

Etiological classification of presbycusis in Turkish population according to audiogram configuration

Türk nüfusunda presbiakuzinin odioqram konfigürasyonuna göre etyolojik sınıflandırılması

Kamil Hakan Kaya, MD., Arzu Karaman Koç, MD., İbrahim Sayın, MD., Selçuk Güneş, MD.,
Sinan Canpolat, MD., Baver Şimşek, MD., Fatma Tülin Kayhan, MD.

Department of Otolaryngology, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey

ABSTRACT

Objectives: This study aims to classify age related hearing loss in Turkish population according to Schuknecht audiometric configurations for presbycusis and investigate the most common etiologies.

Patients and Methods: A total of 1,134 patients (568 males, 566 females; mean age 70.5±7.7 years; range 55 to 80 years) with age related hearing loss were included in the study. Audiograms of patients were classified into three categories: high frequency steeply sloping (HFSS), flat, and high frequency gently sloping (HFGS). Speech discrimination scores were evaluated and compared.

Results: In the study population, HFSS audiogram configuration was the most frequently observed (48.5%), followed by HFGS configuration (26.9%), and flat configuration (24.5%), respectively. While HFSS audiogram configuration was statistically significantly more common in males, flat audiogram configuration was statistically significantly more common in females ($p=0.0001$). HFSS group mean air conduction threshold were statistically significantly higher than flat and HFGS groups ($p=0.0001$). No statistically significant difference was detected in terms of speech discrimination scores between three groups ($p=0.796$).

Conclusion: Results of this study suggest that, in Turkish population, while sensory presbycusis is more common in males, strial presbycusis is more common in females. No difference was detected in terms of the prevalence of cochlear presbycusis in males and females ($p=0.0001$).

Keywords: Age-related hearing loss; audiometric configuration; presbycusis.

ÖZ

Amaç: Bu çalışmada Türk nüfusunda yaşa bağlı işitme kaybı presbiakuzi için Schuknecht odioemetrik konfigürasyonlarına göre sınıflandırıldı ve en sık görülen etyolojiler araştırıldı.

Hastalar ve Yöntemler: Çalışmaya yaşa bağlı işitme kaybı olan 1134 hasta (568 erkek, 566 kadın; ort. yaş 70.5±7.7 yıl; dağılım 55-80 yıl) dahil edildi. Hastaların odyogramları üç kategoriye ayrıldı: yüksek frekanslı ani eğimli (YFAE), düz ve yüksek frekanslı hafif eğimli (YFHE). Konuşmayı ayırt etme puanları değerlendirildi ve karşılaştırıldı.

Bulgular: Çalışma nüfusunda YFAE odyogram konfigürasyonu en sık görüldü (%48.5), bunu sırasıyla YFHE (%26.9) ve düz konfigürasyon (%24.5) izledi. Yüksek frekanslı hafif eğimli odyogram konfigürasyonu erkeklerde istatistiksel olarak anlamlı derecede daha yaygınken düz odyogram konfigürasyonu kadınlarda istatistiksel olarak anlamlı derecede daha yaygındı ($p=0.0001$). YFAE grubu ortalama hava yolu eşikleri düz ve YFHE gruplarından istatistiksel olarak anlamlı derecede yüksek idi ($p=0.0001$). Konuşmayı ayırt etme skorları açısından üç grup arasında istatistiksel olarak anlamlı farklılık bulunmadı ($p=0.796$).

Sonuç: Bu çalışmanın bulgularına göre, Türk nüfusunda sensori presbiakuzi erkeklerde daha yaygın iken strial presbiakuzi kadınlarda daha yaygındır. Erkeklerde ve kadınlarda koklear presbiakuzi görüme sıklığı açısından farklılık bulunmadı ($p=0.0001$).

Anahtar Sözcükler: Yaşa bağlı işitme kaybı; odyometrik konfigürasyon; presbiakuzi.



