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Association Between Audiometric Patterns and Probabilities of Cardiovascular Diseases

Robert A. Bertrand, MD; Zhaoxing Huang, Eng, MD

Objectives: The aim of this study was to analyze the progression of the audiometric pattern of serial screening tests in companies with hearing conservation program (HCP) to clinical audiometric tests to identify individuals more susceptible to develop cardiovascular diseases (CVDs). The procedure is based on the analysis of various audiometric patterns that have been demonstrated to have a statistically significant relation to certain CVDs. Identifying these individuals, based on pattern progression of hearing loss, could result in earlier detection to prevent disease or decrease its morbidity.

Study design: Using the data from the clinical and screening audiograms, pattern analysis was performed and statistical analysis using Fisher's exact test, odds ratios and *P* values were used to calculate the confidence intervals.

Methods: The analysis was based on potential risk factors related to CVD in 29 cohorts of 10,105 subjects. Of these, a total of 704 subjects also had clinical audiometric tests and examination by an ENT to verify the exactitude of the screening test questionnaire and pattern relation with the clinical audiogram.

Results: A first analysis was made on 704 subjects who had clinical evaluation and clinical audiometric tests showed results comparable to those of Friedland. A correlation between the questionnaire of the clinical and the self-reporting screening tests questionnaires was performed and showed a correlation between the following risk factors: diabetes, hypertension, hyperlipidemia and smoking. Analysis of the progression of audiometric patterns suggested a relationship with the predictive probabilities of developing CVDs.

Conclusion: Progression toward low-frequency hearing loss patterns provides early identification of patients whose audiometric pattern progression suggests increased probability of developing CVDs. The treating physician, by prescribing further investigations, could potentially prevent or reduce the morbidity of these diseases.

Key Words: Hearing loss, cardiovascular disease, early detection, audiometric pattern.

Level of Evidence: III

INTRODUCTION

The American Heart Association (AHA)[1] states that heart disease is the primary cause of death in North America. To prevent or reduce the morbidity of cardiovascular diseases (CVDs), the AHA suggests lifestyle management guidelines[2] for patients with common CVD risks, such as diabetes, high blood pressure, hyperlipidemia, and smoking, as well as for patients with no known risks. A possible link between HL and CVDs is not mentioned in the guidelines of the AHA. Friedland demonstrated a statistically significant relationship between audiometric patterns and the probabilities of developing CVDs[3]; he proposed a statistical procedure using audiometric pattern analysis to predict the probability of developing a CVD.

Susmano et al. postulated that patients with ischemic heart disease (IHD) appear to manifest hearing loss (HL) up to eight times more frequently than those without IHD.[4] He considers loss of hearing in the low frequencies as "early marker" preceding the occurrence of heart disease. This noninvasive, easily applicable audiometric pattern analysis procedure can be applied to both clinical and serial screening audiograms performed in industry. Patients presenting audiometric patterns that correspond to greater probabilities of CVDs could then be identified.

Early identification of pathologies based on symptoms, clinical signs, and/or abnormal laboratory tests can lead to an earlier diagnosis, resulting in prevention and/or early treatment of these diseases. Certain risk factors, such as diabetes, arterial hypertension, hyperlipidemia, and smoking, are more prevalent in the presence of CVDs. Moreover, one common factor among these risk factors is the alteration of vascularization, leading to inadequate blood supply to vital organs.

Several authors have demonstrated a relationship between CVD and hearing threshold levels (HTLs). Rubinstein et al. showed a significant difference in pure-tone threshold audiometry between healthy subjects and those presenting cardiovascular symptoms.[5] Gates demonstrated that cardiac diseases and CVD risk factors affect hearing to some extent[7]; Gates also discussed the role of the stria vascularis in hearing loss (HL).[7]

Hull reviewed the relationship between cardiovascular health and the functions of the peripheral and central auditory systems and demonstrated the negative influence of

From the University of Montreal Medical Health Centre (R.A.B.), Montreal, Quebec, Canada; and the Guangzhou Medical University (Z.H.), Guangzhou, China.

