Association of Hearing Loss With Cognitive Decline in Alzheimer's Disease and Vascular Dementia

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Abstract

Background: Alzheimer's disease (AD) and vascular dementia (VaD) are responsible for at least 20 % of diagnosed cases of dementia. It has been established that hearing loss is a risk factor for cognitive impairment and dementia. In this study, the association between hearing impairment and AD/VaD was determined in patients, as well as the characteristics of hearing loss in the two types of dementia.

Methods: 70 participants comprising 30 subjects in control group, 20 patients in AD group, and 20 patients in VaD group, were recruited and assessed with respect to pure-tone audiometric test for peripheral auditory system. On admission, age, gender, body mass index (BMI), smoking and drinking habits, diabetes, stroke, family history, as well as levels of cholesterol (TC), triglycerides (TG), fasting blood glucose (FBG), low-density lipoprotein (LDL), and glycosylated hemoglobin A1c (HbA1c) were measured. Hearing loss results and other clinical indexes were analyzed, and their correlations with severity of dementia were determined.

Results: Degree of hearing impairment and HbA1c level differed significantly between the AD and control groups. However, only age and degree of hearing impairment were positively correlated with grades of cognitive impairment in AD and control groups. Body mass index (BMI) and smoking history; HbA1c level, grades of cognitive impairment, and degree of hearing impairment, as well as related cognitive impairment, differed significantly between VaD and control groups. Results of logistic regression analysis indicated that the degree of hearing impairment could be a predictor for grades of cognitive impairment in AD and VaD. Moreover, the degree of hearing loss in full band hearing was significantly higher in VaD group than in AD group.

Conclusion: Hearing loss may be a potential risk factor for cognitive impairment in AD and VaD, two major types of dementia with different clinical characteristics. The clinical features of hearing loss in the two types dementia might be helpful in their diagnosis and treatment.

Introduction

Progressive cognitive decline has emerged as the greatest global challenge for health. At present, there are more than 30 million dementia patients in the world, and this number is increasing by the millions[1, 2]. The immense burden of dementia on relatives and supporters, and the huge healthcare costs to the society are of great concern. Population studies have estimated the prevalence of significant hearing loss due to dementia. A growing body of research has shown that age-related hearing loss (ARHL) is associated with dementia. Therefore, it is necessary to investigate the link between hearing impairment and cognitive impairment in the dementia.

Alzheimer's disease (AD) and vascular dementia (VaD) seem to be the most important types of dementia. The pathophysiology of AD has been related to β amyloid (β) cascade hypothesis. Clinical/pathological studies have highlighted the role of cerebrovascular disease in VaD[3-5]. There might be differences in clinical characteristics between the two kinds of dementia. Some Case-Control Studies have reported the relationship between hearing loss and AD among the elderly[6, 7]. However, the relationship between hearing loss and cognitive decline has been less studied in VaD. There are a number of studies on the possible mechanisms involved in the relationship between hearing loss and dementia[8]. However, not much is known on the differences in hearing loss between AD and VaD.

In this study, the clinical role of hearing loss as a specific risk factor for cognitive impairment in AD and VaD was investigated. Moreover, the characteristics and differences of hearing loss in the two types of dementia were determined and compared.

Methods

Study population

A total of 70 patients on admission in the Department of Geriatric Neurology were prospectively recruited from the Affiliated Brain Hospital to Nanjing Medical University between January 1, 2020, to December 31, 2020. The inclusion criteria were: age ≥ 50 years, and conformity with neurological scale score and pure tone audiometry. Subjects with BI scores ≥ 60 were able to cooperate during the examination, and were included in the study. Patients in the following categories were excluded: (1) patients with BI scores ≤ 60 or MMSE scores ≤ 10 ; (2) patients with epilepsy, Parkinson's disease, frontotemporal dementia, and other types of dementia; and (3) those with probable conductive hearing loss (air-bone gap ≥ 15 dB), peripheral vertigo, and asymmetric hearing loss, or sudden deafness. Written informed consent was obtained from each participant. The study received approval from the Ethical Committee of the Affiliated Brain Hospital to Nanjing Medical University[9]. The participants were divided into three groups: control group (n=30), AD group (n=20) and VaD group (n=20) according to neurological guidelines[10, 11].

Baseline characteristics of participants

Clinical data were collected from all subjects, with respect to age, gender, body mass index, smoking and drinking habits, diabetes, stroke, family history, as well as TC, TG, FBG, LDL, and HbA1c. Barthel index (BI) was determined for evaluation of behavioral function. Severity of dementia was evaluated using Mini-mental state examination (MMSE). Participants with MMSE greater than 26 were classified as subjects with dementia grade 0. Subjects with MMSE scores ranging from 21 to 26 were placed in dementia grade 1 (mild cognitive impairment). Dementia grade 2 (moderate cognitive impairment) was for subjects with MMSE scores ranging from 10 to 20.

