Long-term Assessment of Systemic Inflammation and the Cumulative Incidence of Age-related Hearing Impairment in the Epidemiology of Hearing Loss Study


Background. Although research has linked systemic inflammation to various diseases of aging, few studies have examined the potential role it may play in the development of age-related hearing impairment.

Methods. Among 1,073 participants free of hearing impairment (pure-tone average 0.5, 1, 2, 4 kHz ≤ 25 dB HL) in the population-based Epidemiology of Hearing Loss Study (1998–2000), serum C-reactive protein, and interleukin-6 were measured at three time points (1988–1990, 1998–2000, and 2009–2010), and tumor necrosis factor-α was measured at one time point (1998–2000), whereas hearing impairment was measured again in 2003–2005 and 2009–2010 to determine the 10-year cumulative incidence.

Results. Inflammatory marker levels from a single time point (1998–2000) were not associated with an increased risk of developing hearing impairment. Associations between long-term serum C-reactive protein levels and incident hearing impairment differed by age (p = .031). Participants less than 60 years with consistently high (>3 mg/L) or increasing levels of serum C-reactive protein over 10 years were nearly two times (hazard ratio: 1.96, 95% confidence interval: 1.19, 3.23) as likely to develop hearing impairment over the subsequent 10-year period, an association not seen in participants more than or equal to 60 years. A statistically significant association (p-trend = .041) was also observed between number of markers in the highest group at baseline and incident hearing impairment in this younger age group.

Conclusions. Associations between long-term serum C-reactive protein levels and incident hearing impairment were observed in the cohort as a whole, but differed significantly by age group, with statistically significant associations observed in adults less than 60 years, participants moving through the peak risk period for hearing impairment over the course of the study.

Key Words: Epidemiology—Hearing—Inflammation—Hearing loss—Sensory.

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Age-related hearing impairment is a highly prevalent condition in older adults and is often associated with a poorer quality of life (1,2). The etiology of age-related hearing impairment, which is no doubt multifactorial, is still being determined. Increasingly, relationships of cardiovascular disease (CVD) and its antecedents as possible risk factors for hearing impairment have been examined (3–8). The prevalence of both hearing impairment and CVD is increased in older adults and these conditions often co-occur, suggesting that there may be some common underlying pathological factors at work. Serum markers of systemic inflammation have been demonstrated to increase with age and have been implicated in adverse cardiovascular outcomes and all-cause mortality (9–14). Yet to date, few studies have examined the potential role that systemic inflammation may play in the development of age-related hearing impairment.

The aim of this study was to determine if circulating markers of inflammation, namely the cytokines interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) and the acute phase protein C-reactive protein (CRP) were associated with the 10-year cumulative incidence of hearing impairment and 10-year hearing sensitivity in a large epidemiological cohort of older adults. Because of the availability of multiple inflammatory measures over many years in this cohort (CRP and IL-6), prospective associations...
between long-term inflammation trajectories and hearing outcomes were examined.

**Methods**

The Epidemiology of Hearing Loss Study (EHLS) is a longitudinal cohort study of older adults in Beaver Dam, Wisconsin (1). The first examination (EHLS1) was conducted between 1993 and 1995 \(^{(N = 3,753; 82.6\% \text{ of those eligible})}\) in a population-based cohort, the Beaver Dam Eye Study, which was begun in 1988–1990 (15). Participants were examined concurrently for both EHLS and Beaver Dam Eye Study every 5 years. For this study, the 5-year follow-up examination (EHLS2; 1998–2000) forms the baseline as it was the earliest exam where both inflammation and hearing data were available \((N = 1,073)\). Participants free of hearing impairment \((N = 1,281; 45.8\%)\) at EHLS2, with inflammatory marker data \((n = 1,215; 94.8\%)\), who had follow-up audiometric data at either EHLS3 (2003–2005) or EHLS4 (2009–2010) or both, were included in these analyses \((N = 1,073)\).

