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Hearing loss is associated with increased stroke risk in the Dongfeng-Tongji Cohort

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HIGHLIGHTS

- Hearing loss levels were associated with stroke or its subtypes prevalence at speech- or high-frequency.
- Stratified analysis and conjoint analysis at speech- or high-frequency.
- Hearing loss might be a useful 'marker' to warn people about stroke risk.

ARTICLE INFO

Keywords:
Hearing loss
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Dose-response relationships
The cross-sectional study

ABSTRACT

Background and aims: The evidence concerning the association between hearing loss and stroke is limited. We aimed to investigate the association of hearing loss with risk of stroke and its subtypes among the middle-aged and older Chinese population.

Methods: We included 19,238 participants aged 64.6 years from the Dongfeng-Tongji Cohort in 2013. Hearing loss was classified into normal, mild, moderate, severe or greater levels by the pure tone average at speech frequency and high frequency, respectively. We calculated the odds ratios of hearing loss and stroke by logistic regression models.

Results: With the increase of hearing loss level, the prevalence risk of stroke has gradually increased. Compared with normal hearing, participants having severe or greater hearing loss had a higher stroke risk of 76% and 39% at speech frequency and at high frequency, respectively. Similarly, individuals with severe or greater hearing loss had an increased risk of ischemic stroke of 69% and 52% at speech frequency and high frequency, respectively; while severe or greater hearing loss was associated with about a 2-fold risk of hemorrhagic stroke than normal hearing only at speech frequency. Stratified analysis suggested that some high cardiovascular risk participants such as male, age ≥ 65, exposed to occupational noise, smoker and with diabetes, hypertension or hyperlipidemia had higher risk of stroke. Furthermore, severe or greater hearing loss combined with age, diabetes, hypertension and hyperlipidemia had joint effects on stroke.

Conclusions: The results have suggested a dose-response relationship between hearing loss and stroke risk in middle-aged and older adults.

Abbreviations: BMHS study, Blue Mountains Hearing Study; DMC, Dongfeng Motor Corporation; ICD, the international classification of diseases; MET, metabolic equivalent; MRI, magnetic resonance imaging; PTA, pure-tone average

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1. Introduction

Stroke is one of the leading cause of death for Chinese and the prevalence of stroke increased rapidly [1]; while hearing loss is a common chronic condition in older adults [2] and it is prevalent in nearly two thirds of Chinese adults aged 60 years and older [3]. Both stroke and hearing loss have become increasingly important public health issues, but there are few studies examining the relationship of hearing loss to stroke or its subtypes.

An earlier cross-sectional study in the Framingham cohort (n = 1662) has shown that low- or high pure-tone average (PTA) of 40-dB hearing level is related to elevated risks of stroke [4]. Gopinath et al. [5] have observed moderate to severe hearing loss (> 40 dB) has a higher risk of reporting previous stroke (n = 1394). Similarly, Friedland et al. [6] have found a cross-sectional relationship of low-frequency hearing loss (> 25 dB) and stroke among Americans (n = 1168). In addition, Liljas et al. have found that British men aged 63–85 years having self-reported hearing impairment are more likely to have prevalent stroke (n = 1074) [7]. However, previous studies are limited by small sample size, self-reported hearing loss or a relatively limited potential confounders. More importantly, these studies have not addressed issues of dose response. Therefore, we aimed to investigate whether there is a dose-response relationship between hearing loss and the prevalence of stroke or its subtypes, whether the association is modified by cardiovascular disease (CVD) risk factors and whether CVD risk factors and hearing loss have joint effects on stroke.

2. Materials and methods

2.1. Study population

The Dongfeng-Tongji Cohort study was launched in 2008 among retirees of Dongfeng Motor Corporation (DMC) in Shiyan City, Hubei province, and the details were described previously [8]. After the first follow-up in 2013, a total of 38,295 retirees were recruited. All participants completed a semi-structured questionnaire, took medical examinations and provided fasting blood samples. Among the 38,295 participants, 20,587 individuals completed the audiometry examination. We excluded missing audiometric data (n = 211) and participants who had conductive hearing loss (n = 106, otitis media, congenital deafness, infective deafness and traumatic deafness), drug-induced deafness (n = 434), sudden deafness (n = 514) and unknown deafness (n = 79) [9] and suspected strokes (n = 6). In the present study, strokes with medical records available for review and then confirmed by physicians were regarded as definite cases; suspected strokes for which confirmatory information was obtained by telephone or medical insurance documents but for which no medical records were available were regarded as probable cases. After these exclusions, 19,238 participants were included in the analysis. Compared to the excluded individuals, the included participants were more likely to be females, non-smokers, drinkers, well-educated, physically active, exposed to less occupational noise, and with a greater proportion of diabetes, hypertension and hyperlipidemia (Supplementary Data 1). The study is approved by the Medical Ethics Committee of the School of Public Health, Tongji Medical College and Dongfeng General Hospital, DMC, and conformed to the ethical guidelines of the 1975 Declaration of Helsinki. All participants have provided written informed consent.

