

# Carotid atherosclerosis is associated with poorer hearing in older adults

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*Journal of the American Medical Directors Association, 2019*

## ABSTRACT

### Objectives

Cardiovascular disease may be linked to hearing loss through narrowing of the nutrient arteries of the cochlea, but large-scale population-based evidence for this association remains scarce. We investigated the association of carotid atherosclerosis as a marker of generalized cardiovascular disease with hearing loss in a population-based cohort.

### Design

Cross-sectional.

### Setting

A population-based cohort study.

### Participants

3,724 participants [mean age: 65.5 years, standard deviation (SD): 7.5, 55.4% female].

### Methods

Ultrasound and pure-tone audiograms to assess carotid atherosclerosis and hearing loss.

### Results

We investigated associations of carotid plaque burden and carotid intima media thickness (IMT) (overall and side-specific carotid atherosclerosis) with hearing loss (in the best hearing ear and side-specific hearing loss) using multivariable linear and ordinal regression models. We found that higher maximum IMT was related to poorer hearing in the best hearing ear [difference in dB hearing level per 1-mm increase IMT: 2.09 dB, 95% (CI): 0.08, 4.10]. Additionally, 3rd and 4th quartile plaque burden as compared to 1st quartile was related to poorer hearing in the best hearing ear (difference: 1.06 dB, 95% CI: 0.04, 2.08; and difference: 1.55 dB, 95% CI: 0.49, 2.60, respectively). Larger IMT (difference: 2.97 dB, 95% CI: 0.79, 5.14), 3rd quartile plaque burden compared to 1st quartile (difference: 1.24 dB, 95% CI: 0.14, 2.35), and 4th plaque quartile compared to 1st quartile (difference: 2.12 dB, 95% CI: 0.98, 3.26) in the right carotid were associated with poorer hearing in the right ear.

### Conclusions and Implications

Carotid atherosclerosis is associated with poorer hearing in older adults, almost exclusively with poorer hearing in the right ear. Based on our results it seems that current therapies for the prevention of cardiovascular disease may also prove beneficial for hearing loss in older adults by promoting and maintaining inner ear health.

## INTRODUCTION

Hearing loss among the older adult population is a growing public health problem causing reduced hearing sensitivity and impaired speech understanding.<sup>1-6</sup> Hearing loss contributes to depression, social isolation, reduced quality of life, and dementia,<sup>7-18</sup> and with an ageing population, the number of people with hearing loss and its consequences will increase.<sup>19</sup> At present, no treatment is available to cure hearing loss. Therefore, prevention of hearing loss might even be more effective but requires more in-depth knowledge on the etiology of hearing loss and possible modifiable risk factors.<sup>6</sup>

Hearing loss is the result of degeneration of the sensorineural structures of the cochlea and the stria vascularis. These parts of the inner ear are highly vascularized tissues, with the main blood supply coming from the labyrinth artery.<sup>20</sup> Given this vascularization, previous studies have focused on the association between cardiovascular risk factors,<sup>11, 21-26</sup> as well as more direct, generalized markers of atherosclerosis including carotid intima media thickness (IMT) and carotid plaque with hearing loss. These studies demonstrated associations between cardiovascular risk factors, markers of atherosclerosis and hearing loss.<sup>22, 23, 25, 27-31</sup> So far, few studies with small to moderate sample sizes have explored the association between atherosclerosis and hearing loss, and mainly assessed atherosclerosis or hearing loss by self-report. Moreover, hearing loss has solely been assessed in the best hearing ear whereas it is known that there are asymmetries between left and right auditory function, expressed in greater sensitivity for simple sounds and processing complex sounds such as speech in the right ear.<sup>32-34</sup> Thus, it could be hypothesized that the right ear may be more vulnerable to changes in cardiovascular health.

Therefore, we investigated the association between carotid atherosclerosis, as a marker of generalized atherosclerosis<sup>27</sup> measured by carotid IMT and plaque burden, and hearing loss within a large, well-characterized population-based cohort.

