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Increased Long-Term Risk of Hearing Loss in Patients With Traumatic Brain Injury: A Nationwide Population-Based Study

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Objectives/Hypothesis: We investigated incidences of hearing loss among patients with traumatic brain injury (TBI) to evaluate whether they had a higher risk of hearing loss than the general population.

Study Design: Cohort study.

Methods: Inpatient data from the Taiwan National Health Insurance Research Database from January 1, 2000 to December 31, 2010 were recorded. Patients with TBI and a retrospective comparison cohort were analyzed. Each subject was individually traced from their index date to identify subjects who subsequently received a diagnosis of hearing loss. Cox regression analyses were applied to determine the risk of TBI-related hearing loss.

Results: Follow-up data from the TBI and comparison cohorts were collected over 10 years for 553,286 and 1,106,572 patients, respectively. Multivariate analyses demonstrated that TBI significantly increased the risk of hearing loss (adjusted hazard ratio = 2.125, 95% confidence interval = 2.045-2.546, $P = .027$). In our subgroup analyses by type of injury, patients with TBI due to traffic injury had the highest associated risk of hearing loss compared with the risk of non-TBI traffic injury patients, followed by patients with crushing/cutting/piercing injuries and falls.

Conclusions: Our study shows that TBI led to a higher risk of long-term hearing loss. Traffic injuries were the most common injury related to hearing loss. Prevention, rather than treatment, may be the best policy for preventing hearing loss.

Key Words: Traumatic brain injury, hearing loss, National Health Insurance Research Database.

Level of Evidence: 2b.

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INTRODUCTION

Traumatic brain injury (TBI) is one of the leading causes of death and permanent disability, and hearing impairment is a common sequela.[1] In the United States, approximately 1.4 million closed TBIs occur annually, with >235,000 hospitalizations and 50,000 deaths.[2] Griffiths et al. proposed that 56% of patients had hearing loss after brain injury at a 6-month follow-up.[3] The authors also reported that >90% of the cases of hearing loss were sensorineural hearing loss. In addition, Kochhar et al. reported that 8% of TBI patients had profound hearing loss.[4]

Patients who have a brain injury with hearing loss in Taiwan are covered by the Taiwanese National Health Insurance (NHI) program. Cassidy et al. conducted a population-based study on mild TBI; however, the inception time was only 2 years.[5] Given the lack of large population-based studies published on hearing loss after brain injury with a long-term follow-up, there is a clear gap in knowledge in this respect. The purpose of this study was to document the incidence and course of hearing loss after brain injury by using the population-based National Health Insurance Research Database (NHIRD).

MATERIALS AND METHODS

Data Source

Taiwan implemented the NHI program on March 1, 1995, and the health insurance coverage rate currently exceeds 99%. The NHI database includes nationwide outpatient/emergency and hospitalization data, and the law requires that all hospitals and clinics report outpatient/emergency and hospitalization expenses to the Bureau of National Health Insurance on a monthly basis. Researchers are required to pass a detailed review by a professional peer review committee before they are allowed to use the Taiwan NHIRD. The study protocol was approved by the institutional review board of Tri-Service General Hospital (Nos. 2-104-05-126, 2-105-05-025).

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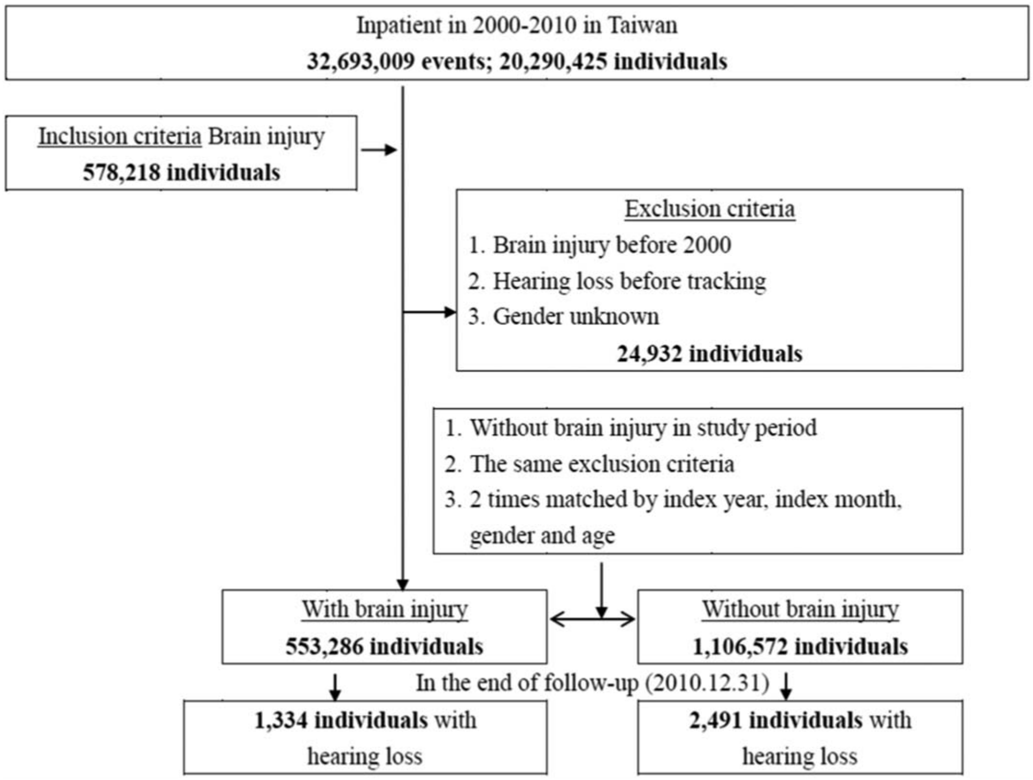