Measurement of hearing

Pure-tone audiometric test was used to measure the sensitivity of the peripheral auditory system and air conduction thresholds in each ear of all subjects at standard octaves from 0.5 to 8 kHz, using a semi-automated testing device (Xeta, GN/otometrics). The measurements were done by trained technicians. All

thresholds were measured in decibels of hearing level. The speech-frequency pure tone average (PTA) of air-conduction thresholds at each frequency was calculated for each patient. Hearing impairment (HI) was defined as PTA > 25 dB in the better-hearing ear, and it was categorized as pure tone average according to clinically defined cut-off points for HI [grade 0 (normal hearing): ≤25 dB; grade 1 (mild HI): 26–40 dB, and grade 2 (moderate/severe HI): >40 dB], based on WHO definition of HI[12].

Statistical analysis

All statistical analyses were performed using the SPSS (Windows, version 16.0 SPSS Inc). Categorical variables for gender are expressed as counts and percentage [n (%)]. Numerical variables are presented as mean±standard deviation (SD). Chi-square statistics for qualitative data was used to determine differences amongst groups, and for determination of correlations with different grades of severity of dementia. The *t*-test for independent samples was used for two-group comparison, while bivariate correlation analysis (Spearman correlation coefficient) for numerical variables was used to determine correlations with different grades of severity of dementia. Logistic regression analyses were carried out to further evaluate the association between grades of HI and dementia severity. Values of *p* values were two-sided. Differences were assumed statistically significant at *p*≤0.05[13, 14].

Results

Clinical characteristics of AD patients and VaD patients

The clinical characteristics of patients in control group, AD group, and VaD group are summarized in Table 1. Overall, 70 subjects comprising 30 patients in control group, 20 patients in AD group, and 20 patients of VaD group, completed the investigation. Chi-square statistics for categorical variables, and *t*-test for numerical variables were used to assess the differences among the three groups. Grades of cognitive impairment based on MMSE scores, degrees of hearing impairment based on threshold of hearing, and HbA1c differed significantly between AD patients and control subjects (*p*≤0.05). Body mass index (BMI), history of cerebral infarction, smoking, HbA1c, grades of cognitive impairment, and degrees of hearing impairment were significantly different between VaD group and control group (*p*≤0.05). Furthermore, history of cerebral infarction and degrees of hearing impairment were significantly different between AD group and VaD group (*p*≤0.05).

Clinical characteristics correlated with grades of cognitive impairment

Chi-square statistics for categorical variables and bivariate correlation analysis for numerical variables were used to assess the relationship amongst clinical characteristics of different grades of cognitive impairment based on MMSE scores (Table 2). In AD group and control group, grades of cognitive impairment were significantly positively correlated with age (*r*=0.28, *p*≤0.05) and degrees of HI based on threshold of hearing ($\chi^2=10.41$, *p*≤0.05). Body mass index (*r*=0.31, *p*≤0.05), HbA1c (*r*=0.35, *p*≤0.05), history of smoking ($\chi^2=6.56$, *p*≤0.05), and degrees of HI ($\chi^2=24.09$, *p*≤0.05) were significantly increased in different grades of cognitive impairment in VaD group and control group.

Logistic regression analyses

To investigate prognostic factors in cognitive impairment, logistic regression analyses were performed based on results of correlation analysis. As shown in Table 3, the degrees of HI, and grades of cognitive impairment based on MMSE scores were significant independent indicators in AD patients and control subjects (*p*≤0.05). Data also showed that the degree of hearing impairment was positively related to grades of cognitive impairment in VaD group and control group (*p*≤0.05).

Pure tone audiograms of HI patients

The hearing thresholds of the HI patients are presented in pure tone audiograms in Figure 1. As shown in Figure 1A, HI in the high-frequency hearing of AD group was significantly increased when compared with control group (*p*≤0.05). It was also found that there was significant impairment in full band hearing in VaD patients, relative to control subjects (Figure 1B, *p*≤0.05). However, there were significant increases in hearing loss in VaD group, when compared with AD group at most frequencies of hearing (Figure 1C; *p*≤0.05).

