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RELATIONSHIP OF STROKE RISK AND HEARING LOSS IN AFRICAN AMERICANS: THE JACKSON HEART STUDY

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Abstract

Objective—To evaluate the relationships among measures of stroke risk and hearing in an African-American cardiovascular study cohort

Study design—Prospective Cohort Study

Methods—The relationships between stroke risk profiles and hearing of 1,107 individuals from a cohort of African-Americans were assessed. Several different hearing pure-tone averages (PTA's) were constructed representing different frequency regions of hearing, namely PTA-low, PTA-mid and PTA-high. Stroke risk profiles were calculated using validated 10-year cardiovascular disease risk scores. Gamma regression analyses were performed for each PTA given as a continuous variable with change in stroke risk score. Logistic regression analyses, presented as odds ratios, were performed with “hearing loss” defined as any PTA > 25 dB hearing level. Stratification models were analyzed for age quarterlies and among sex.

Results—Single unit increases of stroke risk percentage were found to be predictive of increases in all PTA threshold levels in gamma regression analyses for the overall pooled sample. The relationship was influenced by age, where fewer significant relationships were observed at higher ages. When analyzed with respect to stroke risk categories, using low risk as the reference group, there was found to be a significant association between stroke risk and hearing loss in the medium

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and high-risk groups, with a stronger relationship in the high-risk group for all PTA threshold levels.

Conclusion—This study provides evidence that stroke risk has a positive predictive relationship with hearing pure-tone threshold.

Keywords

Stroke risk; sensorineural hearing loss; cerebrovascular disease; ischemic microvascular disease

INTRODUCTION

Stroke is the 5th leading cause of death in the U.S. and a leading cause of long-term disability affecting nearly 800,000 people in the U.S. each year.¹ Auditory dysfunction in patients with stroke has been well described, including both central and peripheral deficits with symptoms ranging from hearing loss to tinnitus and even impairment of higher auditory processes such as sound localization.^{2,3} Associations to stroke have been made with both sudden sensorineural hearing loss (SSNHL) and age-related hearing loss (ARHL).^{4,5} Lin et al examined 1,423 patients with SSNHL and during a 5 year follow-up period found that the hazard for developing stroke was 1.64 times greater than the control group.⁴ In a separate study, 2,802 patients from the Blue Mountain Hearing Study cohort with moderate to severe hearing loss had a significantly higher likelihood of reporting previous stroke.⁵ Although an exact mechanism to explain these findings has not been elucidated, it remains clear that stroke is associated with sensorineural hearing loss.

The cochlea is a complex organ enriched with an equally complex vasculature that is primarily supplied by the spiral modiolar artery, a terminal artery. Therefore the cochlea is vulnerable to changes in blood flow and hypoxia, which occur gradually in arteriosclerosis and is a hallmark of microvascular disease.⁶ There is increasing evidence in the literature reporting associations between cardiovascular disease and its risk factors with hearing loss, possibly in part through a mechanism of microvascular disease leading to ischemia of the cochlea and atrophy of the stria vascularis.^{7–10} Hearing loss has also been associated with other micro-ischemic pathologies such as retinopathy and chronic kidney disease.^{11,12} A histological study of cadaveric temporal bones has shown that strial atrophy is the most prominent finding in the aging cochlea, and this process is more prominent in elderly patients with presbycusis and also in younger patients with generalized arteriosclerosis compared to aged matched controls.^{6,13,14} Although these studies support the hypothesis that compromised cochlear vascularity is involved in hearing loss, the relationship to stroke risk score has not been studied. Moreover, these variables have never been examined in an all-African-American cohort such as the Jackson Heart Study (JHS). Compared to the general population, African Americans have a higher incidence of stroke at a younger age.

Large epidemiological studies are often used to create tools to predict risk of disease in individuals. Recent guidelines referenced data from pooled cohorts in order to develop an estimate of the 10-year risk of developing atherosclerotic cardiovascular disease (ASCVD), which includes stroke and myocardial infarction.¹⁵ The ASCVD risk estimator includes basic risk factors such as age, systolic blood pressure, pharmacologic therapy for

hypertension and hyperlipidemia, diabetes, current smoking status, total serum cholesterol, and serum High-density lipoprotein (HDL) cholesterol. Given the similarities of microvascular disease affecting stroke and hearing loss, the current study examines the relationship between ASCVD risk and hearing loss. For simplicity of description in this paper we will therefore refer to the ASCVD risk score as “stroke risk” score.