Fig. 1. Flowchart of study sample selection from the National Health Insurance Research Database in Taiwan.

Variable Definitions

In our study, inpatient brain injuries included skull fractures (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] 800-804) and intracranial injuries (ICD-9-CM 850-854). The tracked outcome event was hearing loss (ICD-9-CM 389.0-389.2, 389.8-389.9). We excluded patients with presbycusis (ICD-9-CM 388.01) to reduce any influence of presbycusis on trauma-related hearing loss and a family history of deafness or hearing loss (ICD-9-CM V19.2), thus ensuring that the study would be more rigorous and precise.

Low income was defined as a monthly income < 18,000 New Taiwan dollars according to the Ministry of Health and Welfare of Taiwan. In Taiwan's NHI program, patients with any of the 30 categories of catastrophic illness specified by the Bureau of the NHI can apply for catastrophic illness certificates. Any insurant with major diseases such as cancer can apply for a catastrophic illness certification.[6] In accordance with Taiwan National Health Research Institute publications, the urbanization levels in Taiwan were divided into seven strata, with level 1 referring to the "most urbanized" and level 7 referring to the "least urbanized" communities. Urbanization level was based on the population density of the residential area, population ratio of elderly people, number of agricultural workers, educational level, and number of physicians per 100,000 people. Patients in levels 3 to 7 were combined into a single group, which was referred to as the low urbanized group. Therefore, urbanization in our study was categorized into three levels, with high being the most urbanized and low the least urbanized.[7]

Study Sample Selection and Tracking

Of the 20,290,425 individuals with inpatient data recorded from January 1, 2000 to December 31, 2010, 578,218 were hospitalized due to brain injuries. The patients with TBI before 2000 and patients of unknown gender were excluded. In addition, the patients diagnosed with hearing loss before 2000 or before the events of TBI were also excluded. The case group ultimately included 553,286 individuals. The control group met the same exclusion criteria as the case group but did not have a brain injury during the study period. Two individuals for each case patient were matched by index year, index month, gender, and age; therefore, the control group included 1,106,572 individuals. The subjects were tracked until December 31, 2010 (Fig. 1).

Statistical Analysis

Continuous variables are presented as the mean ± standard deviation and categorical variables as frequencies and percentages. Moreover, χ^2 tests, Fisher exact tests, and t tests were used to compare the differences between the groups with and without brain injury at baseline and the tracking endpoint. The difference in the risk of hearing loss between the study and control groups was estimated using the Kaplan-Meier method with log-rank test to assess the difference between groups in the occurrence of cumulative hearing loss. Multivariate Cox proportional hazards regression analyses were used to determine the risk of hearing loss, and the results were presented as hazard ratios (HRs) with a 95% confidence interval (CI). All statistical analyses were performed using SPSS 22.0 (IBM, Armonk, NY), and a two-tailed $P < .05$ was considered the threshold for significance.

RESULTS

The TBI and comparison cohorts comprised data for 553,286 and 1,106,572 patients, respectively. Table I shows the sociodemographic variables and causes of

TABLE I.
Baseline Characteristics of the Study.

