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ORIGINAL ARTICLE

Increased Atherosclerosis Correlates with Subjective Tinnitus Severity

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Abstract The aim of the present study was to investigate whether increased intima media thickness was associated with the severity of subjective non-pulsatile tinnitus and hearing loss. Data of the patients who came to Otorhinolaryngology Department of Isparta Government Hospital with subjective non-pulsatile tinnitus complaint, between January 2012 and June 2013, were evaluated retrospectively. A total of 215 patients were included in the present study. Hearing tests, biochemical analysis, tinnitus handicap inventory (THI), visual analogue scale (VAS) and doppler ultrasonography results of the patients were reviewed and recorded. The patients were classified into two groups as those having an increased intima media thickness and those having a normal intima media thickness. The said groups were compared with respect to age, gender, THI, VAS, hearing test findings and lipid values. Moreover, THI and VAS groups were compared with respect to intima-media thickness. In the group having increased intima-media thickness, THI and VAS average, frequency of hypertension, total cholesterol, low density lipoprotein and triglyceride averages and mean frequencies obtained by hearing test were significantly higher. Comparison of THI and VAS groups showed that intima-media thickness was significantly different between those having a mild tinnitus and those having a severe tinnitus. Increased intima-media thickness was associated with the severity of subjective non-pulsatile tinnitus and hearing loss. For this reason, the carotid system should be examined in subjective non-pulsatile tinnitus patients.

Keywords Atherosclerosis · Hearing loss · Intima-media thickness · Tinnitus

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Introduction

Tinnitus is described as the perception of a noise inside one's head in the absence of auditory stimulation [1]. Both genders are affected equally while 50 % of the cases are bilateral [2]. The prevalence of tinnitus has been reported to be 10–15 % in the adult population [3]. The prevalence of tinnitus shows a tendency to increase with age as follow: 7 % in the 3rd decade and 21 % in the 7th decade [4]. Tinnitus is generally divided into two groups as objective tinnitus (perceived by another individual) and subjective tinnitus (perceived only by the patient). Objective tinnitus is the perception of sounds transmitted to the cochlea or the middle ear by the bones. Subjective tinnitus is the perception of sounds caused by abnormal neural activity that is not evoked by sound [5]. Most cases of tinnitus are subjective.

Subjective tinnitus is generally caused by pathologies in the central nervous system including the central auditory

nervous system [6]. Vascular pathologies are thought to be one of the possible contributing factors. The cochlea is sensitive to the changes in the blood flow and a limited impairment of perfusion causes dysfunction of the organ of corti [7]. Atherosclerosis, which is associated with cerebrovascular diseases and ischemic heart diseases, has been thought to be among factors causing tinnitus. An increase in intima-media thickness (IMT) is accepted as an early sign of atherosclerosis [8, 9]. Doppler ultrasound of carotid artery is commonly used to measure the narrowness of carotid artery and IMT. There is a limited data on the association between subjective non-pulsatile tinnitus and atherosclerotic disease of the carotid artery. For this reason, our aim was to evaluate whether intima-media thickness and serum lipid levels had an effect on the severity of tinnitus and hearing loss in patients with subjective non-pulsatile tinnitus.

Subjects and Methods

Data of the patients who came to Otorhinolaryngology Department of Isparta Government Hospital with subjective non-pulsatile tinnitus complaint, between January 2012 and June 2013, were evaluated retrospectively. For this type of study formal consent is not required. The inclusion criteria were having bilateral subjective non-pulsatile tinnitus for at least 6 months, having no previous treatments for tinnitus, having no external or middle ear infection, having no history of neuro-otological surgery, having no systemic disease other than controlled hypertension or diabetes and having no history of any diseases causing tinnitus such as Meniere disease, otosclerosis, sudden hearing loss and acoustic tumour. Moreover, those found to have conductive hearing loss, mixed hearing loss and A–r, A–d, C and B type curves at audiometry and tympanometry were excluded too. Data of a total of 215 patients composed of 131 (aged 51.11 $\pm$ 14.32) female and 84 (aged 52.33 $\pm$ 11.40) male individuals aged between 18 and 75 years old were studied.