Age-related disorders are important social and economic problems because of low birth rates and longer life expectancy in the second half of the 20th century. The most frequent sensory disability in the elderly is age-related hearing loss (ARHL).^[1] The World Health Organization (WHO) estimates that in 2025, the number of people over 60 years of age will be 1.2 billion and 500 million of them will suffer from presbycusis.^[2] The cognitive and psychosocial consequences of hearing loss are well described in the literature.^[3] The most relevant etiological factors in ARHL are heredity and other preventable factors such as noise exposure, chronic middle ear disease, cardiovascular risk factors, diabetes, smoking, hypertension, hormones, exposure to ototoxic medication or chemicals.^[4]

Histological temporal bone examinations revealed that pathophysiological changes occur in ARHL. Functional loss of sensory and neuronal elements are the primary findings of ARHL.^[5,6] The collected cross-sectional or longitudinal data from previous studies mapping the prevalence of hearing loss in the elderly provide material to create age-related typical audiograms.^[7,8] It has been demonstrated that ageing accelerates hearing loss significantly more at high frequencies than at low frequencies.^[9] Fieuw and Verbeke^[9] additionally suggested that the closer frequencies showed the same threshold progression patterns in audiograms (threshold changes at 8000 Hertz (Hz) correspond to threshold changes at 4000 Hz than to threshold changes at 1000 Hz). In 1964 Schuknecht^[10] demonstrated that there was a correlation between etiology dependent histopathological changes and threshold progression patterns in presbycusis. He classified presbycusis into six categories as follows:

- Sensory (outer hair-cell loss)
- Metabolic (strial atrophy)
- Neuronal (ganglion-cell loss)
- Cochlear conductive (stiffness of the basilar membrane)
- Mixed
- Indeterminate

Additionally in 1999, he concluded that each presbycusis type has a typical audiometric pattern; high frequency steeply sloping (HFSS) loss type for sensory presbycusis,

flat configuration for strial presbycusis, high frequency gently sloping (HFGS) loss type for cochlear presbycusis, loss of word discrimination score for neuronal presbycusis.^[11] Furthermore, each presbycusis type has its own etiological and histopathological features. Gates and Mills^[8] suggested that the exact age-related hearing loss is strial presbycusis. Sensory presbycusis is often found in populations exposed to noise and chemical pollutants.^[11] Heritability is the major cause of strial presbycusis.^[12] Age-related physical changes in basilar membrane cause cochlear presbycusis.^[13] Decreased number of neurons in the cochlea and auditory pathways cause neuronal presbycusis.^[14] Thus, age-related typical audiograms can be simplified to understand the pathophysiological inner ear changes and estimate the etiology in presbycusis.^[15]

In the present study, we aimed to classify the ARHL in the Turkish population according to the Schuknecht's audiometric configurations for presbycusis and to demonstrate their most common etiologies.^[10]

PATIENTS AND METHODS

This retrospective study was performed at Bakırköy Dr. Sadi Konuk Teaching and Research Hospital. The study protocol was approved by the hospital's local ethics board. A card analysis was performed for six months between July 2013 and December 2013 and 1,134 unrelated subjects from residential suburbs of İstanbul (Turkey) between 55 and 80 years old whose bone conductive hearing levels (HLs) were above 20 decibels (dB) in the right or left ear for the average thresholds of 0.5, 1, 2, 4, and 8 kHz were considered for inclusion in this study. The subject's average air and bone conduction HLs and speech discrimination scores (SDS) were evaluated. The Interacoustics Clinic Audiometer AC-33 (Interacoustics, Assen, Denmark) and standard audiometric procedures were used for audiological examination.^[16] The Turkish version of monosyllabic phonetically balanced word lists were used for evaluating the subjects' speech discrimination scores.^[17] Subjects who had chronic otitis media, otitis media with effusion, congenital hearing loss, autoimmune ear disease, Meniere syndrome, previous idiopathic sudden sensorineuronal hearing loss, otologic surgery, cranial trauma, cranial surgery, viral or bacterial labyrinthitis, syphilis, ototoxic drug use, previous acoustic

Table 1. The description of audiogram types according to hearing levels at 0.5, 1, 2, 4, and 8 kHz

Flat (strial presbycusis)	The difference between the mean of 250/500 Hz thresholds, the mean of 1/2 kHz thresholds and the mean of 4/8 kHz thresholds is less than 15 dB
High frequency steeply sloping (sensory presbycusis)	The difference between the mean of 500 Hz/1 kHz thresholds and the mean of 4 kHz/8 kHz thresholds is greater than 30 dB
High frequency gently sloping (cochlear presbycusis)	The difference between the mean of 500 Hz/1 kHz thresholds and the mean of 4 kHz/8 kHz thresholds is greater than 15 dB and less than 29 dB

trauma or occupational noise history or have dementia were excluded from the study. Subjects whose air-bone conduction HL gap was above 15 dB HL and who had asymmetrical hearing loss with differences in (left and right ear) air conduction thresholds greater than 20 dB HL in the average thresholds of 0.5, 1, 2, 4, and 8 kHz were excluded from the study. All audiograms were categorized into three categories: HFSS, flat, HFGS. Characterization of the shapes of the audiograms is shown in Table 1.

