Original Article

Relationships Among Factors Relevant to Abdominal Fat and Age-Related Hearing Loss

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Objectives. Metabolic syndrome is related with abdominal fat and with age-related hearing loss (ARHL). In this study, we evaluated the association between a variety of factors relevant to abdominal fat (FRAs) and hearing thresholds.

Methods. We reviewed retrospectively the medical records of 2,602 subjects aged over 40 years with symmetrical sensorineural hearing loss who underwent abdominal fat computed tomography (CT) scans. Univariate and multivariate linear regression analyses were used to demonstrate the association between each FRA and hearing thresholds at low and high frequencies.

Results. Four of 5 FRAs were associated with hearing thresholds at high frequencies in males. All FRAs examined showed a relationship with hearing thresholds at low frequencies in females. Diabetes mellitus (DM) among clinical factors and visceral adipose tissue (VAT) among the 5 FRAs were the most reflective of hearing thresholds in both males and females.

Conclusion. We found that FRAs were associated with hearing loss with frequency specific characteristics according to sex and reinforced that DM and VAT is particularly an important role for hearing.

Keywords. Hearing Loss; Abdominal Fat; Visceral Fat; Body Mass Index

INTRODUCTION

Age-related hearing loss (ARHL), also known as presbycusis, is the result of the cumulative effects of aging on hearing. It is characterized by progressive, bilateral, symmetrical sensorineural hearing loss, and results from degeneration of the inner ear (the cochlea) or the auditory nerves. It is the second most common disease, following arthritis, affecting 1 in 3 people ≥65 years, and 1 in 2 people ≥75 years [1]. Moreover, the proportion of the population ≥65 years will continue to increase gradually, and will represent one-quarter of the total population by 2030 [2]. Thus, ARHL is expected to become a major public health issue in future decades.

Obesity is a primary preventable cause of morbidity and mortality and is on the rise worldwide. Body mass index (BMI) has been widely used to define and classify obesity according to World Health Organization criteria [3]. However, abdominal obesity has been regarded as a more important risk factor than BMI [4]. Abdominal obesity consists of visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT), the characteristics of which differ in several respects.

Weight, BMI, waist circumference (WC), total adipose tissue (TAT), VAT, and SAT corresponds to factors relevant to abdominal fat (FRAs). Most previous studies that have reported a relationship between obesity and hearing have assessed only 1 of above 6 FRAs, such as BMI [5,6], WC [7], or VAT [8]. To our knowledge, there is only one report showing a relationship between several FRAs and hearing [8]. However, in that study, the sample consisted of 662 adults, which was not sufficient to draw concrete conclusions.

In this study, we sought to evaluate the relationship between several FRAs and hearing thresholds in a larger sample of adults, aged over 40 years. Moreover, we evaluated which factor among the FRAs was most associated with hearing threshold.

MATERIALS AND METHODS

Subjects

Between May 2004 and December 2015, 2,602 subjects ≥40 years (range, 40 to 89 years) of age who attended the Seoul National University Hospital Healthcare System at the Gangnam Center underwent fat measurements by computed tomography (CT), pure tone audiometry for 4 frequencies (0.5, 1, 2, and 4 kHz), and examination of the tympanic membrane by otologists. All subjects answered a medical questionnaire and underwent a medical examination. Subjects (n=31) who underwent external or middle ear surgery and/or showed abnormal tympanic membrane findings were excluded; in total, 2,571 subjects (range, 40 to 89 years) were included in the analysis.

This retrospective study was conducted after approval by the Institutional Review Board of the Clinical Research Institute of Seoul National University Hospital (No. 1512-094-728).

Anthropometric measurements

Each subject's height, weight, and WC were measured after overnight fasting. BMI was calculated by dividing body weight in kilograms by squared height in meters (kg/m^2). WC was measured at the level of the mid-point between the inferior border of the ribs and the upper margin of the iliac crest [4].