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Send correspondence to Robert A. Bertrand, MD, 5995 Gouin Blvd W., Suite 302, Montreal, QC H4J 2P8. Email: info@BJAinc.com

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impaired cardiovascular health on both of these auditory systems.[8] In addition, a potentially positive influence on hearing was demonstrated between improved cardiovascular health and improvement in the auditory systems. Regarding smoking, several authors, such as Ferrite and Santana,[9] Cruickshank et al.,[10] and Pillsbury,[11] have all described the effects of this habit on HL. Moreover, there is overwhelming evidence that decreased vascularization of the auditory system negatively affects hearing. One frequently cited etiology is altered functioning of the stria vascularis resulting in abnormal endolymph potentials.

Several authors, Argawal et al.,[12] Rosenhall et al.,[13] and Talbott et al.,[14] have demonstrated increased arterial blood pressure results in subjects with worsening of hearing threshold levels. Hwang et al.[15] noted increased hearing loss with subjects presenting transient ischemic attacks.

Pathophysiology

The hair cells of the cochlea are stimulated by specific frequencies, with low frequencies at the apex and high frequencies in the basal turn. One important factor in this response is the endolymph potentials generated by the stria vascularis. The stria vascularis is a highly vascularized part of the cochlea, and modification of the vascularization has a considerable influence on the endolymph potential voltages, which vary more in the apex region than in the basal turn. Because frequency stimulation is specific to each area of the cochlea, altered vascularization in various cochlear regions will produce HL in the corresponding area. Endolymphatic potentials apply a voltage to the cochlea amplifier. When the endolymphatic potential is reduced significantly, the function of the cochlea amplifier is affected. Animal experiments have demonstrated that when the endolymphatic potential is 20 mV or lower, the cochlear amplifier is deemed to be "cochlea starving."

Mom et al.[16] demonstrated that decreased vascularization of the cochlea altered the endolymphatic potentials of the cochlea and, as a result, reduced hearing. Johnsson et al.[17] and Sidman et al.[18] described the role of cochlear vascularization in strial atrophy and decreased endolymphatic potentials. Morizane et al.[19] demonstrated in animal models that a short period of transient cochlear ischemia could reduce endolymphatic potentials by up to 17.5 mV within 15 minutes. Lars-Göran and Hawkins[20] demonstrated the association between sensorineural deafness and atrophy of the stria vascularis. Decreased vascularization of the cochlea primarily affects the apical and basal segments of the cochlea, with decreased endolymph voltage resulting in decreased hearing in the low and high frequency ranges.

Friedland's demographic cohorts of 1168 and 90 subjects presented average ages of 67.5 and 69 years, respectively. The analyses in his study were based on a single clinical audiogram. In the general population, clinical audiometric tests are not routinely performed. HL due to presbycusis is a well-known phenomenon that occurs with age. Schuknecht[21] described four histological presbycusis categories: sensorineural, neural, metabolic (strial) and conductive. The most frequently encountered category is neurosensorial, which corresponds to Friedland's high-sloping pattern. Of interest for predicting CVD are the strial, low-sloping and "other" patterns.

MATERIALS AND METHODS

Materials

The audiograms used for the analysis consist of screening tests performed on 10,105 employees in 29 cohorts. All the audiometric tests were performed according to the requirements of the Canadian Standards Association (CSA) and American National Standards Institute (ANSI) standards. The personnel performing the testing were either clinical audiologists or trained in a Council for Accreditation in Occupational Hearing Conservation (CAOHC) equivalent course for hearing conservation. A total of 704 subjects also had clinical audiograms performed by an audiologist and a medical evaluation by an ENT. The medical questionnaire allowed us to have more accurate information in relation to the risk factors. The questionnaire routinely included question in relation to diabetes, hypertension, hyperlipidemia, and smoking. Subjects with mixed and conductive HL were excluded from the study. The clinical audiogram analyses of the pattern progressions were analyzed according to the parameters as described by Friedland. The patterns were analyzed for each ear separately in relation to the potential variable probabilities of CVD. The individuals included in the study were considered "otologically normal," as defined in the International Organization for Standardization (ISO) 7029 standard.

All subjects with serial audiograms completed a self-reporting, pre-test questionnaire. Subjects, who had an otological disease, ear infections, ear surgery, a family history of HL, cranial trauma, or a history of ototoxic drug use, as determined by the questionnaire, were excluded from this study. Among the medical questions routinely asked were whether the subject had diabetes, arterial hypertension, hyperlipidemia/cholesterolemia, or heart disease.