**Hearing Endpoints**

The hearing examination at each phase of the study followed the same standardized methods and included otoscopy, tympanometry (GSI 37 Autotym, Grason-Stadler, Inc., Eden Prairie, MN), and pure-tone air- and bone-conduction audiometry. Audiometric testing was conducted in accordance with guidelines of the American Speech-Language-Hearing Association in a sound-treated booth (Industrial Acoustics Company, New York) (16). A GSI-61 clinical audiometer (Grason-Stadler, Inc.) was used for each phase of the study (EHLS2-4), TDH-50P earphones were used for air-conduction testing, and insert earphones (E-A_Rtone 3A; Cabot Safety Corp., Indianapolis, IN) were used in cases of collapsed ear canals. Masking was used when needed for both air- and bone-conduction audiometry. Participants who were not able to come to the clinical site were examined in their home or nursing home using a Beltone 112 portable audiometer (Beltone Electronic Corp., Chicago, IL) with insert earphones. Audiometers were calibrated every 6 months according to the American National Standards Institute standards (17), and calibration checks were performed daily. Ambient noise levels were measured throughout each study; either in the clinic or at homes and nursing homes to comply with the American National Standards Institute standards (18).

Pure-tone air-conduction thresholds were determined for each ear at 0.5, 1, 2, 3, 4, 6, and 8kHz. A pure-tone average (PTA) was calculated using four thresholds (0.5, 1, 2, and 4kHz) for each ear at each examination phase. Incident hearing impairment was defined as developing a PTA (0.5, 1, 2, and 4kHz) more than 25 decibels (dB) hearing level (HL) in either ear (worse ear) at a follow-up exam among participants without hearing impairment at baseline.

**Exposure Variables**

Nonfasting venous blood draws were conducted at EHLS2 and EHLS4 following similar protocols. In 2011, each participant’s serum samples from EHLS2 and EHLS4 were removed from storage \((-80^\circ \text{C})\), paired and assayed (Advanced Research and Diagnostic Laboratory, University of Minnesota, Minneapolis, MN) on the same plate to eliminate between-run variability. Serum high-sensitivity CRP was measured using a latex-particle enhanced immunoturbidimetric assay kit (Roche Diagnostics, Indianapolis, IN). The reference range for the laboratory was 0–5 mg/L, and the interassay coefficient of variation was 4.5%. In addition, serum high-sensitivity CRP was available in the same cohort from samples drawn at Beaver Dam Eye Study 1 (1988–1990). These samples were stored at −80°C until they were assayed in 2006 using a latex particle-enhanced immunoturbidimetric assay (Kamiya Biomedical Company, Seattle, WA) (reference range: 0–5.5 mg/L; interassay coefficient of variation: 4.5%).

Serum IL-6 was determined in samples from EHLS2 and EHLS4, and serum TNF-α in samples from EHLS2 in 2011 using the quantitative sandwich enzyme technique of ELISA (IL-6: QuantiKine High Sensitivity Kit, R&D Systems, Minneapolis, MN; TNF-α: QuantiGlo immunoassay from R&D Systems, Minneapolis, MN). Interassay coefficient of variations were 11.7% for IL-6 and 13.0% for TNF-α. IL-6 was also available from a random sample of the Beaver Dam Eye Study 1 cohort assayed in 2006 using the quantitative sandwich enzyme technique of ELISA (QuantiKine High Sensitivity Kit, R&D Systems; interassay coefficient of variation: 6.5%–9.6%). Inflammatory marker assays performed in 2006 and in 2011 were analyzed at the same laboratory in accordance with strict quality control procedures.

![Diagram](https://example.com/flowchart.png)

Figure 1. Flow chart for analytic sample construction, the epidemiology of hearing loss study.
Covariates

Behavioral and biomedical variable data were collected by trained examiners following strict protocols, and baseline (1998–2000) levels of covariates were used for statistical adjustment. Total grams of ethanol per week were ascertained by self-report of the number of beer, wine, and liquor beverages consumed in an average week. Alcohol intake groups were created based on previously defined cutoffs in this cohort (19). Participants who had smoked fewer than 100 cigarettes in their lifetime were considered never smokers, whereas those who had smoked at least 100 cigarettes were divided into past (no longer smoking at the time of the exam) and current smokers. The number of blocks walked and flight of stairs climbed per day were combined to create a weekly total physical activity index using the formula of Lee and Paffenbarger (20). Medication data were collected using medication labels or self-report. A history of CVD was defined as self-report of physician diagnosed stroke, myocardial infarction, or angina. The number of years of education a participant had obtained was divided into three groups: less than 12, 12, and more than 12 years of school. Occupational noise was defined as self-report of having a current job that required speaking in a raised voice or louder to be heard within 2 feet of another person, and family history of hearing loss was ascertained by self-report.