Stroke risk and pure-tone auditory data obtained from an ancillary study of the Jackson Heart Study (JHS) was examined. A recent study of the JHS cohort revealed that the stroke risk model correlated with incident stroke in the JHS cohort.¹⁶ We hypothesized that there will be a positive relationship between stroke risk and sensorineural hearing loss, as detected by pure-tone averages.

MATERIALS and METHODS

The study protocol was approved by the institutional review boards of the following participating institutions: the University of Mississippi Medical Center, Jackson State University, and Tougaloo College. All of the participants provided written informed consent.

Study Sample

The Jackson Heart Study (JHS) is a prospective, population-based, longitudinal study of factors that influence the development and progression of cardiovascular disease (CVD) in African Americans. The JHS enrolled a cohort of 5,301 African- American participants from the Jackson, MS metropolitan area, between the ages of 21–94 years-of-age, between September 2000 and March 2004.¹⁷ Demographic and health information was collected during a series of home interviews and clinical examinations that took place during three exam periods: Exam 1 (2000–2004), Exam 2 (2005–2008), and Exam 3 (2009 – 2012). The data presented in this report were obtained from a sample of 1107 individuals participating in the JHS cohort with stroke risk profile data from Exam 2, except smoking which was obtained from Exam 1, and who underwent hearing evaluations in an ancillary study coinciding with Exam 2.

Audiological Assessment

Data obtained from individuals who presented with occluded ear canals, middle ear disorders with conductive hearing losses, or had known histories of hearing loss related to head injury, radiotherapy or chemotherapy, were removed from analyses.

Audiometry was performed with insert earphones (ER-3A type, GN Otometrics, Denmark) on a two channel diagnostic audiometer (Madsen Conera, GN Otometrics, Schaumburg, IL.), calibrated yearly to American National Standards Institute (ANSI) specifications for diagnostic audiometers.¹⁸ All participants were evaluated in a commercially available test room, which met the ANSI standards for permissible ambient noise.¹⁹ Pure– tone audiometric testing was performed in accordance with procedures recommended by the American Speech-Language-Hearing Association.²⁰ Thresholds were determined for octaves from 250 Hz to 8000 Hz by air-conduction and for octaves from 500 Hz to 4000 Hz by bone-conduction. Several different pure-tone averages (PTAs) were used in this study. PTA3, the average of thresholds at frequencies 500, 1000, and 2000 Hz was used as a crosscheck

with the speech reception threshold (SRT) as an estimate of pure-tone testing reliability. SRT and PTA3 agreement within 10 dB HL was considered acceptable reliability. The addition of a fourth frequency (4000 Hz) to the PTA3 was used as a clinical estimate of functional impairment in statistical analyses, referred to as “PTA4”.²¹ Other PTAs were used for analyses, including: 1) PTA-high (the average of 4000 and 8000 Hz), 2) PTA-mid (the average of 1000 and 2000 Hz), and 3) PTA-low (the average of 250 and 500 Hz). Hearing loss was defined as PTA > 25 dBHL. Data were examined for each ear independently. Assessment of middle ear compliance and pressure were assessed with a conventional tympanometer (Madsen Capella, GN Otometrics, Schaumburg, IL.)^{22,23}

Risk Factors and Covariate Assessment

Data used for the current analyses were collected through an in-home interview and study examinations. Age, sex, blood pressure (BP), medication use, cigarette smoking, and history of stroke were collected during the study interview. Hypertension was defined as blood pressure greater than 140/90, self-report of hypertension, or antihypertensive medication use in the previous two weeks. Diabetes mellitus was defined as fasting glucose of 126 mg/dL or greater, random glucose of 200 mg/dL or greater, self-report of diabetes mellitus, or hypoglycemic medication use. Fasting blood samples were collected according to standardized procedures and the assessments of plasma glucose and lipids were processed at the Central Laboratory (University of Minnesota) as previously described.¹⁷

The 10-year atherosclerotic cardiovascular disease (ASCVD) risk scores, which reflect risk estimates for non-fatal stroke and myocardial infarction and fatal stroke and coronary heart disease, were calculated using race-specific equations as recommended by the ACC/AHA.¹⁵ These risk scores were then multiplied by 100 to calculate the stroke risk percentage. A previous study from the JHS revealed that the 10-year cardiovascular risk scores did correlate with incident stroke in the JHS cohort.¹⁶ Again, for simplicity of description in this paper we will therefore refer to the 10-year ASCVD risk scores as “stroke risk” score. To better assess the clinical relevance of stroke risk we analyzed categories of risk according to already established thresholds in the literature: low risk (0–<5.0%), medium risk (5.0–<7.5%), and high risk (>7.5%).²⁴

Statistical Analysis

This study was limited to participants who had (1) available data for each component of the stroke risk score, (2) age between 40–79yo and SBP between 70–200, which are limits set by the stroke risk profile. Patients were excluded from the study if they had a history of prior stroke. We started with 1314 participants and after the above inclusion and exclusion criteria were met we were left with 1107 participants (84.2%).