Statistical analysis

For statistical analysis, the Number Cruncher Statistical System (NCSS) 2007 Statistical Software (NCCS, Kaysville, UT, USA) was used. Along with the descriptive statistical methods (mean, SD), one-way analysis of variance was used for comparison between groups and Tukey's multiple comparison test was used for subgroup

comparison. Binary groups were compared using the unpaired t test. Paired t test was used for comparison between right and left ears. A *p* value of <0.05 was deemed to indicate statistical significance.

RESULTS

A total of 1,134 unrelated subjects (568 males, 566 females) met the criteria and were included in the study. The mean age was 70.6±7.1 years (range 55 to 80 years) in the HFSS population, 69.9±8 years (range 55 to 80 years) in the flat population and 71.3±8.4 years (range 55 to 80 years) in the HFGS population. There were no statistically significant differences in age between the three groups (*p*=0.107).

When all three groups were evaluated according to audiogram types the HFSS configuration was most frequently represented

Table 2. Average speech discrimination scores, air and bone conduction hearing levels according to right and left ear

Audiogram configuration	Right ear	Left ear	<i>p</i>
	Mean±SD	Mean±SD	
Flat			
Speech discrimination	79.3±12.8	80.0±12.6	0.148
Air conduction (dB)	45.8±15.1	44.8±14.8	0.101
Bone conduction (dB)	40.5±14.1	39.8±13.9	0.092
HFSS			
Speech discrimination	79.9±11.6	80.1±11.2	0.114
Air conduction (dB)	41.2±12.4	40.5±12.2	0.097
Bone conduction (dB)	36.3±11.7	36.3±11.6	0.257
HFGS			
Speech discrimination	79.1±10.3	79.8±10.6	0.324
Air conduction (dB)	44.9±12.3	44.4±12.0	0.419
Bone conduction (dB)	40.0±11.0	39.9±11.0	0.194

SD: Standard deviation; HFSS: High frequency steeply sloping; HFGS: High frequency gently sloping.

Table 3. Average speech discrimination scores, air and bone conduction hearing levels according to gender

Audiogram configuration	Male	Female	<i>p</i>
	Mean±SD	Mean±SD	
Flat			
Speech discrimination	79.3±12.7	79.7±12.7	0.788
Air conduction (dB)	46.0±15.0	44.4±15.0	0.436
Bone conduction (dB)	41.1±14	39.1±14	0.292
HFSS			
Speech discrimination	79.3±11.5	80.8±11.1	0.157
Air conduction (dB)	41.1±12.3	38.9±12.3	0.057
Bone conduction (dB)	36.5±11.5	34.6±11.7	0.067
HFGS			
Speech discrimination	78.7±11.8	79.8±9.3	0.375
Air conduction (dB)	45.2±12.6	43.3±11.8	0.168
Bone conduction (dB)	40.5±11.6	38.9±10.4	0.216

SD: Standard deviation; HFSS: High frequency steeply sloping; HFGS: High frequency gently sloping.

(48.5%), followed by the HFGS configuration (26.9%) and the flat configuration (24.5%). When the right and left ear average SDS, air and bone conduction HLs were compared in the three groups separately, there were no statistically significant differences found ($p>0.05$ for all comparisons) (Table 2). When the average SDS, air and bone conduction HLs were compared according to gender in the three groups separately, there were no statistically significant differences found ($p>0.05$ for all comparisons) (Table 3). When the average SDS were compared according to three groups, there were no statistically significant differences found ($p=0.796$) (Figure 1). When the average air conduction

HLs were compared according to three groups, the HFSS group average air conduction HL was found to be statistically significantly lower than the flat and HFGS groups ($p=0.0001$) and there were no statistically significant difference between the flat and HFGS groups ($p=0.833$) (Figure 2). When the average bone conduction HLs were compared according to three groups, the HFSS group average HL was found to be statistically significantly lower than the flat and HFGS groups ($p=0.0001$) and there were no statistically significant differences between the flat and HFGS groups ($p=0.999$) (Figure 2). When the three groups were compared according to gender, the HFSS-configuration was found to be

