Smoking, Central Adiposity, and Poor Glycemic Control Increase Risk of Hearing Impairment

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Abstract

Objectives—To determine associations between smoking, adiposity, diabetes, and other cardiovascular disease (CVD) risk factors and the 15-yr incidence of hearing impairment (HI).

Design—The Epidemiology of Hearing Loss Study (EHLS) is a longitudinal population-based cohort study (1993–95 to 2009–2010).

Setting—Beaver Dam, WI.

Participants—Participants in the Beaver Dam Eye Study (1988–90; residents of Beaver Dam, WI ages 43–84 years in 1987–88) were eligible for the EHLS. There were 1925 participants with normal hearing at baseline.

Measurements—15-year cumulative incidence of HI (pure-tone average (PTA) of hearing thresholds at 0.5, 1, 2 and 4 kHz > 25 decibels Hearing Level (dB HL) in either ear). Cigarette smoking, exercise, and other factors were ascertained by questionnaire. Blood pressure, waist circumference, body mass index and glycosylated hemoglobin were measured.

Results—Follow-up examinations (1) were obtained from 87.2% (n=1678; mean baseline age 61 years). The 15-year cumulative incidence of HI was 56.8%. Adjusting for age and sex, current smoking (Hazard Ratio (HR) =1.31, p=0.048), education (<16 yrs; HR=1.35, p=0.01), waist circumference (HR=1.08 per 10 cm, p=0.017), and poorly controlled diabetes (HR=2.03, p=0.048) were associated with increased risk of HI. Former smokers and people with better controlled diabetes were not at increased risk.

Conclusion—Smoking, central adiposity and poorly controlled diabetes predicted incident HI. These well-known CVD risk factors, suggest vascular changes may contribute to HI in aging. Interventions targeting reductions in smoking and adiposity, and improved glycemic control in people with diabetes, may help to prevent or delay the onset of HI.

INTRODUCTION

Older adults with aging changes in hearing may have significant communication problems that may contribute to poorer quality of life and depression.[1–4] Among older adults, the risk of hearing impairment (HI) is high.[5,6] In a population-based cohort study using audiometric threshold testing, the 10-yr cumulative incidence of HI was 22% among people ages 48–59 years of age at baseline and 74% among adults 70–79 years of age.[6]

Changes in the cochlea, a hallmark of age-related HI, result in impaired signal transduction, but generalized auditory system changes affecting neural transmission and central processing also are likely to be involved in this slowly progressing degenerative disorder.[7–9] Typically, these sensorineural hearing impairments are measured by audiometry using a pure-tone-threshold average to identify people with hearing losses in the frequency range important for communication. Older adults also may experience conductive hearing losses (a large problem in pediatric populations), middle-ear changes which affect signal transmission to the inner ear and are measured by differences between air and bone conduction thresholds and/or tympanometry. However, these are rare in older adults and most often occur in ears also experiencing typical sensorineural changes, leaving sensorineural hearing losses the predominate problem in aging populations.[5]

Some studies have linked HI with risk of cognitive impairment and mortality, but the mechanisms underlying these associations are unclear.[10,11] Hearing aids may be beneficial in treating HI, but uptake and utilization rates are low and they may not be effective in some cases.[12] There are no available treatments to completely restore auditory function in most cases of adult-onset HI, suggesting that primary prevention is needed to reduce the burden of hearing loss in aging populations. Therefore, it is important to identify modifiable risk factors for HI.