## METHODS

### Setting and study population

This study was embedded in the population-based Rotterdam study, the Netherlands, which originated in 1990, investigating determinants and consequences of ageing.<sup>35</sup> At study entry and subsequently every 3 to 4 years, all participants were invited for extensive examinations in the dedicated research centre. By 2008, 14,926 participants aged 45 years and older compromised this population-based study.<sup>35</sup>

Hearing assessment was added to the study protocol from 2011 onward. Between 2011 and 2014, 4,219 participants underwent pure-tone audiometry to assess hearing

abilities. Of those 4,219 participants, 4,190 participants also had data available on carotid IMT and plaque. We additionally excluded participants with present conductive hearing loss ( $n = 79$ ) and those who did not have carotid ultrasound assessment and hearing assessment within the same year ( $n = 387$ ), leaving 3,724 participants for the current analysis. Median time between atherosclerosis assessment and hearing assessment was 0.002 months.

All participants provided written informed consent to participate in the study and to have their information obtained from treating physicians.

## **Carotid atherosclerosis**

### *Carotid plaque*

By use of ultrasonography, the common carotid artery, carotid bifurcation, and internal carotid artery were visualized over a length as large as possible. Both left and right sides were analysed for the presence of plaques, which were defined as focal widenings relative to adjacent segments, with protrusion into the lumen, composed of calcified or non-calcified components. Researchers assessing the amount of plaques were blinded to all clinical information of the participants.<sup>36</sup> A weighted plaque score ranging from 0 to 6 was calculated by adding the number of sites at which a plaque was detected, divided by the total number of sites for which an ultra-sonographic image was available and multiplied by 6, which is the maximum number of sites.<sup>36</sup> Participants of whom at least 2 of the 6 sites did not have available information on the presence of plaques were excluded from the study. Additionally, we categorized plaque burden into quartiles.

### *Carotid intima-media thickness*

The maximum IMT was determined as the maximum IMT of the near- or far-wall of the common carotid artery over a length of 1 cm. Subsequently, the average of left and right maximum common carotid IMT in millimetres was computed.<sup>36</sup>

## **Hearing**

To determine decibel (dB) hearing levels, pure-tone audiometry was performed in a soundproof booth by 1 trained health care professional. A computer-based clinical audiometry system (Decos Technology Group, version 210.2.6 with AudioNigma interface) and TDH-39 headphones were used.<sup>35</sup> dB hearing levels were measured according to the ISO-standard 8253-1 [International Organization for Standardization (ISO), 2010]. Air conduction (frequencies 0.25, 0.50, 1, 2, 4, and 8 kHz) and bone conduction (0.50 and 4 kHz) were tested for both ears. According to the method of Hood,<sup>37</sup> masking was performed. dB hearing levels per ear were determined by taking the average thresholds over all frequencies. The better hearing ear was determined for every participant by comparing the average thresholds over all frequencies. If both ears were equal, we alternately chose

either the right or the left ear. Low-frequency dB hearing level was determined as the average of 0.25, 0.50, and 1 kHz and high-frequency dB hearing level was determined as the average of 2, 4, and 8 kHz. We categorized hearing loss into 3 categories: no hearing loss (0 – 20 dB), mild hearing loss (20 – 35 dB), and moderate/severe hearing loss ( $\geq 35$  dB).<sup>38</sup> The last category contains 3 clinical categories (moderate, severe, and profound) that have been merged to maintain sufficient statistical power. Conductive hearing loss was present when participants had an air-bone gap of 15 dB or more.<sup>35</sup>

### Covariables

Information on smoking was collected through questionnaire and was categorized into current, former, and never smoking. Educational level was assessed according to the standard classification of education, which allows comparison to international levels of education.<sup>35, 39</sup> In our analysis, we combined the 4 highest levels into 1 category, thus, obtaining 4 levels: (1) primary education; (2) lower-level vocational education; (3) medium-level secondary education; and (4) medium-level vocational training to university level. Systolic and diastolic blood pressure was measured twice using a random zero-sphygmomanometer and the average of the 2 measurements was used. Type 2 diabetes was defined as having fasting blood glucose concentration  $>7.0$  mmol/L, a non-fasting blood glucose  $>11.1$  mmol/L, use of glucose-lowering medication, or a combination of these. Using an automatic enzymatic procedure serum total cholesterol and high-density lipoprotein (HDL) cholesterol were measured from fasting blood samples. Information on body weight and length was obtained by physical examination and body mass index (BMI) was calculated. Information on use of blood pressure medication and lipid-lowering medication was collected. The prevalence of coronary heart disease (CHD) and stroke was determined at baseline interview, with verification from medical records.<sup>35, 40</sup>