2.2. Ascertainment of hearing loss

Audiometric testing was performed by trained professional staffs, using Micro-DSP ZD-21 audiometer (Sichuan Micro-DSP Technology Co, Ltd, China) in a sound-isolating room at the DMC-owned hospital. We measured air-conduction hearing thresholds using pure tone at five frequencies (0.5, 1, 2, 4 and 8 kHz), and the intensity range of instrument is −10 to 120 dB. Hearing loss levels were defined as normal hearing (≥0 dB, ≤ 25 dB), mild hearing loss (> 25 dB, ≤ 40 dB), moderate hearing loss (> 40 dB, ≤ 60 dB) and severe or greater hearing loss (> 60 dB) in accordance with the definition of the World Health Organization [10,11], and based on the arithmetic mean of hearing thresholds (in decibels) at speech frequency (0.5, 1 and 2 kHz) or high frequency (4 and 8 kHz) in each ear [6,9,12,13].

2.3. Assessment of covariates

We collected information on socio-demographic characteristics (age, sex, education and marital status), smoking status (current, former, never), alcohol drinking status (current, former, never), physical activity, occupational history, and family and personal disease histories in face-to-face interviews. Never smokers were defined as persons who had never been smoking more than one cigarette a day in their lifetime; former smokers were daily smokers who were abstinent for at least 6 months; current smokers were those who reported having smoked at least one cigarette daily for more than 6 months. We classified smokers as former smokers and current smokers in this analysis. Never drinkers were defined as persons who had never been drinking more than once a week in their lifetime; those who had abstained the previous drinking six months or more were defined as former drinkers. Participants who were drinking at least once a week for more than six months were defined as current drinker [14]. Similarly, former drinkers and current drinkers were considered as drinkers. We defined physical activity as metabolic equivalent (MET) hours per week ≥7.5 MET-hours/week in accordance with the recommended minimum of World Health Organization (WHO) physical activity guidelines [15], and MET was calculated by the following formula: MET coefficient of activity × duration (hours per time) × frequency (times per week) [16]. Occupational exposure records including noise exposure in DMC each year were also obtained. Participants with being exposed to greater than 80 dB at work for at least a year were classified as "occupational noise exposure" [17]. Height and weight were measured once by trained personnel. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters square. Participants also were asked about previous medical diagnoses and about their family history of chronic disease (limited to first-degree family members and doctor diagnosed conditions), including stroke, coronary heart disease and others [8,18]. Hypertension was defined as participants with blood pressure ≥140/90 mmHg, or self-reported physician diagnosis of hypertension, or current use of anti-hypertensive medication [19]. Diabetes was defined as self-reported physician diagnosis of diabetes, plasma glucose level ≥7.0 mmol/L, or taking oral hypoglycemic medication or insulin [20]. Hyperlipidemia was defined as total cholesterol ≥5.72 mmol/L or triglycerides ≥1.70 mmol/L at medical examination, or a previous self-reported physician diagnosis of hyperlipidemia, or taking lipid-lowering medication [18].

2.4. Stroke ascertainment

The outcome of interest was prevalent stroke (the *International Classification of Diseases, Tenth Revision* [ICD-10] codes [21]: I60−I61, I63−I64, I69.0-I69.1, and I69.3-I69.4) that first occurred at the first follow-up in 2013. A panel of physicians reviewed the medical records and confirmed stroke diagnoses following the WHO criteria as a constellation of sudden or rapid onset of a neurological deficit of vascular origin that persisted more than 24 h or till death [22]. A stroke diagnosis was made when the patient had typical clinical symptoms and supporting evidence from computed tomography (CT) and/or magnetic resonance imaging (MRI) was found. Stroke subtypes were carefully classified by physicians according to CT and/or MRI diagnoses into two major categories: a) ischemic stroke, including subtypes of large-artery occlusive infraction, lacunar infarction, cardioembolic infarction and other demonstrated cause of infraction according to the TOAST classification [23]; b) hemorrhagic stroke, including subtypes of intracerebral hemorrhage and subarachnoid hemorrhage. Totally, 877 stroke cases (737 ischemic stroke and 140 hemorrhagic stroke) have been observed in the present study.

