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A Prospective Study of Cardiovascular Risk Factors and Incident Hearing Loss in Men

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Abstract

Objective—Hearing loss is the most common sensory disorder in the US, afflicting over 36 million people. Cardiovascular risk factors have been associated with hearing loss risk in cross-sectional studies, but prospective data are currently lacking.

Methods—We prospectively evaluated the association between diagnosis of hypertension, diabetes mellitus, hypercholesterolemia, smoking and body mass index (BMI) and incidence of hearing loss. Participants were 26,917 men in the Health Professionals Follow-up Study, aged 40-74 years at baseline in 1986. Study participants completed questionnaires about lifestyle and medical history every two years.

Information on self-reported professionally diagnosed hearing loss and year of diagnosis was obtained from the 2004 questionnaire, and cases were defined as hearing loss diagnosed between 1986 and 2004. Multivariable-adjusted hazard ratios (HRs) were calculated using Cox proportional hazards regression models.

Results—3,488 cases of hearing loss were identified. History of hypertension (HR 0.96, 95% CI 0.88-1.03), diabetes mellitus (HR 0.92, 95% CI 0.78-1.08), or obesity (HR 1.02, 95% CI 0.90-1.15 for BMI≥30 compared to normal range of 19-24.9) was not significantly associated with hearing loss risk, while hypercholesterolemia (HR 1.10, 95% CI 1.02-1.18) and past smoking history (HR 1.09, 95% CI 1.01-1.17) were associated with a significantly increased risk of hearing loss after multivariate adjustment.

Conclusion—A history of hypertension, diabetes mellitus, or obesity is not associated with increased risk of hearing loss, while a history of past smoking or hypercholesterolemia has a small but statistically significant association with increased risk of hearing loss in adult males.

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Introduction

Hearing loss is the most common sensory disorder afflicting US adults, with over 36 million Americans suffering from this condition[1]. The highest prevalence of hearing loss is in the older adult population, with over half of the cases found in people over the age of 65[2]. In this older adult age group, the majority of new cases are attributed to age- related hearing loss[3]. As this segment of the population has grown, the prevalence of age-related hearing loss has continued to increase[4]. Despite the high prevalence of hearing loss, limited epidemiologic data currently exist on the risk factors and potential mechanisms for this condition. Cross-sectional studies have evaluated the relation between a limited number of risk factors and the prevalence of hearing loss, however there is scant prospective human information on potential risk factors for hearing loss[2,5].

Common cardiovascular risk factors may play an important role in the pathogenesis of age-related hearing loss by affecting the cochlear microvasculature. Specifically, the vascular nature of the stria vascularis may make it especially vulnerable to vascular compromise[6]. Strial presbycusis, a distinct class of age-related hearing loss described by Schuknecht[7,8], has been shown in cross-sectional analyses to be significantly associated with incident cardiovascular disease, with a demonstrated increased risk of stroke, coronary artery disease and myocardial infarction in individuals with this condition[6]. Nationally representative prevalence data have also indicated an increased prevalence of hearing loss in individuals with a history of hypertension, diabetes mellitus or smoking[2]. These results, however, have only been shown in cross-sectional analyses.

The potential relation between common cardiovascular risk factors, including elevated BMI, smoking, hypertension, diabetes mellitus, and elevated cholesterol and incident hearing loss is yet to be definitively determined in human subjects. The significance of identifying such associations could lead to enhanced understanding of potential underlying pathophysiologic mechanisms for age-related hearing loss. Therefore, we prospectively evaluated the association between cardiovascular risk factors and development of hearing loss in an adult male cohort.

Methods

Participants

The Health Professionals Follow-up Study enrolled 51,529 male dentists, optometrists, osteopaths, pharmacists, podiatrists, and veterinarians who were 40-74 years of age at baseline in 1986. Participants filled out a detailed questionnaire about diet, medical history, and medication use. These questionnaires have been administered every other year, and the 20-year follow-up exceeds 90%. The 2004 long form questionnaire included a question regarding whether the participant had been professionally diagnosed with hearing loss, and if so, the date of diagnosis. Of the 34,884 men who responded to the long form questionnaire, 7092 (20.3%) reported a diagnosis of hearing loss. Those who reported hearing loss diagnosed before 1986 (n=2445) or cancer other than non-melanoma skin cancer were excluded from the analysis. Recent data from the National Health and Nutrition Examination Survey (NHANES) demonstrated that 43% of white men aged 60-69 exhibit hearing loss in the low-mid frequency range, and 93% exhibit high frequency hearing loss[2]. Thus, because age is such a strong risk factor and the prevalence of hearing loss is so high among the elderly, we also excluded men as they reached age 75 during follow-up.

