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ARTICLE

Inner Ear Disorders in the Elderly with Carotid Artery Disease Requiring Revascularization: Prevalence, Characteristics, and Association

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ABSTRACT

Background: Aging is almost assocaited with inner ear disorders (InEarDs) by means of age-related hearing impairment (ARHI) or vertigo-and-dizziness as well as the carotid artery disease requiring revascularization (CAD-R). **Objective:** The present study aimed to study the prevalence and characteristics of InEarDs in older adults diagnosed with CAD-R. The other aim was to determine if InEarDs in CAD-R patients is age-related or might be explained by a concomitant CAD-R. **Method:** A retrospective, case-control study was conducted at the Mayo Clinic, Florida. The study cohort includes 919 patients who had CAD-R. The control group consisted of 244 age- and gender-matched patients presenting with cardiac or peripheral artery disease. The InEarDs were assessed based on the diagnosis upon presentation to the Audiology Clinic and follow-up. **Results:** Of the 919, 348 had ARHI that includes significant peripheral signs and central symptoms (24.9%), vertigo-and-dizziness events that are recurrent and persistent with normal objective vestibular testing (12.9%), or a combination of both (11.0%). These percentages were significantly higher in the study group relative to the control group. After adjustment for the vascular risk factors, the study group had significantly higher odds of ARHI (OR= 1.94; 95% CI: 1.09-3.44; P<0.05). **Conclusion:** CAD-R patients had significantly higher InEarDs than the control group. CAD-R is more likely to be associated with ARHI rather than the vertigo-and-dizziness even after adjusting for the vascular risk factors.

1. Introduction

Atherosclerosis that predisposes carotid artery disease requiring revascularization (CAD-R) is a chronic inflammation process associated with conventional risk factors; these include age, gender, smoking, hyperlipidemia, hypertension, genetic, diabetes, and cardiovascular events [1-7]. Treatment options for CAD-R include the following: medical therapy and carotid endarterectomy (CEA), with a primary goal to prevent cerebrovascular events (strokes) or chronic cerebral hypoperfusion that increase risk of mental ill-health (e.g., dementia,

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depression, cognitive impairment no dementia) [8-13].

Inner ear disorders (InEarDs) by means of age-related hearing impairment (ARHI), also known as presbycusis, and vertigo-and-dizziness are prevalent in the aging population, in which the common vascular risk factors, the associated disorders, and the cerebrovascular events chronic cerebral hypoperfusion found to play a significant role in the incidence and progression of ARHI and recurrent, persistent events of vertigo-and-dizziness [14-21].

The present study aimed to study the prevalence and characteristics of InEarDs in older adults diagnosed with CAD-R. The other aim was to determine if InEarDs in CAD-R patients is age-related or might be explained by a concomitant CAD-R.

2. Methods

2.1 Study Design

This was a retrospective, case-control cohort study conducted at the Mayo Clinic, Florida, and approved by the Institutional Review Board. The study cohort includes 919 patients who had CAD requiring revascularization. Revascularization carried out between December 1, 1995, and June 30, 2016. The control group consisted of 244 age-matched patients who diagnosed with cardiac or peripheral artery disease between January 1, 2014, and December 31, 2017. The InEarDs were assessed based on the diagnosis upon presentation to the Audiology Clinic and follow-up. The selection criteria of the patient sample and the grouping of InEarDs are listed in the Figure 1.