Systolic and diastolic blood pressure was measured using the Hypertension Detection and Follow-up Protocol (21). Hypertension was defined as systolic blood pressure more than or equal to 140 mmHg, diastolic blood pressure more than or equal to 90 mmHg, or physician-diagnosed hypertension and current use of hypertension medication. Diabetes was defined as either a self-report of physician diagnosis of diabetes, taking medications for diabetes (pills or insulin injection), or hemoglobin A1C level more than or equal to 6.5% at the time of the exam (1998–2000). Height and weight were measured, and body mass index was calculated by dividing weight in kilograms by height in meters squared. Obesity was defined as a body mass index more than or equal to 30 kg/m$^2$. Serum high-density lipoprotein cholesterol was measured using colorimetric spectrometry (Vitros Analyzer, Beaver Dam Community Hospital Laboratory).

Statistical Analysis

Participants were divided into three CRP risk groups (<1, 1–3, and >3 mg/L) according to established cut-points, whereas three IL-6 groups and three TNF-α groups were defined according to tertiles of the distribution at EHLS2 (22). Previous studies have demonstrated that both sustained high levels of inflammation and increases in inflammation are associated with negative health outcomes in older age (11–14). Therefore, a 10-year higher risk inflammatory profile was defined as remaining in the highest level or increasing a level between exams at 1988–1990 and 1998–2000. To test whether baseline inflammation levels and 10-year inflammatory profiles were associated with the 10-year cumulative incidence of hearing impairment (1998–2000 to 2009–2010), discrete-time Cox proportional hazards models were used (PROC PHREG. Ties=discrete; SAS 9.3) due to the small number of follow-up intervals. An event was defined as the first occurrence of hearing impairment during the follow up. Participants who died or did not participate in subsequent follow-up exams were censored at their last examination. No violations to the proportional hazards assumption were identified. Interactions between inflammatory markers and age were also tested.

To determine whether inflammatory markers were associated with hearing sensitivity measured by PTA as a continuous variable, 2009–2010 PTA levels were regressed on 1998–2000 inflammatory markers and on 10-year inflammatory profiles in those without hearing impairment at 1998–2000 using linear regression. Progression of PTA was also analyzed by modeling the odds of increasing more than or equal to 10 dB HL over the 10-year follow-up period.

Several sensitivity analyses were also performed. To check the robustness of final results, models were rerun after removal of participants with signs of a possible acute infection defined as having a CRP value more than 10 mg/L at either the 1988–1990 or the 1998–2000 examinations (n = 124) (22). To better capture the long-term nature of inflammatory exposure, a duration of inflammatory profile was created. A 10-year higher risk inflammatory profile was defined as being sustained high or increasing in inflammatory level between exams at 1998–2000 and 2009–2010, and a 20-year higher risk inflammatory profile was defined as being sustained high or increasing a level over the entire 20-year period (1988–1990 to 2009–2010). Because end-level inflammatory markers were used to define exposure groups, the outcome modeled was hearing impairment at 2009–2010 using logistic regression. Given the evidence that statin use may have significant effects on inflammatory levels, and that the use of these medications increased substantially over the course of this study (1998–2000 [19.2%], 2003–2005 [35.5%], 2009–2010 [46.1%]), these analyses were run after removing statin users (23,24). Lastly, an inflammatory index was created using baseline levels of CRP, IL-6, and TNF-α and was defined as the number of markers (0–3) in the highest group. Associations between this inflammatory index and the 10-year cumulative incidence of hearing impairment were examined.

Results

The average age of participants free of hearing impairment at baseline (1998–2000) was 63.8 years (range 53.2–88.0 years), and 30.8% (N = 330) were male (Supplementary Table 1). A high percentage of participants was obese (45.8%), was past or current smokers (50.7%), and was hypertensive (52.7%), whereas a small percentage reported
a history of CVD (8.2%). The geometric means for CRP, IL-6, and TNF-α were 2.33 mg/L (95% confidence interval [CI]: 2.19, 2.47), 1.52 pg/mL (95% CI: 1.48, 1.62), and 1.19 pg/mL (95% CI: 1.15, 1.22), respectively. The mean worse-ear PTA at baseline was 15.5 dB (SD = 6.0 dB), and the 10-year cumulative incidence of hearing impairment in this cohort was 44.9%.