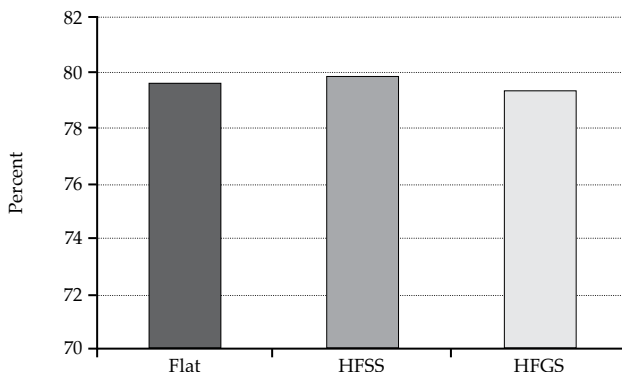


Figure 1. Average speech discrimination scores according to audiogram types ($p=0.796$). HFSS: High frequency steeply sloping; HFGS: High frequency gently sloping.

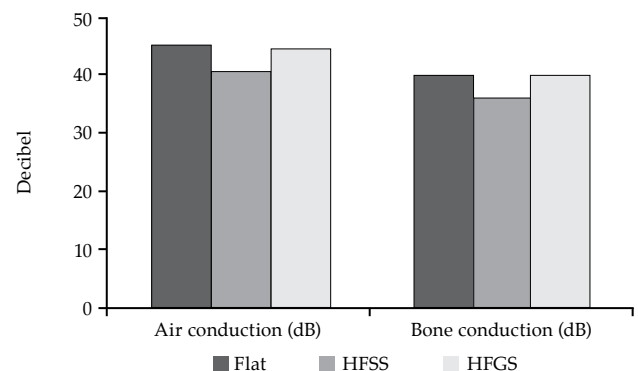


Figure 2. Average air and bone conduction hearing levels according the audiogram types ($p=0.0001$). HFSS: High frequency steeply sloping; HFGS: High frequency gently sloping.

Table 4. The frequency of the audiogram types according to gender

	Flat	HFSS	HFGS	p
	%	%	%	
Gender				
Male	25.90	64.40	45.80	} 0.0001
Female	74.10	35.60	54.20	

HFSS: High frequency steeply sloping; HFGS: High frequency gently sloping.

statistically significantly higher among males (n=354, 64.4%) than the flat (n=72, 25.9%) and HFGS configurations (n=140, 45.8%) (p=0.0001). Among females, the flat configuration was found to be statistically significantly higher (n=206, 74.10%) than the HFSS (n=196, 35.6%) and HFGS configurations (n=166, 54.2%) (p=0.0001) (Table 4).

DISCUSSION

In the present study we analyzed a sample of 1,134 otologically screened subjects between 55-80 years old to determine the etiology of ARHL in the Turkish population depending the prevalence of the three different audiogram configurations. We found that the HFSS configuration was the most common configuration (48.5%) in the study population. Flat-configurations were significantly more common in females whereas HFSS configurations were more common in males. In addition, females with a flat audiogram tended to have a larger amount of overall hearing loss compared to males.

The hearing level is not only associated with age because the rate of changes by age is highly variable.^[18] Davies and Fleishman^[19] reported that the proportion of hearing impairment was 14% between ages 60 and 64 years, 34% between ages 70 and 74 years, and 50% at ages 80 years and over in the elderly population. The higher frequencies are initially affected in presbycusis.^[20] Both peripheral and central auditory pathways can be affected in presbycusis. Most of the studies that evaluated the central pathology in presbycusis revealed the predominant abnormality as hair cell loss.^[21,22] Arlinger^[23] suggested that hearing loss in presbycusis can depend on cochlear, retrocochlear and central lesions together and can be a part of decreased cognitive functioning. In contrast, there was no reduction of the neuron population in the ventral cochlear nucleus found

in the elderly population when compared with younger persons.^[24] Heritability is one of the most putative causes of ARHL.^[25] The changes in expression of 4,000 cochlear genes is responsible for ARHL.^[26] Sensory presbycusis is the most common type and strial presbycusis is less common.^[27]

It can be suggested that ARHL does not have a single cause and is a multifactorial disease affected by various intrinsic and extrinsic factors. In previous studies, it was demonstrated that smoking, elevated blood pressure and cholesterol levels may increase the degree of ARHL.^[28,29] Elevated oxidant levels in the cochlea can lead to hearing loss in aging. An animal study found that mice with antioxidant enzyme deficiency showed the same characteristic phenotype as ARHL.^[30] Caloric diet restriction and antioxidants may reduce age-related hearing loss.^[31]

Langenbeck's law indicates that genetic hearing loss must be symmetric because heritability should affect both ears.^[32] Additionally, Schuknecht defined presbycusis as a bilateral, symmetrical, and slowly progressive hearing loss.^[33] In our study, all subjects in the three groups had symmetrical threshold progression patterns in audiograms in both right and left ears since we had excluded the effects of asymmetrical expression of heritability, test-retest reliability, or other factors were not clear.

