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An Investigation Into Hearing Functions in Patients With Takayasu Arteritis

Emel Oguz Kökoğlu,[1] Kerem Kökoğlu,[2] Abdurrahman Soner Şenel,[1] Nezaket Tektaş,[2] Melih Kızıltepe,[1] Emre Solguntekin,[2] Kadir Aydın[2]

[1]Division of Rheumatology, Department of Internal Medicine, Erciyes University Faculty of Medicine, Kayseri, Türkiye
[2]Department of Otolaryngology, Erciyes University Faculty of Medicine, Kayseri, Türkiye

ABSTRACT

Objective: Takayasu arteritis is a systemic vasculitis. There have been some cases reported in the literature that suggest distortion of hearing in this disease. Patients may experience hearing loss as the first symptom or during the course of the disease. This study aims to investigate disturbances in hearing function in patients with Takayasu arteritis by comparing them to healthy subjects.

Materials and Methods: Patients and randomly selected age-gender compatible healthy subjects were enrolled in the study. Subjects who previously had congenital hearing loss, otologic surgery, severe head trauma, ototoxicity, were exposed to noise, or worked in noisy environments beforehand were excluded. Pure Tone Audiometry (PTA), tympanometry, and Otoacoustic Emissions (OAE) were performed on all subjects. The Indian Takayasu Arteritis Activity Score (ITAS 2010) was also estimated for the Takayasu group. Statistical comparisons of air and bone-conduction thresholds and OAE values between the Takayasu and control groups were performed.

Results: A total of 31 subjects were included in each group, comprising 27 women and 4 men. The mean ages were 45.3±2 for the Takayasu group and 44.8±1.8 for the control group, respectively. Both groups were similar in age and gender composition ($p>0.05$). No significant differences were found between the Takayasu and healthy control groups in terms of PTA averages and OAE values ($p>0.05$). However, significant differences were observed at the right and left 8000 Hz frequencies ($p<0.05$), with higher values in the Takayasu group. Additionally, two patients in the Takayasu group experienced idiopathic sudden sensorineural hearing loss (ISSHL).

Conclusion: Hearing function was similar between the Takayasu group and age-gender-matched healthy controls, except at the 8000 Hz frequency in PTA. Takayasu arteritis may manifest with ISSHL.

Keywords: Autoimmune, hearing loss, vasculitis.

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Address for correspondence:
Kerem Kökoğlu.
Department of Otolaryngology, Erciyes University Faculty of Medicine, Kayseri, Türkiye
Phone: +90 507 540 72 70
E-mail: dr.kokoglu@gmail.com

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INTRODUCTION

Takayasu arteritis is a systemic autoimmune vasculitis that can affect large arteries such the aorta and its major branches, including the pulmonary artery, as well as medium-sized arteries.[1,2] While the main symptoms of Takayasu arteritis include limb claudication, heart murmurs, and asymmetric arterial blood pressure, central nervous system manifestations are also common, particularly in the chronic phase.[3] Notably, small vessel involvement, like that of cerebral arteries, can severely impact prognosis and may be the initial manifestation of the disease.[4] Thus, Takayasu arteritis can lead to neurological symptoms.

Furthermore, Takayasu arteritis may coexist with chronic inflammatory diseases such as ulcerative colitis, Crohn's disease, ankylosing spondylitis, sarcoidosis, rheumatoid arthritis, Behçet's syndrome, and antiphospholipid syndrome.[5] Systemic autoimmune diseases can cause otolaryngologic manifestations that pose diagnostic challenges for clinicians.[6,7] As part of the systemic disease or as a manifestation of autoimmune hearing loss, vasculitis can affect hearing.[8]

Given the previous literature, there are some case reports of hearing loss in Takayasu arteritis.[9,10] Although the inner ear is supplied by the labyrinthine artery, immune complexes can cause cochlear damage. These complexes can lead to hearing loss at the onset or during the course of Takayasu arteritis.[11] Central nervous system involvement may further contribute to hearing loss in this condition.

Penwal et al.[12] reported defective central auditory processing skills in five cases of Takayasu arteritis. They hypothesized that the decrease in blood flow to the central nervous system, following stenosis of the major arteries, leads to functional abnormalities of the brainstem.

Patients with Takayasu arteritis may experience hearing loss as the first symptom or during the course of the disease, not only due to immune complexes but also due to reduced blood supply to the central nervous system. Although there are some case reports, to the researchers' knowledge, no clinical study has examined the audiological findings in Takayasu arteritis. Therefore, the present study aims to address this gap by focusing on the hearing functions in a case group with Takayasu arteritis compared to healthy subjects.