Previously, we reported smokers were more likely to have prevalent HI (Odds Ratio = 1.69, 95%CI=1.31, 2.17) in the population-based Epidemiology of Hearing Loss Study (EHLS).[13] Higher circulating levels of reactive oxygen species or inflammatory markers and

atherosclerotic changes associated with smoking may damage the cochlea or result in neurodegeneration.[14,15] Other cross-sectional population-based studies also have reported associations between smoking and prevalent HI.[16,17] However, most longitudinal studies of the incidence of audiometrically-assessed HI have found no associations with smoking[16,18–20] although positive associations have been found in studies relying on self-reported hearing loss.[21,22] One five-yr follow-up study of male Japanese office workers which tested hearing at two frequencies found that men who smoked > 31 cigarettes/day were more than twice as likely as non-smokers to develop a hearing loss at 4kHz.[23]

Cross-sectional studies have suggested that obesity and diabetes may be associated with HI.[24–29] Recently, the Nurses' Health Study reported that larger waist circumference, a marker of central adiposity, was associated with increased risk of self-reported hearing loss.[30] Diabetes has not been associated with HI incidence in longitudinal studies.[22,28] Obesity and diabetes may affect the auditory system through mechanisms similar to those hypothesized for smoking: oxidative stress, inflammation, and vascular insufficiency. The purpose of the present longitudinal study of adults was to determine the prospective associations between smoking, adiposity, diabetes, and other CVD risk factors and the 15-yr incidence of HI in a large population-based cohort study.

METHODS

Population

Participants in the EHLS were residents of the Beaver Dam, WI who were 43–84 years of age in 1987–88 and had participated in the Beaver Dam Eye Study (BDES).[5,6,13] The baseline study for the EHLS occurred in 1993–95 with follow-up examinations in 1998–2000, 2003–2005 and 2009–2010. Baseline participants who were 75 years were eligible to participate in an additional examination (1995–1998). This study was approved by the Health Sciences Institutional Review Board of the University of Wisconsin and informed consent was obtained at each examination.

Analyses were restricted to participants (n=1925) with normal baseline hearing (defined as a pure-tone average (PTA) of the thresholds at 0.5, 1, 2, and 4 kHz 25 dB HL in both ears) and therefore at risk of developing HI during follow-up. Participation was high (>85%) at each examination (Table 1). Overall, 1678 (87.2%) participated in at least one subsequent examination.

Examinations

The same standardized methods were used at each examination by certified examiners.[5,6,13,31] The examination included an otoscopic evaluation, screening tympanogram (GSI 37 Autotymp, Grason-Stadler, Inc., Madison, WI), and pure-tone air- and bone-conduction audiometry. Audiometric testing was conducted in sound-treated booths using clinical audiometers equipped with TDH-50P earphones and ER-3A insert earphones.[32] Pure-tone air-conduction thresholds were obtained for each ear at 0.5, 1, 2, 3, 4, 6 and 8 kHz. Bone conduction thresholds were measured at 0.5 and 4 kHz at the baseline

examination and at 0.5, 2, and 4 kHz at subsequent examinations. Masking was used as necessary.

All audiometers were calibrated every six months.[33] People who were home-bound, lived in nursing homes or group homes and unable to come to the clinic site were tested with a portable audiometer with insert earphones. Ambient noise levels were routinely monitored at the examination site in Beaver Dam and measured at each home or nursing home visit to ensure that testing conditions complied with ANSI standards.[34] Incident hearing impairment was defined as a PTA > 25 dB HL in either ear at any follow-up examination. This definition has been used frequently in epidemiological studies to measure clinically significant sensorineural hearing loss.

Questionnaires were administered each examination to ascertain medical history, occupational history, and lifestyle and behavioral factors. Some risk factor data were collected as part of the BDES.[31] Education was classified as less or greater than 16 years. Occupations were coded according to the 1980 census classifications and major occupation classified as production, operator or farmer vs managerial, technical or service. History of a noisy job was defined as holding a fulltime job where one needed to speak in a raised voice or louder to be heard two feet away, being a farmer and driving a tractor without a cab, or having served in the military as a pilot, or airplane or tank crew member, or worked in the engine room of a ship, or used grenades, mortars, shoulder-held grenade launchers or multi-person weapons systems. Smoking status was classified as non-smoker (less than 100 cigarettes in their lifetime), ex-smoker, or current smoker. Total pack-years were defined as the number of cigarettes smoked per day divided by 20 multiplied by the years of smoking. Alcohol consumption was measured by a quantity and frequency questionnaire about beer, wine and liquor and converted to grams of ethanol per week.[31] Heavy alcohol consumption was defined as ever drinking 4+ drinks per day. Exercise was sufficient to work up a sweat at least once a week. A history of CVD was defined as reported stroke, angina or myocardial infarction. Current medications were ascertained and we created indicator variables for use of non-steroidal anti-inflammatory medications, lipid lowering agents, and statins (statins were relatively new in 1993–1995 so many participants were using other agents for treating hypercholesterolemia).