Threshold assessments were made at 250, 500, 1000, 2000, 4000, 6000 and 8000 Hz using pure tone audiometry. The pure tone thresholds for statistical purposes were classified as follows: mean of all tested frequencies (mean total: arithmetic mean of pure tone thresholds at 250, 500, 1000, 2000, 3000, 4000, 6000 and 8000 Hz.), mean at high frequencies (mean acute: arithmetic mean of pure tone thresholds at 4000, 6000 and 8000 Hz), conventional tritone mean (mean tri: arithmetic mean of pure tone thresholds at 500, 1000 and 2000 Hz), quadritone mean (mean quadri: arithmetic mean of pure tone thresholds at 500, 1000, 2000 and 4000 Hz).

Serum lipid levels, complete blood count, folic acid and vitamin B12 values of the patients were examined. Total cholesterol (Total-C) level less than 200 mg/dl was considered normal and $\geq$200 mg/dl was considered high. High density lipoprotein (HDL) level less than 40 mg/dl was considered and $\geq$40 mg/dl was considered desired. Low density lipoprotein (LDL) level less than 130 mg/dl was considered desired and >130 mg/dl was considered high. Triglyceride (TG) level less than 200 mg/dl was considered normal and >200 mg/gl was considered high [10].

Tinnitus Handicap Inventory (THI) and visual analogue scale (VAS) were used to evaluate the severity of tinnitus. The answers of the THI composed of 25 questions prepared for Turkey were: No: 0, Sometimes: 2 and Yes: 4 [11]. The lowest score was 0 and the highest score was 100. The five severity scores were: 0–16 points negligible (I), 18–36 points mild (II), 38–56 points moderate (III), 58–76 points severe (IV) and 78–100 points catastrophic (V). VAS scores were grouped similarly: 1–2 points negligible (I), 3–4 points mild (II), 5–6 points moderate (III), 7–8 points severe (IV) and 9–10 points catastrophic (V).

In all the patients, ultrasound evaluation of carotid artery was performed using 7.5-MHz linear-type B-mode probe by a radiologist blind to the medical status of the patients. Tests were performed at supine position. Measurements of the common, internal and external carotid arteries were made at both sides while the maximum IMT was defined as the distance from the leading edge of the lumen–intima interface to the leading edge of the media–adventitia interface of the far wall. Increased blood vessel wall thickness was diagnosed when IMT $\geq$1 mm [12]. The patients were divided into two groups as those having a normal IMT (<1 mm) and those having an increased IMT ($\geq$1 mm).

The statistical analyses were performed between those having normal and increased IMT and between THI and VAS groups. It was examined whether IMT was associated with age, gender, pure tone audiometry and whether there was a significant association between THI and VAS results. SPSS.17 package program was used for the statistical analysis. Kolmogorov–Smirnov test was used to check the normal distribution of the data. In the comparison of intergroups, Chi square was used for the personal data while Independent Sample *T* test and Mann Whitney *U* test were used for the measurement data. The correlation analyses were conducted using Pearson correlation analysis. Percentage and mean $\pm$ standard deviation values were given as descriptive statistics. $p < 0.05$ was regarded as significant.

Informed form was obtained from the participants of the study and their details was collected from the recorded data of the patients' files.

Results

Fifty-three (24.6 %) of the patients were found to have increased intima-media thickness. Characteristics of the patients are shown in Table 1. While the mean age of the group having increased IMT was 59.40 ± 7.79, the mean age was 49.04 ± 13.67 in the group having normal IMT ($p = 0.001$). IMT was found to be increased in 35.7 % of the males and 17.6 % of the females ($p = 0.003$). Mean IMT was 0.96 mm in males and 0.86 mm in females ($p = 0.003$). In both genders, IMT increased significantly with age ($p = 0.0001$; $r = 0.36$). In the group having increased IMT, the mean THI and VAS scores, frequency of hypertension, total cholesterol, mean LDL and triglyceride values (Table 1) and mean frequencies (mean total, mean acute, mean tri, mean quadri) obtained in hearing tests (Table 2) were significantly higher. There was a significant correlation between IMT and hearing test and between THI and VAS findings (Table 3).

