Association of hearing loss with total and cause-specific mortality in US adults

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Abstract
We expected to explore the associations of hearing loss and hearing thresholds at different frequencies with total and cause-specific mortality. In this study, 11,732 individuals derived from the National Health and Nutrition Examination Survey (NHANES) 1999–2012 were included. Data of death was extracted from the NHANES Public-Use Linked Mortality File through December 31, 2015. Cox proportional hazards models were used to explore the associations between hearing loss, hearing thresholds at different frequencies, and total or cause-specific mortality. A total of 1,253 deaths occurred with a median follow-up of 12.15 years. A significant positive dose-response relationship between hearing loss in speech frequency and total mortality was observed, and the HRs and 95% CIs were 1.16 (0.91, 1.47), 1.54 (1.19, 2.00), and 1.85 (1.36, 2.50), respectively, for mild, moderate, and severe speech-frequency hearing loss (SFHL) with a \( P_{\text{trend}} \) of 0.0003. In addition, moderate (HR: 1.90, 95% CI: 1.20–3.00) and greater (3.50, 1.38–8.86) SFHL significantly elevated risk of heart disease mortality. Moreover, hearing thresholds of >25 dB at 500, 1000, or 2000 Hz were significantly associated with elevated mortality from all causes (1.40, 1.17–1.68; 1.44, 1.20–1.73; and 1.33, 1.10–1.62, respectively) and heart disease (1.89, 1.08–3.34; 1.95, 1.21–3.16; and 1.89, 1.16–3.09, respectively). Hearing loss is associated with increased risks of total mortality and heart disease mortality, especially for hearing loss at speech frequency. Preventing or inhibiting the pathogenic factors of hearing loss is important for reducing the risk of death.

Keywords Hearing loss · Hearing impairment · Hearing thresholds · Total mortality · Cause-specific mortality

Introduction

Hearing loss has become an increasingly prevalent disability and has been the fourth leading cause of disability globally (Cunningham and Tucci 2017). As a major concern for global health, hearing loss mainly results from congenital or acquired causes, including genetic mutations, aging, chronic middle ear infections, noise exposure, and ototoxic drugs (WHO 2020; Cunningham and Tucci 2017). The reach of hearing loss extends far beyond sensory impairment (Lancet 2016). As a result of communication disorder, hearing loss may bring series of profound effects on independence, wellbeing, quality of life, and daily function (Lancet 2016), which further result in various adverse health effects such as depression (Scinicariello et al. 2019), dementia (Gallacher et al. 2012), falls (Viljanen et al. 2009), metabolic syndrome (Han et al. 2018), and cardiovascular diseases (Fang et al. 2018). Apart from such effects, previous literature also explored the association between hearing loss and mortality (Engdahl et al.
early noise-induced hearing loss (Anonymous 2003). It was at speech frequency is lower than that at high frequency in addition based on the large size and long follow-up cohorts. More studies are warranted to explicit and verify such association between hearing loss and total mortality, it was not a universal finding (Karpa et al. 2010; Schubert et al. 2017). No significant association between hearing loss and total mortality was observed in the Epidemiology of Hearing Loss Study with 2,418 participants aged 53–97 years (Schubert et al. 2017). A study using data from the National Health and Nutrition Examination Survey (NHANES) 2005–2006 and 2009–2010 did not observe a significant association between hearing loss and the increased risk of mortality in the fully adjusted models among 1666 adults aged equal to and over 70 years (Contrera et al. 2015). In addition, Karpa et al. (2010) also obtained similar non-significant results after multivariable adjustment. Thus, more studies are warranted to explicit and verify such association based on the large size and long follow-up cohorts.

To our knowledge, the effect of noise on hearing often begins at high frequency, and the influence of hearing levels at speech frequency is lower than that at high frequency in early noise-induced hearing loss (Anonymous 2003). It was estimated that the prevalence of hearing loss was 31.1% for high-frequency hearing loss (HFHL) and 14.1% for speech-frequency hearing loss (SFHL) in US adults (Hoffman et al. 2017). However, as initial hearing impairment, HFHL is rarely studied, especially for relevant unhealthy effects. In addition, few researches have focused on the relationships between hearing levels at different frequencies and total and cause-specific mortality. Hence, we conducted this prospective study to investigate the associations of HFHL, SFHL, and hearing levels at different frequencies with total and cause-specific mortality among 11,732 representative US residents in the NHANES 1999–2012.

Methods

Study population

Participants were originated from the NHANES, which was administered by the National Center for Health Statistics (NCHS) and was described in details elsewhere (CDC 2017). In short, the NHANES is an ongoing health-related program conducted with a complex, multistage, probability sampling design for representative sample of the US residents. The continuous NHANES was started in 1999 and was implemented in 2-year cycles. Questionnaire survey, standardized physical examinations, and laboratory tests were carried out to collect data. In this study, we enrolled individuals with audiometric testing (n=16,854) at the baseline survey in the continuous NHANES 1999–2012 with 7 cycles. After excluded participants with uncompleted audiometric information (n=1,774) and those aged under 18 years or without mortality data (n=3,348), 11,732 individuals were finally included for analysis. The NHANES protocol was approved by the NCHS Ethics Review Board, and written informed consent was obtained from all participants.