Measuring the area of abdominal adipose tissue by computed tomography

We used a standard technique to measure abdominal adipose tissue, as described previously [9,10]. Briefly, subjects were scanned in a supine position using a 16-detector CT scanner (Somatom Sensation 16, Siemens AG, Erlangen, Germany). A slice image at the level of the umbilicus, 5 mm in thickness was used to calculate the abdominal adipose tissue. Using Rapidia 2.8 CT software (Infinitt, Seoul, Korea), the surface area that came within –250 to –50 Hounsfield units was deemed to be abdominal adipose tissue. The TAT and VAT were demarcated by manual tracing with a cursor and the difference between TAT and VAT was deemed to be SAT. This was performed by 2 researchers affiliated to Seoul National University Hospital Healthcare System at the Gangnam Center and the mean of 2 values was used for analysis.

Measuring hearing thresholds

Hearing thresholds were measured at 4 frequencies (0.5, 1, 2, and 4 kHz) in both ears for each subject in a double-walled sound booth using audiometry (Madsen Itera II, GN Otometrics, Taastrup, Denmark). The average of the thresholds at 0.5 and 1 kHz was regarded as pure tone audiometry (PTA)-low, and the average at 2 and 4 kHz was regarded as PTA-high.

Classification of the variables

Weight, BMI, WC, TAT, VAT, and SAT were categorized as FRAs. The other factors–age, sex, height, hypertension (HTN), diabetes mellitus (DM), smoking, and alcohol consumption–were categorized as clinical factors.

Statistical analyses

Continuous variables are presented as means±standard deviations (SDs). Categorical variables are presented as frequencies and percentages. Student *t*-test for continuous variables and chi-square tests for categorical variables were used to compare differences between sexes. We conducted univariate linear regression to identify clinical factors associated with PTA thresholds. The significant clinical factors in univariate analyses and one of the FRAs were then considered as independent variables in a multiple linear regression. A step-wise multiple linear regression analysis was performed to determine the relationships between risk factors and PTA thresholds. The statistical significance level was set at 0.05. 'R' software ver. 3.2.2 (R Foundation for Statistical Computing, Vienna, Austria; http://www.R-project.org) was used for statistical analyses.

RESULTS

Demographic and anthropometric characteristics

Subject characteristics are summarized in Table 1. In total, 2,571 subjects (n=1,435 males and n=1,136 females) were included in the final analysis. The mean age was 57.6±7.3 years (males, 57.5±7.6 years; females, 57.8±7.0 years) with no significant difference. The mean height, weight, BMI, and WC were 165.0± 8.3 cm, 65.1±11.9 kg, 23.8±3.2 kg/m^2, and 85.2±9.0 cm, respectively, with significant differences between males and females (height, 170.5±5.8 cm vs. 158.0±5.2 cm; weight, 71.6± 10.0 kg vs. 57.0±8.7 kg; BMI, 24.6±2.9 kg/m^2 vs. 22.8±3.2 kg/m^2; and WC, 88.5±7.9 cm vs. 81.2±8.6 cm; all *P*<0.001). For all subjects, the mean PTA-low and PTA-high hearing levels were 16.7±8.3 dB HL and 23.4±13.2 dB HL, respectively. The PTA-low hearing level did not differ between the sexes. Howev-

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HIGHLIGHTS

- Factors relevant abdominal fat (FRAs) were correlated with hearing at high frequencies in men.
- In women, FRAs were correlated with hearing at low frequencies.
- Visceral adipose tissue has major implications for hearing.