IMT was 0.93 ± 0.24 mm in 158 patients having hearing loss in at least one of the frequencies while it was 0.81 ± 0.15 mm in 57 patients having no hearing loss in any of the frequencies. The difference between the said groups was significant ($p = 0.001$) (Table 1). In the correlation test between THI and VAS, there was a moderately significant difference between the tests (Pearson correlation 0.565, $p = 0.001$). This finding shows that using both tests together in evaluating the severity of tinnitus may increase the reliability of a study.

When THI was used, 15 (7 %) patients had grade I, 79 (36.7 %) patients had grade II, 79 (39.7 %) patients had grade III, 36 (16.8 %) patients had grade IV and 6 (2.8 %) patients had grade V severity scores. Based on VAS scores, 34 (15.8 %) patients had grade I, 56 (26 %) patients had grade II, 84 (39 %) patients had grade III, 40 (18.6 %) patients had grade IV and 1 (0.5 %) patient had grade V severity scores. IMT values of THI and VAS groups are shown in Table 4. Moreover, the significance values obtained when THI and VAS groups were compared are given in Table 5. Especially, IMT showed a significant difference between those having a mild tinnitus and those having a severe tinnitus. These findings show that the severity of tinnitus increases parallel to an increase in IMT.

Discussion

Damaged outer hair cells and more specifically modified stereocilia in hair cells is the most commonly accepted theory in the pathophysiology of tinnitus [6]. The cochlea

Table 1 Demographic data of patients having normal and abnormal IMT

	IMT		p
	<1 mm (n:162) mean ± SD	≥1 mm (n:53) mean ± SD	
Gender			
Male	54 (33.3 %)	30 (56.6 %)	0.003*
Female	108 (66.7 %)	23 (43.4 %)	
Age (years)	49.04 ± 13.67	59.40 ± 7.79	0.001*
Duration of Tinnitus (month)	42.29 ± 45.56	48.16 ± 47.57	0.421
Hearing loss			
Present	111 (68.5 %)	47 (88.7 %)	0.004*
Non-present	51 (31.5 %)	6 (11.3 %)	
Diabetes	14 (8.6 %)	6 (11.3 %)	0.560
Hypertension	26 (16.0 %)	15 (28.3 %)	0.049*
THI	39.22 ± 17.77	45.07 ± 16.63	0.036*
VAS	4.55 ± 1.79	5.37 ± 1.88	0.005*
Haemoglobin	14.08 ± 1.86	14.56 ± 1.39	0.086
Total-C (mg/dl)	193.99 ± 41.52	212.83 ± 46.14	0.006*
VLDL (mg/dl)	31.91 ± 18.67	39.21 ± 25.60	0.059
LDL (mg/dl)	113.18 ± 36.71	131.51 ± 38.12	0.002*
HDL (mg/dl)	47.69 ± 11.63	45.60 ± 11.72	0.257
Triglyceride (mg/dl)	155.98 ± 85.66	196.28 ± 130.12	0.039*
B12	371.80 ± 219.84	386.54 ± 262.29	0.687
Folic acid	7.52 ± 3.61	7.32 ± 2.43	0.813

Total-C total cholesterol, *VLDL* very low density lipoprotein, *LDL* low density lipoprotein, *HDL* high density lipoprotein, *HDL* high density lipoprotein, *THI* tinnitus handicap inventory, *VAS* visual analogue scale

* $p < 0.05$

Table 2 Distribution of audiological findings in patients having normal and abnormal IMT

	IMT		p
	<1 mm mean ± SD	≥1 mm mean ± SD	
Mean total			
Right	24.22 ± 14.83	32.41 ± 15.73	0.001*
Left	25.22 ± 16.86	31.95 ± 13.14	0.009*
Mean acute			
Right	32.91 ± 21.85	45.88 ± 21.80	0.001*
Left	34.77 ± 23.32	46.42 ± 21.11	0.001*
Mean tri			
Right	17.98 ± 13.17	23.45 ± 15.80	0.013*
Left	18.36 ± 15.74	22.01 ± 12.50	0.126
Mean quadri			
Right	20.85 ± 13.52	28.56 ± 15.58	0.001*
Left	21.71 ± 16.45	27.78 ± 12.82	0.015*