In our study the flat audiogram configuration (strial presbycusis) was most frequently represented (74.1%) in female subjects. Heritability is one of the major causes of strial presbycusis and we demonstrated that the genetic component was found more in female than male subjects in the Turkish population. Gate's study supported our findings that familial aggregations for age-related HLs were stronger in women than in men.^[12] Additionally, the highest heritability was found for low frequencies. The loss of 30% or more strial tissue caused presbycusis. However, acoustic trauma, ototoxic drugs, and venous obstruction caused the same degeneration.^[34,35] Additionally Johnsson and Hawkins^[34] found association between capillary loss in the spiral ligament and atrophy of the stria vascularis in strial presbycusis. In contrast, Schuknecht et al.^[36] suggested that heritability was the most important cause of stria vascularis degeneration. Additionally they stated that atrophy of the stria

vascularis was frequently initiated in younger ages and there was no histological evidence of vascular disease found in the stria vascularis. Nelson et al.^[37] compared the presbycusis population with normal hearing subjects. They found significant differences between outer and inner hair cell populations between groups. However they did not find any significant differences between the stria vascularis volume and the ganglion cell population. They suggested that these results could not exclude atrophy of the stria vascularis because the stria vascularis is a metabolically active organ and histopathological studies cannot give exact information about the metabolic process. The importance of stria vascularis atrophy in presbycusis is still controversial.^[38,39] However, the hormonal differences between males and females have superimposed effects on stria vascularis. In an animal study, König et al.^[40] demonstrated that estrogen-deficiency accelerates hearing loss in mice. Additionally, Hederstierna et al.^[41] found that hormone replacement therapy has protective effects on hearing in postmenopausal women.

However, the rate of heritability is greater in stria vascularis. It was estimated that heritability is responsible for 35-55% of subjects in sensory presbycusis (SSHF configuration).^[42] Sensory presbycusis is primarily caused by damaged outer hair cells in 10 mm at the basal turn of the cochlea.^[43] In histopathological studies, the most frequent finding in aging ears was outer hair cell loss.^[14] In an animal study, it was observed that the mice with a genetic mutation and hair cell loss that began a few months after birth showed profound sensory hearing loss with age.^[44] The aging alone does not cause outer hair-cell loss in sensory presbycusis but accumulated environmental noise toxicity has superimposed effects.^[8] Additionally, Fuente and McPherson^[45] demonstrated that solvents, asphyxiant gases (CO), and heavy metals may interact synergistically with noise. The prevalence of HFSS configurations significantly increases with increasing noise and environmental pollutants.^[46] In our study the HFSS audiogram configuration was most frequently represented in the male population is consistent with the fact that the male population is more exposed the noise and pollutants than females in Turkish population.

Neuronal loss in the spiral ganglion is the major cause of the decreased word discrimination scores.^[11] Spiral ganglion neurons (SGN) serve as a station between the hair cells and central nervous system. The damage to inner hair cells, loss of supporting elements and injury of dendritic fibers were putative findings in temporal bone histopathologic studies in neuronal presbycusis.^[47] Takeno suggested that after hair cells were damaged, spiral ganglion neurons began to die because the hair cells provide a trophic support to SGNs.^[48] The loss of cochlear neurons in the 15-22 mm region in the cochlea which is the locus for the speech frequencies correlated strongly with the decrease of word discrimination scores.^[49] The neuronal population numbers approximately 30,000 in younger ages and is decreased to less than 15,000 in patients who have neuronal presbycusis.^[50] Patients who have rapidly progressive neuronal presbycusis show diffuse degenerative changes of the central nervous system.^[51] In previous studies it was demonstrated that decreased word discrimination scores is a common finding in presbycusis and associated with sloping pure-tone thresholds.^[52] Decrement in word discrimination scores was attributed to ARHL in some studies but other studies indicated that it occurs in addition to ARHL.^[53,54] In our study we did not find statistically significant differences in SDS between the three groups.