### Statistics

First, we assessed associations of degree of carotid plaque burden (second quartile, third quartile, and fourth quartile compared to first quartile) and IMT with decibel hearing levels in the best hearing ear (all, high, low frequencies) using multivariable linear regression models. In the first model, we adjusted for age and sex. In the second model, we additionally adjusted for age-squared (to account for nonlinear age effects), education, BMI, smoking, systolic and diastolic blood pressure, use of blood pressure-lowering medication, cholesterol levels (HDL and LDL), diabetes mellitus, and lipid-lowering medication use. Exploratory analyses were performed to account for possible confounding by prevalent coronary heart disease, stroke and antiplatelet medication use. Adding those variables into the models did not change the effect estimates and were therefore left out of the final analysis. Second, we performed a similar multivariable

linear regression analysis in which we studied the association of side-specific atherosclerosis (left and right carotid) and side-specific hearing loss (left and right ear). Third, we investigated the association of atherosclerosis with degree of hearing loss (no, mild, moderate/severe) using ordinal regression with similar multivariable adjusted models. The proportional-odds assumption was checked and it held for every association ( $P > .05$ ). As prevalence of hearing loss increases substantially with age,<sup>11</sup> we further explored whether associations differed by midlife (50-70 years) vs late life (70-98 years). Additionally we checked whether associations differed by sex. All analyses were performed using IBM SPSS statistics for Windows, version 24.0 (International Business Machines Corporation, Armonk, New York). A  $P$  value  $\leq 0.05$  was considered statistically significant.

## RESULTS

Population characteristics are described in Table 1. Mean age was 65.5 years (SD: 7.5), 55.5% were female. Mean maximum IMT was 1.0 mm (SD: 0.2). The first quartile included a plaque score of 0.00, second quartile included a plaque score of 0.10 to 1.49, the third quartile included a plaque score of 1.50 to 2.49, and the fourth quartile included a plaque score of 2.50 to 6.00. Mean hearing loss was 23.6 dB (SD: 12.1) across all hearing frequencies. Important to note for the interpretation of our results is that the amount of hearing loss is expressed in dB; that is, a higher dB value reflects greater hearing loss.

**Table 1.** Population characteristics (N = 3,724)

Characteristic	
Age, years	65.5 (7.5)
Age range, years	51.5 – 98.6
Female, %	55.5
Education level, %	
Primary	7.8
Lower-level vocational	36.9
Medium-level secondary	29.4
Medium-level vocational to university level	25.3
Systolic blood pressure, mmHg	139.6 (20.9)
Diastolic blood pressure, mmHg	83.1 (11.2)
Blood pressure medication use, %	40.9
Cholesterol, mmol/L	5.5 (1.1)
HDL-cholesterol, mmol/L	1.5 (0.4)
Lipid-lowering medication use, %	25.9

**Table 1.** Population characteristics (N = 3,724) (continued)

Characteristic	
Diabetes, %	9.1
Smoking, %	
Yes	17.1
No	82.9
<b>Atherosclerosis</b>	
Degree of total plaque burden, %	
1 <sup>st</sup> quartile	19.4
2 <sup>nd</sup> quartile	28.5
3 <sup>rd</sup> quartile	21.6
4 <sup>th</sup> quartile	27.5
Degree of left carotid plaque burden, %	
1 <sup>st</sup> quartile	30.6
2 <sup>nd</sup> quartile	24.5
3 <sup>rd</sup> quartile	19.4
4 <sup>th</sup> quartile	25.6
Degree of right carotid plaque burden, %	
1 <sup>st</sup> quartile	30.3
2 <sup>nd</sup> quartile	24.6
3 <sup>rd</sup> quartile	20.4
4 <sup>th</sup> quartile	24.7
Total maximum IMT, mm	1.0 (0.2)
Left maximum IMT, mm	1.0 (0.2)
Right maximum IMT, mm	1.0 (0.2)
<b>Hearing loss</b>	
All frequencies, dB	23.6 (12.1)
Low frequencies, dB	14.3 (9.2)
High frequencies, dB	32.0 (17.5)
Left ear, dB	27.0 (14.5)
Right ear, dB	26.2 (13.6)
Degree of hearing loss in the best hearing ear, %	
No	43.2
Mild	40.1
Moderate/severe	16.5