By excluding subjects with HL from known etiologies, air conduction thresholds were assumed to be similar to bone conduction thresholds. Audiograms performed in HCPs were reviewed. Subjects in this study ranged from 18 to 70 years of age. The audiograms of 10,105 subjects in 29 cohorts were included in a second analysis to determine the progression of the patterns. All cases were reviewed in relation to the following criteria: age, gender, presence of pathologies such as diabetes, high blood pressure, hyperlipidemia, and heart disease. Smoking was also considered a risk factor for CVD.

Methods

The first analysis consists of analyzing the 704 clinical audiograms according to the parameter as proposed by Friedland. For these 704 subjects the pattern categories and analyses were performed. A statistical correlation was also performed by using the Fisher's test including odds ratio (OR) and *P* values for using the serial audiograms of these same 704 subjects. Upon validation of the correlation of the 704 subjects with clinical and serial audiograms, after eliminating from the medical questionnaire subjects with pathologies that could have diseases that could have influenced the evolution of hearing or from the clinical audiogram identifying subjects with mixed and conductive hearing loss it was assumed that the hearing threshold levels (HTLs) of the screening tests corresponded to the neurosensorial hearing loss of these subjects.

Medical data of serial screening tests was obtained using a pre-screening audiometric test questionnaire to identify subjects

having pathologies that included diabetes, hyperlipidemia, arterial hypertension, heart disease and smoking. Using the data obtained from the questionnaire and audiometric pattern analysis of each year, logistic regression analyses were performed to establish the probabilities of developing a CVD based on risk factors and specific audiometric patterns.

Revision of the pre-screening test questionnaire allows us to eliminate subjects with known causes of hearing loss due to personal pathologies such as otological diseases, ear surgery, and use of ototoxic drugs or trauma. Following this review, it is assumed that subjects present a neurosensorial hearing loss. As a second step, the pattern progression analyses were performed for each test and each ear separately in order to follow the progression of the audiometric pattern.

Based on the positive answers of the pre-screening test and clinical audiogram questionnaires, the pattern progression of each ear was analyzed in relation to the probabilities of CVD. The final evaluation is based on the last audiometric test.

The pathologies considered in relation to the probabilities were myocardial infarction (MI), coronary artery disease (CAD), cerebrovascular accident (CVA), and transient ischemic attack (TIA). Claudication was not considered in the analysis considering the fact that this question was not routinely asked in the pre-screening questionnaire and was rarely noticed in the clinical evaluation. The age factor was not considered given that the tests were performed in a working population and no subject was aged 75 or more. The probabilities of each disease were based on the logistic regression using the same formula as suggested by Friedland.

Audiometric Patterns

Friedland described parameters to classify the analysis of the audiometric pattern in relation to the predictive probabilities of acquiring CVD. In our study, we applied the same parameters as Friedland's approach to establish the probabilities of CVD. Six mathematically defined and distinct patterns of the audiogram were identified based on thresholds in low, middle, and high frequencies. These patterns were classified as normal, strial, low-sloping, mid-sloping, and high-sloping. Audiograms that did not meet the mathematically defined parameters were classified as "other."

The following criteria were used for pattern analysis: (a) normal hearing, a hearing level of ≤25 dB averaged across the frequencies 500 to 8000 Hz; (b) strial pattern, ≥ 25 dB HL averaged between 500 and 2000 Hz with ≤ 15 dB variability; (c) low-sloping, ≥ 25 dB HL averaged between 500 and 2000 Hz with > 15 dB variability, (d) mid-sloping, > 25 dB HL averaged between 2000 and 4000 Hz with > 15 dB variability and normal thresholds at the lower frequencies of 500 and 1000 Hz; and (e) high-sloping, > 25 dB HL averaged between 4000 and 8000 kHz with > 15 dB variability and normal thresholds at the lower frequencies of 500 and 1000 Hz. Audiograms that did not meet these criteria were classified as "other."

Using these parameters, serial and clinical audiograms were analyzed separately. An example of each pattern is presented in Figure 1. Using the logistic regression medical questionnaire data, analyses of probabilities as developed by Friedland was performed.