Continuous data are described using mean (standard deviation) and categorical data are described using n (%). Unadjusted models were created to examine the associations between stroke risk score and hearing measures. Gamma regression analysis was modeled between stroke risk score as the independent variable, or predictor and hearing with PTA as a continuous dependent variable, or outcome. Logistic regression was used to examine odds of hearing loss based on risk category, hearing loss defined as PTA > 25 dBHL. We were

unable to perform adjustment models for age and sex as they are variables of the risk score, and this would produce co-linearity issues. We therefore assessed the effect of age and sex in select analyses by dividing participants into quartiles by age group (Age 0 = 40.21–52.64; Age 1 = 52.69–60.07; Age 2 = 60.08–68.52; Age 3 = 68.54–78.97) and by dividing participants by male and female sex. All analyses were performed using SAS software, Version 9.4 (SAS Institute, Inc., Cary, NC). Statistical significance was set as $p < 0.05$.

RESULTS

The study group of 1107 participants was comprised entirely of African Americans who were predominately female (69.2%) with an average age of 60.4 years. The majority of study participants fell into the high stroke risk group (59.4%), compared to 12.1% in the medium risk group and 28.5% in the low risk group. Hearing loss was defined for the worse ear by PTA4, which is the four-frequency average of pure-tones 500, 1000, 2000, and 4000Hz. Normal hearing was defined as PTA4 ≤ 25 dB (73.9% of participants), mild hearing loss between 26–40 dB (19.4% of participants), moderate hearing loss between 40–70 dB (5.9% of participants), and marked hearing loss was > 70 dB (1.4% of participants). Regarding stroke risk variables, mean systolic blood pressure (BP) was 125.1 mm/Hg, mean total cholesterol 197.3 and HDL cholesterol 54.3 mg/DL. Only 10.1% reported smoking history, 24.3% had diabetes, 27.5% were on a statin medication, and 61.4% were on an antihypertensive medication.

Stroke risk categories are compared to participants with hearing loss, defined by PTA4 > 25 dB in the worse ear (Figure 1). There was found to be an increasing percentage of participants with hearing loss as the risk group increased. In the high-risk group, 36.17% of the participants had hearing loss compared to only 6.98% in the low risk group. Of the patients with hearing loss, 82.64% are in the high-risk group, 9.72% in the medium risk group and 7.64% in the low risk group.

Gamma regression analysis of the pooled sample was stratified by sex and age (Table I, II, and III). Single unit increases of stroke risk percentage were found to be predictive of increases in all PTA threshold levels in gamma regression analyses for the overall pooled sample (Table I). The relationship was influenced by age, where fewer significant relationships were observed at higher ages. Similarly, sex-stratified analyses and significant findings were seen at low, mid, and high PTAs (Table II and III).

Logistic regression of stroke risk and hearing loss was analyzed with respect to stroke risk categories (Table IV, V, and VI). Using low risk as the reference group, there was found to be a significant relationship between stroke risk and hearing loss in the medium and high-risk groups, with a stronger relationship in the high-risk group for all PTA threshold levels. This relationship was observed in the pooled and sex-stratified samples. Again, the observed relationship was dependent on age group.

DISCUSSION

A relationship between stroke risk and hearing loss is identified which supports the study hypothesis. The most robust relationships were noted in the high frequency ranges of

hearing (4000 Hz and 8000 Hz). When broken down into stroke risk categories there was found to be an increasing percentage of participants with hearing loss as the risk group increased. Of the patients with hearing loss, 82.64% are in the high-risk group, 9.72% in the medium risk group, and 7.64% in the low risk group.

Stratification models did not identify significant differences in sex, despite prior studies demonstrating cardiovascular risk factors were more likely to affect hearing thresholds in females.^{7,10,11} Given the influence of age on hearing loss and the stroke risk profile, participants were organized by age defined quartiles. Interestingly, there was a stronger relationship in the younger age quartiles. Intuitively, sensory presbycusis associated with high frequency hearing loss increases with age. However, similar age-adjusted results have been found in prior studies. Bainbridge *et al*/looked at hearing impairment in adults with diabetes and found a stronger association to hearing loss in the younger, <60yo group.²⁵ The authors argued this was due to the greater relative contribution of diabetes and other cardio-metabolic risk factors on hearing in the younger group, as additional comorbid factors are found to influence hearing with age.

