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Hearing in older adults with exfoliation syndrome/exfoliation glaucoma or primary open-angle glaucoma

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ABSTRACT.

Purpose: **To determine whether adults, aged 66–96 years, with exfoliation syndrome (XFS)/exfoliation glaucoma (XFG), or primary open-angle glaucoma (POAG) have poorer hearing than controls of similar age.**

Methods: **Case (XFS/XFG and POAG) and control status was diagnosed in the Reykjavik Glaucoma Studies (RGS) using slit-lamp examination, visual field testing and optic disc photographs; the RGS data were merged with the Age, Gene/Environment Susceptibility–Reykjavik Study that collected hearing data using air-conduction, pure-tone thresholds obtained at 0.5, 1, 2, 3, 4, 6 and 8 kHz categorized by better ear and worse ear, based on pure-tone averages (PTAs) calculated separately for low and middle frequencies (PTA_{512} – mean of thresholds at 0.5, 1 and 2 kHz) and high frequencies (PTA_{3468} – mean of thresholds at 3, 4, 6 and 8 kHz). Multivariable linear regression was used to test for differences in PTAs between cases and controls.**

Results: **The mean age for 158 XFS/XFG cases (30.4% male) was 77.4 years, 95 POAG cases (35.8% male) was 77.9 years, and 123 controls (46.3% male) was 76.8 years. Using multivariable linear regression analysis, there were no consistent, statistically significant differences in PTAs between the two case groups and controls in either the low- or high-frequency range, even when stratified by age group.**

Conclusion: **Among the older individuals examined in this study hearing loss is highly prevalent and strongly associated with male gender and increasing age. As we did not find consistent statistically significant difference in hearing between cases and controls the diagnosis of XFS/XFG or POAG does not as such routinely call for audiological evaluation.**

Key words: adjustment for age and sex – exfoliation glaucoma – hearing – primary open-angle glaucoma

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Introduction

Exfoliation syndrome (XFS), also called pseudo-exfoliation, is a generalized disease of the extracellular matrix characterized by a pathologic accumulation of microfibrillar material, mainly made up of basement membrane proteins and found in the eye and other tissues (Schlotzer-Schrehardt et al. 2008). Exfoliative material has been found in various tissues of the body, suggesting that XFS may be associated with some systemic conditions (Schlotzer-Schrehardt et al. 2008). The condition has been associated with cardiovascular and cerebrovascular comorbidities as well as diabetes, although these findings have not been confirmed in all studies (Mitchell et al. 1997; Schumacher et al. 2001; Tarkkanen et al. 2008; Wood et al. 2011).

The prevalence of XFS varies with age, sex, race/ethnicity and geographic location and is reported to be 10.7% in Icelanders 50 years and older as compared to 2.4% in North Chinese (Arnarsson et al. 2007, 2009; You et al. 2013). Among Icelanders 80 years and older, the prevalence of XFS is

increased to 40.6% (Jonasson et al. 2003). Longitudinal epidemiological studies have found XFS to be an independent risk factor for open-angle glaucoma (Ekström 1993; Leske et al. 2003), so-called exfoliation glaucoma (XFG), responsible for about two-third of glaucoma blindness in Iceland.

Using the present glaucoma cohort, coding variants in the lysyloxidase like 1 gene were discovered in Iceland to be strongly associated with XFS (Thorleifsson et al. 2007). These findings have now been replicated worldwide (Fan et al. 2011; Ritch 2014).

Most studies on possible non-ocular clinical consequences of XFS have reported an association between sensorineural hearing loss (SNHL) and exfoliation syndrome with or without glaucoma (Cahill et al. 2002; Shaban & Asfour 2004; Aydogan et al. 2006; Turacli et al. 2007; Detorakis et al. 2008; Yazdani et al. 2008; Papadopoulos et al. 2010; Samarai et al. 2012; Singham et al. 2014). It has been suggested that in XFS, the cochlea might be affected through exfoliation microfibrillar deposits that lead to dysfunction of the mechanoreceptors in the inner ear (organ of Corti) and thus impact on hearing (Cahill et al. 2002). Hearing impairment may also be associated with vascular pathology related to XFS, as studies have shown aggregation of exfoliative material in vessel walls (Schlotzer-Schrehardt et al. 2008). Hearing impairment is, however, not found to be associated with degree of XFG damage (Aydogan et al. 2006). Paliobei et al. (2011) considered none of the previous studies to have sufficiently large cohort and selection of suitable age- and sex-matched control groups to assess the association of hearing and XFS reliably. They found an association of XFS/XFG and hearing, in their participants 50–70 years of age, and their findings suggested retrocochlear pathology. Their study is the largest previous publication on the issue including 110 XFS/XFG cases.