MATERIALS AND METHODS

The study was designed as a case-control study. After receiving approval from the Erciyes University Ethical Committee of Clinical Research (decision date: 22. 04. 2022, number: 2022/344), patients with Takayasu arteritis who were under the care of the Rheumatology Department were recruited for the study. They provided informed consent. The diagnosis of Takayasu arteritis was based on the American College of Rheumatology criteria.[13]

Patients' otolaryngological histories and physical examination findings were recorded. Patients with a history of congenital hearing loss, otologic surgery, severe head trauma, exposure to noise, employment in noisy environments, ototoxicity, or tympanogram types other than type A were excluded. They were asked whether they had experienced idiopathic sudden sensorineural hearing loss (ISSHL) in the past. All patients underwent pure tone audiometry (PTA), tympanometry, and distortion product otoacoustic emissions (DPOAE) testing. Their results were compared with those of age and gender-compatible healthy subjects who underwent the same tests. Healthy subjects were randomly selected from the database of the institutional hearing and vestibular unit, forming an archive of individuals tested during routine health screenings. The same exclusion criteria were applied to the control group.

The Indian Takayasu Arteritis Activity Score (ITAS 2010) was used to assess disease activity. This score includes clinical parameters such as hypertension, stroke, heart murmur, claudication, pulselessness, pulse-tension inequality, and laboratory parameters like erythrocyte sedimentation rate and C-reactive protein. A patient scoring more than 1 point is considered to have active disease.[14]

The Takayasu group was divided into subgroups based on disease activity (active/inactive), carotid involvement (positive/negative), and history of cerebrovascular events (positive/negative). Evaluations over time were also conducted for the Takayasu group. These subgroups were compared in terms of PTA thresholds, pure tone averages, and DPOAE values.

Pure Tone Audiometry: All examinations were performed by the same audiologist, who was blinded to the patients' group affiliations. The tests were conducted in a soundproof room using a clinical audiometer (Madsen Astera, Natus Medical, Taastrup, Denmark) equipped with TDH-39 earphones. Air-conduction hearing thresholds were measured at frequencies ranging from 125 to 8000 Hz, and bone-conduction hearing thresholds were measured from 250 to 4000 Hz. The pure tone average was calculated using the hearing thresholds at four frequencies: 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz.

Tympanometry was performed in a soundproof room using a 226 Hz stimulating sound with the AT235 device (Interacoustics, Middelfart, Denmark). The environmental noise level was maintained below 30 dB. The procedure started at an initial pressure of +200 daPa, decreased to -400 daPa, with the pressure change direction from positive to negative. Subjects with a tympanogram type other than Type A were excluded.

Table 1. Median thresholds (25th–75th percentiles) of groups by sides and frequencies

Right ear	Takayasu	Control	p	Left ear	Takayasu	Control	p
125 Hz – AC	15 (10–25)	12.5 (10–20)	0.116	125 Hz – AC	15 (10–20)	15 (10–25)	0.515
250 Hz – AC	15 (10–20)	10 (10–15)	0.059	250 Hz – AC	15 (10–20)	10 (5–20)	0.722
250 Hz – BC	10 (5–10)	10 (5–15)	0.857	250 Hz – BC	10 (5–10)	10 (5–11.25)	0.646
500 Hz – AC	10 (10–20)	10 (5–15)	0.109	500 Hz – AC	10 (10–16.25)	10 (5–15)	0.358
500 Hz – BC	10 (5–20)	10 (5–15)	0.174	500 Hz – BC	10 (5–15)	10 (5–15)	0.442
1000 Hz – AC	10 (5–20)	10 (5–15)	0.271	1000 Hz – AC	10 (5–15)	10 (5–15)	0.803
1000 Hz – BC	10 (5–15)	10 (5–11.25)	0.610	1000 Hz – BC	10 (5–15)	5 (5–10)	0.501
2000 Hz – AC	10 (5–20)	10 (8.75–15)	0.950	2000 Hz – AC	12.5 (5–20)	10 (5–15)	0.250
2000 Hz – BC	10 (5–16.25)	10 (5–15)	0.943	2000 Hz – BC	10 (5–20)	10 (5–15)	0.412
4000 Hz – AC	15 (10–30)	10 (5–20)	0.063	4000 Hz – AC	15 (10–35)	10 (5–20)	0.127
4000 Hz – BC	10 (5–26.25)	10 (5–15)	0.176	4000 Hz – BC	12.5 (8.75–26.25)	10 (5–15)	0.089
8000 Hz – AC	25 (13.75–35)	15 (10–22.5)	**0.042**	8000 Hz –AC	25 (15–40)	15 (10–26.25)	**0.023**

Thresholds are given in Db HL. AC: Air conduction; BC: Bone conduction.