The current results are significant across all PTA thresholds in the overall groups. This contrasts with other studies who have found associations between cardiovascular disease and its risk factors to low frequency hearing loss.^{7,10,11,26,27} The proposed mechanism for these results from prior studies suggest microvascular disease leading to ischemic degeneration of the stria vascularis, particularly at the more distal apical parts of the cochlea, causing low-frequency hearing loss. The findings in our study may be due to the differences in the study cohorts and demographics. Many of the prior study cohorts consisted of elderly participants with a higher prevalence of active CVD and history of prior stroke. In contrast, the JHS cohort consists of a population-based sample of healthy participants. Patients with a stroke history were excluded as a condition of the stroke risk score. Prior studies have also identified some cardiovascular risk factors such as smoking and diabetes to be linked to high frequency hearing loss.^{9,25} Evidence of microvascular disease affecting the high and low frequency regions of the cochlea has been found in multiple temporal bone studies. Nomiva *et al* performed a temporal bone cadaver study of young adults (23–36 years old) with generalized arteriosclerosis compared to age matched controls and found degeneration of the cochlea, especially in the basal turn, of the arteriosclerosis group.⁶ Moreover, histopathological studies of aging gerbils has shown similar results with atrophy of the stria vascularis in the apical and basal turns, providing evidence for microvascular involvement in age-related hearing loss.²⁸ Schuknecht first described this phenomenon in 1955, as one of the four major pathological types of presbycusis. He coined the term metabolic presbycusis, or stria atrophy, where degeneration of the stria vascularis leads bilateral symmetric SNHL affecting all frequencies leading to an audiogram with a flat pattern.²⁹

There are several limitations that affect the generalizability of results. Study participants were from an all-African-American cohort, which can limit making comparisons to the general population, particularly given the fact that African-Americans have higher rates of stroke and lower rates of hearing loss compared to other ethnic groups. However, this may also be seen as a strength given the population-based sample of healthy volunteers who have less confounders to hearing loss than an older or unhealthy cohort. The stroke risk score

does not allow for age adjustment or determining the influence of each risk factor composing the final score, hence the need for stratified models. This stratification also limited our sample size and ability to examine risk in higher age groups, as all participants in the highest age-quartile were considered high-risk. One strength however is that the components of the risk score are easily obtained and the risk score itself has been validated with regards to race. Lastly, cross-sectional study design does not allow for clinical/causal significance of the relationships.

CONCLUSION

The current study provides evidence that as computed stroke risk increases, assessed hearing loss also increases across all thresholds, but most notably at the highest frequencies. Future longitudinal studies of repeat measures of hearing and stroke risk will help to further strengthen knowledge of these relationships.

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Abbreviations

PTA	Pure-tone average
dB	decibel
Hz	hertz
ACC	American College of Cardiology
AHA	American Heart association (AHA)
ASCVD	atherosclerotic cardiovascular disease
HDL	High-density lipoprotein
JHS	Jackson Heart Study
CVD	Cardiovascular disease
ANSI	American National Standards Institute
SRT	speech reception threshold
BP	Blood pressure

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Figure 1.

Distribution of participants with hearing loss versus stroke risk group. Bar graph comparing hearing loss, defined by PTA4>25dB in the worse ear, with stroke risk categories according to cut points in the literature: Low (0–<5%), Medium (5–7.5%), and high (>7.5%).

PTA4 = four-frequency average of pure- tones 500, 1000, 2000, and 4000 Hz

* Percentage of participants with hearing loss in that risk group (i.e. 36.17% of participants in the high stroke risk group had hearing loss)

** Of participants with hearing loss, percentage in each stroke risk group (i.e. 82.64% of participants with hearing loss are also in the high stroke risk group)