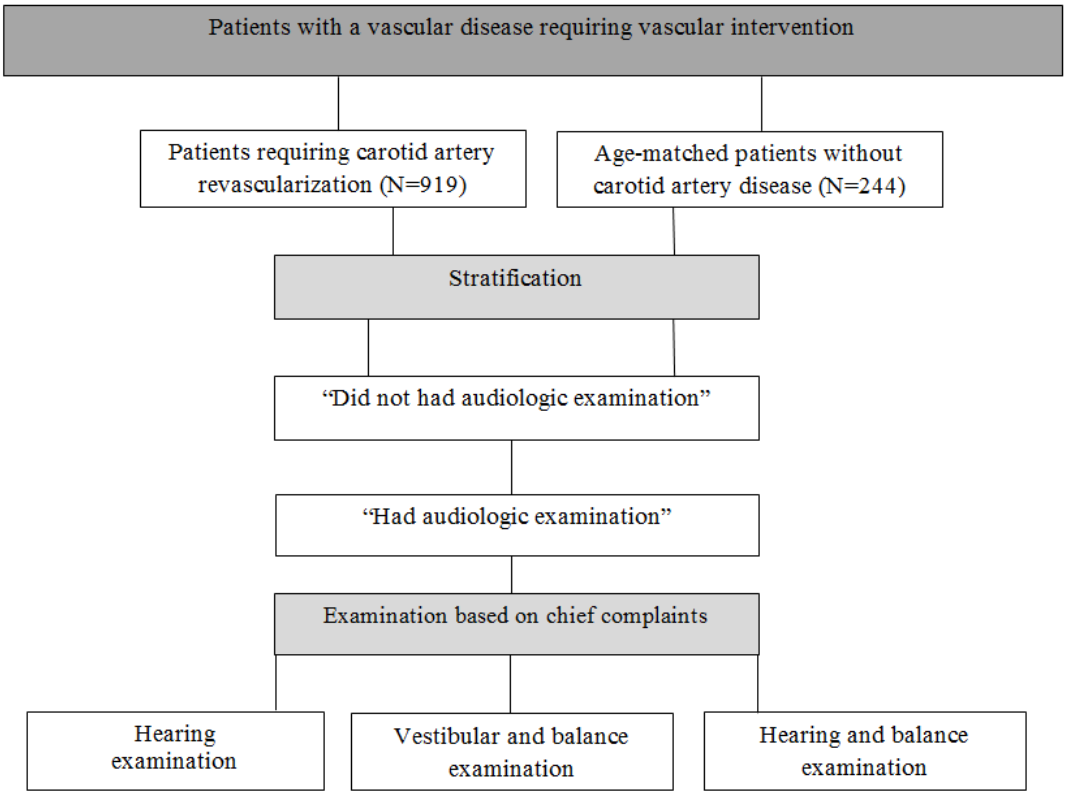

Figure 1. The selection criteria of the patient sample

2.2 Analysis of Results

All analyses were performed using SPSS version 25 (SPSS, Inc, an IBM Company, Chicago, Ilinois) and reviewed by a statistician at the Mayo Clinic, Florida. Descriptive statistics for quantitative variables are presented as prevalence. The Chi-square test was used to evaluate the preoperative characteristics difference in each group. Logistic regression was performed to assess the association of identified inner ear disorders with CAD-R.

3. Results

3.1 Demographic Data

The baseline characteristics of the study and control groups are shown in Table 1. A non- significant differences (P>.05) in age, sex, diabetes mellitus, and hypertension were noted between the two groups. Howevere, a substan-

tial difference ($P \leq .001$) in dyslipidemia and cardiovascular events were noted.

The reported degree of stenosis of the common carotid artery on the surgical site at the time of operation in the carotid group was as follows: more than 70% to 99% in 96.6%, less than 50% to 69% in 2.94%, less than 50% in 0.22%, and occluded in 0.22%. Eight hundred and eighty-eight of patients in the carotid group had carotid stenosis of more than 70% to 99% in the surgical site, based on ultrasonography and computed tomography. In comparison, 61 of patients in the carotid group had stenosis of more than 50% in the non-surgical side. All patients in the study group were under the lipid-lowering treatment, 80% under antihypertensive therapy, and 75% under antiplatelet therapy. Carotid endarterectomy with cerebral protection was the surgical procedure for all the carotid subjects.