Blood pressure, height, weight, waist circumference, white blood cell count and hematocrit were measured.[31] Serum total and HDL cholesterol were measured by reflectance spectrophotometry on non-fasting samples. Non-HDL cholesterol was calculated. Glycoslyated hemoglobin (GHb) was measured by the Gly-Affin assay (Isolab, Inc. Akron, OH); according to the manufacturer the normal range for this assay was 4–8% and 'good control' was 9–12%.

Hypertension was defined as a diagnosis of hypertension with current medication use or systolic blood pressure 140 mmHg or diastolic blood pressure 90 mmHg. Body mass index was calculated (BMI; kg/m^2) and obesity defined as 30 kg/m^2. Diabetes was defined as a diagnosis of diabetes or a GHb > 8% (which corresponds to an A_1C 6.5%).[35] Central retinal arteriolar equivalent (CRAE) and central retinal venular equivalent (CRVE) were measured in right eye fundus photographs.[36]

Analyses were conducted using SAS version 9.4 software (SAS Institute, Inc., Gary, NC). Univariate analyses used the chi-square test of association for categorical variables, Mantel Haenszel chi-square test of trend for ordinal data, and t-tests of mean differences for continuous data. Product-limit (Kaplan-Meier) survival estimates were used to calculate 15-yr cumulative incidence.[37] Discrete-time Cox proportional hazards models were used because of the relatively small number of follow-up intervals.[38] Participants unimpaired at the end of follow-up were treated as censored. GHb also was incorporated into an age- and sex-adjusted discrete-time proportional hazards model using a cubic spline function in order to examine potential nonlinear associations. After constructing an age- and sex-adjusted model, additional risk factor associations were assessed in age-sex-factor Cox proportional hazards models and subsequently with a multivariable model, retaining independent risk factors and confounders.

RESULTS

Incidence of HI

The 15-yr cumulative incidence of HI was 56.8% (Table 2). The incidence increased by age among both men and women leaving few adults who were age 70 years at baseline with normal hearing by the 15-yr follow-up. Men were more than twice as likely as women to develop HI (Hazard Ratio (HR) = 2.23 (95% Confidence Interval (CI) = 1.86, 2.66) and risk increased by 90% for each 5 years of age (HR =1.90, 95%CI = 1.79, 2.02). By age 74 years, half of the men had HI with 50% of women having HI by age 80 years. The mean age at the examination with incident HI was 69.8 years for men and 75.4 years for women, (p<0.0001).

Risk Factors

Table 3 shows the age-sex-adjusted HR for each potential risk factor considered. As shown previously with 10-years of follow-up[6], participants with less education (HR vs 16+ years=1.40, 95% CI= 1.13, 1.75) and those whose major occupation was production, operator or farmer (HR vs management, technical, serice) =1.35, 95%CI=1.11,1.63) were at higher risk of HI.

Current smokers were more likely to develop HI than never-smokers (HR=1.36, 95%CI=1.05, 1.77); former smokers were similar to never-smokers (Table 3). To explore the effect of smoking cessation, we constructed indicator variables for the time since stopped smoking. Participants stopping < 5 years had a slight, but not statistically significant increased risk (HR=1.24, 95%CI=0.88, 1.75) and those who stopped 5+ years had a risk close to never smokers (HR=1.10, 95%CI=0.91, 1.35). A test of trend (never, stopped 5+ years, stopped < 5 years, current) was significant (HR=1.11, 95%CI-1.02,1.20, p=0.013). Among smokers, there was no association between pack-years and HI (data not shown).