Table I**Stroke Risk and Hearing Level Gamma Regression: Pooled**

		Left	Right
overall	PTA4	1.017 (1.014, 1.020) ***	1.019 (1.016, 1.022) ***
	PTA high	1.024 (1.020, 1.028) ***	1.024 (1.020, 1.027) ***
	PTA low	1.013 (1.009, 1.016) ***	1.013 (1.010, 1.017) ***
	PTA mid	1.017 (1.013, 1.020) ***	1.018 (1.015, 1.021) ***
age0	PTA4	1.023 (1.009, 1.038) **	1.037 (1.022, 1.052) ***
	PTA high	1.019 (1.002, 1.038) *	1.034 (1.016, 1.053) ***
	PTA low	1.015 (0.997, 1.033)	1.035 (1.018, 1.054) ***
	PTA mid	1.023 (1.007, 1.039) **	1.036 (1.020, 1.052) ***
age1	PTA4	1.011 (1.002, 1.020) *	1.008 (1.000, 1.017) *
	PTA high	1.013 (1.003, 1.024) *	1.007 (0.997, 1.018)
	PTA low	1.009 (0.999, 1.018)	1.001 (0.992, 1.011)
	PTA mid	1.007 (0.997, 1.017)	1.005 (0.997, 1.014)
age2	PTA4	1.002 (0.995, 1.008)	1.007 (1.001, 1.013) *
	PTA high	1.005 (0.998, 1.013)	1.010 (1.003, 1.017) **
	PTA low	1.000 (0.992, 1.007)	1.005 (0.997, 1.013)
	PTA mid	1.000 (0.993, 1.007)	1.007 (1.001, 1.013) *
age3	PTA4	1.006 (1.001, 1.012) *	1.004 (1.000, 1.009)
	PTA high	1.004 (0.999, 1.010)	1.002 (0.997, 1.007)
	PTA low	1.008 (1.002, 1.014) **	1.004 (0.998, 1.010)
	PTA mid	1.007 (1.001, 1.013) *	1.005 (1.000, 1.010)

Statistical significance:

*
p<0.05,

**
p<0.01,

p<0.001

Age quartiles equally divided and defined as: Age 0 = 40.21–52.64; Age 1 = 52.69–60.07; Age 2 = 60.08–68.52; Age 3 = 68.54–78.97

PTA4 (500, 1000, 2000, 4000 Hz), PTA Low (250, 500 Hz), PTA Mid (1000, 2000 Hz), and PTA High (4000, 8000 Hz).

PTA = pure- tone average; Hz = hertz

Table II

Stroke Risk and Hearing Level Gamma Regression: Males

		Left	Right
overall	PTA4	1.021 (1.016, 1.027) ***	1.021 (1.016, 1.027) ***
	PTA high	1.028 (1.020, 1.035) ***	1.025 (1.018, 1.032) ***
	PTA low	1.016 (1.010, 1.022) ***	1.014 (1.008, 1.021) ***
	PTA mid	1.021 (1.015, 1.028) ***	1.021 (1.015, 1.027) ***
age0	PTA4	1.016 (0.987, 1.047)	1.041 (1.010, 1.074) **
	PTA high	1.007 (0.967, 1.052)	1.029 (0.987, 1.075)
	PTA low	1.009 (0.973, 1.048)	1.032 (0.997, 1.069)
	PTA mid	1.014 (0.984, 1.047)	1.046 (1.015, 1.080) **
age1	PTA4	1.019 (1.003, 1.035) *	1.021 (1.006, 1.036) **
	PTA high	1.024 (1.005, 1.044) *	1.020 (1.001, 1.039) *
	PTA low	1.010 (0.995, 1.027)	1.006 (0.989, 1.024)
	PTA mid	1.020 (1.002, 1.039) *	1.017 (1.002, 1.033) *
age2	PTA4	1.008 (0.997, 1.020)	1.012 (1.000, 1.025)
	PTA high	1.006 (0.991, 1.022)	1.011 (0.997, 1.025)
	PTA low	1.005 (0.989, 1.023)	1.010 (0.994, 1.028)
	PTA mid	1.008 (0.994, 1.023)	1.015 (1.001, 1.029) *
age3	PTA4	1.007 (0.999, 1.017)	1.002 (0.994, 1.010)
	PTA high	1.007 (0.998, 1.017)	1.001 (0.993, 1.010)
	PTA low	1.014 (1.004, 1.024) **	1.007 (0.996, 1.018)
	PTA mid	1.005 (0.995, 1.016)	1.001 (0.992, 1.010)

Statistical significance:

*
p<0.05,

**
p<0.01,

p<0.001

Age quartiles equally divided and defined as: Age 0 = 40.21–52.64; Age 1 = 52.69–60.07; Age 2 = 60.08–68.52; Age 3 = 68.54–78.97

PTA4 (500, 1000, 2000, 4000 Hz), PTA Low (250, 500 Hz), PTA Mid (1000, 2000 Hz), and PTA High (4000, 8000 Hz).