Ascertainment of Exposure

Exposures of interest were body mass index (BMI), smoking, hypertension (HTN), diabetes mellitus (DM), and elevated cholesterol. Questionnaire responses were used to compile the

participants' medical information. Height and weight were obtained on the baseline questionnaire and self-reported weight has been updated every two years. BMI was calculated as weight in kilograms divided by the square of height in meters. Participants were asked if they currently smoke cigarettes and the number of cigarettes per day (1-4, 5-14, 15-24, 25-34, 35-44, and >34). Those who answered no to currently smoking cigarettes but had reported smoking cigarettes in the past were defined as past smokers.

Participants were defined as having hypertension if they had been diagnosed with hypertension by a health professional or if they were taking an antihypertensive medication. Self-reported hypertension has previously been validated in this cohort[9,10]. Similarly, they were defined as having elevated cholesterol if they reported being diagnosed with the condition by a health professional or if they were taking a cholesterol lowering medication. Participants were defined as having diabetes mellitus if they had been diagnosed with the condition by a health professional. Self-reported diabetes has been shown to be highly sensitive in this cohort[11].

Ascertainment of Outcome

The primary outcome, self-reported professionally diagnosed hearing loss, was defined as a "yes" response to the question "Have you ever had professionally diagnosed hearing loss?" This question was asked only on the 2004 Long Form Questionnaire. Those who answered "yes" were additionally asked for the year of first diagnosis (before 1986, 86-87, 88-89, 90-91, 92-93, 94-95, 96-97, 98-99, 00-01, 02, 03, 04).

Ascertainment of Covariates

Covariates considered in the multivariate analysis included: age, race, physical activity and regular aspirin, acetaminophen, or NSAID use. Age and race were obtained from the biennial questionnaires. Information on physical activity was updated every 2 years and has been previously validated in this cohort[12]. Regular intake, defined as two or more times per week, of aspirin, acetaminophen, or NSAIDs[13] was updated every two years.

Statistical Analyses

All analyses were prospective, using exposure information that was collected prior to the diagnosis of hearing loss. For the primary analyses, history of hypertension, diabetes, and elevated cholesterol were categorized as either having or not having a history of the given condition. BMI was categorized as <19, 19-24 (reference group), 25-29, ≥30 kg/m^2, according to the WHO international classification[14]. . Smoking was categorized into never smoker (reference group), past smoker, and current smoker (1-4, 5-14, >14 cigarettes/day).

For each participant, person-time was allocated based on the response to the medical history questions at the beginning of each follow-up period. The medical history questions were updated every two years, and the person-time was measured between the response to the medical history question and either a diagnosis of hearing loss or censoring. Participants were censored at the date of diagnosis of hearing loss, age 75, or the date of death, whichever came first. Age and multivariable-adjusted hazard ratios (HRs) were calculated using Cox proportional hazards regression models. Multivariable models were adjusted for potential confounders listed above as well as simultaneously for each of the exposures of interest.

To examine whether the relation between cardiovascular risk factors and hearing loss varied by age, we performed analyses stratified by age <55 years, 55-64, and 65 and older. For all HRs, we calculated 95% confidence intervals (CIs). All P values were two-tailed. Statistical tests were performed using SAS statistical software, version 9 (SAS Institute Inc, Cary, NC).

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Results

Characteristics of the participants at study onset in year 1986 are shown in Table 1. Although updated information was used for the analysis, the characteristics presented are from the initiation of follow-up to provide representative values. During 369,079 person-years of follow-up, 3488 cases of hearing loss were reported. Past smoking and elevated cholesterol were independently associated with an increased risk of hearing loss; there was no association with BMI, hypertension and diabetes (Table 2). After adjusting for age, race, profession, BMI, smoking, hypertension, diabetes, elevated cholesterol, and regular use of aspirin, NSAIDs and acetaminophen, the multivariate HR of hearing loss in participants with a history of past smoking compared to nonsmokers was 1.09 (95%CI 1.01-1.17). The multivariate HR for elevated cholesterol compared to those with no history of elevated cholesterol was 1.10 (95%CI 1.02-1.18).

Given the age-related differences in prevalence of cardiovascular risk factors, we examined whether the relation between these risk factors and hearing loss varied by age. The association between BMI, smoking, hypertension, and diabetes and incident hearing loss did not vary significantly by age (Table 3). For elevated cholesterol, the association with incident hearing loss was greatest among men younger than 55 years of age, as men in that age group with a history of elevated cholesterol had a 28% higher risk of developing hearing loss (HR 1.28; 95%CI 1.08-1.51). The interaction between age and the association between elevated cholesterol and hearing loss, however, was not significant (p, interaction=0.32).