Relative to the control group, the study group had significantly ($P<0.001$) a higher percentage of ARHI [229 (24.9%)] or recurrent, persistent vertigo-and-dizziness [119 (12.9%)] or a combination of both [100 (11.0%)]. Percentages were presented in Tables 2 and 3.

Table 1. Characteristics of Study Groups (CAD-R)

Variable	Carotid Group (n=919), No. (%)	Control Group (n=244), No. (%)	*P*-Value
Mean (SD) age, y	81.7 (8.90)	80.7 (4.72)	>.05
Sex			>.05
Male	592 (64.4)	142 (58.2)	
Female	327 (35.6)	102 (41.8)	
Degree of carotid stenosis in the surgical side, %			
<50	2 (0.22)	NA	
<50-69	27 (2.94)	NA	
≥70-99	888 (96.6)	NA	
Occluded	2 (0.22)	NA	
Degree of carotid stenosis in the non-surgical side, %			
<50	636 (69.2)	NA	
<50-69	179 (19.4)	NA	
≥70-99	61 (6.6)	NA	
Occluded	43 (4.0)	NA	
Associated risk factors and related disorders			
Hypertension	736 (80.1)	202 (82.8)	> .05
Hyperlipidemia	725 (78.9)	164 (67.2)	≤.001
Diabetes mellitus[a]	220 (23.9)	64 (26.2)	>.05
Cardiovascular [b]	249 (27.1)	89 (36.5)	≤.001

Notes:
Abbreviation: *NA, not applicable (control group did not have stenosis).*
[a] *Diabetes mellitus (type 1 or type 2).*
[b] *Cardiovascular (with remote myocardial infarction [more than 6 months], stable angina, and ejection fraction 25% to 45%).*

Table 2. Prevalence of Risk Factors of CAD-R by identified InEarDs

Variable	ARHI No. (%)	Vertigo-and-Dizziness No (%)	Combined No. (%)
Mean age, y	81.8	81.8	81.8
Sex			
Male	152 (66.3)	74 (62.2)	61 (61.0)
Female	77 (33.6)	45 (37.8)	39 (39.0)
Risk factor and related disorders			
Hypertension	191 (83.4)	92 (77.3)	80 (80.0)
Hyperlipidemia	183 (79.9)	97 (81.5)	81 (81.0)
Diabetes mellitus [a]	57 (24.9)	24 (20.2)	21 (21.0)
Cardiovascular [b]	62 (27.0)	32 (26.9)	25 (25.0)

Notes:
Abbreviation: *NA, not applicable (control group did not have stenosis).*
[a] *Diabetes mellitus (type 1 or type 2).*
[b] *Cardiovascular (with remote myocardial infarction [more than 6 months], stable angina, and ejection fraction 25% to 45%).*

Table 3. InEarDs in the Study Groups with a Degree of Carotid Stenosis in the Surgical Side

Variable	Carotid Group (n=919), No. (%)	Control Group (n=244), No. (%)	*P*-Value
ARHI	229 (24.9)	35 (14.3)	≤.001
Vertigo-and-Dizziness	119 (12.9)	12 (4.9)	≤.001
ARHI & Vertigo-and-Dizziness	100 (10.9)	6 (2.5)	≤.001

3.2 Characteristics of InEarDs

In the study group, the early- and late-onset of ARHI was seen in 54% and 45% based on the revascularization date. The onset is often described as a 'sudden onset of bilateral tinnitus followed by hearing changes' or 'gradual hearing changes.' Features of central auditory processing deficits - i.e., communicative/perceptual difficulties, environmental sound detection difficulty, sound localization difficulty, and understanding spoken speech in quiet, in noise, over distances difficulty - were evident in all patients. The magnitude of ARHI ranged from mild to severe based on the audiometric results. The audiometric profile consists of high-frequency hearing changes or high- and low-frequency hearing changes. Low-frequency dB hearing level was determined as the average decline occurred within the range of 0.25, 0.50, and 1 kHz, and high-frequency dB hearing level was defined as the average of occurred within the range 2, 4, and 8 kHz. The audiometric pattern of ARHI in the study group includes significant changes in only-high-frequency hearing or high- and low-frequency hearing [(x^2= 6.628, P ≤ 0.01)] relative to the control

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group.