Discussion

In this study, pure tone audiometry electricity was determined in order to assess hearing loss in patients with AD and vascular dementia. The two different types of dementia patients had different clinical characteristics, but both had a certain degree of hearing impairment. The degree of the hearing impairment was positively correlated with cognitive damage. Thus, hearing impairment can be used for evaluation of cognitive impairment in AD and VaD. This study also found that the hearing loss in AD patients occurred at high frequency hearing, but hearing loss in patients with vascular dementia were at most frequency bands of hearing. The hearing loss in patients with vascular dementia at most frequency bands, was more significant than that of patients with AD.

Alzheimer's disease and vascular dementia are two important types of dementia, and they account for over 50 % of cognitive impairments in the crowd[15]. The "amyloid cascade hypothesis" is the main theoretical construct for AD[16-18]. In AD, αβ-peptides accumulate in neurons and trigger series of reactions such as inflammatory response, apoptosis, and blood-brain barrier injury[19-21]. Vascular dementia caused directly by stroke arises as a direct consequence of arterial pathology which triggers profound changes in the neurovascular unit and the normal physiology of neurovascular coupling[22, 23]. There are differences in the pathogenesis of the two kinds of dementia. There are also some differences in the clinical manifestations of these types of dementia. In this study, blood glucose control was significant for AD patients. Obesity index, history of smoking and drinking habits, and blood glucose control were more significant as high-risk factors of stroke in patients with vascular dementia than in AD patients. These suggest that although the clinical characteristics of the two types of dementia are different, there are some correlations between them. In the pure tone hearing threshold test, it was found that AD patients and VaD

patients had hearing impairment, but there was also a certain degree of difference between two groups. The degree of hearing loss in VaD group was greater than that in AD group. Moreover, VaD patients had both high-frequency and low-frequency HI, but the degree of impairment was more severe in AD patients at most frequency bands. These characteristics might be related to nerve injury and ear lesions.

Several cross-sectional studies have shown that accelerated rate of decrease in brain volume in temporal lobe in AD is not only important in cognitive impairment, but also in auditory function[24, 25]. Research has also shown that difficult auditory perception may be accompanied by extra burden of severe cognitive load that exhausts cognitive reserve[26-28]. At the same time, AD-related pathology which has been observed in the retina and cochlea, might be associated with cochlear pathology and hearing loss. This pathological mechanism of AD is closely related to age[29]. Some studies have reported age-related hearing loss in AD patients[30]. In the present study, it was also found that the hearing impairment in AD patients was mainly high-frequency hearing loss, and it was more significant with increase in audio frequency. This is consistent with the characteristics of age-related hearing loss. In vascular dementia, there are multiple-infarct lesions and white matter injury in the brain. In cerebral infarction, the internal carotid artery is the most easily blocked vessel. Acute ischemia of the internal carotid artery system often leads to basal ganglia infarction or temporal cortex infarction[31]. Similarly, in some patients with chronic cerebral ischemia, there is damage to the communication system in white matter[32]. Lesions in these functional structures cause decline in processing of spoken language, leading to impairment of cognitive function[33]. In some studies, it was found that there was an association between hearing impairment and speech function in patients with vascular dementia[34, 35]. There is a significant relationship between speech disorder and low-frequency hearing loss. These findings indicate that the damage to brain structure had an impact on hearing function. Furthermore, in some studies, the degree of sclerosis or occlusion of vertebrobasilar artery or internal auditory artery was higher in vascular dementia; this may affect the blood supply of the ear[36]. Therefore, vascular pathology may also occur in the cochlea as a potential contributor to the hearing loss associated with vascular dementia[37]. In this study, patients with vascular dementia had hearing impairment at low sound frequencies. At the same time, compared with AD patients, the degree of hearing damage was more serious in low-frequency and high-frequency ranges. The hearing loss of AD patients was mainly mild high-frequency hearing loss, but in VaD patients, it was mainly moderate or above hearing loss in full frequency. Therefore, hearing loss exists in AD and vascular dementia, but there might be differences in their pathogenesis and pathological mechanisms, leading to different clinical manifestations of hearing impairment.

In this study, there was a correlation between the degree of hearing loss and severity of dementia in AD patients. In results of logistic regression analysis, hearing impairment significantly contributed to the prognosis of severity of dementia in AD group. Furthermore, in VaD group, body mass index, history of cerebral infarction, history of smoking, HbA1c, and the degree of hearing loss were correlated with dementia severity[38, 39]. However, logistic regression analysis showed that hearing impairment was the only significant risk factor for prognosis of severity of dementia in VaD group. These results indicated that hearing impairment was important for cognitive function. Mounting evidence suggests a link between hearing loss and dementia. Some potential causal pathways would explain the relationship between hearing loss and dementia. The mechanism involved in the occurrence of dementia may be similar to the corresponding pathological mechanism in the cochlea, such as formation of α -amyloid in the internal auditory artery, resulting in decline of auditory nerve function[40]. This means that dementia might be the cause of hearing loss[41]. In patients with vascular dementia, the occlusion of internal auditory artery or the aggravation of arteriosclerosis in the inner ear decreases auditory conduction function[36]. Some animal studies on rodents have demonstrated that decline of auditory function led to the simplification of exogenous stimuli, which in turn led to the degeneration of cortex-related memory formation and storage. A third mechanism suggests that hearing impairment uses greater cognitive resources for listening; this negatively affects cognitive tasks such as attention, working memory, or language processing[42].