This last mentioned study by Paliobei et al. (2011) also found primary open-angle glaucoma (POAG) to be associated with hearing impairment contrary to a previous publication by Shapiro et al. (1997). As the otopathology associated with possible hearing impairment in XFS/XFG is not fully understood and neither is the pathogenesis of POAG, there might be a similar pathway leading to hearing impairment in both glaucoma types and both types are treated with the same glaucoma medication which might possibly affect hearing.

Material and Methods

All the cases and controls participated in at least one of the Reykjavik Glaucoma Studies (RGS) and in the Age, Gene/Environment Susceptibility–Reykjavik Study (AGES-R). The AGES-R is a population-based study designed to investigate the genetic and environmental factors contributing to health, disability and disease in older people (Harris et al. 2007; Jonasson et al. 2011; Fisher et al. 2014). The AGES-R was approved by the Icelandic National Bioethics Committee (VSN: 00-063), which acts as the Institutional Review Board for the Icelandic Heart Association, and by the Institutional Review Board for the U.S. National Institute on Aging (NIA), National Institutes of Health (NIH). The RGS were approved by the Icelandic National Bioethics Committee (VSN: 00-024). All participants provided written informed consent and the studies adhered to the tenets of the Declaration of Helsinki. The Reykjavik Eye Study is a population-based study, examining the prevalence and incidence of age-related eye disease, including a glaucoma study (RGS1) (Jonasson et al. 2003), and the second Reykjavik Glaucoma Study (RGS2) is a clinical (non-population-based) study whose focus was on glaucoma and genetics (Thorleifsson et al. 2010).

Both RGS included slit-lamp examination for XFS after dilatation of the pupil, optic disc biomicroscopy and photography, and visual field testing. Those with XFS, open angle, glaucomatous optic neuropathy (GON) and glaucomatous field defect (GVFD) were deemed to have XFG. The definition of exfoliation syndrome includes complete or partial peripheral band and/or a central shield of exfoliative material on the anterior lens capsule in at least one eye of the person. Adults with POAG comprised a separate case group participating in AGES-R and also diagnosed in at least one of the two RGS, including again slit-lamp examination after dilatation, optic disc photography and visual field testing, having open angle, GON and GVFD.

The control group includes persons who participated in AGES-R and at least one of the two RGS and who did not show evidence of XFS/XFG or POAG.

During AGES-R, all participants completed a hearing evaluation which included an otoscopic examination, tympanometry (an evaluation of middle ear function) and air-conduction, pure-tone audiometric threshold testing (Fisher et al. 2014). Individuals who had blocking cerumen in the ear canal had this removed. Middle ear testing was conducted using a Micro Audiometrics Earscan™ acoustic impedance tympanometer (Murphy, NC, USA). Tympanograms were classified based on the Lidén–Jerger procedure as Type A (considered 'normal') where any hearing loss is assumed to be SNHL (SNHL), Type B (flat) or Type C (admittance peak is shifted left or negative), typically suggesting an acute or chronic infection in the ear that can result in conductive or mixed (both conductive and SNHL) hearing loss (Lidén 1969; Jerger 1970).

Air-conduction, pure-tone threshold testing of each ear was accomplished using Interacoustics Model AD229e audiometers (Assens, Denmark) using standard TDH-39P headphones with acoustically transparent disposable hygienic covers. EARtone™ 3A insert earphones with disposable foam tips were used when the subject had collapsing ear canals or large intra-aural differences in hearing thresholds. The pure-tone thresholds in the audiogram were obtained manually at seven frequencies, namely at 0.5, 1, 2, 3, 4, 6 and 8 kHz, using the modified Hughson-Westlake technique with 5-dB hearing level (HL) step size (Carhart & Jerger 1959). If individuals wore hearing aids, these were removed. To determine the better hearing ear (BE), pure-tone averages (PTAs) across all tested frequencies were calculated for each ear; the ear with the lowest average was designated as the BE and the contralateral ear was designated the worse ear (WE). PTAs at 0.5, 1 and 2 kHz, or PTA_{512}, were calculated in the low- and middle-frequency range; better (lower) values of PTA_{512}, preferably less than or equal to 25 dB HL, are important for understanding speech in quiet conditions. In addition, PTAs at 3, 4,

6 and 8 kHz, or PTA_{3468}, were calculated for the high-frequency range; better (lower) values of PTA_{3468} are important for distinguishing consonants that have high-frequency acoustic energy that contributes to the understanding of speech in noisy environments.