Audiometric measurement

Audiometry measurement was performed by a trained examiner using an audiometer (AD226; Interacoustics AS, Assens, Denmark) with standard headphones (TDH-39; Telephonics Corporation, Farmingdale, NY) and insert earphones (EARtone 3A; Etymotic Research, Elk Grove Village, IL) in a dedicated, sound-isolating room. Hearing threshold testing was conducted on both ears of participants at seven frequencies (500, 1000, 2000, 3000, 4000, 6000, and 8000 Hz) across an intensity range of 0 to 120 dB. The 1000 Hz frequency was tested twice in each ear to keep the reliability of the measurement. More details of the audiometric measurement are available online (NHANES 2001).

Pure-tone average (PTA) of hearing thresholds at 500, 1000, 2000, and 4000 Hz (≥25 dB) was calculated to define SFHL, and the PTA of hearing thresholds at 3000, 4000, and 6000 Hz (≥25 dB) was applied to define HFHL (Scinicariello et al. 2019). Based on the PTA, grades of SFHL and HFHL were categorized according to the World Health Organization classifications (WHO 2021): normal (≤25 dB), mild (25–≤40 dB), moderate (40–≤60 dB), and severe (>60 dB).

Ascertainment of mortality outcomes

The data including cause and date of death was extracted from the NHANES Public-Use Linked Mortality File through December 31, 2015, which was from death certificate records from the National Death Index (NCHS 2019). Causes of death were ascertained according to the International Statistical Classification of Diseases, 10th Revision (ICD-10) (Brämer 1988). The outcomes in our study mainly included mortality from all causes, heart disease (codes I00-I09, I11, I13, and I20-I51), cancer (codes C00-C97), and other causes. Follow-up time was counted as the interval from baseline to the date of death, loss to follow-up, or December 31, 2015, for those who were censored.

Assessments of covariates

Covariates were collected from the questionnaire survey and physical examination, which covered information on
demographic (age, gender, race/ethnicity, education level, family income-poverty ratio (PIR), and marital status), lifestyles (smoking status, drinking status, physical activity, and dietary intake), occupational noise exposure, history of diseases (diabetes, cardiovascular disease, hypertension, and cancer), and so on. Multiple imputations were used for all missing values with MI procedure (Yuan 2011). Body mass index (BMI) was calculated as weight (kg) divided by square of height (m²) and was classified into three groups: <25, 25–30, and ≥30 kg/m². The race/ethnicity was mainly including Mexican American, non-Hispanic white, and non-Hispanic black. Education level was categorized as less than high school, high school or equivalent, and college or above. PIR was divided into three categories: 0–1.0, 1.1–3.0, and >3.0 (Chen et al. 2019). Marital status was grouped as married, separated (including widowed and divorced), and never married. We divided smoking status into never smokers (smoked less than 100 cigarettes in life), former smokers (smoked more than 100 cigarettes but not smoked at the time of the survey), and current smokers (smoked at least 100 cigarettes and smoked at the time of the survey). And we categorized drinking status into three groups: never drinker (0), low to moderate drinker (<2 drinks/day), and heavy drinker (≥2 drinks/day) (Chen et al. 2019). Physical activity was also categorized into three groups according to the frequency of exercise: 0, 1–2, and ≥3 times/week (Chen et al. 2019). The overall quality of dietary was assessed by Healthy Eating Index-2015 (HEI-2015), which was calculated as previously reported and categorized in quartiles for analysis (Krebs-Smith et al. 2018). Besides, general health condition was mainly grouped into three categories: very good to excellent, good, and poor to fair.

Statistical analysis

Based on the complex, multistage, probability sampling design in the NHANES, we accounted for sampling weights, cluster, and strata in our analysis according to the NHANES Tutorials (NCHS 2020). Categorical variables were expressed as number (weighted proportion) and compared by the Rao-Scott χ² test, while continuous variables were presented as mean/median (95% confidence interval (CI)) and compared by analysis of variance/Kruskal-Wallis test. We used the Kaplan-Meier method to plot the survival curves associated with high-frequency and speech-frequency PTA. Cox proportional hazards models were used to estimate the hazard ratios (HRs) with 95% CIs for total and cause-specific mortality for the mild (25–40 dB), moderate (40–60 dB), and severe (>60 dB) hearing loss at different frequencies, with comparison to normal hearing level (≤25 dB). For trend was calculated by including the median of PTA in each grade of hearing loss as a continuous variable in the models. Restricted cubic splines were furtherly used to examine the dose-response relationships between high-frequency/speech-frequency PTA and total/cause-specific mortality. Stratified analyses were conducted by gender, age, BMI, smoking status, drinking status, physical activity, occupational noise exposure, and general health condition. Moreover, we also explored the associations between hearing thresholds at different frequencies (500, 1000, 2000, 3000, 4000, and 6000 Hz) and total or cause-specific mortality. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and R version 4.0.2 (R Core Team 2020) with a 2-sided P < 0.05 considered statistically significant.