The Strial Pattern

The metabolic presbycusis category, also called strial presbycusis, is well documented. Histological analysis has demonstrated abnormalities in the stria vascularis and little or no damage in the hair cells. In a histopathological study, Schuknecht demonstrated that, for an audiogram compatible with strial presbycusis, the pathology was located mainly in the stria vascularis. Abnormal functionality of the stria vascularis in the cochlear apex can result in two of the patterns described by Friedland: strial and low-sloping. Strial pathology is present predominantly in the apex and basal regions of the cochlea. Clinically, strial and low-sloping patterns can be treated as a unique pattern for predicting CVD.

STATISTICAL ANALYSIS

Using the pattern analysis of the 704 clinical tests, correlation was evaluated between the number of risks and the various patterns.

A first analysis was performed on 704 subjects who had clinical audiograms. In the first analysis, which corresponds to the clinical audiogram with both bone and air conduction, we noted the following results: The two groups of subjects, those with clinical evaluation and those with serial audiometric screening tests, were analysed separately. Using the screening test closest to do clinical audiogram, there was a good concordance of the pattern progression with those of the clinical audiograms.

As a first analysis for the clinical tests, we applied a logistic regression to arrive at prediction probabilities. The logit function of logistic regression is $\text{logit}\,(\text{MI}) = \log \frac{p(\text{MI})}{1-p(\text{MI})}$

The prediction model used by Friedland consists of different variables including age greater than 75 or not, history of smoking, hyperlipidemia, diabetes, hypertension and different patterns of audiogram. Each prediction formula for different predicted disease has a corresponding set of coefficients for the variables. $p(MI)$ is the probability of acquiring MI.

$$p(MI) = \frac{\exp(\beta_x^T)}{1 + \exp(\beta_x^T)}$$

where, $\beta_x^T = \beta_0 + \beta_1 * var_1 + \beta_2 * var_2 + \cdots + \beta_x * var_x$ and: β_0 = intercept, β_x = coefficient for variable x and var_x = 1 if present; and 0 if not present

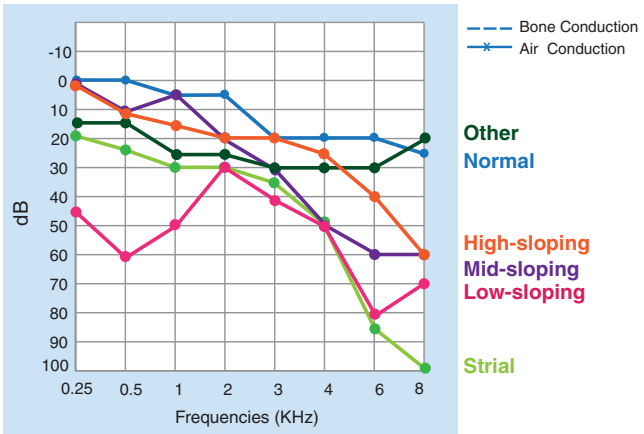

Fig. 1. Examples of the audiometric patterns of 704 subjects with clinical audiograms. Patterns mathematically defined by Friedland normal, strial, low-sloping, mid-sloping, high-sloping, and other.

TABLE I.
Correlation of Pattern to Risk Factors

# of Risks	Normal	Strial	L-Sloping	M-Sloping	H-Sloping	Other
None	102 (21%)	107 (22%)	66 (13%)	181 (36%)	9 (2%)	32 (6%)
One	13 (12%)	20 (19%)	15 (14%)	44 (41%)	2 (2%)	14 (13%)
Two	4 (6%)	13 (20%)	18 (28%)	24 (37%)	0 (0%)	6 (9%)
Three	2 (8%)	7 (28%)	2 (8%)	14 (56%)	0 (0%)	0 (0%)
Four	0 (0%)	5 (56%)	2 (22%)	1 (11%)	0 (0%)	1 (11%)

Clinical Audiogram: Relationship of Risk Factors to Audiometric Patterns.

In Table I, the relation between the number of risks and various patterns is presented. The risks used are: Smoking, diabetes, hyperlipidemia and hypertension. As the number of risks increases, the percentage of various patterns varies. These 4 risks are the variables that were used for the prediction of cardiovascular diseases.

The age variable of 75 was not included as a variable since none of our subjects were 75 years of age or more.

