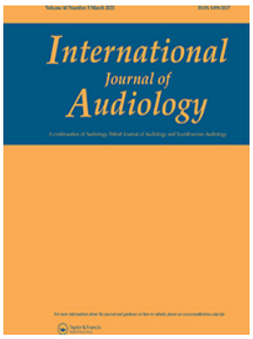

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ORIGINAL ARTICLE

A population-based case–control study of the association between cervical spondylosis and tinnitus

Yen-Fu Cheng[a,b,c,d,e], Sudha Xirasagar[f], Tzong-Hann Yang[g,h], Chuan-Song Wu[g], Nai-Wen Kuo[i] and Herng-Ching Lin[i,j]

[a]Department of Otolaryngology-Head and Neck Surgery, Taipei Veterans General Hospital, Taipei, Taiwan; [b]Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan; [c]Faculty of Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan; [d]Institute of Brain Science, National Yang-Ming University, Taipei, Taiwan; [e]Research Center of Sleep Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan; [f]Department of Health Services Policy and Management, Arnold School of Public Health, University of South Carolina, Columbia, SC, USA; [g]Department of Otorhinolaryngology, Taipei City Hospital, Taipei, Taiwan; [h]Department of Speech Language Pathology and Audiology, National Taipei University of Nursing Health Sciences, Taipei, Taiwan; [i]School of Health Care Administration, College of Management, Taipei Medical University, Taipei, Taiwan; [j]Sleep Research Center, Taipei Medical University Hospital, Taipei, Taiwan

ABSTRACT

Objective: This population-based study aimed to study the association between tinnitus and cervical spondylosis.

Design: A case–control study.

Study sample: We retrieved data from the Taiwan Longitudinal Health Insurance Database. We identified 2465 patients with tinnitus (cases) and 7395 comparison patients by propensity score matching. Multivariable logistic regressions were conducted to estimate the odds (OR) of a diagnosis of cervical spondylosis preceding the tinnitus diagnosis relative to controls.

Results: We found that 1596 (16.19%) of 9860 sample patients had received a diagnosis of cervical spondylosis before the index date, significantly different between the tinnitus group and control group (17.20% vs. 15.85%, $p < 0.001$). Logistic regression analysis showed an adjusted OR for prior cervical spondylosis of 1.235 for cases vs. controls (95% confidence interval [CI]: 1.088–1.402). Further, the adjusted ORs were 1.246 (95% CI: 1.041–1.491) and 1.356 (95% CI: 1.016–1.811), respectively, among patients aged 45 ~ 64 and >64 groups. No difference in cervical spondylosis likelihood between cases and controls was found among patients aged 18 ~ 44 groups.

Conclusions: In conclusion, the study shows a positive association between cervical spondylosis and tinnitus. The findings call for greater awareness among physicians about a possible somatosensory component of cervical spine function which may contribute to tinnitus.

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Tinnitus; cervical spondylosis; epidemiology

Introduction

Tinnitus is a phantom auditory sensation in the absence of external auditory stimuli. The prevalence of tinnitus is estimated to range from 5.2% in Egypt, 10.4% in China, to 25.3% in the United States (Khedr et al. 2010; Shargorodsky, Curhan, and Farwell 2010; Yang et al. 2018). While tinnitus may not represent a pathologically destructive process, it may impact the quality of life for some patients by causing debilitating problems such as insomnia, anxiety and depression (Aazh and Moore 2019; Sahlsten et al. 2018; Salazar et al. 2019; Wakabayashi et al. 2018).

Tinnitus is commonly linked to damage to the auditory apparatus, most often the cochlea and auditory nerve. Tinnitus can occur in patients with normal cochlear function with or without changes to hearing threshold (Bramhall et al. 2017, 2018; Eggermont 1990; Jastreboff 1990; Kujawa and Liberman 2009). Thus, it may have an origin other than the peripheral auditory system such as medial geniculate body (MGB) and inferior colliculus (IC) (Caspary and Llano 2017; Shore, Roberts, and Langguth 2016). A growing body of evidence suggests that the cochlear nucleus (CN) located in the brainstem portion of the central auditory pathway is involved at the earliest stage of hearing signal processing, and this may play an important role in tinnitus (Costa and Caria 2017; Koehler and Shore 2013; Lanting et al. 2010; Levine 1999; Marks et al. 2018; Ralli et al. 2017; Shore, Roberts, and Langguth 2016; Wu et al. 2016).