2.5. Statistical analysis

The differences of basic characteristics among groups according to hearing loss levels were evaluated by *t*-test for continuous variables and chi-square test for categorical variables. Test for trend was evaluated with linear or logistic regression using the median value of each hearing loss level as an ordinal variable after adjusting for age and sex. Multivariate logistic regression models were used to assess the associations of hearing loss levels with the risk of stroke or its subtypes. Test for linear trend was performed using the median hearing threshold for each level as a continuous variable in the models. Stratified analyses were also conducted by CVD risk factors, and we also included an interaction product term in the model to analyze potential interactions between hearing loss and main factors. Statistical data were analyzed with SAS, version 9.4 (SAS Institute Inc. Cary, NC, USA) and all statistical tests were two-sided, and *p* values below 0.05 were considered statistically significant.

3. Results

The demographics and other selected characteristics of the studied population by categories of hearing loss levels are shown in Table 1. Participants' age mean is 64.6 (age range: 36.7–93.0) years. Compared with normal hearing, participants with severe or greater hearing loss were more likely to be older adults, males, smokers, drinkers, less educated, physically inactive, exposed to less occupational noise, and to have a greater proportion of diabetes, hypertension and hyperlipidemia at speech frequency. Similar characteristics were also found at high frequency, except for more occupational noise exposure and lower prevalence of hyperlipidemia.

As shown in Table 2, after multivariate adjustment for potential confounders, increasing hearing loss levels were independently associated with an elevated risk of stroke. Compared to participants with normal hearing, the multivariate-adjusted odd ratio (OR) (95% CI) of stroke was 1.13 (0.96, 1.33), 1.21 (0.97, 1.50), 1.76 (1.30, 2.38) for mild-, moderate- and severe or greater hearing loss at speech frequency (p for trend = 0.001), and 1.08 (0.79, 1.47), 1.18 (0.88, 1.59), 1.39 (1.02, 1.89) at high frequency (p for trend = 0.006), respectively. Similarly, there was a dose-response relationship observed but with slightly higher ORs between hearing loss and ischemic stroke both at speech frequency and high frequency; while the positive relationship of hearing loss were observed with the risk of hemorrhagic stroke only at speech frequency (OR = 2.23; 95% CI: 1.09 to 4.57; p for trend = 0.031), but not at high frequency. Cubic spline regression further showed that the risk of stroke or ischemic stroke increased gradually with prolonged hearing loss thresholds (Fig. 1).

Stratified analyses found that the association between severe or greater hearing loss and increased odds of stroke (Fig. 2) or ischemic stroke (Supplementary Data 2) was seen in individuals who were male, age ≥ 65, smoker, exposed to occupational noise, and with diabetes, hypertension or hyperlipidemia, but no significant interactions. Furthermore, severe or

Table 1
Basic characteristics of the study population according to hearing loss levels.

Characteristics	Hearing loss levels (dB)				p trend
	Normal (≥0, ≤25)	Mild (> 25, ≤40)	Moderate (> 40, ≤60)	Severe or greater (> 60)	
Speech frequency (0.5, 1 and 2 kHz)					
No. of subjects	9522	6698	2349	669	
Age (years)	61.5 ± 7.7	66.5 ± 7.5	69.8 ± 8.2	71.1 ± 8.3	< 0.001
Sex (male, %)	38.4	47.6	52.5	52.8	< 0.001
BMI (kg/m^2)	24.1 ± 3.3	24.4 ± 3.4	24.3 ± 3.4	24.3 ± 3.5	0.403
Education (%)					< 0.001
Primary school or below	15.8	24.7	31.1	39.0	
Junior school	35.7	36.6	35.2	33.5	
Senior or above	48.5	38.7	33.7	27.5	
Physical activity (%)	80.1	79.3	75.7	73.6	< 0.001
Occupational noise exposure (%)	37.5	37.5	35.9	32.8	< 0.001
Smokers (%)	24.2	30.4	30.9	31.9	0.094
Drinkers (%)	29.6	31.1	31.9	30.0	0.198
Diabetes (%)	19.0	23.5	26.2	27.0	0.003
Hypertension (%)	58.7	68.0	71.1	74.3	0.853
Hyperlipidemia (%)	51.4	54.2	53.7	51.5	0.089
Stroke (%)	35.5	39.1	17.4	8.0	< 0.001
Family history of stroke (%)	8.3	6.0	4.7	5.4	0.345
High frequency (4 and 8 kHz)					
No. of subjects	3330	4585	6210	5113	
Age (years)	57.3 ± 6.6	61.8 ± 7.1	66.1 ± 7.2	70.0 ± 7.4	< 0.001
Sex (male, %)	14.0	31.7	49.6	67.0	< 0.001
BMI (kg/m^2)	23.9 ± 3.2	24.3 ± 3.3	24.4 ± 3.3	24.3 ± 3.4	0.009
Education (%)					< 0.001
Primary school or below	9.0	16.7	23.5	31.6	
Junior school	32.2	36.5	37.3	35.9	
Senior or above	58.8	46.8	39.2	32.5	
Physical activity (%)	79.2	79.5	79.5	77.8	< 0.001
Occupational noise exposure (%)	35.3	36.2	37.8	38.3	< 0.001
Smokers (%)	8.8	21.0	31.2	40.8	< 0.001
Drinkers (%)	20.7	26.1	32.7	37.8	0.013
Diabetes (%)	15.1	19.2	23.7	25.8	< 0.001
Hypertension (%)	50.2	58.7	67.9	72.8	0.070
Hyperlipidemia (%)	51.7	53.9	53.9	50.6	< 0.001
Stroke (%)	7.2	16.0	33.8	43.0	< 0.001
Family history of stroke (%)	10.1	7.8	6.4	4.9	0.409