At present, it has been found that many factors affect cognitive function. These include uncontrollable factors such as age, gene and gender, as well as acquired controllable factors such as chronic disease history, obesity, bad habits, and levels of blood lipids and blood glucose[43]. Hitherto, there were no known factors that may be used for early detection of the existence of cognitive impairment and improve cognitive impairment after intervention. However, in this study, there was a close relationship between hearing and the degree of cognitive impairment, such that hearing impairment may be an index of mild cognitive impairment. There are different characteristics of pure-tone audiometry in patients with different types of dementia. Pure-tone audiometry might be an important method for evaluating cognitive impairment and for distinguishing between the two types of cognitive impairment. Furthermore, the issue of the effect of hearing interventions on the development of dementia has aroused interest amongst researchers. Some prospective randomized controlled trials provided the existing evidence related to the effect of hearing aid on recovery of cognitive function. Hearing intervention could reduce the degree of brain atrophy and play a role in nerve remodeling in auditory cortex. Therefore, it is of great significance to further study the relationship between hearing and cognitive function.

Limitations of the study

This investigation has some limitations. Expansion of sample size or a multi-center clinical trial would help to avoid the possibility of bias in case selection. The relationship amongst hearing function, speech function and cognitive function can be further elucidated using speech audiometry. There are also potential ethical issues such as economic burden and physical tolerance in patients with dementia with implanted hearing aid.

Conclusion

Dementia has been described as the greatest global health challenge. Early detection and differentiation of different types of cognitive impairment is of great significance. Pure tone hearing threshold is a simple and easy hearing detection method which might be an important method for identifying cognitive impairment and distinguishing amongst different types of dementia, and it might also become an important method for treating dementia.

Declarations

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None

Disclosures

None

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Tables

Table 1: Clinical demographics of AD patients, VaD patients and control subjects

Variable	Controls (n=30)	AD n=20	VaD n=20	p value
Age	66.47±9.23	70.9±8.93	70.85±8.05	0.05
Sex (% female)	16(53)	12(60)	8(40)	0.05
Body mass index	23.34±2.25	24.93±3.38	25.09±2.08	0.05 **
Hypertension(yes)	19(63)	13(65)	17(85)	0.05
Diabetes(yes)	5(17)	3(15)	4(20)	0.05
Coronary heart disease(yes)	2(6)	4(20)	3(15)	0.05
Cerebral infarction(yes)	14(47)	8(40)	15(75)	0.05 **, #
Smoking (yes)	3(10)	2(10)	7(35)	0.05 **
Drinking(yes)	1(3)	0	3(15)	0.05
MMSE (%)				0.05 *, **
MMSE ≥26	30(100)	0	0	
26≤MMSE <21	0	14(70)	8(40)	
21≤MMSE <10	0	6(30)	12(60)	
HI(%)				0.05 *, **, #
HI≥25	17(56)	3(15)	1(5)	
25≤HI<40	9(30)	9(45)	3(15)	
40≤HI	4(14)	8(40)	16(80)	
UA	290±85.21	308.3±108.87	314.5±84.38	0.05
TG	1.19±0.53	1.26±0.57	1.28±0.58	0.05
TC	4.09±0.87	3.78±0.73	4.02±1.14	0.05
HbA1c	5.64±1.61	6.2±1.23	6.03±1.5	0.05 *, **
LDL	2.13±0.68	1.86±0.59	2.08±0.83	0.05
HDL	1.12±0.31	1.17±0.35	1.13±0.37	0.05

The clinical data of the three groups include control group, Alzheimer's disease group and Vascular dementia group were counted. Categorical variables are expressed as n (%), and were analyzed with Chi-square statistics. Numerical variables are presented as mean±SD, and were analyzed with *t*-test. **p* < 0.05, AD group versus control group; ***p* < 0.05, VaD group versus control group; #*p* < 0.05, AD group versus VaD group.