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Table 1. Comparisons between male and female subjects regarding to demographic, auditory, and factors relevant abdominal fat

Variable	All (n=2,571)	Male (n=1,435)	Female (n=1,136)	P-value
Age (yr)	57.6±7.3	57.5±7.6	57.8±7.0	0.234
Height (cm)	165.0±8.3	170.5±5.8	158.0±5.2	<0.001
Weight (kg)	65.1±11.9	71.6±10.0	57.0±8.7	<0.001
BMI (kg/m²)	23.8±3.2	24.6±2.9	22.8±3.2	<0.001
WC (cm)	85.2±9.0	88.5±7.9	81.2±8.6	<0.001
PTA-low (dB HL)	16.7±8.3	16.8±8.4	16.6±8.2	0.435
PTA-high (dB HL)	23.4±13.2	26.3±14.1	19.7±11.0	<0.001
TAT (cm²)	292.0±161.1	290.0±125.4	294.5±197.2	0.504
VAT (cm²)	122.7±70.4	144.4±65.2	95.3±67.2	<0.001
SAT (cm²)	169.3±116.8	145.6±71.8	199.3±150.9	<0.001
HTN				<0.001
No	1,065 (77.9)	614 (74.2)	451 (83.5)	
Yes	303 (22.1)	214 (25.8)	89 (16.5)	
DM				0.007
No	1,256 (91.9)	746 (90.2)	510 (94.4)	
Yes	111 (8.1)	81 (9.8)	30 (5.6)	
Smoking				<0.001
No	854 (82.3)	523 (75.4)	331 (96.2)	
Yes	184 (17.7)	171 (24.6)	13 (3.8)	
Alcohol				<0.001
No	267 (18.5)	65 (7.4)	202 (36.1)	
Yes	1,176 (81.5)	818 (92.6)	358 (63.9)	

Values are presented as number (%) or mean±standard deviation.
BMI, body mass index; WC, waist circumference; PTA-low, hearing thresholds at low frequencies; PTA-high, hearing thresholds at high frequencies; TAT, total adipose tissue; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; HTN, hypertension; DM, diabetes mellitus.

er, females had a significantly lower PTA-high hearing level (26.3±14.1 dB HL vs. 19.7±11.0 dB HL, *P*<0.001). VAT was significantly higher in males than in females and SAT was higher in females than in males (*P*<0.001). Total adipose tissue showed no significant difference between males and females. The incidences of HTN and DM were higher in males than in females (*P*<0.001), and the incidences of smoking and alcohol consumption were higher in males than in females (*P*<0.001).

Relationship between hearing threshold, clinical factors, and FRAs

Univariate analysis

VAT and SAT was significantly different between sexes (Table 1). This means that sex played a part when hearing and FRAs were analyzed by regression analysis. For this reason, we reanalyzed this relationship with every regard to sex.

Regarding PTA-low, univariate analysis showed that age, height, BMI, WC, VAT, HTN, DM, and alcohol consumption correlated with hearing regardless of sex; weight correlated with hearing only in male. Regarding PTA-high, age, height, weight, BMI, WC, VAT, HTN, and DM correlated with hearing regardless of sex; alcohol consumption correlated with hearing in female and male (Table 2).