Otoacoustic Emissions: Measurements were conducted by the same audiologist in a quiet room using the Madsen Capella device (Natus Medical, Taastrup, Denmark). The DPOAE values were evaluated using the Madsen Capella otoacoustic emission instrument by Natus Medical (Taastrup, Denmark), with OTOsuite as the operating software. The excitation range was a click with a duration of 80 µs and an excitation density of 80 dB Sound Pressure Level (SPL). The frequency of the signal was 25.6 kHz, and the duration was 20 ms. DPOAEs were measured using two primary short pure tones to assess the 2f1–f2: L1=65, L2=55 dB SPL, with an f2/f1=1.22. A band-pass filter from 0.6 to 6 kHz was applied, with the procedure repeated 260 times. The signal strength was recorded at $2\times f1-f2\geq -10$ dB SPL.

Statistical Analysis

Data analysis was conducted using the Statistical Package for the Social Sciences (SPSS) software (version 24.0; IBM, New York, USA). The Shapiro-Wilk test was used to assess the normality of data distribution. Normally distributed data were reported as mean±standard deviation (SD), while non-normally distributed data were presented as medians with the 25th to 75th percentiles. The Mann-Whitney U test was also utilized. Correlation analyses were conducted to examine the impact of disease duration on hearing function. A p-value of less than 0.05 was considered indicative of statistical significance.

RESULTS

The study included 31 subjects in each group (27 women and 4 men). The mean ages were 45.3±2 for the Takayasu group and 44.8±1.8 for the control group, respectively. Both groups were similar in terms of age and gender (p>0.05).

Four patients in the Takayasu group were recently diagnosed. The mean follow-up duration for patients with Takayasu arteritis was 5.1 years, with a maximum of 19 years.

Two patients had a history of ISSHL. No other patients or healthy subjects reported previous episodes of ISSHL. The middle ear pressures for all subjects were within the range of ±50 daPa, and all had Type A tympanograms.

There were no differences between the Takayasu and control groups in median air and bone-conduction thresholds, except at one frequency. A statistically significant difference was observed between the two groups at the right and left 8000 Hz air-conduction thresholds (p<0.05), with the Takayasu group exhibiting higher mean thresholds at these frequencies. The mean air and bone-conduction thresholds for both groups are presented in Table 1 and Figure 1. No difference was found between the Takayasu and healthy groups in terms of median air and bone pure tone averages (p>0.05).

Median DPOAE values were similar between the two groups, except at two frequencies. The median otoacoustic emission value was higher in the Takayasu group at the right and left 1500 Hz frequencies (p<0.05). Median DPOAE values are detailed in Table 2 and Figure 2.

Within the Takayasu group, patients were categorized based on their involvement pattern. No differences were observed in median air and bone-conduction thresholds, median

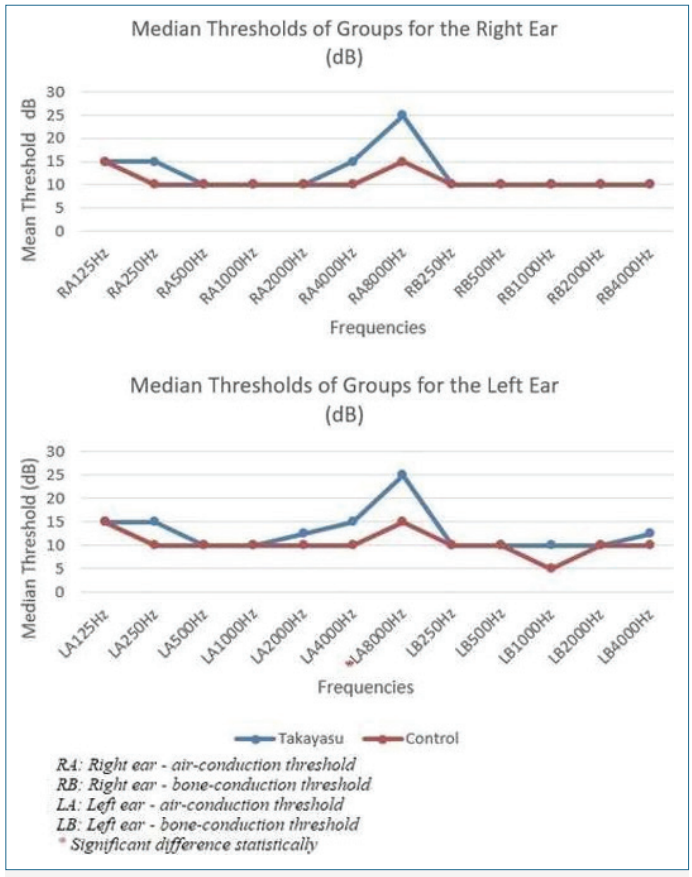

Figure 1. Comparison of median thresholds of groups by pure tone frequencies.