Results

Baseline characteristics

The baseline characteristics of the 11,732 participants were analyzed by categories of high-frequency and speech-frequency PTA (Table 1). Among the total participants, 14.67% (1,721/11,732), 12.33% (1,447/11,732), and 10.97% (1,287/11,732) showed mild, moderate, and severe HFHL, respectively. Meanwhile, 13.41% (1,573/11,732), 7.05% (827/11,732), and 2.57% (302/11,732) had mild, moderate, and severe SFHL, respectively. There were significant differences in BMI, PIR, married status, smoking status, drinking status, and HEI across the different hearing status. In addition, compared with individuals with normal high-frequency and speech-frequency hearing level, those with hearing loss were more likely to be men, older, non-Hispanic white, less educated, physically inactive, exposed to occupational noise, and with a history of diabetes, cardiovascular diseases, hypertension, or cancer.

Association between hearing loss and total or cause-specific mortality

Among 11,732 participants, a total of 1,253 deaths occurred during a median follow-up of 12.15 years, including 218 deaths from heart disease and 286 deaths from cancer. Table 2 shows the associations of HFHL and SFHL with total and cause-specific mortality. Significant dose-response relationships were observed between HFHL or SFHL with total mortality. Compared with individuals with normal high-frequency hearing level, those with mild, moderate, and severe HFHL were significantly associated with 20% (HR: 1.20, 95% CI: 0.86–1.68), 27% (1.27, 0.94–1.72), and 42% (1.42, 1.05–1.92) increased risk of total mortality (P trend=0.0207). However, the HR was elevated without statistically significant for heart disease [0.84 (0.36–1.98), 1.28 (0.60, 2.73), and 1.50 (0.62, 3.60) for mild, moderate, and severe HFHL, respectively] and cancer mortality [1.28 (0.73, 2.22), 1.21 (0.71, 2.04), and 1.37 (0.74, 2.52) for mild, moderate, and severe HFHL, respectively], after adjusting for potential confounders. When
|                         | HFHL P value       | SFHL P value       |
|-------------------------|--------------------|--------------------|
| Participants            | Normal 9,030       | Normal 1,148       |
|                         | Mild 9,573         | Mild 924           |
|                         | Moderate 827        | Moderate 509        |
|                         | Severe 302         | Severe 187         |
| Male                    | Normal 3,026 (40.43)| Normal 4,148 (45.92)| |
| Age, years, mean (95% CI)| Mild 912 (56.90)  | Mild 924 (61.70)  |
|                         | Moderate 868 (64.54)| Moderate 509 (60.54)| |
|                         | Severe 962 (77.92) | Severe 187 (55.37) |
| BMI, kg/m²              | <0.0001            | <0.0001            |
| <25                     | Normal 2,710 (38.40)| Normal 3,183 (35.98)| |
|                         | Mild 465 (26.21)   | Mild 426 (26.00)   |
|                         | Moderate 390 (25.42)| Moderate 573 (37.50)| |
|                         | Severe 382 (28.78) | Severe 317 (34.99) |
| Race/ethnicity          | <0.0001            | <0.0001            |
| Mexican American        | Normal 1,360 (8.78)| Normal 1,675 (8.43)| |
|                         | Mild 304 (6.98)    | Mild 238 (4.93)    |
|                         | Moderate 235 (5.96)| Moderate 167 (4.78)| |
|                         | Severe 167 (3.81)  | Severe 108 (4.78)  |
| Non-Hispanic White      | Normal 2,799 (65.19)| Normal 3,636 (36.10)| |