Brain Injury Variables	Total No.	Total %	With No.	With %	Without No.	Without %	*P*
Total	1,659,858		553,286	33.33	1,106,572	66.67	
Gender							.999
Male	1,022,916	61.63	340,972	61.63	681,944	61.63	
Female	636,942	38.37	212,314	38.37	424,628	38.37	
Age, yr, mean ± SD	41.95 ± 24.90		42.07 ± 22.45		41.84 ± 25.45		.743
Low income							<.001
Without	1,639,197	98.76	544,911	98.49	1,094,286	98.89	
With	20,661	1.24	8,375	1.51	12,286	1.11	
Catastrophic illness							<.001
Without	1,513,663	92.19	502,899	93.95	1,010,764	91.34	
With	128,195	7.81	32,387	6.05	95,808	8.66	
CCI, mean ± SD	0.52 ± 1.50		0.16 ± 0.61		0.69 ± 1.79		<.001
Cause of injury							<.001
Traffic injuries	202,796	53.71	177,874	62.55	24,922	26.75	
Poisoning	2,641	0.70	826	0.29	1,815	1.95	
Falls	73,043	19.35	54,163	19.05	18,880	20.26	
Burns and fires	619	0.16	150	0.05	469	0.50	
Drowning	195	0.05	45	0.02	150	0.16	
Suffocation	1,186	0.31	192	0.07	994	1.07	
Crushing/cutting/piercing	25,324	6.71	13,470	4.74	11,854	12.72	
Other unintentional injuries	48,990	12.98	20,431	7.18	28,559	30.65	
Suicide	3,533	0.94	1,053	0.37	2,480	2.66	
Homicide/abuse	17,453	4.62	15,458	5.44	1,995	2.14	
Undetermined	1,785	0.47	725	0.25	1,060	1.14	
Intentionality of injury							<.001
Unintentional injury	354,794	94.42	267,151	94.18	87,643	95.14	
Intentional injury	20,986	5.58	16,511	5.82	4,475	4.86	
Urbanization level							<.001
High	526,401	31.71	127,790	23.10	398,611	36.02	
Middle	692,975	41.75	225,710	40.79	467,265	42.23	
Low	440,482	26.54	199,786	36.11	240,696	21.75	
Level of care							<.001
Hospital center	500,269	30.14	114,371	20.67	385,898	34.87	
Regional hospital	614,445	37.02	230,691	41.69	383,754	34.68	
Local hospital	545,144	32.84	208,224	37.63	336,920	30.45	
Surgery							<.001
Without	1,052,991	63.44	419,806	75.88	633,185	57.22	
With	606,867	36.56	133,480	24.12	473,387	42.78	
Number of days, mean ± SD	6.85 ± 9.13		6.81 ± 8.83		6.87 ± 9.28		<.001
Prognosis							<.001
Survival	1,635,289	98.52	539,289	97.47	1,096,000	99.04	
Mortality	24,569	1.48	13,997	2.53	10,572	0.96	

Probability values for categorical variables: χ^2/Fisher exact test; for continuous variables: *t* test.

Traffic injuries: ICD-9-CM E800-849; Poisoning: ICD-9-CM E850-E869; Falls: ICDCM E880-E889; Burns and fires: ICD-9-CM E890-E899; Drowning: ICD-9-CM E910; Suffocation: ICD-9-CM E911-E915; Crushing/cutting/piercing: ICD-9-CM E916-E920; Other unintentional injuries: E870-E879, E900-E909, E921-E949; Suicide: ICD-9-CM E950-E959; Homicide/abuse: ICD-9-CM E960-E969; Undetermined: ICD-9-CM E980-E989; Unintentional injury: ICD-9-CM E800-E949; Intentional injury: ICD-9-CM E950-E979, E990-E999. Some patients did not provide information about cause and intentionality of injury.

CCI = Charlson Comorbidity Index; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; SD = standard deviation.

injury for the hearing loss and control patients. No significant differences in age distribution were found between the TBI and comparison cohorts. The majority of patients in the brain injury cohort were male (61.63%). More than 60% of injuries that caused hearing loss in the TBI group were a result of traffic injuries. Falls were the second

TABLE II.
Factors of Hearing Loss at the End of Follow-up Stratified by Variables Listed in the Table by Using Cox Regression.