IMT: intima media thickness. dB: decibel. Values are mean (standard deviation) for continuous variables and percentages for dichotomous variables. The amount of hearing loss is expressed in dB; that is, a higher dB value reflects greater hearing loss. Degree of hearing loss: no 0–20 dB; mild = 20–35 dB; moderate/severe: ≥ 35 dB. Ranges for quartiles were 0, 0.50–1.49, 1.50–2.00, and 2.50–6.00 for overall plaque score, 0, 1.00–1.99, 2.00–2.99, and 3.00–6.00 for left carotid plaque score, and 0, 1.00–1.99, 2.00–2.99, and 3.00–6.00 for right carotid plaque score.

We found that higher maximum IMT and higher plaque burden were associated with poorer hearing in the best hearing ear for all, low, and high frequencies (Table 2; model 1). After additional adjustment for educational level and cardiovascular risk factors (model 2), we found that especially third quartile and fourth quartile plaque burden, as compared to first quartile plaque burden, related to poorer hearing across all frequencies [difference in dB hearing levels: 1.06 dB (95% CI: 0.04, 20.8), and difference: 1.55 dB (95% CI: 0.49, 2.60), respectively] (Table 2, model 2). Effect estimates in the low and high frequencies were comparable to all frequencies (Table 2, model 2). Additionally, larger maximum IMT related to poorer hearing in all hearing frequencies [difference in dB hearing levels per 1-mm increase in maximum IMT: 2.09 dB (95% CI: 0.08, 4.10)] (Table 2, model 2).

**Table 2.** Association between atherosclerosis and hearing loss in the better-hearing ear

Carotid atherosclerosis	All hearing frequencies	Low hearing frequencies	High hearing frequencies
	Difference in dB (95% CI)	Difference in dB (95% CI)	Difference in dB (95% CI)
<b>Model 1</b>			
Maximum IMT, mm	<b>2.76 (0.94, 4.59)</b>	<b>2.06 (0.53, 3.59)</b>	<b>3.35 (0.72, 5.99)</b>
Plaque burden			
1 <sup>st</sup> quartile	<i>Reference</i>	<i>Reference</i>	<i>Reference</i>
2 <sup>nd</sup> quartile	0.32 (-0.60, 1.23)	-0.01 (-0.78, 0.75)	0.57 (-0.75, 1.88)
3 <sup>rd</sup> quartile	0.75 (-0.23, 1.73)	0.31 (-0.51, 1.13)	1.20 (-0.21, 2.61)
4 <sup>th</sup> quartile	<b>1.52 (0.55, 2.49)</b>	<b>1.18 (0.36, 1.99)</b>	<b>1.95 (0.54, 3.35)</b>
<b>Model 2</b>			
Maximum IMT, mm	<b>2.09 (0.08, 4.10)</b>	1.36 (-0.32, 3.03)	2.82 (-0.09, 5.74)
Plaque burden			
1 <sup>st</sup> quartile	<i>Reference</i>	<i>Reference</i>	<i>Reference</i>
2 <sup>nd</sup> quartile	0.47 (-0.48, 1.41)	0.10 (-0.69, 0.88)	0.75 (-0.62, 2.12)
3 <sup>rd</sup> quartile	<b>1.06 (0.04, 2.08)</b>	0.56 (-0.30, 1.41)	<b>1.59 (0.11, 3.08)</b>
4 <sup>th</sup> quartile	<b>1.55 (0.49, 2.60)</b>	<b>1.08 (0.20, 1.96)</b>	<b>2.15 (0.62, 3.68)</b>

dB, decibel; CI, confidence interval; IMT, intima media thickness; mm, millimetre.

Difference represents the difference in dB hearing loss per 1-mm increase in maximum IMT or the difference in dB hearing loss in the better hearing ear per degree of plaque burden (2<sup>nd</sup>-, 3<sup>rd</sup>-, and 4<sup>th</sup>-quartile) compared to 1<sup>st</sup>-quartile plaque burden. The amount of hearing loss is expressed in dB; that is, a higher dB value reflects greater hearing loss. Model 1: adjusted for age and sex; model 2: additionally adjusted for age-squared, education, BMI, smoking, systolic blood pressure, diastolic blood pressure, use of blood pressure lowering medication, cholesterol (HDL and LDL), prevalent diabetes mellitus, and lipid-lowering medication use. Significant values ( $P \leq 0.05$ ) are indicated in bold.