Data was presented as means ± SD for continuous variable and numbers (percentage) for category variables. p for trend tested with linear regression for continuous variables or logistic regression for category variables using the median hearing threshold for each hearing loss level after adjusting for age and sex, except for itself. BMI: body mass index.

Table 2
Adjusted ORs (95% CIs) for stroke by hearing loss levels.

Hearing loss levels	Speech frequency (0.5, 1 and 2 kHz)			High frequency (4 and 8 kHz)		
	Case/participants	Model 1	Model 2	Case/participants	Model 1	Model 2
Stroke						
Normal	311/9522	1.00 (Ref.)	1.00 (Ref.)	63/3330	1.00 (Ref.)	1.00 (Ref.)
Mild	343/6698	1.20 (1.01, 1.40)	1.13 (0.96, 1.33)	140/4585	1.16 (0.86, 1.57)	1.08 (0.79, 1.47)
Moderate	153/2349	1.24 (1.00, 1.54)	1.21 (0.97, 1.50)	297/6210	1.36 (1.02, 1.81)	1.18 (0.88, 1.59)
Severe or greater	70/669	1.94 (1.50, 2.59)	1.76 (1.30, 2.38)	377/5113	1.63 (1.21, 2.21)	1.39 (1.02, 1.89)
p for trend		< 0.001	0.001		< 0.001	0.006
Hearing loss (per 10 dB)	877/19238	1.11 (1.06, 1.16)	1.09 (1.04, 1.14)	877/19238	1.09 (1.05, 1.13)	1.07 (1.02, 1.11)
Ischemic stroke						
Normal	258/9469	1.00 (Ref.)	1.00 (Ref.)	47/3314	1.00 (Ref.)	1.00 (Ref.)
Mild	292/6647	1.19 (1.00, 1.42)	1.12 (0.94, 1.35)	124/4569	1.35 (0.96, 1.90)	1.27 (0.90, 1.80)
Moderate	130/2326	1.22 (0.97, 1.53)	1.18 (0.94, 1.50)	248/6161	1.47 (1.05, 2.04)	1.28 (0.92, 1.80)
Severe or greater	57/656	1.80 (1.31, 2.46)	1.69 (1.22, 2.35)	318/5054	1.75 (1.25, 2.47)	1.52 (1.07, 2.15)
p for trend		0.001	0.003		0.001	0.016
Hearing loss (per 10 dB)	737/19098	1.10 (1.04, 1.15)	1.08 (1.03, 1.14)	737/19098	1.07 (1.03, 1.12)	1.06 (1.01, 1.11)
Hemorrhagic stroke						
Normal	53/9264	1.00 (Ref.)	1.00 (Ref.)	16/3283	1.00 (Ref.)	1.00 (Ref.)
Mild	51/6406	1.18 (0.79, 1.76)	1.18 (0.80, 1.77)	16/4461	0.56 (0.28, 1.14)	0.49 (0.24, 1.01)
Moderate	23/2219	1.39 (0.83, 2.34)	1.36 (0.80, 2.31)	49/5962	1.04 (0.56, 1.92)	0.90 (0.49, 1.67)
Severe or greater	13/612	2.84 (1.49, 5.41)	2.23 (1.09, 4.57)	59/4795	1.28 (0.67, 2.44)	1.04 (0.54, 1.99)
p for trend		0.003	0.031		0.044	0.164
Hearing loss (per 10 dB)	140/18501	1.16 (1.04, 1.29)	1.11 (0.99, 1.25)	140/18501	1.15 (1.05, 1.27)	1.11 (1.01, 1.23)