	With			Without						
Brain Injury Variables	Event	PYs	Rate, per 10^5 PYs	Event	PYs	Rate, per 10^5 PYs	Ratio*	Adjusted HR†	95% CI	*P*
Total	1,334	909,779.56	146.63	2,491	3,625,907.40	68.70	2.134	2.125	2.045-2.546	.011
Gender										
Male	888	539,911.26	164.47	1,852	2,257,681.35	82.03	2.005	2.015	1.982-2.346	<.001
Female	446	369,868.30	120.58	446	1,368,226.05	32.60	3.699	2.448	2.103-3.195	<.001
Low income										
Without	1,296	884,258.62	146.56	2,422	3,538,421.69	68.45	2.141	2.345	2.124-2.602	<.001
With	38	25,520.94	148.90	69	87,485.71	78.87	1.888	1.945	1.756-2.118	.001
Catastrophic illness										
Without	1,148	783,168.33	146.58	2,422	2,938,296.52	82.43	1.778	2.338	2.102-2.774	<.001
With	38	126,611.23	30.01	69	678,610.88	10.17	2.952	1.978	1.765-2.125	<.001
Cause of injury										
Traffic injuries	163	64,065.49	254.43	12	74,145.36	16.18	15.720	13.978	3.445-25.797	<.001
Poisoning	0	2,255.35	0.00	5	5,817.53	85.95	0.000	0.000	—	.893
Falls	55	34,499.90	159.42	25	77,149.65	32.40	4.920	5.121	2.447-6.970	<.001
Burns and fires	0	413.62	0.00	0	971.53	0.00	—	—	—	—
Drowning	0	128.18	0.00	0	227.28	0.00	—	—	—	—
Suffocation	0	690.26	0.00	2	2,851.83	70.13	0.000	0.000	—	.849
Crushing/cutting/ piercing	4	14,862.56	26.91	1	26,577.17	3.76	7.153	7.442	3.151-10.065	<.001
Other unintentional injuries	107	41,593.42	257.25	67	116,818.51	57.35	4.485	4.454	1.026-7.523	.022
Suicide	1	3,176.58	31.48	3	7,376.75	40.67	0.774	0.864	0.304-1.346	.227
Homicide/abuse	12	6,309.53	190.19	2	4,447.40	44.97	4.229	4.196	2.941-7.008	.002
Undetermined	4	1,682.18	237.79	4	4,242.75	94.28	2.522	2.597	1.022-3.448	.017
Intentionality of injury										
Unintentional injury	346	169,677.07	203.92	121	320,625.76	37.74	5.403	4.445	3.012-5.453	<.001
Intentional injury	13	9,486.11	137.04	5	11,824.15	42.29	3.241	2.011	1.003-2.446	.049
Urbanization level										
High	444	220,627.72	201.24	806	1,091,734.62	73.83	2.726	2.167	2.051-2.522	<.001
Middle	558	378,949.98	147.25	1,333	1,623,710.50	82.10	1.794	1.985	1.345-2.215	<.001
Low	332	310,201.87	107.03	352	910,462.28	38.66	2.768	2.485	2.245-2.672	<.001
Level of care										
Hospital center	598	216,420.82	276.31	1,279	1,195,054.85	107.02	2.582	2.310	2.104-2.617	<.001
Regional hospital	622	421,809.10	147.46	983	1,585,629.51	61.99	2.379	2.121	2.009-2.286	<.001
Local hospital	114	271,549.65	41.98	229	845,223.05	27.09	1.549	1.875	1.234-2.059	<.001
Surgery										
Without	872	558,656.24	156.09	1,999	2,298,894.47	86.95	1.795	2.032	1.713-2.235	<.001
With	462	351,123.32	131.58	492	1,327,012.53	37.08	3.549	3.445	2.944-4.106	<.001

*Ratio = rate in case ÷ rate in control.
†Adjusted for variables listed in the table.
CI = confidence interval; HR = hazard ratio; PY = person-year.

most common mechanism of injury in the TBI group, followed by homicide and crushing. In the non-TBI group, the most common cause of injury was other unintentional injuries, followed by traffic injuries, falls, and crushing. Participants in both cohorts had monthly income levels that were not low income and tended to live in more urbanized areas (63.89% vs. 78.25% for high and middle urbanization levels, respectively). Our data showed that over the 10-year follow-up, 1,334 brain injury patients developed hearing loss, for an overall rate of 146.63 cases per 100,000 person-years, whereas 2,491 non–brain injury individuals had hearing loss, for an overall rate of 68.70 cases per 100,000 person-years (Fig. 1 and Table II). At the end of the follow-up period, the TBI group had a higher risk of developing hearing loss than the non-TBI control group (Table III). Table IV reveals the results of the Cox regression analysis of the comparison between the risk of developing hearing loss in the TBI group and

TABLE III.
Characteristics of Study at the End of Follow-up.