* $p < 0.05$

Table 3 Correlation analyses of IMT and hearing test, THI and VAS findings

	Pearson correlation*	p**
THI	0.234	0.001
VAS	0.257	0.001
Mean total		
Right	0.260	0.001
Left	0.195	0.004
Mean acute		
Right	0.298	0.001
Left	0.255	0.001
Mean tri		
Right	0.177	0.009
Left	0.103	0.132
Mean quadri		
Right	0.251	0.001
Left	0.174	0.011

THI tinnitus handicap inventory, *VAS* visual analogue scale

* Correlation is significant at the 0.01 level (2-tailed). ** Correlation is significant at the 0.05 level (2-tailed)

is sensitive to the changes in the blood flow while a limited impairment of perfusion causes dysfunction of the organ of corti [7]. Atherosclerosis may cause changes in cochlear microcirculation and turbulence or decrease of blood flow in the inner ear [13, 14]. Tinnitus can be the first symptom of atherosclerosis [15, 16]. IMT is used as a criterion for atherosclerosis [8, 9]. Increased IMT detected by ultrasound reflects morphological changes including thickening and calcification of carotid artery [17]. Increased IMT is considered as an indicator of increased risk for myocardial infarction and stroke [9, 18]. We believe that IMT can be reflecting intracranial arterial sclerosis in patients who present with the complaint of tinnitus. In a study on 1348 patients attending a brain -scan program, Fukatsu et al. [19] reported that IMT was significantly higher in patients having tinnitus (242 patients) when compared to those having no tinnitus. In a study on 100 patients having pulsatile tinnitus, Sismanis and Smoker [15] reported the presence of atherosclerotic carotid artery disease as 15 %. Gutmann et al. [20] stated that the risk of atherosclerotic stenosis of the extracranial arteries was 18 % in patients having tinnitus and 1 % in asymptomatic patients. Waldvogel et al. [21] found atherosclerosis of the internal carotid artery in 8 % of 84 patients having pulsatile tinnitus. In our study, we found increased IMT in 24.6 % of the patients. THI and VAS scores, showing the severity of tinnitus, had a positive correlation with IMT while the severity of tinnitus increased parallel to an increase in IMT. As the aim of the present study was to evaluate the effect of an increased IMT on the severity of subjective non-pulsatile tinnitus, no control group composed of individual without tinnitus was formed.

It is known that tinnitus is associated with age, male gender, hearing loss and exposure to noise. Moreover, tinnitus is thought to be associated with some metabolic diseases such as hypertension, hypercholesterolemia and diabetes mellitus [22]. On the other hand, etiological mechanisms have to be explained clearly. In most of the patients having tinnitus, there can be at least one risk factor for atherosclerotic carotid artery disease [13]. High serum LDL and low HDL are regarded as the most important

Table 4 Intima media thicknesses in THI and VAS groups

	I	II	III	IV	V
THI					
N	15	79	79	36	6
Mean ± SD	0.86 ± 0.29	0.84 ± 0.18	0.93 ± 0.21	0.98 ± 0.30	0.86 ± 0.05
VAS					
N	34	56	84	40	1
Mean ± SD	0.81 ± 0.23	0.84 ± 0.15	0.93 ± 0.23	0.98 ± 0.28	0.80 ±

N number of patients, *Mean* ± *SD* mm, *THI* tinnitus handicap inventory, *VAS* visual analogue scale

Table 5 p values obtained when IMT values of THI and VAS groups were compared

	I–II	I–III	I–IV	I–V	II–III	II–IV	II–V	III–IV	III–V	IV–V
THI	0.812	0.195	0.145	0.527	0.002*	0.010*	0.329	0.798	0.535	0.631
VAS	0.340	0.014*	0.015*	0.920	0.029*	0.030*	0.635	0.656	0.401	0.438