As shown in Table 3, obesity was associated with increased risk of HI (HR=1.19, 95%CI=1.00, 1.41) as was larger waist circumference, a measure of central adiposity (HR per 10 cm=1.08, 95%CI=1.02, 1.15).

Diabetes was associated with a slight, but not statistically significant, increased risk of HI (HR=1.26, 95% CI=0.93, 1.71). However, GHb appeared to be associated with an increased

risk on a continuous scale (Table 3). To further explore these findings, we analyzed GHb with indicator variables grouping as 4–6.0% (referent group), 6.1–8%, 8.1–10%, 10.1–12%, and 12.1% or higher (people with levels greater than 8.0% were considered to have diabetes). High GHb levels (12.1% or higher) were associated with a doubling of risk of HI (HR=2.19, 95%CI=1.08, 4.61), but there was no statistically significant excess risk for those with better controlled diabetes (HR for GHb =10.1–12% = 0.98, 95%CI=0.48,2.01 and HR for GHb=8.1–10% =1.36, 95%CI=0.84,2.19); there was a modest excess risk for high normal levels of GHb (HR for GHb 6.1–8.0% =1.21, 95%CI= 1.01,1.44). We also used a cubic spline function with the discrete-time proportional hazards model to examine nonlinear associations between GHb and HI, adjusting for age and sex. The positive association was most pronounced at GHb levels above 12.0%.

There were no associations between baseline occupational noise exposure, alcohol consumption, exercise, history of CVD, hypertension or blood pressure, CRAE, CRVE, non-HDL cholesterol, hematocrit, white blood cell count, or use of medication (statins, lipid lowering agents, non-steroidal anti-inflammatory medications) and HI risk (Table 3). Results from sex-specific models were similar (data not shown).

Multivariable models

All factors associated with HI in age-sex-adjusted models were considered for the final multivariable model. When collinearity was an issue (obesity and waist circumference, for example) separate models were constructed and compared. As shown in Table 4, in addition to age, sex, and education, current smoking (HR=1.31, 95%CI=1.003, 1.71, p=0.048), central adiposity (HR per 10 cm = 1.08 95% CI=1.02,1.15, p=0.017), and poorly controlled diabetes (HR=2.03, 95% CI=1.01,4.08, p=0.048) were independent risk factors for HI. Other levels of GHb were not significantly associated with HI and were not retained. Estimated 15-yr risk of HI is shown for various risk factor profiles (Figure). The risk for men with the lowest risk profile (educated, thin, non-smoker, with lower GHb levels) was 47.3% and 93.0% for men with all risk factors. The risk estimates for women with the various risk factor combinations varied from 27.0% to 73.0%.

We repeated the multivariable model using only 5 or 10 years of follow-up data to understand the effects of duration of follow-up time. At five years of follow-up smoking (HR=1.16, 95%CI=0.76, 1.79) and high GHb (HR=1.79, 95%CI=0.73, 4.40) were associated with slightly elevated, but not statistically significant, risks; by 10-yrs of follow-up effect sizes were larger but did not reach statistical significance (Smoking HR=1.26, 95%CI=0.92, 1.74 and High GHb HR=2.04, 95%CI=0.95, 4.36).

DISCUSSION

We identified three modifiable factors that predicted the development of HI in this population-based cohort: smoking, central adiposity and poor glycemic control. These results suggest that it may be possible to delay age-related HI, and retain good hearing longer. The long-term risk of HI was high as the 15-yr cumulative incidence was 56.8%, with higher rates among older ages, men, and less educated participants, patterns consistent with previous reports with shorter follow-up time.[5,6] Controlling for age, sex, and education,

current smokers were 31% more likely to develop HI than life-long non-smokers, for every 10 cm larger waist circumference risk increased 8% and having poor glycemic control doubled the risk of HI. The probability of developing HI was 57.9% for a non-smoking, 60-yr-old man with less than a college education, a waist circumference of 80 cm, and a GHb 12 % whereas for a similar man with all three risk factors (smoked, larger waist (100 cm) and GHb>12%), the probability of developing HI was 93%, a difference similar to the effects of about ten years of aging. Interventions targeting multiple risk factors may be important for lowering risk of this common disorder of aging.

