-related illness, and anxiety (Table 2). Furthermore, the rate of depression increased with age and was higher in women than in man. To minimize the influence from smoking, we have used an alternative way and adjusted for smoking-related diseases (including COPD, CAD, stroke, asthma) in our analysis in accordance with previous studies.[35] Indeed, we have listed the association between smoking-related diseases and SHL, and we also noted the COPD, CAD, stroke, and asthma were more

prevalent in the SHL cohort (Table 2). After adjustment for age, sex, and comorbidities, hearing loss was observed as an independent risk factor for depression (Table 3). The results are consistent with the results of a US study.[11] Li et al[11] reported a significant association between moderate hearing loss and depression in women, particularly those aged <70 years, but not in men or patients aged ≥70 years. These findings are different from our results. Our study revealed that the age-specific relative risk of depression for the SHL cohort compared with the non-SHL cohort was significant in all age groups, except in the age group of 50 to 64 years, which also exhibited a trend of an increased risk. The risk in patients in different age groups and with psychosocial ailments differs, probably because of differences in race, ethnicity, lifestyle, responsibility, and circumstances. We found that the relative risk of depression was significantly higher in both men and women (Table 3). However, while Gopinath et al[36] reported that depression is more common in women than in men with hearing loss, Harada et al[37] reported that hearing loss is associated with depression in men. Furthermore, several comorbidities, such as CAD, alcohol-related illness, and anxiety, were associated with both SHL and depression in the present study (Table 3).

Our study has some limitations. First, we did not classify the severity of hearing impairment and demonstrate its effect on

Table 2

The incidence and hazard ratio for depression and depression-associated risk factor.

Variable	Event	PY	Rate#	Crude HR (95% CI)	Adjusted HR† (95% CI)
Sensory hearing loss					
No	534	111,744	4.78	1.00	1.00
Yes	273	28,740	9.50	1.99 (1.72, 2.31)‡	1.73 (1.49, 2.00)‡
Age, y					
≤49	165	38,267	4.31	1.00	1.00
50–64	198	37,654	5.26	1.21 (0.99, 1.49)	0.94 (0.76, 1.17)
65+	444	64,564	6.88	1.56 (1.30, 1.87)‡	1.05 (0.85, 1.30)
Sex					
Women	370	54,959	6.73	1.33 (1.15, 1.52)‡	1.35 (1.17, 1.56)‡
Men	437	85,526	5.11	1.00	1.00
Comorbidity					
Cirrhosis					
No	593	114,776	5.17	1.00	1.00
Yes	214	25,709	8.32	1.60 (1.37, 1.87)‡	1.18 (1.00, 1.39)
Rheumatoid arthritis					
No	804	140,221	5.73	1.00	1.00
Yes	3	264	11.4	1.90 (0.61, 5.92)	1.56 (0.50, 4.90)
Hypertension					
No	361	82,152	4.39	1.00	1.00
Yes	446	58,332	7.65	1.71 (1.49, 1.97)‡	1.09 (0.91, 1.31)
Hyperlipidemia					
No	554	110,576	5.01	1.00	1.00
Yes	253	29,908	8.46	1.66 (1.43, 1.93)‡	1.12 (0.95, 1.33)
Diabetes mellitus					
No	684	125,003	5.47	1.00	1.00
Yes	123	15,482	7.94	1.42 (1.17, 1.72)‡	1.03 (0.84,1 .27)
Asthma					
No	709	129,414	5.48	1.00	1.00
Yes	98	11,071	8.85	1.58 (1.28, 1.95)‡	1.05 (0.83, 1.33)
Chronic kidney disease					
No	784	138,005	5.68	1.00	1.00
Yes	23	2480	9.27	1.58 (1.04, 2.39)*	1.10 (0.72, 1.68)
Coronary artery disease					
No	509	110,882	4.59	1.00	1.00
Yes	298	29,602	10.1	2.16 (1.87, 2.50)‡	1.52 (1.28, 1.81)‡
Alcohol-related illness					
No	774	137,382	5.63	1.00	1.00
Yes	33	3103	10.6	1.81 (1.28, 2.57)‡	1.61 (1.12, 2.29)†
Anxiety					
No	674	133,043	5.07	1.00	1.00
Yes	133	7442	17.9	3.42 (2.84, 4.13)‡	2.38 (1.95, 2.89)‡
COPD					
No	614	118,024	5.20	1.00	1.00
Yes	193	22,460	8.59	1.62 (1.38, 1.91)‡	1.15 (0.95, 1.38)
Stroke					
No	741	133,914	5.53	1.00	1.00
Yes	66	6571	10.0	1.58 (1.28, 1.95)‡	1.31 (1.01, 1.70)*
Medication					
Steroid					
No	698	127,001	5.50	1.00	1.00
Yes	109	13,483	8.08	1.43 (1.17, 1.75)‡	1.03 (0.83, 1.27)