Information on age, sex, work history related to noise exposure (type of work and duration of work), bothersome tinnitus (ringing, buzzing or other sounds in the ears or head), frequent ear infections in childhood or as adults, pneumatic equalization tube use, prior middle ear or mastoid surgery, ear diseases, congenital hearing loss and general hearing health history (such as history of meningitis, sudden hearing loss, head trauma and acoustic neuroma) was collected using interviewer-administered questionnaires and collected as part of a standardized protocol (Harris et al. 2007). The protocol also included gathering information on educational attainment, the highest level of completed schooling (primary, secondary, college/university) and self-reported health status measured using a Likert scale (e.g. excellent, very good, good, fair or poor). Tobacco use or smoking status was classified as never smoker, former smoker and current smoker. Alcohol consumption was categorized as <1 drink per month, 1–3 drinks per month, or 1 or more drinks per week. High blood pressure was characterized as hypertension (self-reported history of hypertension or use of antihypertensive drugs or blood pressure ≥140/90 mmHg), prehypertension (blood pressure ≥120/80 but <140/90 mmHg) or normal blood pressure. Diabetes mellitus was determined by self-reported history of diabetes, use

Table 1. Selected characteristics of cases with exfoliation syndrome/exfoliation glaucoma (XFS/XFG) and primary open-angle glaucoma (POAG) and controls by sex.

	Male					Female				
Characteristics	*N**	XFS/XFG *N* = 48 (%)	POAG *N* = 34 (%)	Control *N* = 57 (%)	p-Value†	*N**	XFS/XFG *N* = 110 (%)	POAG *N* = 61 (%)	Control *N* = 66 (%)	p-Value†
Age										
Mean (years)	139	77.5	78.7	76.4		237	77.3	77.5	77.1	
Standard deviation		5.2	5.2	4.6			5.4	5.9	5.8	
Age groups					0.090					0.685
66–74	41	31.3	26.5	29.8		82	36.4	36.1	30.3	
75–79	52	29.2	29.4	49.1		60	23.6	21.3	31.8	
80+	46	39.6	44.1	21.1		95	40.0	42.6	37.9	
Education, lifestyle and chronic diseases										
Education					0.837					0.882
Primary	18	10.4	11.8	15.8		68	27.3	27.9	31.8	
Secondary	67	54.2	47.1	43.9		115	51.8	47.5	43.9	
College/University	54	35.4	41.2	40.4		54	20.9	24.6	24.2	
Health status					0.089					0.805
Excellent/very good	52	37.5	38.2	36.8		94	36.4	42.6	42.4	
Good	57	27.1	47.1	49.1		73	32.7	32.8	25.8	
Fair	26	29.2	14.7	12.3		60	26.4	23.0	25.8	
Poor	4	6.3	0.0	1.8		10	4.6	1.6	6.1	
Smoking					0.344					0.371
Current	10	8.3	5.9	7.0		30	17.3	8.2	9.1	
Former	77	60.4	64.7	45.6		74	28.2	32.8	34.9	
Never	52	31.3	29.4	47.4		133	54.6	59.0	56.1	
Alcohol drinking					0.813					0.748
≥1 per week	39	33.3	29.4	22.8		27	10.0	11.5	13.6	
1–3 per month	36	25.0	23.5	28.1		61	23.6	31.2	24.2	
<1 per month	64	41.7	47.1	49.1		149	66.4	57.4	62.1	
Hypertension‡					0.033					0.097
Hypertension	72	35.4	61.8	59.7		129	49.1	52.5	65.2	
Prehypertension	54	47.9	29.4	36.8		81	41.8	31.2	24.2	
No	13	16.7	8.8	3.5		27	9.1	16.4	10.6	
Diabetes	14	12.5	8.8	8.8	0.788	14	4.6	4.9	9.1	0.432
Hearing variables										
Tinnitus	20	14.6	14.7	14.0	0.995	19	4.6	13.1	9.1	0.132
Noise exposure	71	50.0	55.9	49.1	0.809	41	17.3	19.7	15.2	0.797
Repeated ear infections	11	8.3	2.9	10.5	0.428	24	11.8	9.8	7.6	0.663
Tympanogram type (in better hearing ear)					0.527					0.182
Type A ('normal')	105	68.8	85.3	75.4		181	80.0	67.2	78.8	
Types B or C	10	8.3	5.9	7.0		27	9.1	19.7	7.6	
No tympanogram	24	22.9	8.8	17.5		29	10.9	13.1	13.6	

* *N* = number of males, or females, with the characteristic shown in each row; for example, there are 41 males and 82 females aged 66–74 years of age.
† p-Value based on the chi-square distribution.
‡ High blood pressure was characterized as hypertension (self-reported history of hypertension or use of antihypertensive drugs or blood pressure ≥140/90 mmHg), prehypertension (blood pressure ≥120/80 but <140/90 mmHg) or normal blood pressure.

of glucose lowering medications or fasting blood glucose of ≥7.0 mmol/l.