This is the first longitudinal population-based cohort study to show long-term increased risk of HI among current smokers. In our baseline study[13] and other cross-sectional studies[16,17,26] current cigarette smoking has been associated with prevalent HI. Previous longitudinal studies with audiometric assessments but shorter follow-up time have failed to find an association between current smoking and HI incidence[16,18–20] and studies relying on self-report of hearing[21,22] have had inconsistent results. Only one study found a longitudinal association between heavy smoking and 5-yr incidence of deficits at 4kHz in men but this study lacked complete audiometric assessments.[23] We found a significant trend with risk for former smokers declining as time since smoking cessation increased. However, we did not find a dose-response relation for the number of pack-years of cigarettes smoked. With only five or ten years of follow-up, the smoking effect was not significant suggesting that long-term exposure is needed. As people age, many stop smoking, which may limit the long-term auditory damage as risk declined with years since smoking cessation. Cigarette smoking has been inversely associated with healthy aging and smoking cessation is beneficial in improving long-term health outcome risks.[39] Smoking may have a generalized effect on health as well as damage the cochlea and central auditory system through its effects on inflammation and atherosclerosis.[14, 15]

Obesity and central adiposity were associated with increased risk of HI in this study. These results are consistent with the Nurses' Health Study which relied on self-report of hearing loss and cross-sectional studies.[26, 27, 29, 30] Markers of adiposity have long been recognized to be associated with increased risk of earlier mortality and heart disease.[40–42] Waist circumference which measures central fat distribution, may be an important risk marker for chronic diseases of aging because of associations with dyslipidemia, insulin resistance, and inflammation.[43]

High levels of GHb, but not the diagnosis of diabetes, was associated with an increased risk of HI. Although diabetes and glycemia have been linked with prevalent hearing loss in cross-sectional studies, there have been no longitudinal studies finding a prospective association.[24–28] There may be significant heterogeneity in the type of diabetes, or severity or duration of hyperglycemia and, in cross-sectional studies, hearing loss may have preceded the onset of diabetes. Most large cohort studies, including this one, have small numbers of participants with diabetes, which may limit power to detect statistically significant effects. Alternatively, results of the current study suggest that the degree of metabolic dysregulation, not the diagnosis of diabetes per se, may damage the auditory system. Tight glycemic control is known to reduce risk of complications and excess mortality in people with type 2 diabetes.[44] Hyperglycemia has been associated with cochlear changes including basement

membrane thickening in the stria vascularis and basilar membrane.[45] In NHANES, there was a suggestion that neuropathy and microvascular factors may be involved in the association of diabetes and HI.[46]

We did not find occupational noise exposure, history of CVD or other risk factors associated with incidence of HI, consistent with most longitudinal studies.[16,18,20–22,28] Although the risk factors identified all suggest a common vascular pathway, the lack of associations with other CVD risk factors and high incidence among those with none of the three risk factors, suggest that non-vascular pathways also may be involved in the deterioration of auditory function with aging. Hormonal and neurotransmitter deficits as well as chemical exposures have been implicated in the pathogenesis of HI but additional longitudinal human data are needed to clarify their roles.[47–50] The lack of association with occupational noise exposure may reflect the self-report nature of the measure, or suggest that the study lacked power to detect an association because only a small percent of older adults were exposed, or highlight that at the population level, occupational noise exposure is unlikely to be a common cause of HI at older ages because of the low prevalence of exposure.