Using a subject with the following parameters: age 60, diabetes, hypertension, hyperlipidemia, and smoking, with a strial pattern, the progression of the pattern allowed us to estimate the probabilities of heart disease (MI) at age 58 as follows in Table II:

The probabilities of each employee acquiring MI, CAD, CVA or TIA can be projected for every audiogram for each ear. From Friedland's coefficient sets, we get:

$$\beta_x^T = -4.89 + 0.58*(\text{age} > 75) + 0.91*\text{Smoking} + 1.11*\text{Lipids} + 0.8*DM + 0.65*\text{HTN} + 0.89*\text{Strial} - 0.11*\text{Mid-sloping} + 0.43*\text{Low-sloping} - 0.88*\text{High-sloping}$$

So, $\beta_x^T = -4.89 + 0 + 0.91 + 1.11 + 0.8 + 0.65 + 0.89 = -0.53$; $\exp(\beta_x^T) = 0.5886$

Therefore, $p(MI) = \frac{\exp(\beta_x^T)}{1+\exp(\beta_x^T)} = 0.5886/(1+0.5886) = 37\%$

This procedure is calculated for each of the analyzed probabilities. In our procedure, the variables were limited to diabetes, hyperlipidemia, hypertension and smoking. The age factor was not considered as no subjects were 75 years old or more.

There is a strong correlation between age groups and patterns. As age advances, the pattern progresses. As the pattern progresses, the risk of developing some form of cardiovascular disease increases.

RESULTS

A first analysis consists of analyzing the audiometric pattern according to age groups as presented in Table III below.

Pattern Progression Analysis

For each clinical audiogram a correlation was made with serial audiograms of the same subjects using the tests with the shortest intervals between them. Considering an adequate relationship of the patterns between the two procedures, analyses of the progression of audiometric patterns of screening tests could be used to identify subjects whose results indicate a trend toward a greater predictive probability of developing CVD. With advancing age, HL related to presbycusis becomes more prevalent. According to Gates, 10% of the adult population presents significant HL. Ries[22] states that at age 65, this percentage increases to 40%. Many of these older patients consult with audiologists and hearing aid dealers and may undergo several audiometric tests spanning a number of years. When several audiograms have been performed for an individual, an analysis of the progression of the audiometric pattern can be generated and analyzed, and this pattern may reveal greater probabilities of CVD when it evolves toward the strial or low-sloping patterns. The analysis was focused on the risk of the following diseases: MI, CAD, CVA, and TIA.

TABLE II.
Example of Pattern Evolution

		AGE									
		41	**42**	**43**	**51**	**53**	**54**	**57**	**59**	**60**	**61**
Male	**RE**	N	M	M	M	M	M	M	L	S	L
Heart disease	**LE**	N	M	N	M	L	M	L	L	S	L
Hypertension	**MI**	1%	1%	1%	2%	1%	1%	14%	13%	37%	13%
High cholesterol	**CAD**	1%	1%	1%	1%	4%	1%	55%	100%	100%	100%
Diabetes	**CVA**	1%	1%	1%	1%	3%	1%	11%	13%	37%	13%
Smoking	**TIA**	0%	0%	0%	0%	1%	0%	0%	4%	8%	4%

At age 58, this subject had an MI.

CAD, coronary artery disease; CVA, cerebrovascular accident; L, low-sloping; M, mid-sloping; MI, myocardial infarction; N, normal; S, serial; TIA, transient ischemic attack; RE, right ear; LE, left ear.

TABLE III.
Correlation of Pattern to Age Group

Pattern	Age 25	30	35	40	45	50	55	60	65+	Correlation
Normal	98%	98%	96%	93%	86%	76%	66%	42%	25%	-0.93
Strial	1%	1%	1%	2%	4%	6%	7%	14%	22%	0.88
Low-sloping	1%	1%	1%	1%	2%	2%	3%	6%	10%	0.83
Mid-sloping	0%	1%	1%	2%	4%	10%	18%	28%	32%	0.92
High-sloping	0%	0%	0%	1%	2%	3%	4%	6%	6%	0.97
Other	0%	0%	1%	1%	2%	3%	8%	3%	3%	0.69

Percentage of subjects in each age group and patterns.

Industrial Applications

A total of 10,105 employees in 29 cohorts were analyzed. The progression of the audiometric pattern of each employee in the 29 cohorts evaluated is presented in Figure 2 for the entire workforce based on the last audiogram.