|                         | Mild 755 (73.39)   | Mild 887 (78.32)   |
|                         | Moderate 807 (78.43)| Moderate 544 (79.80)| |
|                         | Severe 900 (85.46)| Severe 194 (79.29)| |
| Non-Hispanic Black      | Normal 1,908 (13.46)| Normal 2,269 (12.93)| |
|                         | Mild 405 (9.77)    | Mild 264 (6.80)    |
|                         | Moderate 233 (5.85)| Moderate 94 (4.87) |
|                         | Severe 120 (3.82)  | Severe 39 (7.00)   |
| Others                  | <0.0001            | <0.0001            |
| Educational level       | Normal 1,486 (14.67)| Normal 1,986 (15.48)| |
|                         | Mild 512 (19.69)   | Mild 556 (24.68)   |
|                         | Moderate 520 (25.78)| Moderate 335 (32.37)| |
|                         | Severe 480 (26.30)| Severe 121 (28.01)| |
| PIR                     | 0.0002             | <0.0001            |
| 0–1.0                   | Normal 1,671 (15.71)| Normal 2,006 (15.04)| |
|                         | Mild 356 (13.87)   | Mild 271 (11.24)   |
|                         | Moderate 255 (11.72)| Moderate 139 (13.22)| |
|                         | Severe 189 (9.97)  | Severe 55 (16.46)  |
| Married status          | <0.0001            | <0.0001            |
| Married                 | Normal 3,085 (50.55)| Normal 4,148 (53.69)| |
|                         | Mild 967 (61.45)   | Mild 912 (62.84)   |
|                         | Moderate 835 (65.25)| Moderate 440 (57.55)| |
|                         | Severe 755 (63.93)| Severe 142 (50.47)| |
| Separated               | Normal 1,487 (17.63)| Normal 1,919 (18.25)| |
|                         | Mild 463 (23.26)   | Mild 487 (23.60)   |
|                         | Moderate 463 (23.71)| Moderate 320 (32.64)| |
|                         | Severe 435 (26.57)| Severe 122 (36.44)| |
| Never married           | Normal 2,705 (31.82)| Normal 2,963 (28.06)| |
| Smoking status          | <0.0001            | <0.0001            |
| Never smoker            | Normal 4,084 (55.04)| Normal 4,888 (52.51)| |
|                         | Mild 844 (45.62)   | Mild 694 (42.10)   |
|                         | Moderate 642 (41.38)| Moderate 354 (42.14)| |
|                         | Severe 502 (37.00)| Severe 136 (44.35)| |
| Former smoker           | Normal 1,759 (21.52)| Normal 2,303 (23.49)| |
|                         | Mild 477 (27.11)   | Mild 563 (32.17)   |
|                         | Moderate 524 (34.48)| Moderate 357 (41.25)| |
|                         | Severe 585 (42.90)| Severe 122 (33.88)| |
| Current smoker          | Normal 1,434 (23.44)| Normal 1,839 (24.01)| |
| Drinking status         | 0.0025             | <0.0001            |
| Never drinker           | Normal 1,420 (17.72)| Normal 1,819 (17.16)| |
|                         | Mild 467 (18.51)   | Mild 454 (21.49)   |
|                         | Moderate 395 (20.39)| Moderate 260 (26.50)| |
|                         | Severe 367 (21.40)| Severe 116 (36.01)| |
| Low to moderate drinker | Normal 2,165 (29.10)| Normal 2,700 (29.23)| |
|                         | Mild 520 (30.15)   | Mild 530 (31.67)   |
|                         | Moderate 496 (32.78)| Moderate 321 (38.26)| |
|                         | Severe 490 (33.74)| Severe 120 (34.54)| |
| Heavy drinker           | Normal 3,692 (53.18)| Normal 4,511 (53.61)| |
|                         | Mild 734 (51.34)   | Mild 589 (46.84)   |
|                         | Moderate 556 (46.83)| Moderate 246 (35.24)| |