Brain Injury Variables	Total		With		Without		
	No.	%	No.	%	No.	%	*P*
Total	1,659,858		553,286	33.33	1,106,572	66.67	
Hearing loss							.022
Without	1,656,033	99.77	551,952	99.76	1,104,081	99.77	
With	3,825	0.23	1,334	0.24	2,491	0.23	
Subgroup of hearing loss							<.001
Without	1,656,033	99.77	551,952	99.76	1,104,081	99.77	
Conductive	291	0.02	185	0.03	106	0.01	
Sensorineural	1,127	0.07	340	0.06	787	0.07	
Mixed	118	0.01	58	0.01	60	0.01	
Others	2,289	0.14	751	0.14	1,538	0.14	
Gender							.999
Male	1,022,916	61.63	340,972	61.63	681,944	61.63	
Female	636,942	38.37	212,314	38.37	424,628	38.37	
Age, yr, mean ± SD	44.66 ± 25.29		44.49 ± 22.83		44.90 ± 26.40		.793
Low income							<.001
Without	1,631,977	98.32	542,882	98.12	1,089,095	98.42	
With	27,881	1.68	10,404	1.88	17,477	1.58	
Catastrophic illness							<.001
Without	1,443,876	86.99	500,945	90.54	942,931	85.21	
With	215,982	13.01	52,341	9.46	163,641	14.79	
CCI, mean ± SD	0.88 ± 2.29		0.47 ± 150		1.08 ± 2.57		<.001
Cause of injury							<.001
Traffic injuries	202,796	53.71	177,874	62.55	24,922	26.75	
Poisoning	2,641	0.70	826	0.29	1,815	1.95	
Falls	73,043	19.35	54,163	19.05	18,880	20.26	
Burns and fires	619	0.16	150	0.05	469	0.50	
Drowning	195	0.05	45	0.02	150	0.16	
Suffocation	1,186	0.31	192	0.07	994	1.07	
Crushing/cutting/piercing	25,324	6.71	13,470	4.74	11,854	12.72	
Other unintentional injuries	48,990	12.98	20,431	7.18	28,559	30.65	
Suicide	3,533	0.94	1,053	0.37	2,480	2.66	
Homicide/abuse	17,453	4.62	15,458	5.44	1,995	2.14	
Intention unknown	1,785	0.47	725	0.25	1,060	1.14	
Intentionality of injury							<.001
Unintentional injury	354,794	94.42	267,151	94.18	87,643	95.14	
Intentional injury	20,986	5.58	16,511	5.82	4,475	4.86	
Urbanization level							<.001
High	513,091	30.91	139,377	25.19	373,714	33.77	
Middle	713,332	42.98	229,783	41.53	483,549	43.70	
Low	433,435	26.11	184,126	33.28	249,309	22.53	
Level of care							<.001
Hospital center	520,598	31.36	135,369	24.47	385,229	34.81	
Regional hospital	671,975	40.48	242,529	43.83	429,446	38.81	
Local hospital	467,285	28.15	175,388	31.70	291,897	26.38	
Surgery							<.011
Without	1,037,368	62.50	380,838	68.83	656,530	59.33	
With	622,490	37.50	172,448	31.17	450,042	40.67	

TABLE III.
(Continued)

Brain Injury Variables	Total No.	Total %	With No.	With %	Without No.	Without %	P
Length of days, mean ± SD	17.42 ± 19.78		17.03 ± 18.76		17.62 ± 20.23		<.001
Prognosis							<.001
Survival	1,531,617	92.27	517,802	93.59	1,013,815	91.62	
Mortality	128,241	7.73	35,484	6.41	92,757	8.38	

the non-TBI control group. The adjusted HR was 2.125 (95% CI = 2.045-2.546, $P = .011$). The results revealed that patients with brain injury had a 2.125 times (95% CI = 2.045-2.546) higher risk of developing hearing loss than individuals without brain injury. Males also had a higher risk of hearing loss than females (adjusted HR = 1.384). For each additional year of age, the risk of hearing loss increased by 0.7% (adjusted HR = 1.007; Table IV). The Kaplan-Meier analysis showed that patients with brain injury had a significantly higher incidence of hearing loss than the matched controls (log-rank test $P = .027$; Fig. 2). Table II shows the stratification analysis of the cause of injury associated with the risk of hearing loss in the TBI group compared to the control group after controlling for other factors. The TBI group had a higher risk of hearing loss than the control group. For the subgroup of traffic injuries, the risk of hearing loss in the TBI group was 13.978 times higher than that of the non-TBI subgroup of traffic injuries, followed by crushing/cutting/piercing injuries with 7.442 times, falls with 5.121 times, and homicide/abuse with 4.196 times. Table V shows the distribution of the type of hearing loss among the patients at the end of follow-up based on the Cox regression. The highest percentage of patients had sensorineural hearing loss, followed by conductive and mixed type hearing loss. Figure 2 shows the time of onset of hearing loss stratified by brain injury. The results at 0.5 year approached statistical significance ($P = .052$), whereas at the 1-year follow-up all the results were significant ($P < .05$). The average follow-up in both groups was approximately 7 years.