As the age of the subject increases, a greater number of subjects present one or more of the usual risks considered a precursor of increased probabilities of CVDs. The percentages of subjects according to age group and pattern are presented in Table II.

Health professionals, such as physicians, audiologists, hearing aid dealers, nurses, or technicians, who perform clinical tests or audiometric screening tests, can apply the suggested pattern analysis to provide industry and patients with potentially valuable health information. The progression analysis identifies patients whose pattern modification demonstrates greater probabilities of CVD so that early strategies can be implemented to prevent CVD or decrease the risk of morbidity. The audiometric data was analyzed by a computer software program called Corti 7.0 which is developed by Bertrand Johnson Acoustics, Inc. The pattern analysis progression and prediction features were added in Corti version 7. This procedure analyzed the progression of audiometric patterns according to the predictive probabilities of developing CVD for each individual. The procedure estimated the evolving probabilities based on the occurrence of risks factors and the evolving pattern. The analysis below was based on the last audiogram.

The number of patterns differs according to age group between serial screening in industry and subjects with clinical tests. This is attributed to the fact that clinical audiograms were performed for employees who had worsening of their hearing, frequently above 35 or 40 years of age, whereas serial audiograms were performed from the beginning of employment.

The relationship between the number of risks and different patterns between clinical and screening audiograms are presented in Tables IV and V.

The analysis comparing audiometric pattern progression and the four selected risks revealed a pattern of increased CVD risk, occasionally even in the absence of any of these risks. This finding suggests that there might be other causes for this pattern progression that have yet to be determined.

The probability analysis was limited to the risk of MI, CAD, CVA, and TIA. A first analysis of odd ratios was performed for the risk factors of diabetes, hypertension, hyperlipidemia, heart disease, and smoking. In the validation analysis, heart diseases included MI and CAD. An additional group, including subjects with none of the four risks and the presence of patterns susceptible to risk probabilities of CVD, was added to the data analysis. This data is presented in Table VI.

Clinical and screening tests showed a similar response. If a subject has a specific pattern, such as strial or low-sloping, the probabilities of developing a CVD are greater than subjects with normal hearing.

DISCUSSION

As expected, many subjects with known CVDs presented normal hearing, whereas many subjects with strial and low-sloping patterns showed none of the usual risk factors for CVD. Audiometric patterns predicted the increased probabilities of developing CVDs based on logistic regression analysis using Friedland's approach and audiometric pattern parameters. With regard to the pattern analysis, Friedland's analyses demonstrated a statistically significant relationship between HL and the following aspects of vascular disease: MI, CAD, CVA, TIA, CABG (coronary artery bypass grafting), PTCA (percutaneous transluminal coronary angioplasty), and claudication. While such an analysis was performed by

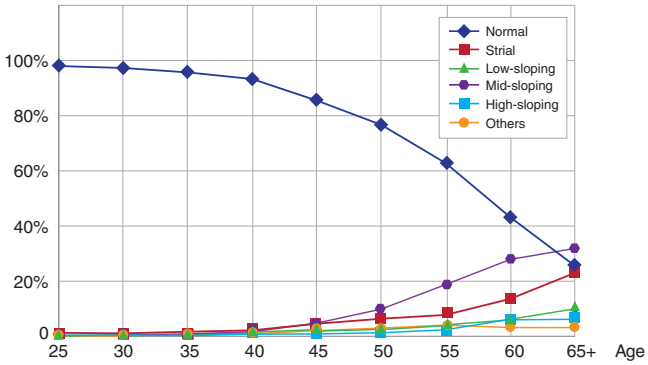

Fig. 2. Graphic representation of the progression of the various patterns for various age groups for subjects with both clinical and serial screening test audiograms.

TABLE IV.
Risk Factor to Audiometric Pattern Correlation (Screening Tests)

# of Risks	Normal	Strial	Low-sloping	Mid-sloping	High-sloping	Other
None	76%	6%	2%	11%	3%	2%
One	57%	10%	5%	20%	5%	3%
Two	48%	11%	8%	23%	5%	4%
Three	46%	12%	5%	31%	4%	2%
Four	24%	30%	16%	16%	9%	5%

Percentage of subjects according to the number of risks and audiometric pattern in 29 cohorts consisting of 10,105 subjects with screening tests audiograms.