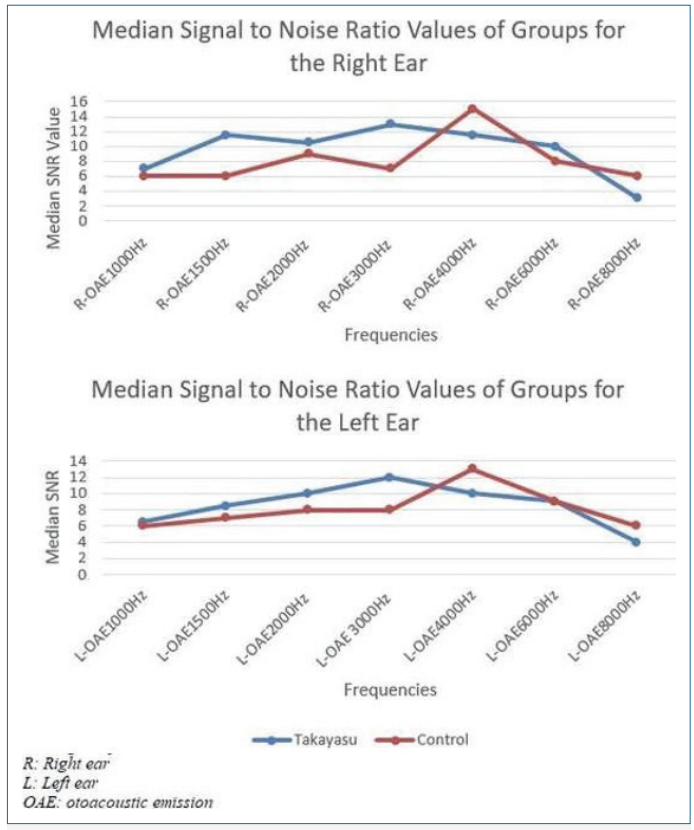

Figure 2. Comparison of median otoacoustic emission values among groups according to testing frequencies.

pure tone averages, and median DPOAE values when compared by carotid artery involvement or experience of cerebrovascular events.

Based on the ITAS 2010, Takayasu patients were classified as having active or inactive disease. There were no differences between these subgroups in terms of median air and bone-conduction thresholds, median pure tone averages, and median DPOAE values ($p>0.05$). The distribution of patients within the Takayasu subgroups is provided in Table 3.

Correlation analyses were performed between disease follow-up duration, pure tone thresholds, and otoacoustic emissions values. The maximum Pearson correlation coefficients were 0.29 and 0.36, respectively, indicating a weak correlation between disease duration and hearing functions.

Based on the median follow-up time (4.5 years), the Takayasu groups were divided into short and long follow-up categories. No difference in hearing functions was observed between these subgroups ($p>0.05$).

DISCUSSION

Takayasu arteritis may present with neurological and hearing symptoms. Our study aimed to evaluate the hearing functions of patients in comparison with healthy controls. No differences were observed across all frequencies except for two (right and left air-conduction at 8000 Hz) in PTA. Similarly, no differences were found in all DPOAE values except for two frequencies (right and left 1500 Hz). When Takayasu patients were categorized into different subgroups based on carotid involvement (positive and negative), cerebrovascular events (positive and negative), and disease activity (active and under control), no significant differences were noted between these subgroups. The study revealed that hearing functions in patients with Takayasu arteritis may be specifically affected at 8000 Hz in PTA and 1500 Hz in DPOAE, with disease activity having no discernible effect on hearing functions within the study group. Takayasu arteritis may cause ISSHL rather than a global distortion in PTA and DPOAE values.