Cervical spondylosis is a chronic degenerative condition of the cervical spine that affects not only the vertebral bodies and the intervertebral discs in the neck, but also the facets, other joints and associated soft tissue supports. Progression of the spondylosis process may cause narrowing of the spinal canal and intervertebral formina, resulting in neurological deficits. Because the spinal cord integrates and relays somatosensory inputs, mechanical deformity caused by cervical spondylosis may interfere with the dorsal root ganglia (DRG) and dorsal column, from which sensory input to the central nervous system are relayed in the CN of the brainstem (Kelly et al. 2012). Disruption of the somatosensory pathway from the DRG or the dorsal column may trigger hyperactivity in the CN manifesting as tinnitus (Koehler and Shore 2013; Marks et al. 2018; Wu et al. 2016).

Previously, the presence of tinnitus has been reported in patients with cervical spondylosis (Fleming, Vora, and Harrigan

CONTACT Herng-Ching Lin henry11111@tmu.edu.tw School of Health Care Administration, Taipei Medical University, 250 Wu-Hsing Street, Taipei, 110, Taiwan

Table 1. Demographic characteristics and co-morbidities among patients with tinnitus and controls in Taiwan, 2010–2016 ($n = 9860$).

	Patients with tinnitus ($n = 2465$)		Controls ($n = 7395$)		
Variable	Total No.	%	Total No.	%	p Value
Age, mean (standard deviation)	48.06 (15.62)		50.57 (16.16)		<0.001
Sex					
Male	1055	42.80%	2842	38.43%	<0.001
Female	1410	57.20%	4553	61.57%	
Monthly income					
15,840≥	513	28.01%	1596	21.58%	0.217
NT$15,841–25,000	1155	46.86%	3546	47.95%	
≥NT$25,001	797	32.33%	2253	30.47%	
Geographic region					
Northern	1140	46.25%	3247	43.91%	0.099
Central	644	26.13%	1973	26.68%	
Eastern	59	2.39%	227	3.07%	
Southern	622	25.23%	1948	26.34%	
Urbanisation level					
1 (most urbanised)	658	26.69%	1822	24.64%	<0.001
2	693	28.11%	1912	25.86%	
3	383	15.54%	1058	14.31%	
4	410	16.63%	1724	23.31%	
5 (least urbanised)	151	6.13%	492	6.65%	
Others	170	6.90%	387	5.23%	
Hyperlipidaemia	978	39.68%	1487	40.77%	0.337
Diabetes	578	23.45%	2098	28.37%	<0.001
Hypertension	1057	42.88%	3831	51.81%	<0.001
Coronary heart disease	600	24.34%	2564	34.67%	<0.001
Asthma	382	15.50%	2013	27.22%	<0.001
Hearing loss	876	35.54%	2628	35.54%	>0.999

2013; Li et al. 2014; Melding and Goodey 1979; Olszewski, Kowalska, and Kuśmierczyk 2008; Sun et al. 2013). However, these studies were generally lacking a control group and had small sample sizes. This population-based case–control study was undertaken to assess the association between tinnitus and prior diagnosis of cervical spondylosis.

Methods

Database

Data were retrieved on patients included in the Taiwan Longitudinal Health Insurance Database 2005 (LHID2005). Taiwan implemented its National Health Insurance (NHI) program in 1995. There were approximately 25.68 million individuals covered by the NHI program in 2005. The LHID2005 includes all healthcare claims data for two million enrolees who were randomly sampled from the 25.68 million NHI beneficiaries. The National Health Research Institutes have reported that there is no significant difference in age, sex or average insured payroll-related insurance premium between the LHID2005 sample and the population of NHI beneficiaries.

The study was approved by the Institutional Review Board of Taipei Medical University (TMU-JIRB N201911025) and is compliant with STROBE guidelines for research reporting standards. Since this study used deidentified administrative data for analyses, informed consent was not needed.

Study sample

To select study patients, we first identified 2465 patients aged ≧18 years where diagnosed with tinnitus (ICD-9-CM code 388.3) at outpatient settings (private clinics or hospital outpatient departments between 1 January 2010 and 31 December 2016. The date of the first-ever tinnitus diagnosis during this period was set as the index date for these patients. We further assured that none of these selected patients had a history of Ménière's disease and otitis media prior to index date.

To select controls out of the remaining patients, we first excluded those aged less than 18 years and those who received a diagnosis of tinnitus. Thereafter, we selected three propensity score-matched controls per case. Variables used in propensity score-matching were patient demographics (age, sex, monthly income, geographic location and urbanisation level of the patient's residence) and presence of selected medical comorbidities, hyperlipidaemia, diabetes, coronary heart disease, hypertension, asthma and hearing loss. Furthermore, we matched the controls to a tinnitus case based on utilisation of medical services in the same index year as the case. For controls, the date of their first utilisation of ambulatory care during that matched year was assigned as the index date. We also confirmed that none of these selected controls had a history of Ménière's disease and otitis media before the index date. A total of 2465 cases and 7395 controls were analysed in this study.