|                         | Severe 430 (44.86)| Severe 66 (29.45)| |
|                      | HFHL | SFHL |                      | SFHL | SFHL |
|----------------------|------|------|----------------------|------|------|
|                      | Normal | Mild | Moderate | Severe | P value | Normal | Mild | Moderate | Severe | P value |
| Physical activity, times/week | <0.0001 | 0.0003 |                      | <0.0001 | 0.0003 |
| 0                    | 2,303 (25.49) | 745 (36.03) | 701 (39.60) | 665 (41.84) | 3,040 (27.27) | 766 (40.78) | 441 (44.02) | 167 (44.62) | <0.0001 | 0.0003 |
| 1–2                  | 3,257 (53.60) | 668 (49.75) | 516 (45.11) | 422 (40.97) | 3,935 (52.58) | 555 (45.56) | 281 (43.04) | 92 (37.64) | <0.0001 | 0.0003 |
| ≥3                   | 1,717 (20.92) | 308 (14.21) | 230 (15.29) | 200 (17.19) | 2,055 (20.15) | 252 (13.66) | 105 (12.94) | 43 (17.74) | <0.0001 | 0.0003 |
| General health condition | <0.0001 | <0.0001 |                      | <0.0001 | <0.0001 |
| Very good to excellent | 3,133 (49.52) | 566 (40.50) | 479 (39.51) | 429 (39.90) | 3,755 (48.23) | 518 (39.55) | 244 (32.40) | 90 (38.40) | <0.0001 | <0.0001 |
| Good                 | 3,087 (39.85) | 725 (41.60) | 585 (40.62) | 524 (40.67) | 3,828 (40.28) | 624 (38.94) | 350 (44.35) | 119 (36.91) | <0.0001 | <0.0001 |
| Poor to fair         | 1,057 (10.63) | 430 (17.90) | 383 (19.87) | 334 (19.43) | 1,447 (11.48) | 431 (21.51) | 244 (32.40) | 90 (38.40) | <0.0001 | <0.0001 |
| Healthy eating index | <0.0001 | 0.0004 |                      | <0.0001 | <0.0001 |
| Q1                   | 2,059 (29.46) | 342 (21.52) | 269 (23.84) | 263 (23.06) | 2,397 (27.95) | 307 (23.76) | 169 (22.74) | 60 (23.15) | <0.0001 | <0.0001 |
| Q2                   | 1,902 (25.66) | 400 (25.74) | 351 (24.18) | 280 (23.09) | 2,316 (25.74) | 364 (23.76) | 190 (24.04) | 63 (18.15) | <0.0001 | <0.0001 |
| Q3                   | 1,725 (23.29) | 470 (25.96) | 397 (28.25) | 341 (24.27) | 2,193 (23.75) | 442 (27.68) | 223 (25.56) | 75 (24.03) | <0.0001 | <0.0001 |
| Q4                   | 1,591 (21.59) | 509 (26.78) | 430 (23.73) | 403 (29.58) | 2,124 (22.56) | 460 (24.80) | 245 (27.65) | 104 (34.67) | <0.0001 | <0.0001 |
| Occupational noise exposure | 1,724 (23.06) | 563 (34.37) | 532 (39.80) | 613 (47.99) | 2,390 (26.41) | 566 (37.07) | 348 (42.85) | 128 (37.97) | <0.0001 | <0.0001 |
| History of diseases  |                      |                      |                      |                      |                      |                      |                      |                      |                      |
| Diabetes             | 364 (3.69) | 287 (10.70) | 254 (15.37) | 225 (15.18) | 632 (4.98) | 293 (14.84) | 152 (18.49) | 53 (15.09) | <0.0001 | <0.0001 |
| Cardiovascular disease | 250 (3.20) | 192 (8.90) | 292 (16.71) | 355 (21.91) | 452 (4.41) | 316 (15.81) | 239 (25.85) | 82 (21.27) | <0.0001 | <0.0001 |
| Hypertension         | 1,452 (18.59) | 753 (36.51) | 705 (40.17) | 700 (47.67) | 2,196 (21.81) | 803 (42.35) | 446 (49.06) | 165 (51.27) | <0.0001 | <0.0001 |
| Cancer               | 285 (5.08) | 181 (10.64) | 220 (13.91) | 284 (16.92) | 480 (6.13) | 246 (17.53) | 178 (19.56) | 66 (17.04) | <0.0001 | <0.0001 |
| Follow up time, years, median (95% CI) | 12.42 (12.10–12.74) | 12.15 (11.70–12.61) | 11.14 (10.46–11.81) | 9.71 (8.13–11.29) | 12.35 (12.06–12.65) | 11.28 (10.74–11.85) | 9.48 (8.73–10.54) | 7.35 (6.48–8.64) | <0.0001 | <0.0001 |