This study has several strengths including the large population-based cohort, high retention rates, use of audiometry to measure hearing thresholds over time, standardized risk factor assessment methods, and long-term follow-up. However, limitations include the lack of ethnic/racial diversity, small number of people with diabetes, lack of objective measures of lifetime noise exposure, absence of data on environmental tobacco smoke exposure at baseline, and absence of a direct measure of visceral fat. Because most alcohol consumers drank beer (data not shown) any protective effect due to wine consumption may have been masked.

This study has provided new evidence that HI risk may be modifiable as smoking, central adiposity and poor glycemic control were independent predictors of HI. Although randomized controlled trials of exposure to these factors aren't ethical, intervention trials designed to improve health behaviors and reduce risk of other chronic diseases may be warranted in also measuring hearing changes, to determine if smoking prevention or cessation, obesity prevention or reduction, and good glycemic control may help to reduce the incidence of HI and contribute to healthy sensory aging.

Acknowledgments

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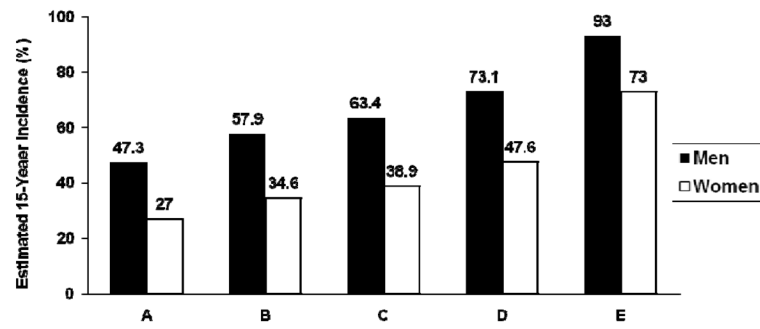
Education (y)	≥16	<16	<16	<16	<16
Waist (cm)	80	80	100	100	100
Smoking	Never	Never	Never	Current	Current
High GHb	No	No	No	No	Yes

Figure.

Estimated 15-yr hearing impairment (HI) risk in 60-yr old adults by risk factor profiles (education, waist circumference, smoking status, and glycosylated hemoglobin (GHb) level) and sex

Table 1

Participation at Follow-up: Normal Hearing at Baseline (N=1925; 1993–1995)

Time Period	Eligible[*] N	Participated N (%)	Deceased N (%)	Non-participants N (%)
1995–1998	174[**]	162 (93.1)	7 (4.0)	5 (2.9)
1998–2000	1837	1636 (89.1)	36 (2.0)	165 (9.0)
2003–2005	1688	1465 (86.8)	66 (3.9)	157 (9.3)
2009–2010	1451	1240 (85.5)	47 (3.2)	164 (11.3)

[*] Indicates the number with normal hearing at baseline who were alive at the beginning of the follow-up period

[**] Only subjects 75 years of age or older at baseline were eligible for this follow-up examination

Table 2

15-year Cumulative Incidence of Hearing Impairment by Baseline Age and Sex

Age group (yrs)	At risk at Baseline	Cases	Rate per 100 (95%CI)
48–59	990	315	39.1 (35.6, 42.5)
60–69	544	314	74.7 (70.3, 79.1)
70–79	303	177	93.4 (88.9, 97.9)
80–92	38	29	100.0 (--)
Total	1925	835	56.8 (54.2, 59.4)
Women			
48–59	605	145	29.5 (25.4, 33.6)
60–69	407	208	71.1 (65.6, 76.6)
70–79	242	140	93.0 (87.9, 98.2)
80–92	34	25	100.0 (--)
Total	1288	518	52.8 (49.6, 56.0)
Men			
48–59	385	170	54.3 (48.6, 59.9)
60–69	187	106	83.5 (76.4, 90.6)
70–92[*]	65	41	95.3 (69.8, 100.0)
Total	637	317	64.9 (60.5, 69.3)

[*] The number of men 80–92 yrs at baseline was too small to report separately so the two oldest age groups were collapsed