Model 1: Adjusted for age and sex.
Model 2: Additional adjustment for BMI, education, physical activity, occupational noise exposure, smokers, drinkers, hypertension, diabetes, hyperlipidemia and stroke family history.

greater hearing loss combined with age, diabetes, hypertension and hyperlipidemia had joint effects on stroke (all *p* for trend < 0.05). The risk of stroke for age ≥65, diabetes, hypertension and hyperlipidemia subjects with severe or great hearing loss was ranging from about 2- to 4-fold compared with either at speech frequency (Fig. 3), and a similar combined effect was observed at high frequency (Supplementary Data 3).

The prevalence of hearing loss increased with occupational noise in different age groups. The prevalence of hearing loss was significantly higher among subjects exposed to occupational noise than those without occupational noise exposure at 1 kHz, 2 kHz, 4 kHz and 8 kHz after controlling age groups (all *p* values < 0.05) (Supplementary Data 4).

4. Discussion

Our study has found a dose-response between hearing loss and risk of stroke or ischemic stroke at speech- and high-frequency, while only has found a positive association of hearing loss with hemorrhagic stroke at speech frequency.

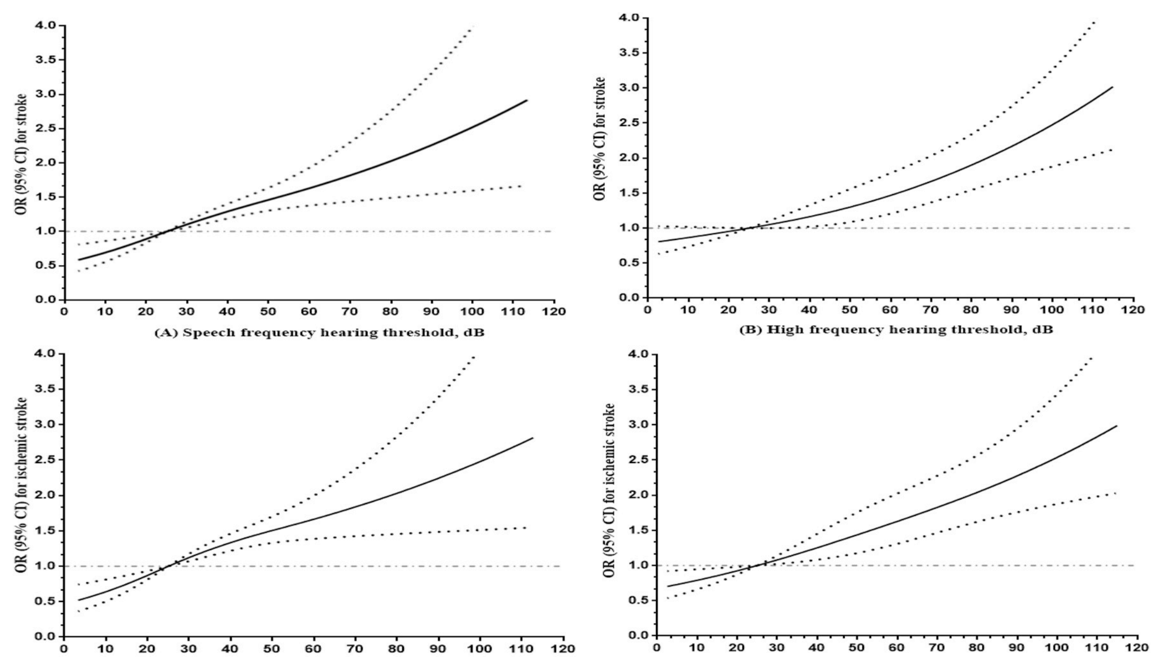

Fig. 1. Multivariable adjusted spline curves for relation between hearing loss with stroke or its subtypes.
(A) Speech or (B) high frequency hearing loss and stroke, (C) speech or (D) high frequency hearing loss and ischemic stroke. All covariates were age, sex, BMI, education, physical activity, occupational noise exposure, smokers, drinkers, hypertension, diabetes, hyperlipidemia and stroke family history. Each group adjusted for the other covariates except itself. The reference groups were normal hearing.