TABLE V.
Risk Factor to Audiometric Pattern Correlation (Clinical Tests)

# of Risks	Normal	Strial	Low-sloping	Mid-sloping	High-sloping	Other
None	21%	27%	9%	38%	1%	4%
One	12%	23%	9%	44%	7%	5%
Two	6%	26%	22%	37%	3%	6%
Three	8%	28%	8%	56%	0%	0%
Four	0%	56%	22%	11%	0%	11%

Percentage of subjects according to the number of risks and audiometric pattern consisting of 704 clinical tests

reviewing the subjects of Friedland's cohorts, the aim of the proposed approach was not to identify the probabilities of a specific type of CVD but rather to identify the probabilities of a subject developing any type of CVD. The probabilities of treatments such as CABG and PTCA were not the aim of this study.

In correlating the audiometric pattern progressions with the occurrence of various risk factors, one common factor was decreased vascularization of the peripheral and/or central auditory system. According to the literature, decreased or modified vascularization of the cardiovascular system has been described in relation to decreased hearing.

CVD risk factors can affect hearing by decreasing vascularization of the peripheral and central auditory systems. The cochlea is a highly vascularized organ, especially in the stria vascularis. Noise-induced HL is caused by destruction of the hair cells in the basal segment of the cochlea. A decreased blood supply affects the maintenance of adequate endolymphatic potentials

TABLE VI.
Association of Pattern Comparison and Cardiovascular Disease

	No Disease		HD		Diabetes		HTN		HL	
Pattern Comparison	*Screening test*	*Clinical test*	*Screening test*	*Clinical test*	*Screening test*	*Clinical test*	*Screening test*	*Clinical test*	*Screening test*	*Clinical test*
Strial vs. normal	0.37	0.55	4.04	4.98	2.63	4.87	1.95	2.12	1.9	2.81
	0.31–0.45	0.31–0.97	2.76–5.81	1.11–45.93	1.82–3.73	1.4–26.16	1.32–2.81	0.96-5.07	1.39–2.56	1.38–6.14
	($P \leq .0001$)	($P \leq .05$)	($P \leq .0001$)	($P \leq .05$)	($P \leq .0001$)	($P \leq .01$)	($P \leq .001$)	($P = .06$)	($P \leq .0001$)	($P \leq .01$)
Strial+low-sloping vs. Normal	0.35	0.51	4.2	5.21	2.98	4.73	1.78	2.25	1.92	3
	0.30–0.41	0.30–0.86	3.03–5.77	1.24–46.58	2.21–3.99	1.42–24.78	1.27–2.46	1.07-5.21	1.46–2.48	1.53–6.37
	($P \leq .0001$)	($P \leq .01$)	($P \leq .0001$)	($P \leq .05$)	($P \leq .0001$)	($P \leq .01$)	($P \leq .001$)	($P \leq .05$)	($P \leq .0001$)	($P \leq .001$)
Low-sloping vs. normal	0.30	0.43	4.47	5.71	3.8	4.38	1.4	2.57	1.94	3.43
	0.23–0.38	0.22–0.84	1.33–11.93	1.05–57.65	2.39–5.84	1.01–26.4	0.7–2.54	1.01–6.78	1.22–2.98	1.51–8.17
	($P \leq .0001$)	($P \leq .05$)	($P \leq .01$)	($P \leq .05$)	($P \leq .0001$)	($P \leq .05$)	($P = .29$)	($P \leq .05$)	($P \leq .01$)	($P \leq .01$)
Mid-sloping vs. normal	0.35	0.53	3.96	4.23	2.72	2.97	2.24	2.82	1.63	2.52
	0.31–0.41	0.31–0.88	2.92–5.35	0.99–38.22	2.04–3.58	0.85–15.95	1.69–2.95	1.36–6.43	1.26–2.09	1.28–5.36
	($P \leq .0001$)	($P \leq .05$)	($P \leq .0001$)	($P \leq .05$)	($P \leq .0001$)	($P = .095$)	($P \leq .0001$)	($P \leq .01$)	($P \leq .001$)	($P \leq .01$)
High-sloping vs. normal	0.36	0.37	1.63	N/A	2.39	4.7	2.34	1.86	2.09	2.48
	0.28–0.49	0.14–0.95	0.68–3.37		1.34–4	0.6–37.12	1.36–3.82	0.39–7.14	1.32–3.19	0.69–8.08
	($P \leq .0001$)	($P \leq .05$)	($P = .17$)		($P \leq .01$)	($P = .078$)	($P \leq .01$)	($P = .296$)	($P \leq .01$)	($P = .107$)

The upper figure odds ratio, the middle figure 95% CI, and *P* value using individual audiometric pattern analyses in either ear. Only the significant results are presented.

of the cochlea, especially in the apex, which corresponds to the hair cell stimulation at low frequencies.