VAS visual analogue scale

* $p < 0.05$, THI: tinnitus handicap inventory

vascular risk factors. Daneshi et al. [23] reported that patients having pulsatile tinnitus had at least one risk factor for atherosclerotic carotid artery disease. Histochemical studies conducted on animals having hypercholesterolemia revealed vacuolar degeneration in vessels at stria vascularis [24] and clusters of amorphous material in outer hair cells and strial marginal cells [25]. Cholesterol, other than its role in atherosclerosis development and blood viscosity increase, may damage cochlear microcirculation by decreasing the release of nitric oxide (NO), which is a strong vasodilator, from the endothelial cell [26]. As it has been reported previously, we found that carotid IMT had a direct and significant correlation with total cholesterol, LDL cholesterol, triglyceride and HDL cholesterol (negative correlation) [27]. Moreover, in our study, IMT was higher in patients of male gender and hypertension while there was no significant difference in patients having diabetes. This finding is consistent with the ones obtained in previous studies [28].

There is a close association between tinnitus and hearing loss [29]. Tinnitus has been found in 50 % of those having sudden sensorineural hearing loss, 70 % of those having presbycusis and 50–90 % in those having chronic acoustic trauma [30]. The Pearson correlation analysis in our study verifies that there is a positive association between IMT and hearing loss ratios. In this regard, we believe that our results are consistent with the previous results.

Evaluating tinnitus patients with tinnitus inventories and scales helps assessing the impact of tinnitus and contributes to standardization in evaluating the treatment outcomes during patient follow-up. THI is a comprehensive method to assess the severity and impact of tinnitus. VAS is a simple method which is easy to apply especially in older people. In our study, we used THI and VAS together and evaluated the association of IMT to the severity of subjective non-pulsatile tinnitus and audiometric data. We believe that the significant correlation we found between THI and VAS increased the reliability of our study.

Conclusion

As a result, there was a significant association between increased IMT and severity of subjective non-pulsatile tinnitus and hearing loss. For this reason, the carotid system should be examined in subjective non-pulsatile tinnitus patients. At the same time, risks for cerebrovascular and cardiovascular diseases can be reduced.

Conflict of interest We have no conflict of interest that we should disclose.

References

1. Jastreboff PJ (1990) Phantom auditory perception (tinnitus): mechanisms of generation and perception. Neurosci Res 8:221–254
2. Meyerhoff WL, Cooper JC (1991) Tinnitus. In: Paparella MM, Shumrick DA, Gluckman JL (eds) Otolaryngology, 3rd edn. WB Saunders, Philadelphia, pp 1169–1179
3. Zöger S, Svedlund J, Holgers KM (2001) Psychiatric disorders in tinnitus patients without severe hearing impairment: 24 month follow-up of patients at an audiological clinic. Audiology 40:133–140
4. Hoke M, Pantev C, Lütkenhöner B, Lehnertz K. (1991) Auditory cortical basis of tinnitus. Acta Otolaryngol Suppl 491:176–81; discussion 182
5. Moller AR (2006) Neural plasticity in tinnitus. Prog Brain Res 157:365–372
6. Moller AR (2003) Pathophysiology of Tinnitus. Otolaryngol Clin North Am 36:249–266
7. Miller JM, Ren TY, Nuttall AL (1995) Studies of inner ear blood flow in animals and human beings. Otolaryngol Head Neck Surg 112:101–113
8. Hunt KJ, Evans GW, Folsom AR, Sharrett AR, Chambless LE, Tegeler CH et al (2001) Acoustic shadowing on B-mode ultrasound of the carotid artery predicts ischemic stroke: the Atherosclerosis Risk in Communities (ARIC) study. Stroke 32:1120–1126
9. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr (1999) Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. N Engl J Med 340:14–22
10. Harris WS, Mozaffarian D, Rimm E (2009) Omega-6 fatty acids and risk for cardiovascular disease: a science advisory from the American Heart Association Nutrition Subcommittee of the Council on Nutrition, Physical Activity, and Metabolism; Council on Cardiovascular Nursing; and Council on Epidemiology and Prevention. Circulation 119:902–907
11. Aksoy S, Fırat Y, Alpar R (2007) The tinnitus handicap inventory: a study of validity and reliability. Int Tinnitus J 13:94–98
12. Cifkova R, Erdine S, Fagard R, Farsang C, Heagerty AM, Kiowski W et al (2003) ESH/ESC Hypertension Guidelines Committee. Practice guidelines for primary care physicians: 2003 ESH/ESC hypertension guidelines. J Hypertens 10:1779–1786
13. Kirkby-Bott J, Gibbs HH (2004) Carotid endarterectomy relieves pulsatile tinnitus associated with severe ipsilateral carotid stenosis. Eur J Vasc Endovasc Surg 24:651–653