Participants reporting the following conditions were excluded: prior ear operation, otosclerosis, cholesteatoma, chronic ear disease, acoustic neuroma and Meniere's disease. Furthermore, individuals who reported a history of meningitis, mumps/measles, sudden deafness or congenital deafness were excluded. To be included, cases and controls were required to have hearing thresholds determined for at least six tested frequencies in each ear.

SAS version 9.3 (SAS Institute Inc. Cary, NC, USA) was used for statistical analysis. Student's *t*-test was used for comparison of means. Multivariable linear regression analysis was used to compare PTAs of XFS/XFG cases versus controls, and PTAs of POAG cases versus controls, adjusting for age and sex. Advanced models adjusted for additional covariates including educational level, health status, smoking, hypertension, tinnitus, noise exposure and repeated ear infections.

Results

A total of 186 participants were identified with XFS/XFG, but 28 (15%) were excluded in accordance with exclusion criteria, leaving 158 XFS/XFG cases for analysis. There were 105 participants with POAG; however, applying the exclusion criteria 10 (10%), participants were excluded and 95 cases remained for analysis. The control group had 123 persons who satisfied the inclusion/exclusion criteria and were diagnosed definitively as not having XFS or POAG. The male/female ratio in the XFS/XFG group was 30.4%/69.6%, and in the POAG group, it was 35.8%/64.2% as shown in Table 1; sex was more evenly distributed in the control group, 46.3%/53.7%. Of the 158 persons with XFS, 47.5% had XFG and 110 (69.6%) of the 158 participants had both eyes affected. Among those with POAG, 86 (90.5%) had bilateral disease.

Selected characteristics for the three groups, stratified by sex and case–control status, are summarized in Table 1. Altogether 67.3% were 75 years and older. Comparing characteristics between cases and controls, only hypertension among males was significant ($p = 0.033$) with controls more likely to be hypertensive compared to the POAG or XFS group. None of the other characteristics shown in Table 1 had significant ($p < 0.05$) distributional differences.

Of all 376 participants analysed in the present study, 53 (14%) had missing tympanograms. Of the 323 individuals with tympanograms, 286 (88.5%) had BE Type A tympanograms (SNHL) as compared to 37 (11.5%)

Table 2. Low/middle (PTA512)- and high (PTA3468)-frequency pure-tone averages of thresholds, in dB (decibels) hearing level (HL), for cases (XFS/XFG and POAG) and controls by age, sex, better and worse hearing ears.

		XFS/XFG		POAG		Controls	
	Age (years)	*N* = 158	PTA Mean (SD)	*N* = 95	PTA Mean (SD)	*N* = 123	PTA Mean (SD)
Males							
PTA_{512}							
Better ear	66–74	15	19.2 (7.3)	9	22.2 (14.8)	17	21.5 (15.0)
	75–79	14	21.4 (13.4)	10	28.2 (13.8)	28	25.8 (11.6)
	80+	19	31.5 (18.0)	15	26.9 (11.3)	12	24.2 (11.6)
Worse ear	66–74	15	24.2 (10.4)	9	23.3 (15.7)	17	25.7 (16.1)
	75–79	14	26.1 (17.5)	10	33.8 (14.7)	28	36.8 (20.7)
	80+	19	38.2 (21.3)	15	32.4 (17.0)	12	28.8 (10.9)
PTA_{3468}							
Better ear	66–74	15	49.0 (17.2)	9	50.0 (17.4)	17	47.3 (17.9)
	75–79	14	53.8 (20.2)	10	57.0 (16.7)	28	60.8 (15.5)
	80+	19	59.1 (12.1)	15	61.4 (11.7)	12	61.9 (11.5)
Worse ear	66–74	15	53.9 (9.2)	9	61.5 (18.2)	17	53.4 (18.1)
	75–79	14	60.5 (20.2)	10	66.4 (14.9)	28	66.7 (16.2)
	80+	19	64.7 (15.3)	15	68.9 (15.4)	12	65.0 (12.7)
Females							
PTA_{512}							
Better ear	66–74	40	18.8 (8.3)	22	20.1 (9.3)	20	19.0 (7.0)
	75–79	26	20.6 (10.1)	13	22.6 (8.6)	21	20.5 (10.7)
	80+	44	29.5 (13.4)	26	30.8 (12.0)	25	25.9 (10.7)
Worse ear	66–74	40	22.5 (9.7)	22	23.3 (12.2)	20	23.6 (10.7)
	75–79	26	24.9 (10.1)	13	27.4 (9.4)	21	29.8 (23.2)
	80+	44	35.9 (19.3)	26	37.2 (13.0)	25	30.7 (11.1)
PTA_{3468}							
Better ear	66–74	40	37.5 (14.1)	22	39.5 (15.0)	20	35.1 (13.5)
	75–79	26	40.1 (13.5)	13	46.4 (18.4)	21	44.5 (13.2)
	80+	44	53.5 (15.9)	26	57.0 (17.4)	25	49.3 (12.9)
Worse ear	66–74	40	43.0 (15.1)	22	41.9 (16.0)	20	39.1 (14.9)
	75–79	26	44.7 (15.5)	13	53.0 (17.3)	21	49.9 (20.0)
	80+	44	60.3 (17.6)	26	61.6 (11.4)	25	55.8 (11.8)