Recurrent positional vertigo, persistent dizziness, imbalance and fall events with normal objective vestibular testing were the commonly observed findings in both groups. Recurrent positional vertigo defined as 'positional vertigo that was lasting more than 2 weeks and after at least 2 weeks of a symptom-free interval following previous successful treatments. Persistent defined as 'dizziness and unsteadiness that were lasting 3 months or more'. In the study group, the early- and late-onset (determined based on the revascularization date) of these findings was seen in 47% and 52%, *respectively*. A history of peripheral vestibular disorders (i.e., benign paroxysmal positional vertigo) was reported in some patients in the study group.

3.3 Logistic Regression

Logistic regression to test the clinical correlate of CAD-R with the InEarDs classified to ARHI, vertigo-and-dizziness, a combination of both was performed. The early and late-onset of HI or vertigo-and-dizziness have been merged to maintain sufficient statistical power. After adjustment for the common risk factors (age, gender, hypertension, hyperlipidemia, diabetes mellitus type 1 or type 2, and cardiovascular conditions), the study group had a significantly higher Odds of ARHI (OR= 1.94; 95% CI: 1.09-3.44; $P<0.05$). The model was statistically significant ($\beta = -2.13$; SE = .121; Wald = 312.26; $P\leq.001$). The overall logistic regression model is presented in Table 4.

Table 4. Odds Ratios in the Study Group Compared With Control Group After Adjustment for Risk Factors

CAROTID STENOSIS		
Predictor	**Odds Ratio (95% CI)**	***P*-Value**
Age	0.97 (0.94-1.00)	>.05
Sex	1.55 (0.91-2.62)	>.05
Hyperlipidemia	1.67 (0.914-3.04)	>.05
Hypertension	0.82 (0.31-0.12)	<.05
Diabetes mellitus [a]	1.56 (0.82-2.98)	>.05
Cardiovascular disease [b]	0.90 (1.09-2.96)	>.05
ARHI	1.94 (1.09-3.44)	<.05

Notes:

[a] *Diabetes mellitus (type 1 or type 2).*

[b] *Cardiovascular (with remote myocardial infarction [more than 6 months], stable angina, and ejection fraction 25% to 45%).*

4. Discussion

The present study aimed to study the prevalence and characteristics of InEarDs in older adults diagnosed with CAD-R. The other aim was to determine if InEarDs in CAD-R patients is age-related or might be explained by a concomitant CAD-R. In age-matched groups, CAD-R patients had higher percentages of ARHI, vertigo-and-dizziness, a combination of both. These percentages were significantly higher relative to the control group. Further, CAD-R is more likely to be associated with ARHI, but not vertigo-and-dizziness, even after adjusting for the common risk factors. This suggests that ARHI in CAD-R patients is not solely due to their age but might be explained by a concomitant CAD-R.

ARHI is one of the most common conditions affecting older and elderly adults. It affects about 30% of people over 65 years of age and 50% of those over 80 years of age [22]. Because of the changes in the auditory system; the early onset of ARHI is often associated with tinnitus. However, beyond the aging effects, we believe that a sudden onset of bilateral tinnitus followed by hearing changes might be related to the global decline in vascular health in CAD-R patients. In support, a study found that the presence of carotid artery plaque and a 0.2 mm difference in carotid intima-media thickness in a predominantly middle-aged cohort is associated with an increased risk of incident hearing loss (Odds Ratio was 1.18) [23]. Importantly, this difference in carotid intima-media thickness is similar to what is seen with five years of aging.