Table 2. Univariate analysis for hearing by several variables

Variable	PTA-low All β±SE	P-value	PTA-low Male β±SE	P-value	PTA-low Female β±SE	P-value	PTA-high All β±SE	P-value	PTA-high Male β±SE	P-value	PTA-high Female β±SE	P-value
Age	0.385±0.021	<0.001	0.34±0.028	<0.001	0.454±0.032	<0.001	0.713±0.033	<0.001	0.758±0.045	<0.001	0.672±0.042	<0.001
Sex	0.258±0.330	0.435	-	-	-	-	6.591±0.510	<0.001	-	-	-	-
Height	-0.104±0.020	<0.001	-0.226±0.038	<0.001	-0.313±0.046	<0.001	0.135±0.031	<0.001	-0.362±0.064	<0.001	-0.332±0.062	<0.001
Weight	-0.017±0.014	0.223	-0.083±0.022	<0.001	0.040±0.028	0.149	0.127±0.022	<0.001	-0.115±0.037	0.002	0.029±0.038	0.440
BMI	0.133±0.052	0.011	-0.09±0.078	0.249	0.348±0.075	<0.001	0.415±0.083	<0.001	-0.006±0.131	0.648	0.331±0.101	0.001
WC	0.082±0.018	<0.001	0.020±0.028	0.473	0.166±0.028	<0.001	0.236±0.029	<0.001	0.035±0.048	0.456	0.180±0.038	<0.001
TAT	0.002±0.001	0.069	-0.001±0.002	0.598	0.003±0.001	0.008	0.001±0.002	0.373	-0.002±0.003	0.510	0.004±0.002	0.030
VAT	0.007±0.002	0.003	-0.001±0.003	0.847	0.016±0.004	<0.001	0.024±0.004	<0.001	0.003±0.006	0.652	0.018±0.005	<0.001
SAT	0.001±0.001	0.467	-0.002±0.003	0.456	0.002±0.002	0.140	-0.006±0.002	0.006	-0.008±0.005	0.119	0.003±0.002	0.218
HTN	1.860±0.566	0.001	1.373±0.691	0.047	2.962±1.005	0.003	2.278±0.889	0.010	0.418±1.131	0.712	3.871±1.374	0.005
DM	2.579±0.861	0.003	1.937±1.019	0.058	4.275±1.630	0.009	5.765±1.347	<0.001	4.298±1.660	0.010	6.733±2.223	0.003
Smoking	0.204±0.702	0.771	0.036±0.777	0.964	0.413±2.333	0.860	1.116±1.111	0.316	-1.195±1.260	0.343	1.481±3.162	0.640
Alcohol	-2.070±0.591	<0.001	-1.653±1.120	0.140	-2.628±0.772	<0.001	-0.974±0.928	0.294	-6.827±1.821	<0.001	-2.901±1.046	0.006

For both PTA-high and PTA-low, age, BMI, WC, VAT, HTN, and DM were correlated with hearing regardless of sex.
PTA-low, hearing thresholds at low frequencies; PTA-high, hearing thresholds at high frequencies; SE, standard error; BMI, body mass index; WC, waist circumference; TAT, total adipose tissue; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; HTN, hypertension; DM, diabetes mellitus.

Table 3. Multivariate analyses for hearing thresholds at low and high frequencies by clinical factors inclusive of each factor relevant to obesity in males

Independent variable	PTA-low			PTA-high		
	β±SE	*P*-value	Model R^2	β±SE	*P*-value	Model R^2
Age, height, HTN, DM, alcohol, weight			0.111			0.176
Age	0.338±0.047	<0.001		0.734±0.074	<0.001	
Height	−0.188±0.061	0.002		−0.287±0.109	0.009	
HTN	-	-		−1.921±1.226	0.118	
DM	1.713±1.085	0.115		4.068±1.755	0.021	
Alcohol	-	-		−5.307±2.122	0.013	
Weight	-	-		0.108±0.065	0.099	
Age, height, HTN, DM, alcohol, BMI			0.111			0.176
Age	0.338±0.047	<0.001		0.735±0.074	<0.001	
Height	−0.188±0.061	0.002		−0.196±0.096	0.040	
HTN	-	-		−1.922±1.226	0.117	
DM	1.713±1.085	0.115		4.065±1.755	0.021	
Alcohol	-	-		−5.316±2.122	0.012	
BMI	-	-		0.326±0.193	0.092	
Age, height, HTN, DM, alcohol, WC			-			-
Age	0.338±0.047	<0.001		0.717±0.073	<0.001	
Height	−0.188±0.061	0.002		−0.228±0.097	0.020	
HTN	-	-		−1.908±1.227	0.120	
DM	1.713±1.085	0.115		4.063±1.756	0.021	
Alcohol	-	-		−5.319±2.123	0.012	
WC	-	-		0.113±0.073	0.125	
Age, height, HTN, DM, alcohol, TAT			0.111			0.173
Age	0.338±0.047	<0.001		0.705±0.073	<0.001	
Height	−0.188±0.061	0.002		−0.199±0.096	0.039	
HTN	-	-		-	-	
DM	1.713±1.085	0.115		3.460±1.697	0.042	
Alcohol	-	-		−5.369±2.126	0.012	
TAT	-	-		-	-	
Age, height, HTN, DM, alcohol, VAT			0.111			0.177
Age	0.338±0.047	<0.001		0.711±0.073	<0.001	
Height	−0.188±0.061	0.002		−0.209±0.096	0.029	
HTN	-	-		−1.946±1.225	0.113	
DM	1.713±1.085	0.115		4.025±1.754	0.022	
Alcohol	-	-		−5.381±2.121	0.011	
VAT	-	-		0.018±0.010	0.061	

