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# Hypertension, Diuretic Use, and Risk of Hearing Loss



Brian M. Lin, MD,<sup>a,b,c</sup> Sharon G. Curhan, MD, ScM,<sup>b,c</sup> Molin Wang, PhD,<sup>b,d,e</sup> Roland Eavey, MD,<sup>f</sup> Konstantina M. Stankovic, MD, PhD,<sup>a,c</sup> Gary C. Curhan, MD, ScD<sup>b,c,d,g</sup>

<sup>a</sup>The Massachusetts Eye and Ear Infirmary, Department of Otolaryngology-Head and Neck Surgery, Boston, Mass; <sup>b</sup>Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Mass; <sup>c</sup>Harvard Medical School, Boston, Mass; <sup>d</sup>Department of Epidemiology, Harvard TH Chan School of Public Health, Boston, Mass; <sup>e</sup>Department of Biostatistics, Harvard TH Chan School of Public Health, Boston, Mass; <sup>f</sup>Vanderbilt Bill Wilkerson Center for Otolaryngology and Communications Sciences, Vanderbilt University School of Medicine, Nashville, Tenn; <sup>g</sup>Renal Division, Department of Medicine, Brigham and Women's Hospital, Boston, Mass.

#### ABSTRACT

**BACKGROUND:** Hearing loss is highly prevalent among adults in the United States. Hypertension also is common and often treated with diuretics. Hypertension may increase the risk of hearing loss by decreasing vascular supply to the stria vascularis. Use of thiazides has been anecdotally associated with hearing loss. In small studies, furosemide use has been associated with hearing loss that is usually reversible, but can be permanent. We investigated the relation among hypertension, diuretic use, and hearing loss in a prospective cohort of 54,721 women in the Nurses' Health Study I, 1994 to 2012.

**METHODS:** Eligible participants included 54,721 female nurses aged 48 to 73 years in 1994 who provided information on thiazide diuretic and furosemide use in 1994, answered the question on hearing loss over their lifetime in 2012, and did not report hearing loss with date of onset before date of onset of hypertension diagnosis or medication use. The outcome was self-reported hearing loss. Cox proportional hazards regression was used to adjust for potential confounders.

**RESULTS:** During 774,096 person-years of follow-up, 19,296 cases of hearing loss were reported (incidence rate, 25 cases per 1000 person-years). At baseline in 1994, the mean age was 57.9 years and mean body mass index was 26.3 kg/m<sup>2</sup>. Some 30.8% of participants had a history of hypertension. History of hypertension was independently associated with a modestly higher risk of hearing loss (multivariable adjusted relative risk, 1.04 [1.01-1.07]). Among women with a history of hypertension, neither thiazide diuretic (multivariable adjusted relative risk, 1.07 [0.99-1.16]) nor furosemide use (multivariable adjusted relative risk, 0.91 [0.75-1.09]) was significantly associated with risk of hearing loss when compared with women not taking antihypertensive medications. There was no significant effect modification by age.

**CONCLUSIONS:** History of hypertension was associated with a small increased risk of hearing loss. Thiazide diuretic use and furosemide use were not associated with risk of hearing loss among women with a history of hypertension.

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Requests for reprints should be addressed to Brian M. Lin, MD, Channing Division of Network Medicine, Brigham and Women's Hospital, 181 Longwood Ave, Boston, MA 02115.

E-mail address: brian\_lin@meei.harvard.edu

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Hearing loss is highly prevalent in adults in the United States. Approximately one third of women aged 50 to 59 years and approximately two thirds of women aged 60 to 69 years have hearing loss.<sup>1</sup> As the life expectancy of individuals has increased, so has the prevalence of age-related hearing loss.<sup>2</sup> Hearing loss can be disabling; therefore,

identification of potential modifiable risk factors is an important public health issue.<sup>3,4</sup>

Hypertension also is common in the United States and affects approximately 35% of women aged 40 to 59 years, and more than 65% of women aged more than 65 years.<sup>5</sup> Hypertension may increase the risk of hearing loss via decreased vascular supply to the stria vascularis.<sup>6</sup> However, current

evidence regarding the relation between hypertension and risk of hearing loss is inconsistent, with cross-sectional studies suggesting a positive association<sup>1,7</sup> and a prospective study suggesting no association.<sup>8</sup>

The Joint National Committee recommends thiazide diuretics as initial drug therapy for patients with uncomplicated hypertension.<sup>9</sup> The relation between thiazides and hearing loss is largely anecdotal, with no published reports in the literature. Thus, the mechanism by which thiazides may alter hearing is unclear.