Inflammatory Markers and the 10-Year Incidence of Hearing Impairment

In separate models, higher levels of baseline (1998–2000) CRP (hazard ratio [HR]: 1.16, 95% CI: 0.84, 1.59; >3 mg/L vs <1 mg/L), IL-6 (HR: 0.97, 95% CI: 0.73, 1.28; >2.06 vs <1.08 pg/mL), and TNF-α (HR: 1.17, 95% CI: 0.87, 1.56; >1.44 vs <0.99 pg/mL) were not associated with developing hearing impairment over the 10-year follow-up period after adjustment for age and sex, and after further covariate adjustment (data not shown). Having a 10-year higher risk CRP profile (1988–1990 to 1998–2000) was associated with the development of hearing impairment over the next 10 years (HR: 1.31, 95% CI: 1.03, 1.65) adjusting for age and sex (Table 1). This association was not observed with long-term IL-6 levels. The interaction between 10-year CRP inflammatory group and age was statistically significant (p = .031), and therefore further analyses were stratified at age 60 years. Participants less than 60 years of age at baseline with a 10-year higher risk CRP profile were nearly two times (HR: 1.98, 95% CI: 1.22, 3.20) as likely to develop hearing impairment over the subsequent 10-year period adjusting for age and sex. This result was robust after further covariate adjustments. A 10-year higher risk CRP profile was not associated with the incidence of hearing impairment in participants aged more than or equal to 60 years. After further removal of those participants with signs of possible acute infection, results were also similar (data not shown).

Inflammatory Markers, PTA at Last Examination (2009–2010), and 10-Year PTA Progression

Higher levels of baseline CRP, IL-6, or TNF-α were not associated with higher end-level PTA adjusting for age and sex, or other covariates (data not shown). In participants less than 60 years, end-level PTA was statistically significantly higher for those with a 10-year higher risk CRP profile (21.0 vs 18.8 dB; p = .045) than those without a high-risk profile after controlling for age and sex, and results were similar after further covariate adjustment. Also, within this age group, participants with a 10-year higher risk CRP profile were more likely to have more than or equal to 10 dB progression of PTA over 10 years (OR: 2.31, 95% CI: 1.35, 3.96) adjusting for age, sex, and further covariates. Pure-tone average at the last examination or odds of a PTA progression more than or equal to 10 dB HL did not statistically differ by 10-year CRP profile in those more than or equal to 60 years nor did it differ by 10-year IL-6 profile (data not shown).

Duration of Inflammatory Profile and Hearing Impairment at Last Examination (2009–2010)

Among participants less than 60 years at baseline (1998–2000) who never used statins throughout the study, after adjusting for age, sex, obesity, and smoking, those with a 20-year inflammatory profile were more than three times as likely to have hearing impairment at the final examination as those without a long-term inflammatory profile (Table 2). However, within this group, the mean outcome PTA (2009–2010) was not statistically significantly worse in

Table 1. Hazard Ratios (HR) and 95% Confidence Intervals (CI) for the Development of Hearing Impairment Over the 10-Year Follow-up by 10-Year Inflammatory Risk Groups* (1988–1990 to 1998–2000), the Epidemiology of Hearing Loss Study

<table>
<thead>
<tr>
<th>Inflammation Marker Group</th>
<th>N at Risk*</th>
<th>Incident Cases</th>
<th>Model 1, HR (95% CI)</th>
<th>Model 2, HR (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>C-reactive protein</td>
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<tr>
<td>Whole population</td>
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<tr>
<td>Lower risk</td>
<td>497</td>
<td>201</td>
<td>1 [Ref]</td>
<td>1.31 (1.03, 1.65)*</td>
</tr>
<tr>
<td>Higher risk</td>
<td>573</td>
<td>237</td>
<td>1.31 (1.03, 1.65)*</td>
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<tr>
<td>&lt; 60 years</td>
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<td>168</td>
<td>31</td>
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<td>1 [Ref]</td>
</tr>
<tr>
<td>Higher risk</td>
<td>223</td>
<td>61</td>
<td>1.98 (1.22, 3.20)</td>
<td>1.96 (1.19, 3.23)</td>
</tr>
<tr>
<td>≥60 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower risk</td>
<td>329</td>
<td>170</td>
<td>1 [Ref]</td>
<td>1 [Ref]</td>
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<tr>
<td>Higher risk</td>
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<td>176</td>
<td>1.14 (0.87, 1.50)</td>
<td>1.06 (0.80, 1.41)</td>
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<td>Interleukin-6</td>
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<tr>
<td>Lower risk</td>
<td>302</td>
<td>118</td>
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<td>1 [Ref]</td>
</tr>
<tr>
<td>Higher risk</td>
<td>139</td>
<td>60</td>
<td>1.33 (0.90, 1.96)</td>
<td>1.14 (0.76, 1.71)</td>
</tr>
</tbody>
</table>

Notes: Model 1, adjusted for age, sex; Model 2, <60 years: adjusted for age, sex, obesity, smoking, and alcohol use; ≥60 years: adjusted for age, sex, obesity, and smoking.