DISCUSSION

To our knowledge, this is the first large-scale nationwide population cohort study investigating the association between brain injury and hearing loss. Patients with TBI had an increased risk of hearing loss, and males had a higher risk than females. This result may be due to the differences in daily activities and work circumstances between males and females. Males are more prone to TBI than females, and >60% of the patients in our study were male. De Silva et al. conducted a study that included patients with TBI from 46 countries, and >81% of the patients were male.[8] In our study, there was a trend toward statistical significance from trauma to after 0.5 year, suggesting that hearing loss occurred relatively late in most patients with brain injury because their hearing tests had been delayed for a few months after they had awoken in the hospital (Fig. 2). Furthermore, some trauma patients may have died within a few days or months; we cannot determine the incidence of hearing loss within this group of patients. Ghajar proposed that most of the deaths from TBI that occur in the first week are from intracranial hypertension, and this belief might support our explanation of the results of this study.[9] The 1.5% difference in the mortality rate between the two groups may be because the TBI group had more severe disease, and this discrepancy suggests that the percentage of hearing loss may be underestimated. After 1 year, the P values in the brain injury group were statistically significant for hearing loss from 1 year to 11 years. Therefore, brain injuries were clearly related to all types of hearing impairment. The P value for the comparison of TBI and non-TBI was .022, and not <.001, due to the follow-up duration. As both groups were older than 50 years at the end of follow-up, hearing loss in both groups could have occurred due to aging. Robinson and Sutton proposed that age had an effect on hearing threshold.[10] Age-related hearing loss occurs after 50 years of age, and the American Academy of Family Physicians and American Speech-Language-Hearing Association recommend that adults older than 50 to 60 years receive screening for hearing loss.[11]

In Taiwan, most medical centers are located in highly urbanized areas. Hospitals in highly urbanized areas receive more patients with TBI and more complicated forms of TBI. This may explain why more hearing loss was observed in the highly urbanized areas. Medical centers may receive patients with more severe and complicated diseases, which may explain why the risk of hearing loss was the highest in this group. Patients at medical centers often have several comorbidities and more complicated illnesses.

Surgery was associated with the lowest risk of hearing loss, which may be because the surgical intervention ameliorated the damage related to hearing loss. Stein et al. proposed that aggressive intracranial pressure (ICP) monitoring and treatment of patients with TBI resulted in better outcomes.[2] In addition, Fujii et al. emphasized the importance of treating patients with TBI by removing mass lesions, which can reduce elevated ICP and local mass effects. Surgical evacuation to remove space-occupying lesions such as intracranial hematomas is a well-accepted procedure with favorable outcomes.[12]

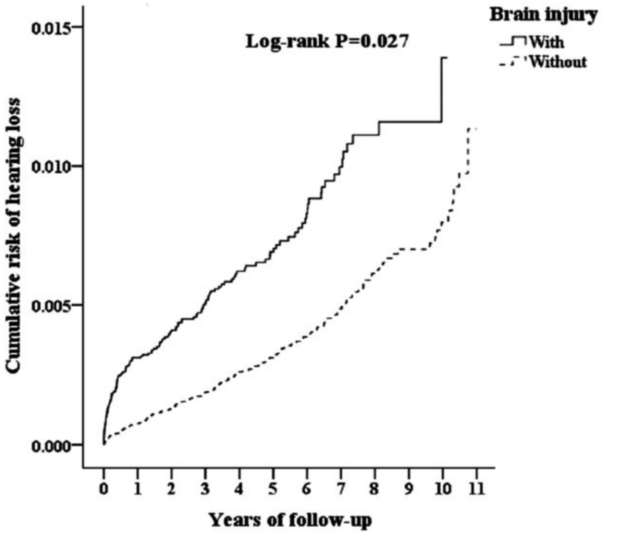
The mechanisms of hearing loss related to brain injury are as follows: 1) injury to the central auditory

TABLE IV.
Factors of Hearing Loss at the End of Follow-up by Using Cox Regression.