The Rao-Scott $\chi^2$ test was used to compare for categorical variables, and analysis of variance adjusted for sampling weights was used to compare for continuous variables. Categorical variables were expressed as number (percentage), and continuous variables were shown as mean/median (95% CI). Abbreviation: HFHL high-frequency hearing loss, SFHL speech-frequency hearing loss, BMI body mass index, PIR family income-poverty ratio, CI confidence interval.
### Table 2. Associations of hearing loss levels with total and cause-specific mortality (N=11,732)

| HRs (95% CIs) by different hearing status | P for trend |
|------------------------------------------|------------|
| Normal | Mild | Moderate | Severe |
| **HFHL** |
| Total mortality |
| Age adjusted mortality rate# | 6.00 (4.98–7.01) | 9.27 (7.16–11.39) | 12.75 (10.58–14.93) | 18.06 (9.97–26.16) |
| Number of deaths/person years | 311/66,870 | 207/15,151 | 302/11,686 | 433/9,566 |
| Model 1 | 1 (ref.) | 1.42 (1.04, 1.94) | 1.83 (1.47, 2.27) | 2.23 (1.82, 2.72) |
| Model 2 | 1 (ref.) | 1.25 (0.90, 1.73) | 1.38 (1.05, 1.82) | 1.56 (1.17, 2.09) |
| Model 3 | 1 (ref.) | 1.20 (0.86, 1.68) | 1.27 (0.94, 1.72) | 1.42 (1.05, 1.92) |
| Heart diseases mortality |
| Number of deaths/person years | 40/66,870 | 28/15,151 | 55/11,686 | 95/9,566 |
| Model 1 | 1 (ref.) | 1.30 (0.61, 2.77) | 2.53 (1.20, 5.34) | 3.51 (1.74, 7.10) |
| Model 2 | 1 (ref.) | 1.00 (0.44, 2.25) | 1.60 (0.76, 3.34) | 1.91 (0.81, 4.51) |
| Model 3 | 1 (ref.) | 0.84 (0.36, 1.98) | 1.28 (0.60, 2.73) | 1.50 (0.62, 3.60) |
| Cancer mortality |
| Number of deaths/person years | 87/66,870 | 55/15,151 | 61/11,686 | 83/9,566 |
| Model 1 | 1 (ref.) | 1.43 (0.81, 2.51) | 1.61 (1.05, 2.49) | 1.93 (1.14, 3.28) |
| Model 2 | 1 (ref.) | 1.20 (0.69, 2.09) | 1.19 (0.73, 1.93) | 1.37 (0.77, 2.44) |
| Model 3 | 1 (ref.) | 1.28 (0.73, 2.22) | 1.21 (0.71, 2.04) | 1.37 (0.74, 2.52) |
| Other causes mortality |
| Number of deaths/person years | 184/66,870 | 124/15,151 | 186/11,686 | 255/9,566 |
| Model 1 | 1 (ref.) | 1.45 (0.96, 2.19) | 1.77 (1.24, 2.52) | 2.07 (1.50, 2.85) |
| Model 2 | 1 (ref.) | 1.35 (0.88, 2.06) | 1.43 (0.97, 2.12) | 1.55 (1.00, 2.40) |
| Model 3 | 1 (ref.) | 1.27 (0.83, 1.96) | 1.31 (0.87, 1.96) | 1.41 (0.89, 2.21) |
| **SFHL** |
| Total mortality |
| Age adjusted mortality rate# | 6.75 (5.96–7.54) | 12.37 (9.83–14.92) | 23.61 (16.50–30.73) | 16.89 (10.66–23.11) |
| Number of deaths/person years | 515/82,247 | 336/12,970 | 283/6,015 | 119/2,040 |
| Model 1 | 1 (ref.) | 1.59 (1.29, 1.95) | 1.61 (1.05, 2.49) | 1.93 (1.14, 3.28) |
| Model 2 | 1 (ref.) | 1.20 (0.69, 2.09) | 1.19 (0.73, 1.93) | 1.37 (0.77, 2.44) |
| Model 3 | 1 (ref.) | 1.28 (0.73, 2.22) | 1.21 (0.71, 2.04) | 1.37 (0.74, 2.52) |
| Heart diseases mortality |
| Number of deaths/person years | 75/82,247 | 55/12,970 | 55/6,015 | 33/2,040 |
| Model 1 | 1 (ref.) | 1.61 (0.90, 2.88) | 3.50 (2.04, 6.01) | 6.30 (2.52, 15.76) |
| Model 2 | 1 (ref.) | 1.04 (0.59, 1.83) | 2.15 (1.33, 3.46) | 3.90 (1.48, 10.30) |
| Model 3 | 1 (ref.) | 0.88 (0.50, 1.53) | 1.90 (1.20, 3.00) | 3.50 (1.38, 8.86) |
| Cancer mortality |
| Number of deaths/person years | 146/82,247 | 74/12,970 | 50/6,015 | 16/2,040 |
| Model 1 | 1 (ref.) | 1.19 (0.81, 1.76) | 1.36 (0.80, 2.31) | 1.23 (0.55, 2.75) |
| Model 2 | 1 (ref.) | 0.93 (0.61, 1.41) | 1.09 (0.66, 1.82) | 1.00 (0.44, 2.26) |
| Model 3 | 1 (ref.) | 0.94 (0.61, 1.46) | 1.04 (0.62, 1.75) | 0.93 (0.38, 2.28) |
| Other causes mortality |
| Number of deaths/person years | 294/82,247 | 207/12,970 | 178/6,015 | 70/2,040 |
| Model 1 | 1 (ref.) | 1.82 (1.40, 2.38) | 2.58 (1.79, 3.72) | 2.80 (1.97, 3.99) |
| Model 2 | 1 (ref.) | 1.49 (1.10, 2.03) | 1.84 (1.23, 2.76) | 1.83 (1.15, 2.90) |
| Model 3 | 1 (ref.) | 1.40 (1.04, 1.90) | 1.73 (1.15, 2.58) | 1.77 (1.11, 2.84) |

Model 1, adjusted for age; model 2, model 1+adjusted for gender, race, educational levels, BMI, family income-poverty ratio level, married status, smoking status, drinking status, physical activity, general health condition, healthy eating index, and occupational noise exposure; model 3, model 2+adjusted for history of diabetes, cardiovascular disease, hypertension, and cancer

#Mortality rates per 1000 person years, standardized to age distribution of entire study population and represented as estimated mortality rates (95% CIs).