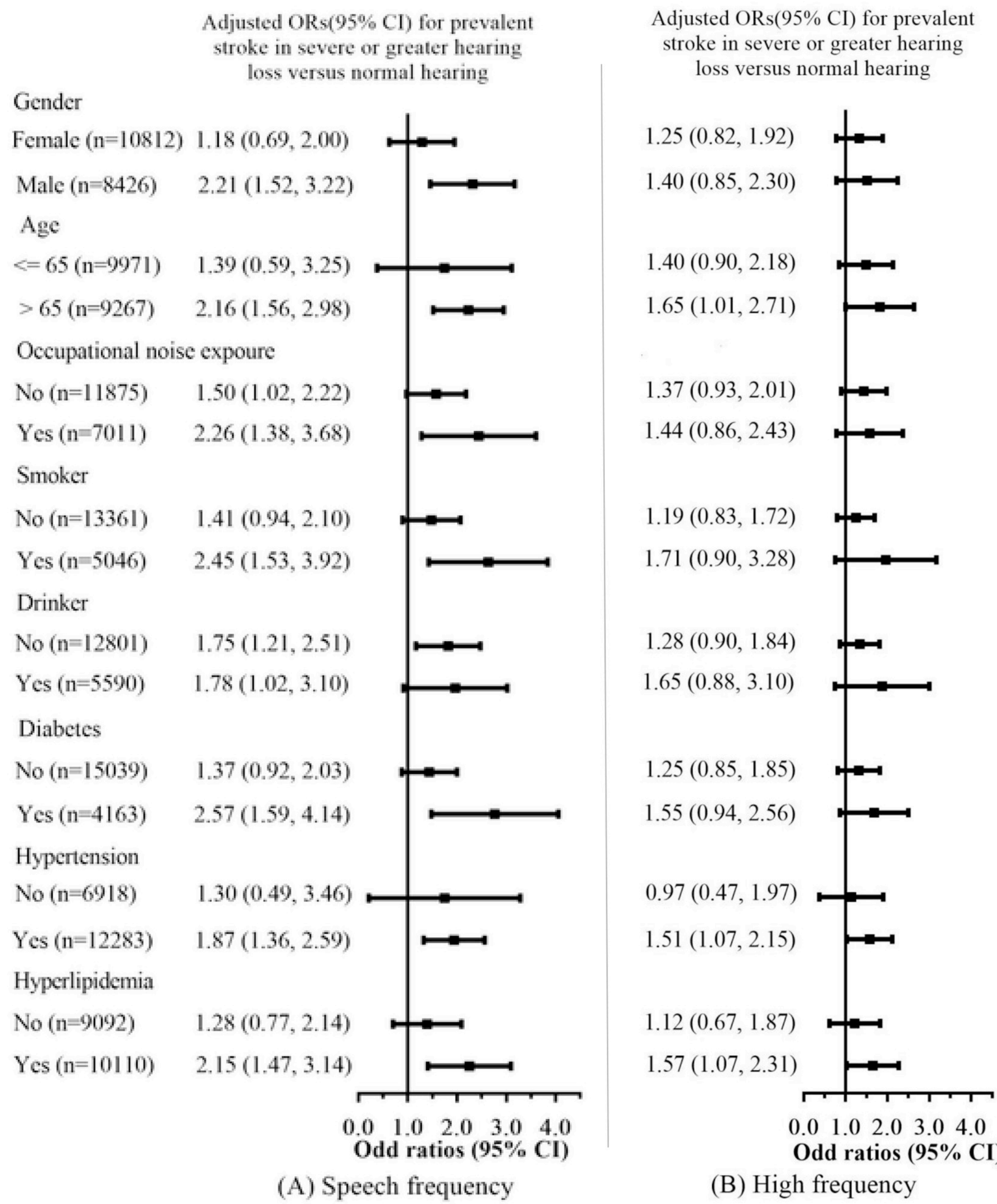

Fig. 2. Adjusted odds ratios (95% CI) for prevalent stroke in individuals with severe hearing loss at (A) speech frequency and (B) high frequency compared with the reference groups.

All covariates were age, sex, BMI, education, physical activity, occupational noise exposure, smokers, drinkers, hypertension, diabetes, hyperlipidemia and stroke family history. Each group adjusted for the other covariates except itself. The reference groups were normal hearing.