Variables	Crude HR	95% CI	*P*	Adjusted HR*	95% CI	*P*
Brain injury						
Without	Reference			Reference		
With	2.168	2.027-2.320	.027	2.125	2.045-2.546	.011
Gender						
Male	1.508	1.412-1.612	<.001	1.384	1.301-1.401	<.001
Female	Reference			Reference		
Age, yr	1.007	1.006-1.009	<.001	1.007	1.006-1.008	<.001
Low income						
Without	Reference			Reference		
With	1.139	0.950-1.365	.159	1.155	0.953-1.486	.129
Catastrophic illness						
Without	Reference			Reference		
With	0.993	0.862-1.011	.090	0.822	0.706-1.095	.082
CCI	0.993	0.981-1.006	.296	0.926	0.503-1.465	.195
Intentionality of injury						
Unintentional injury	Reference			Reference		
Intentional injury	1.041	0.587-1.506	.799	1.090	0.439-1.446	.572
Season						
Spring, March–May	Reference			Reference		
Summer, June–August	0.970	0.892-1.055	.474	0.955	0.862-1.315	.300
Autumn, September–November	0.828	0.761-0.902	<.001	0.798	0.711-0.867	<.001
Winter, December–February	0.854	0.782-0.933	<.001	0.842	0.746-0.913	<.001
Urbanization level						
High	1.680	1.539-1.835	<.001	1.059	0.849-1.325	.338
Middle	1.658	1.526-1.801	<.001	1.112	1.012-1.345	<.001
Low	Reference			Reference		
Level of care						
Hospital center	3.956	3.558-4.398	<.001	4.655	4.006-5.098	<.001
Regional hospital	2.447	2.198-2.724	<.001	2.978	2.195-3.793	<.001
Local hospital	Reference			Reference		
Surgery						
Without	Reference			Reference		
With	0.582	0.543-0.624	<.001	0.512	0.482-0.638	<.001
Length of days†	1.006	1.004-1.007	<.001	1.005	1.004-1.006	<.001

Unintentional injury: ICD-9-CM E800-E949; Intentional injury: ICD-9-CM E950-E979, E990-E999.
*Adjusted for variables listed in the table.
†Medical cost had collinearity with length of days.
CCI = Charlson Comorbidity Index; CI = confidence interval; HR = hazard ratio; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

pathways, which may result in severe deafness; 2) temporal bone fracture with otic capsule involvement, which may result in three types of hearing loss, including sensorineural hearing loss, conductive hearing loss, and mixed type; 3) tympanic membrane rupture with conductive hearing loss; 4) ossicular chain disruption complicated with conductive hearing loss; 5) cochlear disruption due to barotrauma; 6) anterior and posterior movement of the brain by coup or contracoup injuries, resulting in a shearing injury to the auditory nerve[13]; 7) disruption of the membranous labyrinth; 8) avulsion or trauma to the cochlear nerve; 9) interruption of the cochlear blood supply; 10) hemorrhage into the cochlea; 11) perilymphatic fistula; and 12) endolymphatic hydrops.[14] Griffiths et al. reported that the force of a blow to the temporal region is the likeliest and most severe cause of sensorineural hearing loss.[3] The three types of hearing loss related to brain injury include sensorineural hearing loss, conductive hearing loss, and mixed hearing loss. Lew et al. proposed that most TBI-related hearing losses are sensorineural,[15] which is consistent with the results of our study. In our study, Table V shows the distribution of the types of hearing loss in the patients at the end of the follow-up period based on the Cox regression analysis. Sensorineural hearing loss accounted for the highest percentage, followed by conductive and mixed type hearing loss. Griffiths et al. proposed that 56% of



Brain injury	With (N=553,286)	Without (N=1,106,572)	P
Follow-up	Number of events (hearing loss)		
1 month	240	113	0.067
3 months	415	228	0.060
6 months	522	347	0.052
1 year	656	506	0.048
2 years	794	799	0.035
3 years	934	1,094	0.023
4 years	1,042	1,347	0.012
5 years	1,105	1,557	0.008
6 years	1,186	1,789	0.001
7 years	1,247	1,992	<0.001
8 years	1,288	2,195	<0.001
9 years	1,318	2,302	0.004
10 years	1,327	2,396	0.019
11 years	1,334	2,491	0.027

Fig. 2. Kaplan-Meier analysis of the cumulative risk of hearing loss stratified by brain injury with log-rank test (log-rank test: $P = .027$).

hearing loss occurs within 48 hours after minor head injury.[3] Therefore, post-trauma hearing symptoms often begin immediately after the trauma. In general, hearing loss often improves within 6 months, and a spontaneous resolution of mild sensorineural hearing loss at 4 to 8 kHz has also been reported.[16] The sequelae of brain injury related to conductive hearing loss are as follows: hemotympanum, tympanic membrane rupture, and ossicular chain disruption. Hemotympanum is often observed after trauma and often resolves within weeks to months. Traumatic tympanic membrane rupture also heals gradually within 3 months.[16] Ossicular chain disruption may also improve after a duration of 6 months.