Discussion

Several studies have described microvascular disease as a possible mechanism for age-related hearing loss[6,15]. This is the first large prospective epidemiologic human study of the association between cardiovascular risk factors and hearing loss. Our study found no prospective association between variation in BMI or a history of hypertension or diabetes and incident hearing loss. While current smoking was not significantly associated with hearing loss risk, a history of past smoking was associated with a 9% increased risk of hearing loss. A history of elevated cholesterol was also associated with a 10% increase in hearing loss risk.

Although numerous potential mechanisms for age-related hearing loss have been studied, evidence for cardiovascular risk factors as potential risk factors for hearing loss has been demonstrated through several large cross-sectional studies. Hypertension and diabetes were shown to be associated with high frequency hearing loss prevalence in data from NHANES 1999-2004[2,5]. In our prospective analyses, however, neither hypertension nor diabetes was significantly associated with hearing loss risk in age or multivariate-adjusted models. One potential reason for these varying results is that cross-sectional studies fail to determine temporal or causative relations between a given exposure and outcome. As hearing loss has been shown to be a risk factor for cardiovascular disease independent of other cardiovascular risk factors[6], it is possible that the cochlear damage associated with cardiovascular disease occurred prior to the diagnoses of hypertension or diabetes in those studies. There is also evidence that the relation between hearing loss and vascular disease may be sex-specific, with significant associations apparent in women but not in men[16].

While past studies analyzing the relation between BMI and hearing loss have shown conflicting results, the relations between smoking history and elevated cholesterol and

hearing loss seen in our cohort are consistent with past studies. High BMI was associated with hearing loss in a recent cross-sectional European multi-center study[17], while another large cross-sectional study done in 2009 showed no significant association between BMI and hearing loss risk[18]. A weak association between smoking and age-related hearing loss was demonstrated by Rosenhall et al in 1993[19], and this has been further supported by more recent reports[20,21]. One proposed mechanism for the association between smoking history and hearing loss risk is that carbon monoxide, a common ingredient in cigarette smoke, may cause a temporary threshold shift after long-term exposure by reducing the blood's capacity to deliver oxygen to the cochlea[19]. Conversely, short term exposure to cigarette smoke has been shown to potentially reduce the temporary threshold shift following noise exposure[22], which may be a reason for the variation in findings between current and past smokers in our cohort. Although data on the association between elevated cholesterol and incident hearing loss are scant, a case-control study with 4071 cases of hearing loss demonstrated a significant association between hyperlipidemia and noise-induced hearing loss[23]. Moreover, studies have suggested that disturbances to microcirculation caused by hyperlipidemia may lead to inner ear disease[24,25].

Our study has limitations. Assessment of hearing loss was based on self-report of professionally diagnosed hearing loss and individuals who did not report hearing loss were considered not to be hearing impaired. Therefore, it is likely that cases of hearing loss were underreported. Although standard pure-tone audiometry is generally considered the gold standard of hearing loss evaluation, self-reported hearing loss has been demonstrated to be a reliable assessment[26]. Nevertheless, the sensitivity of the questionnaire in identifying cases of hearing loss is likely to be lower than that of an audiogram. Given the likely high prevalence of hearing loss in this population[2], misclassification of outcome would likely bias the results toward the null.

The outcome analyzed in this study does not distinguish among different hearing loss etiologies. While sensorineural, age-related hearing loss is likely to be the dominant pathologic process in this cohort, we were not able to quantify other common entities such as noise induced hearing loss. In addition, the nature of our outcome assessment predisposed our study to potential survival bias. While the exposure data were assessed prospectively, the hearing loss outcome was determined retrospectively with a single question asked in 2004. As the hearing loss question was only asked at the conclusion of our participants' follow-up, it is possible that individuals with cardiovascular risk factors had developed cardiovascular disease and passed away at a rate disproportionate to those without these risk factors. This could have potentially excluded individuals with specific exposures of interest from our study population.

The HPFS questionnaire has been shown to be an accurate and reliable instrument, and has been used to demonstrate numerous associations between our exposures of interest and other disease outcomes[27,28]. Moreover, prospective associations between the outcome measure in this study and several risk factors have recently been demonstrated[13,29]. The participants in this cohort are not representative of the adult population in the U.S., but the follow-up rates are high and the information provided is reliable. The observed associations are likely to apply to other groups inasmuch as the underlying biologic mechanisms are likely to be similar. However, additional studies are needed to examine these relations in women, younger men and racial groups other than caucasian.