When investigating side-specific associations, we found that larger maximum IMT in the left carotid [difference: 2.03 dB (95% CI: 0.04, 4.03)] and in the right carotid [difference: 2.97 (95% CI: 0.79, 5.14)] was associated with poorer hearing exclusively in the right



ear (Table 3). Moreover, it appeared that fourth-quartile plaque burden, as compared to first-quartile plaque burden, in the left carotid is associated with poorer hearing in the right ear [difference: 1.68 dB (95% CI: 0.56, 2.81)] (Table 3). More interestingly, the third- and fourth-quartile plaque burden in the right carotid compared to first-quartile plaque burden [difference: 1.24 dB (95% CI: 0.14, 2.35), and difference: 2.12 dB (95% CI: 0.98, 3.26), respectively] was associated with poorer hearing in the right ear (Table 3). No associations were found for left carotid maximum IMT or plaque burden and left ear hearing loss (Table 3).

**Table 3.** Association between atherosclerosis and hearing loss per side

Carotid atherosclerosis	Left ear hearing loss, Difference in dB (95% CI)	Right ear hearing loss, Difference in dB (95% CI)
<b>Left carotid</b>		
Maximum IMT, mm	-0.07 (-2.27, 2.14)	<b>2.03 (0.04, 4.03)</b>
Plaque burden		
First quartile	Reference	Reference
Second quartile	0.77 (-0.37, 1.91)	1.00 (-0.04, 2.04)
Third quartile	0.67 (-0.57, 1.90)	0.85 (-0.27, 1.98)
Fourth quartile	0.72 (-0.52, 1.95)	<b>1.68 (0.56, 2.81)</b>
<b>Right carotid</b>		
Maximum IMT, mm	2.15 (-0.26, 4.55)	<b>2.97 (0.79, 5.14)</b>
Plaque burden		
First quartile	Reference	Reference
Second quartile	0.07 (-1.06, 1.20)	0.02 (-1.02, 1.05)
Third quartile	0.99 (-0.22, 2.21)	<b>1.24 (0.14, 2.35)</b>
Fourth quartile	<b>1.65 (0.40, 2.90)</b>	<b>2.12 (0.98, 3.26)</b>

dB, decibel; CI, confidence interval; IMT, intima media thickness; mm, millimetre. *Difference* represents the difference in dB hearing loss per 1-mm increase in maximum IMT or the difference in dB hearing loss per degree of plaque burden (2<sup>nd</sup>-, 3<sup>rd</sup>-, and 4<sup>th</sup>-quartile) compared to 1<sup>st</sup>-quartile plaque burden. The amount of hearing loss is expressed in dB; that is, a higher dB value reflects greater hearing loss. Adjusted for age, age-squared, sex, education, BMI, smoking, systolic blood pressure, diastolic blood pressure, use of blood pressure lowering medication, cholesterol (HDL and LDL), prevalent diabetes mellitus, and lipid-lowering medication use. Significant values ( $P \leq 0.05$ ) are indicated in bold.

Finally, we found that both side-specific, as well as overall higher carotid plaque burden and larger IMT was associated with poorer hearing in the better-hearing ear (Table 4). Interestingly, those associations seems to be explained by hearing status of the right ear. To be specific, larger overall maximum IMT and larger IMT in the right carotid were related with the odds of having a higher degree of hearing loss in the right ear [ordered log-odds: 0.50 (95% CI: 0.07, 0.92), ordered log-odds: 0.49 (95% CI: 0.10, 0.89), respectively] (Table 4). Moreover, fourth-quartile plaque burden, as compared to first-quartile

plaque burden, for the overall carotid, but also the left and right carotid, was related with the odds of having a higher degree of hearing loss in the right ear [ordered log-odds: 0.34 (95% CI: 0.12, 0.56), ordered log-odds: 0.26 (95% CI: 0.06, 0.46), and ordered log-odds: 0.32 (95% CI: 0.12, 0.52), respectively] (Table 4).

In general, the effect estimates of the association between atherosclerosis and hearing loss between midlife and late life (Supplementary Table 1) and between males and females (Supplementary Table 2) did not differ.