In cochlear presbycusis (HFSS configuration), there were no light microscopic histopathologic abnormalities of the cochlea found to explain the hearing loss. It was suggested that abnormal motion mechanics of the basilar membrane was the primary cause.^[14] In his histopathological study, Nomura demonstrated lipid deposits in the basilar membrane in some presbycusis subjects.^[55] Nadol observed accumulation of amorphous material and an increased number of fibrils in the markedly thickened basilar membrane in one case with presbycusis.^[56] Bhatt et al.^[57] demonstrated age-related thickening of the basilar membrane in presbycusis but the same changes were not found in the same age population who had normal hearing. In our study it was demonstrated that cochlear presbycusis was seen at the same rate in males and females.

In his review of prevalence of age-related hearing loss in Europe, Roth et al.^[4] demonstrated

that 30% of men and 20% of women have a hearing loss of 30 dB HL or more by age 70 years and 55% of men and 45% of women by age 80 years. A study of the epidemiology of hearing impairment in the Australian population found that 16.6% of the population had a hearing impairment in the better ear at ≥ 25 dB HL and 22.2% in the worse ear at the same level.^[58] In his study Kelly demonstrated that the flat-configuration was most dominantly represented and flat configurations were significantly more common in females whereas HFSS configurations were more common in males in Europe.^[45]

Previous studies revealed that aging causes mixed pathological changes in the organ of corti, spiral ganglion neurons and stria vascularis.^[11,59] Currently, there is no effective medication to prevent or treat presbycusis. Preventing noise and environmental pollution and appropriate treatment of heart disease, hyperlipidemia, and diabetes in the population can help preserve hearing in the older population.

Conclusion

In the Turkish population, the HFSS audiogram configuration was most frequently represented, followed by the HFGS configuration, and the flat configuration. In the male population exposure to noise and environmental pollutants are the most important cause of ARHL besides heritability. In the female population the most prominent cause is heritability. The subjects with a flat or HFGS audiogram configuration tend to have more hearing loss compared to subjects with an HFSS audiogram configuration. Sensory presbycusis is most found in the male population, strial presbycusis most found in the female population and cochlear presbycusis was seen at the same rate in males and females.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Layer LV, Cump GV. Age-related hearing impairment: ensemble playing of environmental and genetic factors. In: Alessandro Martini, Dafydd Stephens, Andrew P, editors. *Genes, Hearing, and Deafness: From Molecular Biology to Clinical Practice*. London: Informa UK Ltd. 2007. p. 79-90.
2. Sprinzi GM, Riechelmann H. Current trends in treating hearing loss in elderly people: a review of the technology and treatment options - a mini-review. *Gerontology* 2010;56:351-8.
3. Monzani D, Galeazzi GM, Genovese E, Marrara A, Martini A. Psychological profile and social behaviour of working adults with mild or moderate hearing loss. *Acta Otorhinolaryngol Ital* 2008;28:61-6.
4. Roth TN, Hanebuth D, Probst R. Prevalence of age-related hearing loss in Europe: a review. *Eur Arch Otorhinolaryngol* 2011;268:1101-7.
5. Nelson EG, Hinojosa R. Presbycusis: a human temporal bone study of individuals with downward sloping audiometric patterns of hearing loss and review of the literature. *Laryngoscope* 2006;116:1-12.
6. Frisina RD, Walton JP. Age-related structural and functional changes in the cochlear nucleus. *Hear Res* 2006;216-217:216-23.
7. CORSO JF. Age and sex differences in pure-tone thresholds. Survey of hearing levels from 18 to 65 years. *Arch Otolaryngol* 1963;77:385-405.
8. Gates GA, Mills JH. Presbycusis. *Lancet* 2005;366:1111-20.
9. Fieuws S, Verbeke G. Pairwise fitting of mixed models for the joint modeling of multivariate longitudinal profiles. *Biometrics* 2006;62:424-31.
10. Schuknecht HF. Further observations on the pathology of presbycusis. *Arch Otolaryngol* 1964;80:369-82.
11. Schuknecht HF, Gacek MR. Cochlear pathology in presbycusis. *Ann Otol Rhinol Laryngol* 1993;102:1-16.
12. Gates GA, Couropmitree NN, Myers RH. Genetic associations in age-related hearing thresholds. *Arch Otolaryngol Head Neck Surg* 1999;125:654-9.
13. Salvi RJ, Ding D, Eddins AC, McFadden SL, Henderson D. Age, noise, and ototoxic agents. In: Hof PR, Mobbs CV, editors. *Functional Neurobiology of Aging*. Chapter 38. San Diego: Academic Press; 2001. p. 549-63.
14. Schuknecht H. *Pathology of the Ear*. Cambridge: Harvard University Press; 1974.
15. Demeester K, van Wieringen A, Hendrickx JJ, Topsakal V, Franssen E, van Laer L, et al. Audiometric shape and presbycusis. *Int J Audiol* 2009;48:222-32.
16. Harrell, RW. Puretone evaluation. In: Katz, J, editor. *Handbook of Clinical Audiology*. Philadelphia: Lippincott Williams & Wilkins; 2002. p. 71-87.
17. Kılınçarslan A. *Türk Dili için Geliştirilmiş Fonetik Dengeli Tek Heceli Kelime Listelerinin Standardizasyonu*. Ankara: Hacettepe University, Master of Science; 1986.
18. Gates GA, Cooper JC. Incidence of hearing decline in the elderly. *Acta Otolaryngol* 1991;111:240-8.
19. Davies AM, Fleishman R. Health status and use of health services as reported by the older residents of the Baka neighborhood, Jerusalem. *Isr J Med Sci* 1981;17:138-44.
20. Gates GA. Central auditory processing in presbycusis: an epidemiological perspective. In: Hickson L, editor. *Proceedings of the Second International Adult Conference: Hearing Care for adults 2009 - the challenge of aging*. Staefa, Switzerland: Phonak AG; 2009. p. 47-52.