There are several studies to observe a significant association between hearing loss and stroke risk, but none have shown a dose-response as our study suggested. Both the Framingham study [4] (n = 1662) and the Blue Mountains Hearing Study (BMHS study) [5] (n = 1394) have found that participants with hearing loss are 2–4 fold more likely to have prevalent stroke than those with normal hearing, but only 1–2 fold in our study. Inherent and environmental differences might explain the discordant results. The mean ages and stroke prevalence of participants (72.9 years and 7.5% in Framingham study; 73.8 years and 10.5% in BMHS study) are higher than our study (64.6 years; 4.6%) In addition, these two studies [4,5] have defined hearing loss as above 40 dB, while our study has defined hearing loss as above 25 dB. And the BMHS study has used speech frequency (PTA of 0.5, 1.0, 2 kHz and 4.0 kHz) to analyze the association, but our study has used speech frequency (PTA of 0.5, 1 and 2 kHz) and high frequency (PTA of 4 and 8 kHz). What's more, both studies [4,5] have not accounted for other important confounders such as BMI, education, physical activity, occupational noise exposure, drinking, hyperlipidemia and family history of stroke, which might have resulted in unmeasured or residual confounding of their risk estimates. Recently, a cross-sectional study of 3981 British men aged 63–85 years has shown that subjects who could not hear despite using hearing aids had 1.81 fold risk for stroke prevalence compared with those could hear [7]. However, the study of self-reported hearing loss based on hearing aid could not further explore the relationship between hearing threshold and stroke at different frequencies. Another study of 1168 patients has reported that low-frequency hearing loss (PTA $>$ 25 dB) is associated with stroke, while the relationship of high frequency hearing loss with stroke is not clear [6].

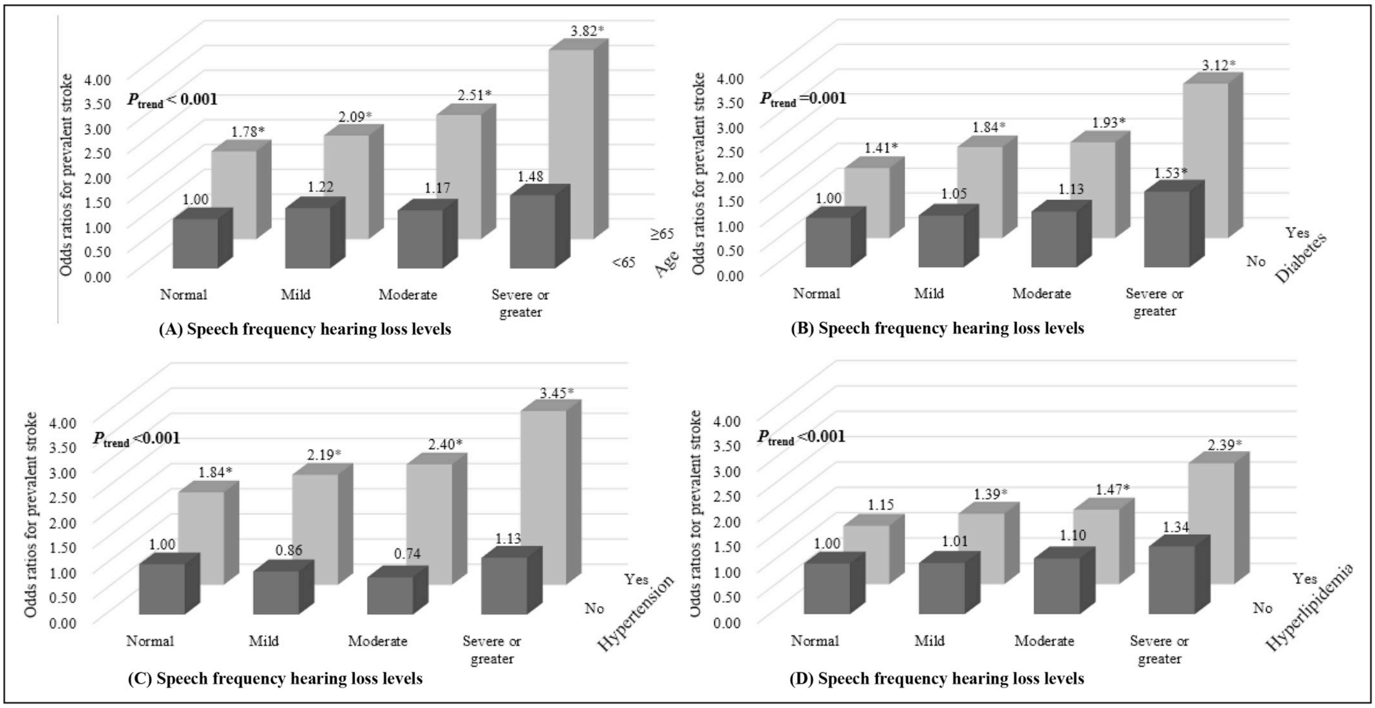

Fig. 3. Combined effects of speech-frequency hearing loss and (A) age ≥ 65, (B) hyperglycemia, (C) hypertension or (D) dyslipidemia on the risk of stroke prevalence. The odds ratio was compared with a reference group (normal hearing and age < 65, non-hyperglycemia, non-hypertension or non-dyslipidemia, respectively), with models adjusted for age, sex, BMI, education, physical activity, occupational noise exposure, smokers, drinkers, hypertension, diabetes, hyperlipidemia and stroke family history, except for combined covariates. *$p < 0.05$.