**Table 4.** Association between atherosclerosis and degree of hearing loss

Carotid atherosclerosis	Better-ear hearing loss	Left ear hearing loss	Right ear hearing loss
	Ordered log-odds (95% CI)	Ordered log-odds (95% CI)	Ordered log-odds (95% CI)
<b>Overall</b>			
Maximum IMT, mm	0.29 (-0.14, 0.71)	0.18 (-0.24, 0.59)	<b>0.50 (0.07, 0.92)</b>
Plaque burden			
1 <sup>st</sup> quartile	Reference	Reference	Reference
2 <sup>nd</sup> quartile	0.09 (-0.12, 0.30)	-0.01 (-0.21, 0.19)	0.11 (-0.09, 0.31)
3 <sup>rd</sup> quartile	0.19 (-0.03, 0.42)	0.11 (-0.10, 0.33)	0.19 (-0.03, 0.41)
4 <sup>th</sup> quartile	<b>0.31 (0.08, 0.53)</b>	0.15 (-0.06, 0.37)	<b>0.34 (0.11, 0.56)</b>
<b>Left carotid</b>			
Maximum IMT, mm	0.23 (-0.13, 0.58)	0.15 (-0.20, 0.50)	0.31 (-0.04, 0.67)
Plaque burden			
1 <sup>st</sup> quartile	Reference	Reference	Reference
2 <sup>nd</sup> quartile	<b>0.28 (0.09, 0.47)</b>	0.14 (-0.02, 0.30)	<b>0.22 (0.04, 0.41)</b>
3 <sup>rd</sup> quartile	0.18 (-0.02, 0.39)	0.09 (-0.12, 0.29)	0.18 (-0.02, 0.38)
4 <sup>th</sup> quartile	<b>0.28 (0.08, 0.48)</b>	0.16 (-0.16, 0.48)	<b>0.26 (0.06, 0.46)</b>
<b>Right carotid</b>			
Maximum IMT, mm	0.22 (-0.17, 0.61)	0.13 (-0.25, 0.52)	<b>0.49 (0.10, 0.89)</b>
Plaque burden			
1 <sup>st</sup> quartile	Reference	Reference	Reference
2 <sup>nd</sup> quartile	0.08 (-0.11, 0.27)	0.02 (-0.16, 0.20)	0.03 (-0.16, 0.21)
3 <sup>rd</sup> quartile	0.13 (-0.08, 0.33)	0.06 (-0.14, 0.25)	0.12 (-0.08, 0.32)
4 <sup>th</sup> quartile	<b>0.28 (0.07, 0.48)</b>	<b>0.25 (0.05, 0.44)</b>	<b>0.32 (0.12, 0.52)</b>

CI, confidence interval; IMT, intima media thickness; mm, millimetre; IMT, intima media thickness; mm, millimetre. Ordered log-odds represents the odds of having a higher degree of hearing loss (no hearing loss, mild hearing loss, or moderate/severe hearing loss) per 1-mm increase in maximum IMT or the odds of having a higher degree of hearing loss (no hearing loss, mild hearing loss, or moderate/severe hearing loss) per degree of plaque burden (2<sup>nd</sup>-, 3<sup>rd</sup>-, and 4<sup>th</sup>-quartile) as compared to 1<sup>st</sup>-quartile plaque burden. Adjusted for age, age-squared, sex, education, BMI, smoking, systolic blood pressure, diastolic blood pressure, use of blood pressure lowering medication, cholesterol (HDL and LDL), prevalent diabetes mellitus, and lipid-lowering medication use. Significant values ( $P \leq 0.05$ ) are indicated in bold.

## DISCUSSION

In this large sample of community-dwelling older individuals, we found that higher burden of carotid atherosclerosis as a measure of generalized atherosclerosis is associated with poorer hearing. Interestingly, this association was most prominent for hearing loss in the right ear.

Strengths of our study include the population-based setting, the large sample size, and the standardized assessment of hearing levels with pure-tone audiometry as well as atherosclerosis assessment. Some limitations of this study should also be acknowledged. First, this is a cross-sectional study, precluding inference on directionality. Second, the participants in this population-based cohort are mainly of European ancestry, which might limit the generalizability of our findings to other ethnicities. Third, data on labyrinthine artery atherosclerosis were unavailable, precluding inference on direct effects of atherosclerosis on hearing loss as blood supply to the inner ear directly comes from the labyrinthine artery.