PTA = pure- tone average; Hz = hertz

Table III**Stroke Risk and Hearing Level Gamma Regression: Females**

		Left	Right
overall	PTA4	1.014 (1.010, 1.017) ***	1.016 (1.013, 1.020) ***
	PTA high	1.020 (1.016, 1.025) ***	1.022 (1.018, 1.027) ***
	PTA low	1.011 (1.007, 1.015) ***	1.014 (1.010, 1.018) ***
	PTA mid	1.014 (1.010, 1.018) ***	1.016 (1.012, 1.019) ***
age0	PTA4	1.022 (1.004, 1.043) *	1.037 (1.017, 1.060) ***
	PTA high	1.022 (1.000, 1.046)	1.044 (1.020, 1.069) ***
	PTA low	1.019 (0.995, 1.046)	1.043 (1.018, 1.072) **
	PTA mid	1.025 (1.003, 1.049) *	1.034 (1.012, 1.057) **
age1	PTA4	1.000 (0.988, 1.012)	0.997 (0.985, 1.009)
	PTA high	0.997 (0.983, 1.013)	0.995 (0.980, 1.011)
	PTA low	1.008 (0.995, 1.022)	0.999 (0.987, 1.013)
	PTA mid	0.997 (0.983, 1.011)	0.997 (0.985, 1.010)
age2	PTA4	0.996 (0.988, 1.003)	1.001 (0.994, 1.008)
	PTA high	0.999 (0.991, 1.007)	1.005 (0.997, 1.013)
	PTA low	0.998 (0.989, 1.007)	1.003 (0.994, 1.012)
	PTA mid	0.994 (0.986, 1.002)	1.001 (0.994, 1.008)
age3	PTA4	1.003 (0.997, 1.009)	1.003 (0.998, 1.009)
	PTA high	1.001 (0.994, 1.007)	1.000 (0.994, 1.007)
	PTA low	1.003 (0.995, 1.010)	1.002 (0.994, 1.009)
	PTA mid	1.005 (0.999, 1.013)	1.005 (0.999, 1.012)

Statistical significance:

*
p<0.05,

**
p<0.01,

p<0.001

Age quartiles equally divided and defined as: Age 0 = 40.21–52.64; Age 1 = 52.69–60.07; Age 2 = 60.08–68.52; Age 3 = 68.54–78.97

PTA4 (500, 1000, 2000, 4000 Hz), PTA Low (250, 500 Hz), PTA Mid (1000, 2000 Hz), and PTA High (4000, 8000 Hz).

PTA = pure- tone average; Hz = hertz

Table IV**Stroke Risk and Hearing Loss Logistic Regression: Pooled**

			Left	Right
overall	HL(yes)	Mid risk	3.29 (1.70, 6.36) ***	3.51 (1.74, 7.09) ***
		High risk	6.73 (4.06, 11.15) ***	9.00 (5.22, 15.51) ***
	HL high	Mid risk	3.95 (2.42, 6.44) ***	3.98 (2.44, 6.51) ***
		High risk	7.80 (5.40, 11.29) ***	7.88 (5.43, 11.43) ***
	HL low	Mid risk	1.71 (0.77, 3.80)	1.83 (0.75, 4.46)
		High risk	2.60 (1.49, 4.53) ***	4.01 (2.16, 7.44) ***
	HL mid	Mid risk	2.96 (1.59, 5.50) ***	2.75 (1.46, 5.20) **
		High risk	4.52 (2.83, 7.22) ***	5.44 (3.38, 8.74) ***
age 0	HL(yes)	Mid risk	2.17 (0.43, 10.98)	3.87 (0.67, 22.15)
		High risk	0.67 (0.08, 5.59)	9.77 (2.72, 35.10) ***
	HL high	Mid risk	3.67 (1.36, 9.86) *	3.46 (1.30, 9.25) *
		High risk	1.45 (0.50, 4.16)	2.37 (0.96, 5.89)
	HL low	Mid risk	1.68 (0.34, 8.18)	1.23 (0.14, 10.6)
		High risk	0.52 (0.06, 4.20)	4.36 (1.27, 15.03) *
	HL mid	Mid risk	2.18 (0.43, 11.04)	2.55 (0.49, 13.31)
		High risk	2.12 (0.53, 8.56)	4.36 (1.27, 15.03) *
age 1	HL(yes)	Mid risk	1.55 (0.56, 4.26)	2.24 (0.83, 6.06)
		High risk	2.39 (1.05, 5.42) *	1.80 (0.74, 4.37)
	HL high	Mid risk	2.32 (1.09, 4.97) *	2.26 (1.06, 4.83) *
		High risk	2.05 (1.07, 3.93) *	1.55 (0.79, 3.02)
	HL low	Mid risk	0.33 (0.04, 2.85)	0.65 (0.12, 3.46)
		High risk	1.12 (0.34, 3.64)	1.12 (0.34, 3.64)
	HL mid	Mid risk	1.42 (0.55, 3.66)	1.26 (0.50, 3.20)
		High risk	1.44 (0.65, 3.19)	1.22 (0.56, 2.68)
age 2	HL(yes)	Mid risk	2.18 (0.42, 11.21)	0.66 (0.15, 2.98)
		High risk	2.13 (0.46, 9.80)	1.51 (0.41, 5.59)
	HL high	Mid risk	1.44 (0.42, 4.98)	2.82 (0.69, 11.48)
		High risk	1.89 (0.61, 5.81)	3.81 (1.03, 14.03) *
	HL low	Mid risk	1.30 (0.24, 6.97)	1.95 (0.21, 17.73)
		High risk	0.58 (0.12, 2.78)	1.85 (0.23, 14.69)
	HL mid	Mid risk	1.02 (0.27, 3.83)	1.15 (0.27, 4.89)
		High risk	0.64 (0.19, 2.12)	1.19 (0.32, 4.43)