Exposure assessment

We identified patients with a prior cervical spondylosis diagnosis among cases controls (ICD-9-CM codes 721.0 and 721.1). We considered a patient as having cervical spondylosis if they had at least one claim with a diagnosis of cervical spondylosis prior to the index date.

Statistical analysis

Statistical analyses were carried out using the SAS system (SAS System for Windows, version 9.4, SAS Institute, Cary, NC). Chi-square test and t-tests as appropriate were performed to examine differences in patient demographics and medical comorbidities between cases and controls. Multivariable logistic regressions were conducted to estimate the odds ratios (ORs) of prior

Table 2. Crude and covariate-adjusted odds ratios for prior cervical spondylosis among sample patients.

	Total sample N = 9860		Patients with tinnitus N = 2465		Controls N = 7395	
Prior cervical spondylosis	No.	%	No.	%	No.	%
Prior cervical spondylosis (total)	1596 (16.19)		424 (17.20)		1172 (15.85)	
Crude OR (95 % CI)	–		1.103 (0.977–1.246)		1.000	
Adjusted OR (95 % CI)	–		1.235 (1.088–1.402)		1.000	

CI: confidence interval; OR: odds ratio; adjustment for age, sex, monthly income, geographic location, urbanisation level, hyperlipidaemia, hypertension, diabetes, coronary heart disease, asthma and hearing loss.

Table 3. Crude and covariate-adjusted odds ratios for prior cervical spondylosis among the sample patients by age group.

	Total patients		Patients with tinnitus		Controls	
Prior cervical spondylosis	No.	%	No.	%	No.	%
Age 18 ~ 44 (years)	N = 3843		N = 1064		N = 2779	
Yes	429 (11.16)		117 (11.00)		312 (11.23)	
Crude OR (95 % CI)	–		0.977 (0.780–1.224)		1.000	
Adjusted OR (95 % CI)	–		1.137 (0.897–1.442)		1.000	
Age 45 ~ 64 (years)	N = 4028		N = 996		N = 3032	
Yes	838 (20.80)		225 (22.59)		613 (20.22)	
Crude OR (95 % CI)	–		1.152 (0.969–1.369)		1.000	
Adjusted OR (95 % CI)	–		1.246 (1.041–1.491)		1.000	
Age >64 (years)	N = 1989		N = 405		N = 1584	
Yes	329 (16.54)		82 (20.25)		247 (15.59)	
Crude OR (95 % CI)	–		1.374 (1.041–1.814)		1.000	
Adjusted OR (95 % CI)	–		1.356 (1.016–1.811)		1.000	

CI: confidence interval; OR: odds ratio; adjusted for age, sex, monthly income, geographic location, urbanisation level, hyperlipidaemia, hypertension, diabetes, coronary heart disease, asthma and hearing loss.

cervical spondylosis among patients with tinnitus vs. controls. We used $p < 0.05$ for statistical significance.

Results

The sample mean age was 49.94 years (±16.03 standard deviation). Despite propensity score matching, there were significant differences in age, sex, urbanisation level, diabetes, coronary heart disease, hypertension and asthma (all $p < 0.001$) between cases and controls (no differences in monthly income ($p = 0.217$), geographic region ($p = 0.099$), hyperlipidaemia ($p = 0.337$) and hearing loss ($p > 0.999$) (Table 1).

The rate of prior cervical spondylosis in the two groups is in Table 2. Of 9860 sample patients, 1596 (16.19%) had received a diagnosis of cervical spondylosis before the index date. Chi-square test showed statistically significant difference in the rate of prior cervical spondylosis between cases and controls (17.20% vs. 15.85%, $p < 0.001$). Logistic regression analysis showed an adjusted OR for prior cervical spondylosis of 1.235 among cases vs. controls [95% confidence interval (CI): 1.088–1.402], adjusted for age, sex, monthly income, geographic location, urbanisation level, hyperlipidaemia, hypertension, diabetes, coronary heart disease, asthma and hearing loss.

The adjusted ORs (AOR) stratified by age group are presented in Table 3. Logistic regressions showed an AOR of 1.246 (95% CI: 1.041–1.491) and 1.356 (95% CI: 1.016–1.811) respectively, among the 45 ~ 64 and >64 age groups. Among patients aged 18 ~ 44 years, the association between tinnitus and prior cervical spondylosis was not significant.