Any among the factors relevant to abdominal fat was not correlated with PTA-low, meanwhile, all factors except TAT were significantly correlated with PTA-high. PTA-low, hearing thresholds at low frequencies; PTA-high, hearing thresholds at high frequencies; SE, standard error; HTN, hypertension; DM, diabetes mellitus; BMI, body mass index; WC, waist circumference; TAT, total adipose tissue; VAT, visceral adipose tissue.

Multivariate analysis

All factors were included in a multivariate analysis, apart from SAT and smoking, which did not show a statistically significant difference between females and males. The 5 clinical factors (age, height, HTN, DM, and alcohol consumption) and each of the FRAs (weight, BMI, WC, TAT, and VAT) were analyzed 5 times independently. That is, 6 factors, 5 clinical factors plus one FRA, were analyzed 5 times, independently.

For males, while no factor among the FRAs showed a significant difference in any analysis in PTA-low, all factors except TAT showed significant differences in PTA-high (Table 3). For females, while all FRAs showed significant differences in PTA-low, 3 of 5 factors (weight, BMI, and WC) showed no significant difference in PTA-high (Table 4).

Among the clinical factors, DM showed significant differences regardless of sexes and hearing thresholds in low/high frequency. The values of R^2 were highest when VAT was included among the FRAs in multivariate analyses in PTA high and PTA low for both males and females (R^2=0.177 and 0.284, respectively).

DISCUSSION

In this study, we showed that the FRAs were correlated with hearing at high frequencies in males, whereas FRAs were correlated with hearing at low frequencies for females. Although there

Table 4. Multivariate analyses for hearing by several factors including factors relevant to obesity in females

Independent variable	PTA-low			PTA-high		
	β±SE	*P*-value	Model R^2	β±SE	*P*-value	Model R^2
Age, height, HTN, DM, alcohol, Weight			0.278			0.260
Age	0.484±0.062	<0.001		0.806±0.082	<0.001	
Height	−0.279±0.084	0.001		-	-	
HTN	-	-		-	-	
DM	4.166±1.701	0.015		5.340±2.358	0.024	
Alcohol	-	-		-	-	
Weight	0.125±0.057	0.029		-	-	
Age, height, HTN, DM, alcohol, BMI			0.278			0.260
Age	0.484±0.062	<0.001		0.806±0.082	<0.001	
Height	0.312±0.142	0.029		-	-	
HTN	-	-		-	-	
DM	4.171±1.700	0.015		5.340±2.358	0.024	
Alcohol	-	-		-	-	
BMI	0.312±0.142	0.029		-	-	
Age, height, HTN, DM, alcohol, WC			0.281			0.260
Age	0.464±0.063	<0.001		0.806±0.082	<0.001	
Height	−0.228±0.079	0.004		-	-	
HTN	-	-		-	-	
DM	4.068±1.698	0.017		5.340±2.358	0.024	
Alcohol	-	-		-	-	
WC	0.130±0.053	0.014		-	-	
Age, height, HTN, DM, alcohol, TAT			0.282			0.263
Age	0.481±0.062	<0.001		0.791±0.082	<0.001	
Height	−0.218±0.079	0.006		-	-	
HTN	-	-		-	-	
DM	4.614±1.670	0.006		5.145±2.358	0.030	
Alcohol	-	-		-	-	
TAT	0.006±0.002	0.011		0.005±0.003	0.139	
Age, height, HTN, DM, alcohol, VAT			0.284			0.266
Age	0.471±0.062	<0.001		0.780±0.083	<0.001	
Height	−0.219±0.079	0.006		4.831±2.365	0.042	
HTN	-	-		-	-	
DM	4.317±1.675	0.010		4.831±2.365	0.042	
Alcohol	-	-		-	-	
VAT	0.015±0.006	0.006		0.014±0.008	0.064	