Conclusion

In conclusion, there was no significant association between variation in BMI or a history of hypertension or diabetes and incident hearing loss. A history of past smoking or elevated

cholesterol was, however, independently associated with a small but statistically significant increase in risk of incident hearing loss. Given the aging of the population and the high prevalence of hearing gloss, identification of potential mechanisms as well as risk factors to reduce the burden of this common condition should be an important public health priority.

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Table 1

Characteristics of men in 1986

Characteristic		
Age yr		51
Race (%)	Caucasian	90.7
	African- American	0.8
	Asian	1.5
BMI kg/m^2		24.9
Smoke %	never	48.6
	past	39.8
	Current 1-4cig/d	1.0
	5-14cig/d	1.4
	15+cig/d	4.5
Hypertension %		17.4
Diabetes %		1.6
Elevated Cholesterol %		11.3
Alcohol g/day		11.2
Aspirin 2+tabs/week %		26.8
NSAID 2+tabs/week %		4.9
Acetaminophen 2+tabs/week %		5.4

means except where noted

Table 2

Multivariate- Adjusted* Hazard Ratios for Cardiovascular Risk Factors and Incident Hearing Loss

		Cases	Age-Adjusted Hazard Ratio	Multivariate-Adjusted Hazard Ratio
BMI	<19	8	0.58 (0.29-1.15)	0.63 (0.31-1.26)
	19-24 (ref)	1276	1 ref	1 ref
	25-29	1505	1.02 (0.95-1.10)	1.00 (0.92-1.08)
	≥30	373	1.11 (0.99-1.25)	1.03 (0.92-1.17)
Smoking none			1 ref	1 ref
Smoking past		1651	1.11 (1.03-1.19)	1.09 (1.01-1.17)
Smoking Current	1-4cig/d	20	0.68 (0.44-1.06)	0.66 (0.43-1.04)
	5-14cig/d	38	0.85 (0.61-1.18)	0.84 (0.60-1.16)
	15+cig/d	84	0.85 (0.68-1.06)	0.83 (0.66-1.04)
Hypertension	no		1 ref	1 ref
	yes	1293	1.04 (0.97-1.11)	0.96 (0.88-1.03)
Diabetes	no		1 ref	1 ref
	yes	164	0.96 (0.82-1.12)	0.92 (0.78-1.08)
Elevated Cholesterol	no		1 ref	1 ref
	yes	1563	1.16 (1.08-1.24)	1.10 (1.02-1.18)

*Adjusted for age, BMI, race, profession, smoking, hypertension, diabetes, elevated cholesterol, aspirin, NSAID, acetaminophen use

Table 3

Age stratified multivariate- adjusted analysis of cardiovascular risk factors and incident hearing loss

		HR (95% CI)		
		Age <55	**Age 55-64**	**Age ≥ 65**
	Cases	**675**	**1427**	**1386**
BMI	<19	No cases	0.88 (0.33-2.38)	0.61 (0.22-1.63)
	19-24	1 (ref)	1 (ref)	1 (ref)
	25-29	1.00 (0.84-1.19)	1.03 (0.91-1.16)	0.97 (0.86-1.09)
	≥30	0.77 (0.56-1.04)	1.20 (1.01-1.44)	0.99 (0.81-1.21)
Smoking None		1 (ref)	1 (ref)	1 (ref)
Smoking past		1.02 (0.86-1.20)	1.13 (1.01-1.26)	1.07 (0.96-1.20)
Smoking Current	1-4cig/d	0.97 (0.47-1.97)	0.23 (0.07-0.73)	1.02 (0.52-1.99)
	5-14cig/d	0.62 (0.27-1.39)	1.00 (0.62-1.61)	0.80 (0.46-1.37)
	15+cig/d	0.79 (0.50-1.23)	0.87 (0.63-1.21)	0.79 (0.51-1.22)
Hypertension	no	1 (ref)	1 (ref)	1 (ref)
	yes	1.01 (0.83-1.22)	0.96 (0.86-1.08)	0.98 (0.88-1.10)
Diabetes	no	1 (ref)	1 (ref)	1 (ref)
	yes	1.23 (0.73-2.07)	0.81 (0.61-1.08)	0.93 (0.75-1.16)
Elevated Cholesterol*	no	1 (ref)	1 (ref)	1 (ref)
	yes	1.28 (1.08-1.51)	1.01 (0.90-1.13)	1.14 (1.01-1.27)

Adjusted for age, BMI, race, profession, smoking, hypertension, diabetes, elevated cholesterol, aspirin, NSAD, acetaminophen use

*p-interaction 0.32