Statistical significance:

*
p<0.05,**
p<0.01,***
p<0.001

Age quartiles equally divided and defined as: Age 0 = 40.21–52.64; Age 1 = 52.69–60.07; Age 2 = 60.08–68.52; Age 3 = 68.54–78.97

PTA4 (500, 1000, 2000, 4000 Hz), PTA Low (250, 500 Hz), PTA Mid (1000, 2000 Hz), and PTA High (4000, 8000 Hz).

Stroke risk categories as defined in the literature with the reference group as low risk (0–<5%) analyzed with Medium risk (5–7.5%), and high risk (>7.5%)

PTA = pure-tone average; Hz = hertz; HL = Hearing loss

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Table V**Stroke Risk and Hearing Loss Logistic Regression: Males**

			Left	Right
overall	HL(yes)	Mid risk	0.94 (0.22, 4.08)	1.67 (0.37, 7.53)
		High risk	5.01 (1.72, 14.57) **	5.96 (1.78, 19.94) **
	HL high	Mid risk	2.10 (0.69, 6.45)	5.23 (1.34, 20.47) *
		High risk	6.16 (2.49, 15.27) ***	11.42 (3.42, 38.12) ***
	HL low	Mid risk	0.97 (0.13, 7.29)	0.97 (0.13, 7.29)
		High risk	2.23 (0.51, 9.76)	2.08 (0.47, 9.10)
	HL mid	Mid risk	0.69 (0.14, 3.30)	1.30 (0.27, 6.22)
		High risk	3.40 (1.16, 9.91) *	4.93 (1.47, 16.51) **
age 0	HL(yes)	Mid risk	1.33 (0.20, 8.86)	2.07 (0.26, 16.13)
		High risk	0.34 (0.03, 3.51)	3.10 (0.55, 17.35)
	HL high	Mid risk	2.33 (0.57, 9.58)	8.45 (1.48, 48.24) *
		High risk	0.62 (0.14, 2.86)	1.72 (0.27, 11.08)
	HL low	Mid risk	4.27 (0.36, 50.83)	2.00 (0.12, 34.09)
		High risk	1.10 (0.07, 18.46)	3.56 (0.35, 36.18)
	HL mid	Mid risk	0.63 (0.06, 6.51)	2.07 (0.26, 16.13)
		High risk	0.71 (0.11, 4.60)	2.38 (0.4, 14.08)
age 1	HL(yes)	Mid risk	0.38 (0.03, 5.57)	0.37 (0.03, 5.57)
		High risk	1.00 (0.10, 10.20)	0.57 (0.05, 5.97)
	HL high	Mid risk	0.92 (0.07, 11.54)	0.92 (0.07, 11.54)
		High risk	1.75 (0.17, 17.64)	1.11 (0.11, 11.31)
	HL low	Mid risk	0.00 (0.00, 2.38)	0.19 (0.01, 3.90)
		High risk	0.17 (0.01, 1.98)	0.21 (0.02, 2.45)
	HL mid	Mid risk	0.38 (0.03, 5.57)	0.37 (0.03, 5.57)
		High risk	0.74 (0.07, 7.60)	0.57 (0.05, 5.97)

Statistical significance:

*
p<0.05,

**
p<0.01,

p<0.001

Age quartiles equally divided and defined as: Age 0 = 40.21–52.64; Age 1 = 52.69–60.07; Age 2 = 60.08–68.52; Age 3 = 68.54–78.97

PTA4 (500, 1000, 2000, 4000 Hz), PTA Low (250, 500 Hz), PTA Mid (1000, 2000 Hz), and PTA High (4000, 8000 Hz).