*Higher risk = remaining in the highest level or increasing a level between 1988–1990 and 1998–2000 examinations. Lower risk = all other participants.

Interaction between CRP risk group and age (p = .031).
those with a 20-year CRP inflammatory profile than those without such a profile (21.6 dB vs 18.8 dB; \( p = .156 \)). There were no significant associations observed between longer duration of CRP inflammatory profile and hearing outcomes in participants more than or equal to 60 years old or between duration of IL-6 inflammatory profiles and hearing outcomes.

**Inflammatory Index and the 10-Year Incidence of Hearing Impairment**

Among participants less than 60 years at baseline, those with levels of CRP, IL-6, and TNF-\( \alpha \) in the highest group, were more than twice (HR: 2.38, 95% CI: 1.12, 5.04; for 3 markers high vs 0 high) as likely to develop hearing impairment over the next 10 years (Figure 2). This association was not observed in those more than 60 years old or between duration of IL-6 inflammatory profiles and hearing outcomes.

**Discussion**

In this study, we found that long-term levels of CRP were associated with the incidence of hearing impairment over a period of 10 years in an aging population. Although this association was statistically significant in the cohort overall, results differed by age group, and long-term CRP levels were predictive of incident hearing impairment in those less than 60 years old at baseline but not those more than or equal to 60 years old. This finding was independent of potential confounders including age, sex, obesity, smoking, and alcohol use. Among participants less than 60 years old, a statistically significant trend was observed between having an inflammatory profile over 10 and 20 years (vs none) and hearing impairment in a subset of participants who had never used statin medications. Inflammatory marker measurements at a single time point did not predict hearing impairment nor did long-term levels of IL-6. To our knowledge, this was the first study to prospectively examine the associations between inflammatory markers and the development of age-related hearing impairment.

It has been demonstrated that increased inflammation is associated with many age-related diseases including cardiovascular disease (11), dementia, and Alzheimer’s disease (25,26). Fewer studies have focused on potential associations between systemic inflammation and age-related hearing impairment. In a cross-sectional study in the Hertfordshire Aging Study, CRP and IL-6 were associated with worse hearing sensitivity, and in a larger cross-sectional study conducted with NHANES data, it was demonstrated that CRP was associated with hearing impairment (high vs low tertile, OR: 1.89, 95% CI: 1.21–2.95) (27,28). This study extends these findings by providing longitudinal data on inflammation and hearing to demonstrate that participants with persistently high inflammatory profiles were more likely to develop hearing impairment over 10 years.

A low-grade proinflammatory state that accompanies aging has been labeled “inflammaging” (29). Increased inflammation with age could be due to the higher prevalence of cardiovascular disease or other morbidities in older adults (9), or to other age-associated processes including oxidative stress (10). Inflammation is associated with

<table>
<thead>
<tr>
<th>Inflammation Marker Group</th>
<th>N</th>
<th>Cases</th>
<th>Model 1 OR (95% CI)</th>
<th>Model 2 OR (95% CI)</th>
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<td>C-reactive protein</td>
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<td>91</td>
<td>17</td>
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<tr>
<td>10 year</td>
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<td>6</td>
<td>1.10 (0.37, 3.34)</td>
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<tr>
<td>20 year</td>
<td>48</td>
<td>15</td>
<td>2.97 (1.20, 7.33)</td>
<td>3.24 (1.23, 8.50)</td>
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<td>( p )-trend</td>
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<td>0.023</td>
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<tr>
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<td>118</td>
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<tr>
<td>10 year</td>
<td>36</td>
<td>18</td>
<td>0.87 (0.37, 2.03)</td>
<td>0.80 (0.34, 1.91)</td>
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<td>20 year</td>
<td>65</td>
<td>29</td>
<td>0.66 (0.33, 1.34)</td>
<td>0.53 (0.25, 1.12)</td>
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<td>1.18 (0.49, 2.87)</td>
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<tr>
<td>( p )-trend</td>
<td></td>
<td></td>
<td>0.364</td>
<td>0.702</td>
</tr>
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</table>

Notes: OR = odds ratio; CI = confidence interval.