Discussion

Several case reports have noted the co-occurrence of cervical spondylosis and tinnitus (Fleming, Vora, and Harrigan 2013; Li et al. 2014; Melding and Goodey 1979; Olszewski, Kowalska, and Kuśmierczyk 2008; Sun et al. 2013). No study has used control groups to establish the association. To the best of our knowledge, this is the first large scale retrospective study to document an association between cervical spondylosis and tinnitus showing an adjusted OR of 1.235 for prior cervical spondylosis relative to control patients without tinnitus after accounting for demographic variables and tinnitus-relevant comorbidities.

The mechanism underlying the association is likely to be related to somatosensory pathway disruptions in cervical spondylosis. Although damage to the peripheral auditory system accounts for majority of tinnitus cases, our study affirms the potential for tinnitus to be evoked by disturbed inputs via the somatosensory pathways. Extensive studies with animal models have shown that neural stimuli originating in the auditory and somatosensory systems are integrated in the cochlea nucleus of the brainstem (CN) (Brozoski and Bauer 2005; Koehler and Shore 2013; Roberts et al. 2010; Zhang et al. 2019). In addition to the ascending auditory pathway from the auditory nerves and descending auditory pathways from the auditory centres in the midbrain and auditory cortex, the somatosensory projection of dorsal column nuclei, trigeminal and cervical ganglia also converge at this site. As a result, dysregulated synchrony across this neural ensemble along the auditory and related somatosensory pathway that converge in the cochlea nucleus can cause tinnitus-generating neural discharges, even in the absence of a permanent shift in the hearing threshold (Koehler and Shore 2013).

Our findings may be supported by the known higher incidence of tinnitus in patients with temporomandibular disorder (TMD), which may be another example of tinnitus caused by disrupted somatosensory pathways (Bousema et al. 2018; Buergers et al. 2014; Hilgenberg et al. 2012; Lee et al., 2016; Levine et al. 2007; McCormack et al. 2016; Park and Moon 2014). Given that the somatic sensation of the temporomandibular joint is mainly conveyed by the trigeminal nerve and the related trigeminal ganglion, it is possible that tinnitus accompanying TMD is caused by disruption of the trigeminal pathway.

Traumatic cervical injury (whiplash), which causes structural instability of cervical spine, has been reported to cause tinnitus (Lee et al. 2019; Pang 1971; Kreuzer et al. 2012). Similarly, structural instability caused by cervical spondylosis may cause disruption of dorsal spiral ganglia or dorsal column pathway and lead to tinnitus.

Consistent with the proposed mechanism of tinnitus causation among cervical spondylosis cases, we find that the odds of prior cervical spondylosis among tinnitus cases increased with age, the highest risk noted among patients aged > 64 (OR = 1.356), followed the 45–64 age group (OR = 1.246) and no association in the 18–44 age group. As cervical spondylosis is associated with aging that causes degenerative changes in the spine, younger patients may have asymptomatic spondylosis or mild symptoms despite radiological evidence of spondylotic changes or the tinnitus may have other origins (Kelly et al. 2012).

A strength of this study is its population-based study design using nation-wide population data on all diagnosed tinnitus cases with prior medical diagnoses data available which ensured a large sample size, minimal selection bias and complete retrospective data on patients. There are some study limitations. First, the NHID2005 database, being an insurance claims database, does not contain data on the results of audiometric tests. While we accounted for hearing loss in assessing the association between cervical spondylosis and tinnitus, one limitation is the absence of data on the severity of hearing loss. Similarly, the severity of co-morbidities was, therefore, unavailable and the available data on ICD codes were used to control for diabetes, hypertension, and hyperlipidaemia and to match controls with cases using propensity score matching to minimise selection bias at baseline. Third, relevant information on patients' occupation is not available in the NHID2005 database. Certain occupational groups involving physically demanding manual labour and noise exposure may be predisposed to spondylosis and tinnitus, respectively. Finally, young patients who had asymptomatic spondylosis or mild symptoms may not seek medical assistance. It is very likely that cervical spondylosis was under-diagnosed in young patients. While in the absence of any epidemiological associations, the amount of cervical spondylosis cases, and the chance of being diagnosed with cervical spondylosis, should be balanced between cases and controls.

In conclusion, our study found a positive association between cervical spondylosis and subsequent tinnitus. The results call for awareness of possible somatosensory factors arising in the cervical spine as a contributing factor to tinnitus, especially among older adults. Our epidemiologic study points to an association that merits further research to validate spondylosis as a risk factor for tinnitus.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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