14. Hartung O, Alimi YS, Juhan C (2004) Tinnitus resulting from tandem lesions of the internal carotid artery: combined extracranial endarterectomy and intrapetrous primary stenting. J Vasc Surg 39:679–681
15. Sismanis A, Smoker WRK (1994) Pulsatile tinnitus: recent advances in diagnosis. The Laryngoscope 104:681–688
16. Sismanis A, Stamm MA, Sobel M (1994) Objective tinnitus in patients with atherosclerotic carotid artery. Am J Otol 15:404–407
17. Yamagishi T, Kato M, Koiwa Y, Hasegawa H, Kanai H (2009) Impact of lifestyle-related diseases on carotid arterial wall elasticity as evaluated by an ultrasonic phased tracking method in Japanese subjects. J Atheroscler Thromb 16:782–791
18. Lin HF, Liu CK, Liao YC, Lin RT, Chen CS, Juo SH (2010) The risk of the metabolic syndrome on carotid thickness and stiffness: sex and age specific effects. Atherosclerosis 210:155–159
19. Fukatsu M, Yamada T, Suzuki S, Yoneyama A, Joh T (2011) Tinnitus is associated with increase in the intima-media thickness of carotid arteries. Am J Med Sci 342:2–4
20. Gutmann R, Wollenberg B, Krampert B, Mees K (1993) Incidence of Doppler ultrasound-detectable stenoses of cervical arteries in patients with cochlear-vestibular symptoms. Laryngorhinootologie 72:502–505
21. Waldvogel D, Mattle HP, Sturzenegger M, Schroth G (1998) Pulsatile tinnitus—a review of 84 patient. J Neurol 245:137–142
22. Crummer RW, Nassan GA (2004) Diagnostic approach to tinnitus. Am Fam Physician 69:120–126
23. Daneshi A, Hadizadeh H, Mahmoudian S, Sahebjam S, Jalesi A (2004) Pulsatile tinnitus and carotid artery atherosclerosis. Int Tinnitus J 10:161–164
24. Saito T, Sato K, Saito H (1986) An experimental study of auditory dysfunction associated with hyperlipoproteinemia. Arch Otorhinolaryngol 243:242–245
25. Gratton MA, Wright CG (1992) Alterations of inner ear morphology in experimental hypercholesterolemia. Hear Res 61:97–105
26. Feron O, Dessy C, Desager JP, Balligand JL (2001) Hydroxymethylglutarylcoenzyme A reductase inhibition promotes endothelial nitric oxide synthase activation through a decrease in caveolin abundance. Circulation 103:113–118
27. Wendelhag I, Wiklund O, Wikstrand J (1992) Arterial wall thickness in familial hypercholesterolemia: ultrasound measurement of intima-media thickness in common carotid artery. Arterioscler Thromb 12:70–77
28. Baldassarre D, Amato M, Bondioli A, Sirtori CR, Tremoli E (2000) Carotid artery intima-media thickness measured by ultrasonography in normal clinical practice correlates well with atherosclerosis risk factors. Stroke 31:2426–2430
29. Dauman R, Cazals Y (1989) Auditory frequency selectivity and tinnitus. Arch Otorhinolaryngol 246:252–255
30. Graham JM (1981) Tinnitus and defness of sudden onset: electrocochleographic finding in 100 patients. J Laryngol Otol 4:111–116