Abbreviation: HFHL high-frequency hearing loss, SFHL speech-frequency hearing loss, HRs hazard ratios, CIs confidence intervals
compared with those with normal speech frequency hearing, the HRs and 95% CIs of mild, moderate, and severe SFHL were 1.16 (0.91, 1.47), 1.54 (1.19, 2.00), and 1.85 (1.36, 2.50), respectively, for total mortality ($P_{\text{trend}} =0.0003$). Different from total mortality, no significant associations were discovered between HFHL and heart disease mortality, while significant associations were observed between SFHL and heart disease mortality. The HRs and 95% CIs of heart disease mortality were 1.90 (1.20, 3.00) and 3.50 (1.38, 8.86), respectively for moderate and severe/greater SFHL.

The dose-response relationships between high-frequency and speech-frequency PTA with total and cause-specific mortality were further intuitively showed by the spline curve in Figure 1. A significantly monotonic increasing dose-response relationship was found between high-frequency PTA and total mortality. Similarly, significant linear dose-response relationships were also observed among speech-frequency PTA and total and heart disease mortality. In addition, Figure 2 showed that the survival probability gradually decreased as the high-frequency and speech-frequency PTA increased during the follow-up time.

In the stratified analyses, significant associations between HFHL and total mortality were mainly observed among female, current smokers, and those with inactive physical activity (Table S1). Likewise, the association between SFHL and total mortality were more significant among females, obese individuals, heavy drinkers, and those with poor to fair general health condition (Table S2).

**Associations between hearing thresholds at different frequencies and total or cause-specific mortality**

We furtherly evaluate the associations between hearing thresholds at different frequencies and total or cause-specific mortality (Figure 3). Compared with hearing thresholds of ≤25 dB at 500, 1000, or 2000 Hz, hearing thresholds of >25 dB were significantly associated with increased total [(1.40 (1.17, 1.68), 1.44 (1.20, 1.73), and 1.33 (1.10, 1.62), respectively] and heart disease mortality [1.89 (1.08, 3.34), 1.95 (1.21, 3.16), and 1.89 (1.16, 3.09), respectively]. In addition, the risk for total and heart disease mortality also showed increasing trends as hearing thresholds at 3000, 4000, and 6000 Hz increased, though they were not statistically significant. The dose-response relationships between hearing thresholds at different frequencies and total or cause-specific mortality were presented in Figure S1, which further yielded significant associations between hearing thresholds of >25 dB at low frequencies (500, 1000, or 2000 Hz) and total/heart disease mortality.

**Discussions**

In this study, we observed positive dose-response associations of total mortality with SFHL and HFHL in US adults. Also, SFHL was associated with heart disease mortality in a positive dose-dependent manner. Moreover, we found that hearing thresholds at speech frequencies (500, 1000, and 2000 Hz) were positively associated with total and heart disease mortality.

Although several epidemiological studies have explored the association between hearing loss and mortality, the results from these researches are not entirely consistent (Engdahl et al. 2019; Genther et al. 2015; Karpa et al. 2010; Miyawaki et al. 2020; Schubert et al. 2017). Genther et al. (2015) reported that hearing loss was associated with an increased risk of mortality among 1,958 older adults in the USA, whereas Schubert et al. (2017) failed to discover significant association between hearing loss and total mortality in the Epidemiology of Hearing Loss Study. The discrepancy might due to different race/ethnicity, different sample sizes, and follow-up time. In addition, most studies except Karpa et al. (2010) and Gopinath et al. just explored the association of SFHL or self-reported hearing loss with total mortality (Gopinath et al. 2013; Karpa et al. 2010). Different from previous studies, the participants in the present study covered a larger age range (18 years or older), and the follow-up time was longer (12.15 years); the number of the participants was larger. Of note, the study could better explore the association between hearing loss, hearing thresholds, and mortality more comprehensively in US adults. As hearing loss is widely prevalent and greatly threatens people’s health (Blackwell et al. 2014; Strawbridge et al. 2000), the findings of our study have important public health implications that more effective measurements are needed to be taken for preventing the occurrence and development of hearing loss.