All factors relevant to abdominal fat were significantly related with PTA-low, meanwhile, 3 of 5 factors were not related with PTA-high.
PTA-low, hearing thresholds at low frequencies; PTA-high, hearing thresholds at high frequencies; SE, standard error; HTN, hypertension; DM, diabetes mellitus; BMI, body mass index; WC, waist circumference; TAT, total adipose tissue; VAT, visceral adipose tissue.

was not a big difference, VAT among the FRAs best described PTA-high and PTA-low for both males and females. To our knowledge, this is the first study to assess the relationship between a variety of FRAs including VAT and hearing thresholds.

The mechanisms interlinking FRAs and ARHL have not been documented clearly. Abdominal fat increase the risk of the type 2 DM and dyslipidemia. Regarding to type 2 DM, it was shown to cause hearing loss due to angiopathy, neuropathy, and oxidative stress and remnants of glycation end products [11]. Regarding to dyslipidemia, it was shown to causes swelling of the strial marginal layer and the outer hair cell in guinea pigs [12]. Therefore, we presume that the mechanism interlinking FRAs and ARHL might include a complicated relevance, comprising angiopathy, imbalance of redox, and neuropathy following to metabolic rem-

nants of abdominal obesity. This gives explanations in part, it is still not clear if abdominal obesity could induce to ARHL.

It is unclear why the association between FRAs and ARHL differed between men and women. However, we suggest that the difference may be due to sex-related differences in the distributions of adipocytokines, hormones, and adipose tissue. Adiponectin is an adipocytokine released from adipose tissue and has a protective effect against atherogenic and inflammatory issues [13]. Concentrations of adiponectin are higher in females than in males [14]. Moreover, estrogen has been found to have a protective effect in the maintenance of the auditory system in females [15,16]. Finally, VAT is higher in males than females, whereas SAT is higher in females than males [17].

Our result that VAT played a role in hearing regardless of sex

is consistent with previous studies showing that VAT is more involved in metabolic disease than is SAT [17-19]. VAT differs from SAT in several respects. First, VAT exists primarily in the mesentery/omentum and passes via the portal circulation to the liver. Second, VAT contains more glucocorticoid/androgen receptors and a greater number of inflammatory/immune cells. Third, VAT is more active in metabolism and more sensitive to lipolysis. Finally, VAT has a greater ability to take up glucose and to release free fatty acids [18].

Early intervention studies demonstrated that physical activity was helpful in reducing visceral adipose fat [20-22]. Haas et al. [23] showed that physical activity correlated with better hearing. Our study might suggest a link between these studies, given that we propose an effect of VAT on hearing.

This study has several limitations. First, this was a cross-sectional study, so we can only interpret the phenomenon, not reveal its pathophysiology. Second, the values of R^2 were similar between the analyses, and the explanatory capacity for hearing might be altered with other study samples. Third, the thresholds at extremely low (0.25 kHz) and high frequencies (8 and 16 kHz) were not assessed. The hearing thresholds were tested at 4 frequencies, 0.5, 1, 2, and 4 kHz, used in routine health checkups.

Our study provides further evidence that FRA is associated with ARHL in males for high frequencies and in females for low frequencies in adults aged over 40 years, and that DM and VAT in particular has major implications for hearing. Further study addressing whether weight loss with a decrease in abdominal fat would slow progression of hearing loss might be interesting.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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