Stroke risk categories as defined in the literature with the reference group as low risk (0–<5%) analyzed with Medium risk (5–7.5%), and high risk (> 7.5%)

PTA = pure-tone average; Hz = hertz; HL = Hearing loss

Table VI**Stroke Risk and Hearing Loss Logistic Regression: Females**

			Left	Right
overall	HL(yes)	Mid risk	4.51 (2.14, 9.49) ***	4.16 (1.87, 9.24) ***
		High risk	5.65 (3.14, 10.17) ***	8.93 (4.81, 16.58) ***
	HL high	Mid risk	4.67 (2.69, 8.12) ***	4.05 (2.34, 7.00) ***
		High risk	7.78 (5.14, 11.78) ***	7.86 (5.23, 11.8) ***
	HL low	Mid risk	2.02 (0.84, 4.83)	2.13 (0.79, 5.77)
		High risk	2.77 (1.50, 5.12) **	5.02 (2.53, 9.98) ***
	HL mid	Mid risk	4.21 (2.13, 8.33) ***	3.38 (1.67, 6.81) ***
		High risk	4.26 (2.50, 7.25) ***	5.18 (3.06, 8.79) ***
age 0	HL(yes)	Mid risk	0.00 (0.00, 2.02)	0.00 (0.00, 1.48)
		High risk	0.00 (0.00, 2.00)	15.45 (1.98, 120.37) **
	HL high	Mid risk	2.94 (0.57, 15.19)	0.98 (0.12, 8.12)
		High risk	2.41 (0.48, 12.14)	6.09 (1.78, 20.85) **
	HL low	Mid risk	0.00 (0.00, 2.66)	0.00 (0.00, 3.59)
		High risk	0.00 (0.00, 1.35)	6.07 (1.06, 34.93) *
	HL mid	Mid risk	4.20 (0.43, 41.16)	0.00 (0.00, 9.34)
		High risk	3.50 (0.36, 33.82)	3.50 (0.36, 33.82)
age 1	HL(yes)	Mid risk	1.85 (0.60, 5.74)	2.94 (0.99, 8.77)
		High risk	1.31 (0.40, 4.27)	1.48 (0.44, 4.95)
	HL high	Mid risk	2.85 (1.23, 6.58) *	2.74 (1.19, 6.31) *
		High risk	1.19 (0.48, 2.94)	1.32 (0.55, 3.19)
	HL low	Mid risk	0.56 (0.06, 5.21)	0.55 (0.06, 5.08)
		High risk	1.57 (0.34, 7.34)	1.00 (0.18, 5.67)
	HL mid	Mid risk	1.74 (0.61, 4.96)	1.52 (0.54, 4.24)
		High risk	0.80 (0.24, 2.71)	1.10 (0.38, 3.20)
age 2	HL(yes)	Mid risk	2.40 (0.47, 12.37)	0.71 (0.16, 3.23)
		High risk	1.26 (0.27, 6.01)	1.15 (0.30, 4.38)
	HL high	Mid risk	1.49 (0.43, 5.19)	2.90 (0.71, 11.91)
		High risk	1.33 (0.42, 4.17)	3.03 (0.81, 11.35)
	HL low	Mid risk	1.41 (0.26, 7.6)	2.11 (0.23, 19.2)
		High risk	0.57 (0.11, 2.86)	2.31 (0.29, 18.63)
	HL mid	Mid risk	1.12 (0.30, 4.24)	1.26 (0.30, 5.37)
		High risk	0.47 (0.14, 1.63)	1.02 (0.27, 3.89)

Statistical significance:

*
p<0.05,**
p<0.01,***
p<0.001

Age quartiles equally divided and defined as: Age 0 = 40.21–52.64; Age 1 = 52.69–60.07; Age 2 = 60.08–68.52; Age 3 = 68.54–78.97

PTA4 (500, 1000, 2000, 4000 Hz), PTA Low (250, 500 Hz), PTA Mid (1000, 2000 Hz), and PTA High (4000, 8000 Hz).

Stroke risk categories as defined in the literature with the reference group as low risk (0–<5%) analyzed with Medium risk (5–7.5%), and high risk (>7.5%)

PTA = pure-tone average; Hz = hertz; HL = Hearing loss

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