Although the underlying mechanisms of the associations between hearing loss and mortality are unclear, several reasons might be considered. Firstly, as described in the study, individuals with hearing loss were more likely to be smokers, physical inactive, exposed to occupational noise, poor to fair general health condition, and with history of diabetes, cardiovascular diseases, hypertension, and cancer, and these characteristics are also risk factors for increased risk of death. Furthermore, individuals with progressive levels of hearing impairment showed a dose-response decreased pattern for physical functioning, mental health, and social functioning (Strawbridge et al. 2000). As reported previously, hearing loss has been associated with cognitive decline/dementia (Lin et al. 2011), depression (Sciniciarlo et al. 2019), walking speed (Li et al. 2013), falls (Viljanen et al. 2009), metabolic syndrome (Han et al. 2018), and cardiovascular diseases (Fang et al. 2018), all of which have been associated with increased risk of death (Houle 2013; Käräjämäki et al. 2020; Mirelman et al. 2016; Studenski et al. 2011; Torisson et al. 2012). The Blue Mountains Hearing Study previously demonstrated that disability in walking, cognitive impairment, and self-rated health mediated the association between hearing loss and total...
mortality by structural equation modeling (Karpa et al. 2010). Herein, our results also showed that the association of hearing loss and mortality was attenuated after adjustment for general health condition and cardiovascular diseases. Meanwhile, the association became stronger among individuals with poor to fair general health condition. In addition, age is an important factor of hearing loss, and the risk of hearing loss would elevate with age increasing (WHO 2020); however, we still obtained significant associations between hearing loss and mortality adjusted for age in the models and in the analysis stratified by age, which could promise the reliability of our study.

Notably, the association between SFHL and total mortality was more obvious than HFHL. It has been reported that
approximately 104 million people are at risk of noise-induced hearing loss in the USA (Hammer et al. 2014). The effect of noise on hearing often begins at the higher frequencies of 3000, 4000, or 6000 Hz, which are more susceptible to noise (Anonymous 2003). And the influence from PTA of speech frequency is lower than that of high frequency in early noise-induced hearing loss (Anonymous 2003). Thus, SFHL may reflect more severe hearing impairment, which is more likely to cause or be associated with a series of negative health outcomes (Fang et al. 2018; Jayakody et al. 2018; Scinicariello et al. 2019). That significant associations between hearing thresholds at low frequencies (500, 1000, and 2000 Hz) and total mortality in this study further proved it. Initial HFHL may partly predict the risk of total mortality at an earlier stage before SFHL as previously mentioned (Feeny et al. 2012), and to prevent the further development of hearing loss may somewhat decrease the risk of death. In addition, inconsistent with the results from Karpa et al. (2010) and Gopinath et al. (2013), they failed to discover a significant association between hearing loss and cardiovascular disease mortality in fully adjusted models. We found SFHL rather than HFHL was significantly connected with heart disease mortality in this study. SFHL has been reported to be associated with microvascular damage (Fang et al. 2019) and often accompanied by cardiovascular disease risk factors such as smoking, inactive physical activity, with a history of hyperglycemia, and hypertension (Han et al. 2018), which would promote the development of heart disease to further increase the risk of heart disease mortality (Fang et al. 2018; Gan et al. 2016; Karpa et al. 2010).

There are some strengths in our study. We first conducted a prospective cohort study to investigate the associations of HFHL and SFHL with total and cause-specific mortality in a large nationally representative US sample. Furthermore, we also evaluated the associations between hearing thresholds at

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**Fig. 2** Association of high-frequency and speech-frequency pure-tone average with the survival probability during the follow-up time (N=11,732).

**Fig. 3** Associations of hearing thresholds at different frequencies with total and cause-specific mortality (N=11,732). Adjusted for age, gender, race, educational levels, BMI, family income-poverty ratio level, married status, smoking status, drinking status, physical activity, general health condition, healthy eating index, occupational noise exposure, history of diabetes, cardiovascular disease, hypertension, and cancer. Abbreviation: HR hazard ratios, CI confidence interval.
different frequencies and total and cause-specific mortality. Several limitations in our study should also be identified. First, the hearing thresholds were measured only once at baseline, and covariates adjusted in our study were also available at baseline. It is unclear whether hearing thresholds and covariates changed during follow-up. Second, we did not differentiate between innate and acquired hearing loss due to a lack of relative data. Thus, studies are needed to explore the differences in the associations of innate and acquired hearing loss with mortality in the future. Third, although we adjusted confounders as well as possible, we might not consider all potential confounders in the analyses. In addition, participants in our study were US adults aged 18–85 years; thus, the results might not be adapted to children or other ethnicities.

Conclusion

Hearing loss and hearing thresholds, especially at speech frequencies, are associated with increased risk of total and heart disease mortality. Prevention for the occurrence and development of hearing loss may markedly reduce the risk of total and heart disease mortality. More research should be conducted to further elucidate the underlying mechanisms responsible for these associations.

Availability of data and materials No additional data available.

Author contribution XF, WC, and DW designed research. XF and DW conducted research, analyzed data, and wrote the paper. WL, MC, WQ, RL, ML, and WC contributed to the acquisition, analysis, or interpretation of the data and revised the manuscript for important intellectual content. DW and WC have primary responsibility for final content and is the study guarantor. All authors read and approved the final manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Declarations

Ethics approval and consent to participate The National Health and Nutrition Examination Survey protocol was approved by the National Center for Health Statistics Ethics Review Board, and written informed consent was obtained from all participants.

Consent for publication Not applicable.

Conflict of interest The authors declare no competing interests.

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