21. Soucek S, Michaels L. Hearing Loss in the Elderly. London: Springer-Verlag; 1990.
22. Collet L, Moulin A, Gartner M, Morgon A. Age-related changes in evoked otoacoustic emissions. *Ann Otol Rhinol Laryngol* 1990;99:993-7.
23. Arlinger S. Audiometric profile in presbycusis. *Acta Otolaryngol Suppl* 1990;476:85-9.
24. Konigsmark BW, Murphy EA. Volume of the ventral cochlear nucleus in man: its relationship to neuronal population and age. *J Neuropathol Exp Neurol* 1972;31:304-16.
25. Christensen K, Frederiksen H, Hoffman HJ. Genetic and environmental influences on self-reported reduced hearing in the old and oldest old. *J Am Geriatr Soc* 2001;49:1512-7.
26. Yamasoba T. Molecular mechanism of age-related hearing loss: toward its prevention. *Nippon Jibiinkoka Gakkai Kaiho* 2009;112:414-21.
27. DeStefano AL, Gates GA, Heard-Costa N, Myers RH, Baldwin CT. Genomewide linkage analysis to presbycusis in the Framingham Heart Study. *Arch Otolaryngol Head Neck Surg* 2003;129:285-9.
28. Cruickshanks KJ, Klein R, Klein BE, Wiley TL, Nondahl DM, Tweed TS. Cigarette smoking and hearing loss: the epidemiology of hearing loss study. *JAMA* 1998;279:1715-9.
29. Brant LJ, Gordon-Salant S, Pearson JD, Klein LL, Morrell CH, Metter EJ, et al. Risk factors related to age-associated hearing loss in the speech frequencies. *J Am Acad Audiol* 1996;7:152-60.
30. McFadden SL, Ohlemiller KK, Ding D, Shero M, Salvi RJ. The Influence of Superoxide Dismutase and Glutathione Peroxidase Deficiencies on Noise-Induced Hearing Loss in Mice. *Noise Health* 2001;3:49-64.
31. Seidman MD. Effects of dietary restriction and antioxidants on presbycusis. *Laryngoscope* 2000;110:727-38.
32. Langenbeck B. Das symmetrigeretz der erblihen taubehelt. *Z Hals Nasen Ohren-heild* 1936;39:223-261
33. Schuknecht HF. Pathology of the Ear. 2nd ed. Philadelphia: Lea & Febiger; 1993. p. 416-36.
34. Johnsson LG, Hawkins JE Jr. Strial atrophy in clinical and experimental deafness. *Laryngoscope* 1972;82:1105-25.
35. Kimura R, Perlman HB. Extensive venous obstruction of the labyrinth. A. Cochlear changes. *Ann Otol Rhinol Laryngol* 1956;65:332-50.
36. Schuknecht HF, Watanuki K, Takahashi T, Belal AA Jr, Kimura RS, Jones DD, et al. Atrophy of the stria vascularis, a common cause for hearing loss. *Laryngoscope* 1974;84:1777-821.
37. Nelson EG, Hinojosa R. Presbycusis: a human temporal bone study of individuals with flat audiometric patterns of hearing loss using a new method to quantify stria vascularis volume. *Laryngoscope* 2003;113:1672-86.
38. Jorgensen MB. Changes of aging in the inner ear. Histological studies. *Arch Otolaryngol* 1961;74:164-70.
39. Pauler M, Schuknecht HF, White JA. Atrophy of the stria vascularis as a cause of sensorineural hearing loss. *Laryngoscope* 1988;98:754-9.
40. König O, Rüttiger L, Müller M, Zimmermann U, Erdmann B, Kalbacher H, et al. Estrogen and the inner ear: megalin knockout mice suffer progressive hearing loss. *FASEB J* 2008;22:410-7.