The study of pattern progression in clinical and screening audiometric tests can help to identify subjects with greater probabilities of developing a CVD. This approach can be developed for use as a screening procedure, although additional studies must be performed to achieve the goal of preventing or decreasing the morbidity associated with CVD. This procedure may be developed as an additional parameter to be added to existing guidelines on the prevention of CVD, stroke and transient ischemic attacks, such as those issued by The American Heart Association. If a patient's audiometric pattern progression indicates a higher than normal probability of developing a CVD, the treating physician may order further tests related to the specific highlighted risk factors or encourage the subject to modify his/her lifestyle, such as through smoking cessation, if indicated. This procedure can also be applied to future studies, such as a retrospective analysis of serial audiograms of HCPs, or by health professionals who perform audiograms. This approach can be enhanced with a pre-screening test questionnaire that includes questions related to CVD risk factors.

The aim of the current analysis was not focused on specific CVD pathologies but rather on the potential for future cardiac pathologies, thus allowing early intervention for treatment and prevention. Another aspect that could be explored is the use of otoacoustic emissions (OAE), as discussed by Hutchinson et al.[23] The application of OAE and distortion product otoacoustic emissions (DPOAE) was evaluated in relation to pure-tone HL and cardiovascular fitness, and a correlation was established between the degree of HL, age, cardiac fitness and certain OAE and DPOAE tests. Thus, it is possible that this test, or a modification based on other parameters, could improve the estimation of CVD risk, which should be addressed in future studies.

The presence of subjects with none of the usual CVD risk factors but with a strial or low-sloping frequency suggests a missing CVD risk factor. For instance, aggressors in the environment are known to produce an increased risk of Ischemic Heart Disease (IHD), as shown by Costello et al.[24] Thus, environmental factors should be considered as additional risk factors.

CONCLUSION

A procedure is proposed to analyze the pattern progression of serial screening audiometric tests in otologically normal subjects. Analysis of the progression of these patterns can help to identify subjects who may present greater probabilities of developing cardiovascular pathology at an earlier stage, thus allowing for earlier intervention and treatment to prevent the onset of or decrease the morbidity associated with these diseases.

The procedure developed is noninvasive and can be applied to any audiometric database currently used in industry or to any audiogram performed by health professionals, such as physicians, audiologists and hearing aid dealers. Abnormal audiometric pattern progression represents an additional metric to identify subjects with greater probabilities of developing CVDs.

CONFLICT OF INTEREST

Dr. Bertrand and Mr. Huang are shareholders of Bertrand Johnson Acoustics, Inc.

FINANCIAL DISCLOSURES

Bertrand Johnson Acoustics, Inc. (BJA) is a local service provider for Hearing Conservation Programs. Dr. Bertrand who founded the company is now retired from active practice for the last 10 years. He acted as an unpaid consultant for research projects in relation to Hearing Conservation Programs. Tax credit grants from the Canadian Federal and Provincial governments were obtained for the R&D aspects to pay 60% of the cost, mainly programmers', statisticians', and secretaries' salaries. The cost of all other expenses was paid for by BJA. Zhaoxing Huang, chief programmer, is a salaried employee of BJA, assigned to R&D. Dr. Bertrand, MD, received no salary during the development of this project working part time as Director of R&D.

Both Dr. Bertrand and Mr. Huang are shareholders of BJA. No dividends have been paid to the shareholders for the last 10 years.

The material included in the manuscript is not subject to commercialization. It is considered by the FDA to be a SaMD (software as a medical device) and we have not made any attempts to obtain FDA approval. At present, no remuneration from sales is foreseen for the material in the manuscript. If more information is required, please contact the author.

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