Our results confirm previous reports regarding the association of the presence and burden of atherosclerosis with age-related hearing loss,<sup>23, 29, 30, 41, 42</sup> but were mainly of a cross-sectional nature, consisted of small sample sizes and assessed atherosclerosis and hearing loss by means of self-report. The only longitudinal study so far has reported an association of increased IMT and a larger number of plaques with a higher 5-year incidence of hearing impairment.<sup>29</sup> Although the reported study included a proper population-based study sample, the included age range (35-64 years) did not include the ages at which hearing loss is most pronounced. As hearing loss is highly prevalent at older ages, it is important to assess the association between atherosclerosis and hearing loss among older adults.

Interestingly, we found that generalized atherosclerosis is associated most prominently with right-ear hearing loss. The existence of asymmetries between right and left auditory function has been described earlier. It has been found that hearing levels in the right ear are poorer than hearing levels in the left ear in both young and older participants,<sup>32-34, 43</sup> for both central and peripheral auditory functions.<sup>32</sup> It has been hypothesized that this lateralization of central hearing abilities is associated with cerebral hemispheric topographic organization. Indeed, processing of phonetic information has been associated with higher activity in the left auditory cortex, resulting in a right ear advantage for complex auditory signals.<sup>44</sup> However, as detection of pure tones is dominated by peripheral function, it is more likely that our results are explained by peripheral hearing asymmetries. A study from 1983 found that with increasing age, the right ear was more vulnerable to peripheral auditory function changes than the left ear,<sup>34</sup> possibly because of a higher vulnerability than the left ear for risk factors such as atherosclerosis influencing inner ear health.<sup>32</sup> But, as the current study is of a cross-sectional design, we cannot determine

whether the right ear over time or with age is more vulnerable to peripheral damage. The above-mentioned hearing asymmetries might be further explained by differences in cochlear blood flow. Animal studies have consistently found poorer hearing in animals with lower cochlear blood flow.<sup>45-47</sup> Interestingly, a study in gerbils demonstrated that cochlear blood flow in the left ear was higher than cochlear blood flow in the right ear.<sup>48</sup> Therefore, we may speculate that abovementioned phenomenon is also applicable in humans. As such, our results might be explained by a lower right-cochlear blood flow and, possibly, the subsequent poorer right-ear hearing for older adults with atherosclerosis. Any change in cardiovascular health may affect the right ear more than the left ear. However, as it is not possible to measure cochlear blood flow in humans, this remains speculative and our results await further confirmation by other (longitudinal) population-based studies.

Nevertheless, as we found associations between both left and right carotid atherosclerosis and hearing loss, our results are more likely explained by a more generalized impact of atherosclerosis through the entire vascular system. We measured atherosclerosis in the carotid artery, but blood supply to the inner ear comes from the labyrinthine artery. The inner ear vessels may anastomose with the middle ear vessels, for which the external carotid artery is the most important supplier of blood.<sup>20</sup> Although not directly, the carotid externa might supply blood or, in light of our results, exert its atherosclerosis impact indirectly on the inner ear through this anastomose. Moreover, it is known that larger IMT in the carotid artery is correlated with atherosclerotic disease elsewhere in the arterial system, including the vertebrobasilar arteries, and with the risk of cardiovascular events.<sup>27, 49, 50</sup> As such, it has been suggested that carotid atherosclerosis can be used as an indicator of generalized atherosclerosis and cardiovascular health. Notably, a recent study reported an association between coronary atherosclerosis and hearing loss, supporting the generalized impact of atherosclerosis.<sup>51</sup> Thus, therapeutic and possibly other lifestyle interventions preventing or deferring progression of atherosclerosis through the entire vascular system<sup>52</sup> might be a promising strategy to prevent or delay the onset or progression of hearing loss in older adults as an added bonus in targeting cardiovascular disease.

## CONCLUSION AND IMPLICATIONS

Carotid atherosclerosis is associated with poorer hearing in older adults. Interestingly, associations are predominantly found with poorer hearing in the right ear. The impact of atherosclerosis, therefore, seems to go beyond merely the risk of cardiovascular events. Early detection and prevention of atherosclerosis carries the promise to not only lower the risk of clinical cardiovascular events and mortality, but also prevent or delay the onset or progression of hearing loss in older adults by promoting and maintaining inner ear health.

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