41. Hederstierna C, Hultcrantz M, Collins A, Rosenhall U. Hearing in women at menopause. Prevalence of hearing loss, audiometric configuration and relation to hormone replacement therapy. *Acta Otolaryngol* 2007;127:149-55.
42. McMahan CM, Kifley A, Rochtchina E, Newall P, Mitchell P. The contribution of family history to hearing loss in an older population. *Ear Hear* 2008;29:578-84.
43. Lee KY. Pathophysiology of age-related hearing loss (peripheral and central). *Korean J Audiol* 2013;17:45-9.
44. Hequembourg S, Liberman MC. Spiral ligament pathology: a major aspect of age-related cochlear degeneration in C57BL/6 mice. *J Assoc Res Otolaryngol* 2001;2:118-29.
45. Fuente A, McPherson B. Organic solvents and hearing loss: The challenge for audiology. *Int J Audiol* 2006;45:367-81.
46. Demeester K, van Wieringen A, Hendrickx JJ, Topsakal V, Franssen E, van Laer L, et al. Audiometric shape and presbycusis. *Int J Audiol* 2009;48:222-32.
47. Spoendlin H. Factors inducing retrograde degeneration of the cochlear nerve. *Ann Otol Rhinol Laryngol Suppl* 1984;112:76-82.
48. Takeno S, Wake M, Mount RJ, Harrison RV. Degeneration of spiral ganglion cells in the chinchilla after inner hair cell loss induced by carboplatin. *Audiol Neurootol* 1998;3:281-90.
49. Pauler M, Schuknecht HF, Thornton AR. Correlative studies of cochlear neuronal loss with speech discrimination and pure-tone thresholds. *Arch Otorhinolaryngol* 1986;243:200-6.
50. Otte J, Schuknecht HF, Kerr AG. Ganglion cell populations in normal and pathological human cochleae. Implications for cochlear implantation. *Laryngoscope* 1978;88:1231-46.
51. Nodal JB. Disorders of aging. In: Merchant SN, Nodal JB, editors. Schuknecht's pathology of the ear. 3rd ed. Shelton, CT: People's Medical Publishing House-USA; 2010. p. 432-74.
52. Crowe SJ, Guild SR, Polvogt LM. Observations on the pathology of high-tone deafness. *Bull Johns Hopkins Hosp* 1934;54:315-79.
53. Divenyi PL, Stark PB, Haupt KM. Decline of speech understanding and auditory thresholds in the elderly. *J Acoust Soc Am* 2005;118:1089-100.
54. Jerger J, Chmiel R. Factor analytic structure of auditory impairment in elderly persons. *J Am Acad Audiol* 1997;8:269-76.
55. Nomura Y. Lipidosis of the basilar membrane. *Acta Otolaryngol* 1970;69:352-7.
56. Nadol JB Jr. Electron microscopic findings in presbycusis degeneration of the basal turn of the human cochlea. *Otolaryngol Head Neck Surg* 1979;87:818-36.
57. Bhatt KA, Liberman MC, Nadol JB Jr. Morphometric analysis of age-related changes in the human basilar membrane. *Ann Otol Rhinol Laryngol* 2001;110:1147-53.
58. Wilson DH, Walsh PG, Sanchez L, Davis AC, Taylor AW, Tucker G, et al. The epidemiology of hearing impairment in an Australian adult population. *Int J Epidemiol* 1999;28:247-52.
59. Sha SH, Kanicki A, Dootz G, Talaska AE, Halsey K, Dolan D, et al. Age-related auditory pathology in the CBA/J mouse. *Hear Res* 2008;243:87-94.