Table 3

Baseline Characteristics and Risk of Hearing Impairment

	N (%) or Mean (SD)	Age-sex-adjusted HR
Age 5 yr	60.7 (8.5)	1.90 (1.79,2.02)[*]
Men (v Women)	545 (32.5%)	2.23 (1.86,2.66)[**]
Education (years)		
<16 (v >16)	325 (19.4%)	1.40 (1.13,1.75)
Occupation:		
Production/Manufacturing/Farming (v Managerial/technical/service)	426 (26.4%)	1.35 (1.11,1.63)
Occupational noise exposure	175 (10.4%)	1.17 (0.88, 1.56)
Smoking		
Never	813 (49.2%)	1.0 referent group
Former	603 (36.5%)	1.13 (0.94, 1.37)
Current	238 (14.4%)	1.36 (1.05, 1.77)
Alcohol consumption (g/wk)		
None	295 (17.9%)	1.05 (0.83,1.33)
1–14	735 (44.7%)	1.0 referent group
15–74	297 (18.0%)	0.83 (0.65, 1.05)
75–140	163 (9.9%)	0.76 (0.57,1.02)
141+	156 (9.5%)	0.93 (0.69, 1.26)
Hx of heavy alcohol consumption (4+/day)	224 (13.5%)	1.23 (0.96,1.58)
Exercise at least once a week	715 (43.2%)	0.88 (0.74,1.04)
History of CVD	121 (7.3%)	0.99 (0.71, 1.37)
Hypertension	730 (44.4%)	1.13 (0.95, 1.34)
Systolic blood pressure (per 5 mmHg)	127 (19)	1.01 (0.98,1.03)
Diastolic blood pressure (per 5 mm Hg)	77 (10)	1.00 (0.95,1.04)
Pulse Rate (per 5 beats/min)	74 (11)	1.02 (0.98,1.06)
CRAE (4th Q vs 1)	416 (26.0%)	1.27 (0.99, 1.62)
CRVE (4th Q vs 1)	354 (22.2%)	1.21 (0.95,1.55)
Obesity (BMI>=30 kg/m^2)	665 (41.0%)	1.19 (1.00,1.41)
Waist (10 cm)	92.6 (15.7)	1.08 (1.02,1.15)
Diabetes	128 (7.7%)	1.26 (0.93, 1.71)
GHb (%)	6.3 (1.4)	1.08 (1.02,1.14)
Non-HDL Cholesterol (per 10 mg/dl)	187 (46)	1.00 (0.94, 1.06)
WBC (k/μL)	7.3 (2.0)	1.03 (0.99,1.08)
HCT (%)	42.6 (3.4)	1.01 (0.98,1.04)
NSAID medications	982 (59.4%)	1.11 (0.93,1.31)
Anti-hyperlipidemia medications	202 (12.2%)	1.16 (0.91,1.48)
Statins	67 (4.1%)	1.06 (0.71,1.59)

HR= Hazard Ratio; BMI= Body Mass Index; CRAE= Central Retinal Arteriolar Equivalent; CRVE = Central Retinal Venular Equivalent; CVD= Cardiovascular disease; GHb= Glycosylated hemoglobin; HCT = hematocrit; Non-HDL = Non-High Density Lipoprotein; NSAID = Non-steroidal anti-inflammatory medications; WBC= White Blood Cell count.

*
Adjusted for sex only;

**
adjusted for age only

Table 4

Multivariable model of risk factors for the 15-yr cumulative incidence of hearing impairment

	HR (95% CI)	p-value
Age (5 yr)	1.89 (1.78,2.01)	<0.0001
Sex (M)	2.04 (1.65,2.51)	<0.0001
Education (<16 y)	1.35 (1.08,1.70)	0.010
Waist (10 cm)	1.08 (1.02,1.15)	0.017
Current Smoking	1.31 (1.003,1.71)	0.048
High GHb (>12%)	2.03 (1.01, 4.08)	0.048

HR= Hazard Ratio; GHb= Glycosylated hemoglobin