Table 2: Clinical features correlated with the degree of dementia severity

Types of cognitive impairment	AD					VaD				
Grade of cognitive impairment	0	1	2	χ^2/r	p value	0	1	2	χ^2/r	p value
Age	66.47±9.23	69±8.45	75.33±9.14	0.28	0.05*	66.47±9.23	72.25±8.38	70.58±8.2	0.22	0.05
Sex (% female)	16(53)	7(50)	5(83)	2.11	0.05	16(53)	4(50)	4(33)	1.39	0.05
Body mass index	23.34±2.25	25.81±3.46	22.85±2.23	0.16	0.05	23.34±2.25	25.08±2.65	25.1±3.03	0.31	0.05*
Hypertension(yes)	19(63)	8(54)	5(83)	1.27	0.05	19(63)	6(50)	11(92)	3.45	0.05
Diabetes(yes)	5(17)	2(14)	1(15)	0.043	0.05	5(17)	2(25)	2(15)	0.32	0.05
Coronary heart disease(yes)	2(6)	2(14)	2(67)	3.46	0.05	2(6)	2(25)	1(8)	2.41	0.05
Cerebral infarction(yes)	14(47)	6(43)	2(33)	0.37	0.05	14(47)	6(75)	9(82)	3.96	0.05
Smoking (yes)	3(10)	2(14)	0	0.95	0.05	3(10)	4(50)	3(25)	6.56	0.05*
Drinking(yes)	1(3)	0	0	0.68	0.05	1(3)	1(15)	2(15)	2.32	0.05
HI(%)				10.41	0.05*				24.09	0.05*
HI≥25	17(56)	3(15)	0			17(56)	0	1(8)		
25<HI≤40	9(30)	6(43)	3(50)			9(30)	2(25)	1(8)		
40<HI	4(14)	5(35)	3(50)			4(14)	6(75)	10(84)		
UC	290±85.21	299.14±99.3	330±139.46	0.07	0.05	290±85.21	281.63±47.59	335.75±96.6	0.18	0.05
TG	1.19±0.53	1.2±0.63	1.41±0.4	0.11	0.05	1.19±0.53	1.28±0.83	1.29±0.38	0.11	0.05
TC	4.09±0.87	3.82±0.73	3.67±0.78	-0.2	0.05	4.09±0.87	3.97±0.72	4.04±1.39	-0.09	0.05
HbA1c	5.64±1.61	6.18±1.36	6.27±0.94	0.27	0.05	5.64±1.61	6.03±0.28	6.02±0.23	0.35	0.05*
LDL	2.13±0.68	1.87±0.46	1.87±0.87	-0.2	0.05	2.13±0.68	2.05±0.56	2.1±1	-0.06	0.05
HDL	1.12±0.31	1.18±0.33	1.14±0.44	-0.069	0.05	1.12±0.31	1.13±0.39	1.12±0.37	-0.15	0.05

The correlation between clinical data and the degree of cognitive impairment were analyzed. The correlation between clinical data and the degree of cognitive impairment was determined. The degree of dementia was assessed according to MMSE score. MMSE score greater than 26 was categorized as grade 0; MMSE scores ranging from 20 to 26 were in grade 1, while patients with MMSE scores ranging from 11 to 20 were in grade 2. Categorical variables are expressed as n (%), and were analyzed with Chi-square test. Numerical variables are presented as mean±SD, and they were analyzed with bivariate correlation analysis (Spearman correlation coefficient). * $P < 0.05$ (correlation of variables to dementia grades).

Table 3: Logistic regression analysis of factors and the degree of severity of dementia

Type of cognitive impairment	AD				VaD			
Factor	B	Wald	p	95 % CI	β	Wald	p	95 % CI
Age	0.05	1.6	0.2	-0.026-0.219	-	-	-	-
Body mass index	-				0.26	2.7	0.1	-0.05-0.57
Smoking	-				-0.02	0	0.98	-1.7-1.7
HI=0	-2.155	5.87	0.02*	-3.9-0.42	-3.68	9.7	0.05*	-0.05-0.59
HI=1	-0.29	0.14	0.71	-1.82-1.24	-2.29	6.77	0.05*	-0.05-0.60
HbA1c					0.46	0.5	0.48	-0.82-1.74

CI = confidence interval; OR = odds ratio

Figures

Pure Tone Audiometry

Figure 1

Pure tone audiograms of individuals with control group (n= 30), AD group (n= 20), and VaD group (n= 20). Hearing threshold of each group was present as mean±standard deviation in each frequency and analyzed by T test. A. Comparison of hearing threshold between control group and AD group. *p < 0.05, AD group versus control group. B. Comparison of hearing threshold between control group and VaD group. *p < 0.05, VaD group versus control group. C. Comparison of hearing threshold between AD group and VaD group. * p < 0.05, AD group versus VaD group.