Further, peripheral signs of the ARHI include the only-high-frequency hearing loss or high- and low-frequency hearing loss. The central symptoms include communicative/perceptual difficulties, environmental sound detection difficulty, sound localization difficulty, and understanding spoken speech in quiet, in noise, over distances difficulty. Although age is the main contributory factor to the progression of ARHL and central symptoms, there is evidence that CAD can account for the abnormal audiologic findings - i.e., high-frequency hearing loss and central changes within the auditory brainstem pathways (inferior colliculus, superior Olivery nucleus, and cochlear nucleus complex) [19]. Importantly, these central changes may mimic the impact of stroke on all levels of the auditory pathway [24-27].

Several types of ARHI have been reported [28]. Sensory presbycusis refers to loss (atrophy) of the outer hair cells in the organ of Corti that produces nerve impulses in response to sound vibrations. With sensory presbycusis, which is slowly progressive and starts in mid-life, there is a sharp high-frequency sounds with relatively intact speech discrimination. Neural presbycusis, which begins early in life and effects are not noticeable until an older age, there is a disproportionately severe decrease in speech discrimination ability compared to their level

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of hearing loss. Metabolic or stria presbycusis, which tends to occur in the last two to three decades of life with a slow progressive nature, the hearing loss represented by a high- and low-frequency hearing loss (meaning the entire cochlea is affected results from atrophy of the stria vascularis.) However, speech discrimination is preserved. Accordingly, the ARHI in CAD-R patients is not solely due to their age but might be explained by a concomitant CAD-R pathology.

With regards to the recurrent positional vertigo and persistent dizziness with normal objective vestibular testing in the CAD-R pateints, this can imply a functional dizziness or space and motion discomfort, which is the is the new term for somatoform or psychogenic dizziness. This results is consisnt with a previous study showed that carotid plaque is a new risk factor for peripheral vestibular disorder [29]. The high prevelane of functional dizziness in CAD-R pateints could be related to a history of peripheral vestibular disorders (i.e., benign paroxysmal positional vertigo) as many patients may complain of residual dizziness even after successful treatment [30-32]. Also, functional dizziness could an adverse effects of CAD-R on brain functions that can impair harmony between the vestibular (balance) functions and brain area known for its role in orientation, navigation, and maintenance of postural control in space [11-13]. It is well accepted that this pathophysiologic process in dizzy pateints with vascular risk factros seem to include precipitating events that trigger anxiety-related changes in postural strategies with an increased attention to head and body motion and a cocontraction of leg muscles. Early diagnosis and management of functional dizziness, whethere it is secondary disorder after a peripheral or central changes syndrome, is very important to prevent further chronification and substantially reduce morbidity.

With that follows, the new task for the otorhinolaryngological physician and audiologists is to impart the main statements to other healthcare providers (particularly to internists of cardiovascular physicians and neurologists) and verse versa. This can be done by developing a scoring system for the association of the CAD-R with InEarDs by combining the audiological-vestibular evaluation with the vascular assessments [20-21]. Such a system is currently lacking and requires further studies to validate and implemented in clinical practice.

Limitations

Limitations of this study include its retrospective nature, for this may lead to a selection bias. Another potential limitation of this study is the use of two separate vascular patient databases with different inclusion time frames for the carotid and control groups. However, the use of a more recent database for the control group allowed for a more accurate exclusion of patients with carotid disease due to more precise imaging with more knowledge in the field, for this was our primary independent variable. The other limitation is related to the considerable number of patients who did not visit the hearing healthcare facility as compared to a number of patients who had visited the Audiology clinic. Information about the neurobehavioral assessments, including the neuroimaging in CAD-R patients, was lacking.

5. Conclusion

CAD-R patients had significantly higher InEarDs than the control group. CAD-R is more likely to be associated with ARHI rather than the vertigo-and-dizziness even after adjusting for the vascular risk factors. Developing a scoring system for the association of the CAD-R with InEarDs is the next wise step if we are aiming to improve outcomes.

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