In small studies, furosemide use has been associated with sudden sensorineural hearing loss that is usually reversible but can be permanent.<sup>10-12</sup> The hearing loss is more likely to occur after intravenous drug administration but can also occur after oral dosing.<sup>10,12</sup> The mechanism by which furosemide may cause hearing loss in humans is unclear. Rodent models have shown that furosemide causes dysfunction of the stria vascularis, resulting in reduced endocochlear potential.<sup>13-17</sup> Chronically impaired endocochlear potential has been shown to reduce auditory nerve activity, thereby impairing hearing.<sup>18</sup>

Although hypertension and diuretic use are common, the relation among hypertension, diuretic use, and hearing loss has not been prospectively studied in women. Therefore, we investigated the relation among hypertension, use of thiazide diuretics and furosemide, and hearing loss in a prospective cohort of 54,721 women in the Nurses' Health Study I. We also compared the use of thiazide diuretics and furosemide with the use of other hypertensive medications among hypertensive women to examine the relation between different hypertensive medications and risk of hearing loss.

## MATERIALS AND METHODS

#### Study Participants

The Nurses Health Study I is a cohort of 121,700 female nurses aged 30 to 55 years when enrolled in 1976.

Questionnaires are administered every 2 years, with an average follow-up rate of more than 90% of the eligible person-time. Participants were asked in 2012, "Do you have a hearing problem?" and, if so, "At what age did you first notice a change in your hearing?" Of the 63,966 women who answered the long-form questionnaire in 2012, 47%

## **CLINICAL SIGNIFICANCE**

- Hypertension is independently associated with a higher risk of hearing loss in women.
- Use of thiazide diuretics and furosemide is not independently associated with risk of hearing loss in women.

reported having a hearing problem. We excluded women who reported a hearing problem that began before 1994 (baseline year of our study) and those who had a history of nonmelanoma skin cancer due to potential exposure to chemotherapeutic agents that can be ototoxic. After excluding these participants, our study population was 54,721 women.

## Ascertainment of Hypertension

On the 1976 questionnaire and every 2 years thereafter, participants were asked whether a clinician had diagnosed them as having high blood pressure. Self-reported hypertension has been shown to be highly reliable in this cohort of women.<sup>19</sup> We classified women who answered "yes" to this question as having a history of hypertension from that time onward.

#### Ascertainment of Medication Use

In 1994 and every 2 years thereafter, information on regular use of thiazide diuretics, furosemide, calcium channel blockers, and beta-blockers was obtained. In 1996, use of angiotensin-converting enzyme inhibitors was first ascertained. We considered women who answered "yes" to have taken the indicated medication for the previous 2 years.

#### Ascertainment of Hearing Loss

The outcome examined in this study was self-reported hearing loss. The 2012 questionnaire inquired whether the women had hearing loss, and if so, the age of onset. Year and age of onset were calculated from participant responses. We defined incident cases of hearing loss as participants who reported a hearing problem first noticed after this study's baseline of 1994.

The gold standard of evaluating hearing loss is pure-tone audiometry. However, it is logistically and financially challenging to obtain audiograms on all participants. Several studies have examined the correlation between self-reported hearing loss and hearing loss diagnosed by audiogram.<sup>20-23</sup> Studies found a single question on self-reported hearing loss to be a relatively reliable indicator of hearing loss.<sup>24</sup> Significant associations between several factors and risk of self-reported hearing loss have been observed using this manner of assessment in the Nurses' Health Study II.<sup>25-27</sup>

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