Although most TBI-related hearing loss events occurred immediately, delayed hearing loss was also noted in our study. Delayed hearing loss may be related to the late degeneration of the central auditory pathway after brain injury. Bergemalm et al. proposed that closed head injuries with or without temporal bone fractures are related to a risk of acute sensorineural hearing loss. Furthermore, hearing loss can progress with time.[17]

In our subgroup analyses by type of injury, patients with TBI due to traffic injury had the highest associated risk of hearing loss compared with the risk of non-TBI traffic injury patients, followed by patients with crushing/cutting/piercing injuries and falls. These findings may be clinically applied by conducting hearing examinations after brain injury to detect and treat hearing loss as soon as possible.

The most common and important pathologic feature of TBI is diffuse axonal injury.[18] In the acute stage, neuroinflammation mobilizes immune cells, astrocytes, cytokines, and chemokines to mount an anti-inflammatory response against brain damage. However, the excess activation of these inflammatory elements in the chronic stage contributes to secondary cell death in TBI.[19] In addition, Oesterle proposed that hair cell repair is limited in the mammalian auditory epithelium and that support cells form permanent scars where replacement hair cells are unable to regenerate. In contrast, in nonmammalian vertebrates, the injured ear generates replacement hair cells to restore hearing function.[20] Alzahrani et al. reported that hearing loss from shaken baby syndrome results from tears in the membranous labyrinth, which may involve both vestibular structures and the cochlea. The force produced by injuries resulting in TBI

TABLE V.
Distribution of Type in Patients With Hearing Loss at the End of Follow-up by Using Cox Regression.

Brain Injury Subgroup of Hearing Loss	With: Event	With: PYs	With: Rate, per 10^5 PYs	Without: Event	Without: PYs	Without: Rate, per 10^5 PYs	Ratio*	Adjusted HR†	95% CI	*P*
Total	1,334	909,779.56	146.63	2,491	3,625,907.40	68.70	2.134	2.125	2.045–2.546	.011
Conductive	185	909,779.56	20.33	106	3,625,907.40	2.92	6.956	6.875	5.976–8.443	<.001
Sensorineural	340	909,779.56	37.37	787	3,625,907.40	21.70	1.722	1.644	1.035–2.974	.030
Mixed	58	909,779.56	6.38	60	3,625,907.40	1.65	3.853	3.421	2.776–4.301	.001
Unspecified	751	909,779.56	82.55	1,538	3,625,907.40	42.42	1.946	1.813	1.245–2.882	.013

*Ratio = rate in case ÷ rate in control.
†Adjusted for variables listed in Cox Regression table.
CI = confidence interval; HR = hazard ratio; PY = person-year.

thus seems strong enough to cause cochlear tears and temporal bone trauma.[21–23] Otic capsule–disrupting fractures often result in severe to profound sensorineural hearing loss.[24]

The large sample size obtained from our nationwide database provided statistical power, and the most clinically important aspect of our study was the 10-year follow-up. To date, few studies have been conducted with large sample sizes and with a long-term follow-up. The patients in our study displayed a wide range of demographic characteristics, which might increase the applicability of our results to the general population. However, this study has several limitations. First, the NHI program includes hearing loss data on brain injury patients who receive a pure tone audiogram (PTA) examination; therefore, NHI data do not include patients with brain injury who cannot perform the PTA examination due to coma or severe disability. The percentage of hearing loss in patients with brain injury may have been underestimated. Second, the NHIRD is a claims-based database; therefore, no detailed clinical information regarding the PTA or other otological examinations is recorded. Third, our study excludes patients with presbycusis, which may make the study group much younger. Finally, the NHIRD documents only the date of hearing loss, not the severity. Therefore, the effect of brain injury on the severity of hearing loss could not be analyzed.

CONCLUSION

The findings of our study show that TBI is associated with a higher incidence of hearing loss. Our study revealed that patients with TBI had a 2.125 times higher risk of developing hearing loss. However, our study excludes patients with presbycusis, which may make the study group much younger. After a long-term follow-up of 10 years, hearing loss after TBI occurred in both the acute and the chronic stage. Our study suggests that clinicians should be aware of the importance of TBI-related hearing loss and take precautions to follow up on long-term hearing among TBI patients. Traffic injuries were the most common injuries associated with hearing loss in our study.

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