Rate#, incidence rate, per 1,000 person-years; Crude HR, relative hazard ratio, Adjusted HR†, multivariable analysis including age, sex, and comorbidities of cirrhosis, hypertension, hyperlipidemia, diabetes mellitus, asthma, chronic kidney disease, coronary artery disease, alcohol-related illness, anxiety, COPD and stroke, and medication of steroid.
* $P<0.05$.
† $P<0.01$.
‡ $P<0.001$.

depression by group. However, after adjustment for age, sex, and comorbidities, the risk of depression was higher in the SHL cohort than in the non-SHL group, suggesting that SHL may be a risk factor for subsequent depression regardless of severity. Second, various studies have established a correlation between tinnitus and psychological illness. Tinnitus typically accompanies hearing impairment during its progression. This study focused on the effect of objective diagnosis of SHL instead of subjective symptoms of tinnitus. Third, the diagnosis of depression in our study was based on ICD-9-CM code. We could not make sure whether those patients receive standard diagnostic interview to make this diagnosis. Even though this limitation could raise the

Table 3

Incidence of depression by age, sex and comorbidity and Cox model measured hazards ratio for patients with sensory hearing loss compared those without sensory hearing loss.

| Variables | Sensory hearing loss | | | | | | Crude HR (95% CI) | Adjusted HR[†] (95% CI) |
| | No | | | Yes | | | | |
	Event	PY	Rate#	Event	PY	Rate#		
Age, y								
≤49	101	30,731	3.29	64	7536	8.49	2.58 (1.89, 3.53)[‡]	2.22 (1.62, 3.06)[‡]
50–64	142	30,125	4.71	56	7529	7.44	1.58 (1.16, 2.15)[†]	1.21 (0.88, 1.67)
65+	291	50,889	5.72	153	13,676	11.2	1.97 (1.62, 2.39)[‡]	1.78 (1.46, 2.17)[‡]
Sex								
Women	256	43,887	5.83	114	11,073	10.3	1.77 (1.42, 2.20)[‡]	1.55 (1.24, 1.95)[‡]
Men	278	67,858	4.10	159	17,668	9.00	2.21 (1.82, 2.68)[‡]	1.88 (1.54, 2.29)[‡]
Comorbidity[‡]								
No	136	47,144	2.88	46	8786	5.24	1.82 (1.30, 2.54)[‡]	1.83 (1.31, 2.55)[‡]
Yes	398	64,600	6.16	227	19,955	11.4	1.86 (1.58, 2.19)[‡]	1.87 (1.58, 2.20)[‡]
Medication								
Steroid								
No	463	101,656	4.55	235	25,345	9.27	2.05 (1.75, 2.39)[‡]	1.78 (1.51, 2.08)[‡]
Yes	71	10,088	7.04	38	3395	11.2	1.58 (1.07, 2.35)[*]	1.40 (0.94, 2.09)

Rate#, incidence rate, per 1000 person-years; Crude HR, relative hazard ratio; Adjusted HR[†], multivariable analysis including age, sex, and comorbidities of cirrhosis, hypertension, hyperlipidemia, diabetes mellitus, asthma, chronic kidney disease, coronary artery disease, alcohol-related illness, anxiety, COPD and stroke, and medication of steroid; Comorbidity[‡], patients with any one of the comorbidities cirrhosis, hypertension, hyperlipidemia, diabetes mellitus, asthma, chronic kidney disease, coronary artery disease, alcohol-related illness, anxiety, COPD and stroke were classified as the comorbidity group.

[*] $P < 0.05$.
[†] $P < 0.01$.
[‡] $P < 0.001$.

concern about the probability of false positive or false negative case, our study demonstrated long-term observation to observe the course between hearing loss and depression. Fourth, suicide was prevalent in patients with depression.[38] Even though suicidal event in depression was not further discussed in our study, we considered this relationship could raise more concern in clinical practice, based on our study. Finally, although SHL and depression are very frequent, our well-designed study protocol and large population cohort have demonstrated the association between SHL and depression. After including the analysis of steroid treatment for SHL (Table 3), we further demonstrated the possible causal association; however, future prospective studies are required.

5. Conclusion

Our data demonstrated that SHL may increase the risk of subsequent depression. However, information on networks and etiologic mechanisms between auditory damage and depression is scant. Additional prospective clinical and biomedical studies on the relationship between hearing loss and depression are warranted to determine the etiopathology.

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