Compared with above studies, our study has demonstrated a strong dose-response relationship between hearing loss and stroke or ischemic stroke at speech- or high frequency after adjusting a wide range of traditional CVD risk factors.

Interestingly, the above-mentioned relationship of severe or greater hearing loss and stroke or ischemic stroke has seemed to be more prominent in male, the older adults, smoker, and participants with occupational noise exposure, diabetes, hypertension or hyperlipidemia. Our observation is partly supported by the Framingham study [4] in which stroke prevalence is more strongly linked to speech-frequency hearing loss in men. Moreover, our earlier study among high CVD risk population similarly has demonstrated a stronger dose–response relationship between hearing loss and risk of coronary heart disease [9]. It might be possible that the effects of traditional CVD risk factors would strengthen the detrimental effect of hearing loss on prevalent stroke in high-risk individuals. Additionally, different results between speech- or high-frequency hearing loss and the ischemic or hemorrhagic stroke might be caused by different mechanisms. Speech frequency hearing loss is felt to be due to cochlear aging [24], stria vascularis involvement [25], smoking [26] and diabetes [27]. While high frequency hearing loss is likely due to occupational noise exposure [28] and outer or inner hair cell dysfunction [29], which has likely a component of ischemia rather than hemorrhage.

Furthermore, we observed joint effects of hearing loss with age, diabetes, hypertension or hyperlipidemia, respectively, on prevalent stroke, and the underlying mechanisms of associations might be explained by these traditional CVD risk factors. Other potential mechanisms concerning hearing loss and stroke might be explained by vascular ischemia. Hearing loss occurred due to microvascular damage [25], which gradually developed into ischemia in vertebrobasilar artery; while vertebrobasilar artery ischemia played an important role in the development of stroke [30,31]. A prior study has reported that patients had hearing loss as an isolated manifestation from 1 day to 2 months before anterior inferior cerebellar artery infarction, indicating that hearing loss can be a characteristic sign of a vertebrobasilar circulatory disturbance [32]. It might be another potential mechanism to explain the relationship of hearing loss and stroke, while our study suggested that stroke lead to hearing loss as a temporal relationship could not be determined. In addition, the common central neurological, anatomical and physiological processes might contribute to the relationship of hearing loss and stroke. Participants with hearing loss, especially moderately or greater hearing loss, had greater odds of depressive, anxiety symptoms and stress, compared to those with normal hearing [33], and a review found that anxiety disorders were associated with risk of stroke increased by 24% [34].

Although it is hard to correlate hearing loss with stroke risk in clinical practice, this clinical relevance could alert doctors to pay more attention to patients with severe hearing loss. Some limitations of the current study should be addressed. Due to its cross-sectional nature, our study could not demonstrate a causal relationship of hearing loss and stroke. In addition, our population is middle-aged and older adults, and thus the results could not generalize to other populations of all ages, different health conditions or other ethnicities. Thirdly, although major potential confounders are included in our analysis, other unselected or unmeasured covariates are not included in our study such as psychological risk factors. Finally, the missing hearing thresholds at 3 and 6 kHz is also one of our study's limitations.

In conclusion, our data have suggested that a dose-response relationship between hearing loss and the prevalence of stroke. Although our study has made the relevance of hearing loss and stroke risk in clinical practice, we are required more future prospective studies and randomized clinical trials to enable relevance and causality of hearing loss and stroke.

Conflicts of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

Author contributions

Q. Fang, X. Zhang had full access to all the data in the study and took responsibility for the integrity of the data and accuracy of the data analysis. Study concept and design: H. Yang, W. Kong, T. Wu, X. Zhang. Acquisition, analysis or interpretation of data: all authors. Drafting of the manuscript: Q. Fang, X. Lai; L. Yang, X. Zhang. Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: Q. Fang, X. Zhang. Obtained funding: T. Wu, and X. Zhang. Administrative, technical, or material support: Z. Wang, Y. Zhan, L. Zhou, Y. Xiao, H. Wang, D. Li, K. Zhang, T. Zhou, H. Guo, M. He. Study supervision: T. Wu, W. Kong, X. Zhang. All authors agree to submit the report for publication.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.atherosclerosis.2019.03.012.

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