Takayasu arteritis is a systemic vasculitis most commonly involving the aorta and its major branches. Aortic diseases

Table 2. Median otoacoustic emission values (25th–75th percentiles) among groups by sides and frequencies

Right Ear	Takayasu	Control	p	Left Ear	Takayasu	Control	p
1000 Hz	7 (4–11.25)	6 (4.25–8)	0.14	1000 Hz	6.5 (3–10)	6 (-1.25–7)	0.113
1500 Hz	11.5 (8–15.25)	6 (4–12)	**0.031**	1500 Hz	8.5 (7–17.5)	7 (6–9.25)	**0.042**
2000 Hz	10.5 (8–17)	8.5 (6.75–12)	0.054	2000 Hz	10 (7–17.25)	8 (6–12.25)	0.152
3000 Hz	13 (7.75–15.25)	7 (6–17.25)	0.114	3000 Hz	12 (8–15.5)	7.5 (6–15.25)	0.190
4000 Hz	11.5 (6.75–16.75)	14 (7–17)	0.538	4000 Hz	10 (3.25–16)	12 (6–18.25)	0.354
6000 Hz	10 (3.5–15)	8 (6.75–12.25)	0.743	6000 Hz	9 (4.75–13.25)	9 (6–17)	0.562
8000 Hz	3 (-0.25–8)	6 (0–7.5)	0.910	8000 Hz	4 (,2.12–7.25)	6 (-1.25–8)	0.344

Emissions are given in dB SPL.

Table 3. Number of patients in Takayasu subgroups

	Positive (n)	Negative (n)
Carotid involvement	14	17
Disease activity	15	16
Cerebrovascular event	7	24

can lead to a range of neurological problems, either directly, indirectly, or secondary to surgical interventions. Although these neurological complications are rare in aortic diseases, potential neurological manifestations, such as stroke and hearing loss, should be considered by clinicians.[15] Mahajan et al.[16] reported a case of Takayasu arteritis initially presenting with amaurosis. Despite being rare, Takayasu arteritis can lead to neurological events.

There have been cases in the literature where Takayasu arteritis was reported to manifest with hearing loss. Siglock and Brookler identified an 18-year-old woman who experienced recurrent attacks of sensorineural hearing loss. They also emphasized that the hearing loss was associated with an increased erythrocyte sedimentation rate and responded well to corticosteroids.[9] Maruyoshi et al.[17] reported on a 49-year-old woman with Takayasu arteritis who experienced sudden sensorineural hearing loss in the left ear, which responded well to corticosteroids. Ralli et al.[18] described a 36-year-old woman with Takayasu arteritis and episodes of sudden sensorineural hearing loss who successfully treated the condition with hyperbaric oxygen therapy.

Autoimmune inner ear disease is characterized as a clinical condition with bilateral sensorineural hearing loss caused by an exaggerated immune system response. It typically benefits from corticosteroid treatment. There are no established diagnostic criteria or reliable laboratory tests for its diagnosis. Therefore, the diagnosis is based on clinical symptoms. A patient is considered to have autoimmune hearing loss when they exhibit progressive, fluctuant, and bilateral hearing loss that responds well to steroid treatment, and other causes have been excluded.[19] Sensorineural hearing loss may appear as an initial symptom or develop during the course of Takayasu arteritis. There were two patients who had experienced ISSHL in the past. Takayasu arteritis may lead to ISSHL, affecting high frequencies rather than causing hearing loss across all frequencies.

There were some limitations to the study. Although the auditory brainstem response (ABR) is the most reliable test for examining hearing, it was not utilized in this study. PTA and Otoacoustic Emissions (OAE) were employed, which are also widely recognized tests in the field. The patient group was relatively small; however, this was considered acceptable given the rarity of Takayasu arteritis. To the best of our knowledge, this was the first study to focus on the hearing functions of patients with Takayasu arteritis in a case group.

CONCLUSION

In this cross-sectional study, there were no differences in terms of Pure Tone Averages and Otoacoustic Emission results between patients with Takayasu arteritis and age-gender-matched healthy subjects.

Ethics Committee Approval: The Erciyes University Clinical Research Ethics Committee granted approval for this study (date: 22.04.2022, number: 2022/344).

Author Contributions: Concept – EOK, KK, ASŞ, NT, MK, ES, KA; Design – EOK, KK, ASŞ, NT, MK, ES, KA; Supervision – EOK, KK, ASŞ, NT, MK, ES, KA; Resource – EOK, KK, NT, MK; Materials – KK, ES, KA; Data Collection and/or Processing – EOK, NK, MK, ES, KA; Analysis and/or Interpretation – EOK, KK, ASŞ; Literature Search – EOK, KK, ASŞ; Writing – KK, ASŞ; Critical Reviews – KK, ASŞ.

Conflict of Interest: The authors have no conflict of interest to declare.

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