Ten-year higher risk inflammatory profile was defined as being sustained high or increasing in inflammatory level between exams at 1998–2000 and 2009–2010, and 20-year higher risk inflammatory profile was defined as being sustained high or increasing a level over the entire 20-year period (1988–1990 to 2009–2010).

Model 1, adjusted for age and sex; Model 2, adjusted for age, sex, obesity, and smoking.

*All participants were never statin users.*
pathophysiological processes of aging, including vascular damage and neurodegeneration (10,25). Both the cochlea and the tissues of the central auditory pathway are reliant on an adequate blood supply and therefore vascular damage may have deleterious effects on their function (3,30,31). For example, Trune and colleagues and others have shown that circulating inflammatory molecules can negatively affect tissues of the cochlear vasculature, both proximally in the spiral modiolar artery and distally among the capillaries of the stria vascularis (31,32). Inflammation is also involved in many neurodegenerative diseases such as dementia and Alzheimer’s disease, and similar inflammatory processes may also occur along the central auditory pathway in the brain (25,26).

The associations between inflammatory markers and age-related hearing impairment appeared to be age dependent. Age-related hearing impairment is a slowly progressing condition whereby the majority of people are first affected between 60 and 70 years of age, and nearly everyone has developed some degree of hearing impairment by 80 years of age (1). Therefore, given a statistically significant interaction between long-term CRP risk group and age, analyses were stratified at 60 years of age. Participants less than 60 years at the baseline examination were moving through the peak risk period over the course of this study. Because higher levels of systemic inflammation are associated with older age, and hearing impairment often co-occurs with other negative health conditions such as diabetes, CVD, and hypertension (8), selection bias may have disproportionally affected associations in the older age stratum making it difficult to detect risk factor associations. Despite the results of this study, prior studies have demonstrated that inflammation may have negative consequences even in the oldest old (17).

Circulating inflammatory marker levels at any one time point can be influenced by factors such as acute infections and medication use. The use of multiple measures collected longitudinally should serve to better place participants into an inflammatory profile than a single measure. Sensitivity analysis results that showed long-term marker results to be similar after the removal of acute CRP values support this hypothesis. When combining data from three inflammatory markers, CRP, IL-6, and TNF-α, younger participants (<60 years) with high levels of each were more likely to develop hearing impairment over the next 10 years. Creating inflammatory biomarker panels may be one way in which observational studies without longitudinal measures could better capture inflammatory burden. It has also been demonstrated in both observational and randomized trials that
levels of CRP, and to some extent levels of other inflammatory markers, may be lower in statin users compared with nonusers (23,24). To address the concern of medication effects on inflammatory levels, sensitivity analyses were performed among statin never-users only, and results demonstrated that a 20-year duration of inflammatory profile was a predictor of hearing impairment while a duration of 10 years was not.

The results of this study should be interpreted in light of several limitations. This was a longitudinal study in older adults and therefore selective survival may have biased results toward the null. Less data were available for IL-6 over all time points, and therefore lack of power may explain why associations were observed for CRP but not for IL-6. It was also not possible to define long-term profiles of TNF-α, as multiple measures were not available. Over the course of the study, too few participants reached a PTA more than 40 dB HL to allow for an analysis of incident severe hearing impairment by inflammatory level. This study also lacked data on dietary factors that may have potentially led to uncontrolled confounding. Despite these limitations, this study was a population-based cohort study which including a large number of participants with standardized audiometric data measured longitudinally. Few cohort studies are available to study longitudinal risk factor associations with incident hearing impairment within populations. Several commonly used inflammatory markers, measured using reproducible assays, and available from three examinations in a 20-year period for CRP and IL-6, allowed for a better characterization of inflammatory profiles over time.

This study demonstrated that long-term inflammatory profiles characterized by increasing or sustained high levels of CRP were associated with the development of age-related hearing impairment, most predominantly among younger adults (<60 years at baseline) in this study. Recent reports have demonstrated that hearing impairment appears to be decreasing among younger cohorts of Americans, and therefore may be, in part, preventable (8). The results of this study offer evidence for one potential underlying process for the development of hearing impairment associated with aging. Given that treatment options for age-related hearing impairment are limited once onset has occurred, research should continue to focus on the potential for delaying or preventing this common chronic condition.

**SUPPLEMENTARY MATERIAL**

Supplementary material can be found at: http://biomedgerontology.oxfordjournals.org/

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**REFERENCES**