XFS/XFG = exfoliation syndrome/exfoliation glaucoma; POAG = primary open-angle glaucoma; SD = standard deviation; PTA_{512} = low/middle-frequency range; PTA_{3468} = high-frequency range.

Table 3. Multivariable regression estimates of pure-tone average hearing differences in dB HL by age for cases (XFS/XFG and POAG) compared to controls for better ear (BE) and worse ear (WE).

	Model 1		Model 2		Model 3	
	Estimates	p-Value	Estimates	p-Value	Estimates	p-Value
66–74 years						
XFS/XFG						
BE PTA_{512}	−1.2	0.553	−1.7	0.417	−1.8	0.414
WE PTA_{512}	−1.6	0.514	−2.2	0.375	−2.9	0.332
BE PTA_{3468}	−0.1	0.988	0.8	0.820	−0.8	0.817
WE PTA_{3468}	0.3	0.924	0.8	0.804	−0.2	0.946
POAG						
BE PTA_{512}	0.6	0.863	2.8	0.933	2.5	0.224
WE PTA_{512}	−1.2	0.706	−2.3	0.482	−5.1	0.128
BE PTA_{3468}	1.8	0.641	2.4	0.538	1.4	0.730
WE PTA_{3468}	1.9	0.668	2.2	0.577	0.4	0.923
75–79 years						
XFS/XFG						
BE PTA_{512}	−2.6	0.287	−1.9	0.434	−1.8	0.466
WE PTA_{512}	−8.5	0.034	−7.6	0.063	−7.4	0.099
BE PTA_{3468}	−8.7	0.016	−0.6	0.092	−6.7	0.056
WE PTA_{3468}	−9.3	0.026	−5.7	0.137	−5.9	0.153
POAG						
BE PTA_{512}	1.5	0.605	2.0	0.493	1.1	0.736
WE PTA_{512}	−3.5	0.471	−3.0	0.539	−3.2	0.561
BE PTA_{3468}	−2.8	0.522	−1.9	0.647	−3.7	0.366
WE PTA_{3468}	−0.7	0.887	0.5	0.907	−1.5	0.756
80+ years						
XFS/XFG						
BE PTA_{512}	4.8	0.088	5.1	0.067	5.6	0.065
WE PTA_{512}	6.5	0.067	6.9	0.049	7.8	0.048
BE PTA_{3468}	1.8	0.540	2.4	0.391	3.7	0.254
WE PTA_{3468}	2.9	0.376	3.4	0.284	3.7	0.283
POAG						
BE PTA_{512}	4.0	0.122	3.8	0.124	4.3	0.094
WE PTA_{512}	5.4	0.069	5.2	0.069	6.1	0.053
BE PTA_{3468}	5.2	0.120	4.4	0.150	5.3	0.111
WE PTA_{3468}	5.5	0.067	4.8	0.081	4.9	0.099

PTA_{512} = pure-tone average of thresholds in the low/middle-frequency range (0.5, 1 and 2 kHz); PTA_{3468} = pure-tone average of thresholds in the high-frequency range (3, 4, 6 and 8 kHz); XFS/XFG = exfoliation syndrome/exfoliation glaucoma; POAG = primary open-angle glaucoma.
Model 1: unadjusted; Model 2: adjusted for age and sex only; Model 3: adjusted for age, sex, education level, health status, smoking, hypertension, tinnitus, noise exposure and repeated ear infections.

individuals that had either a BE Type B or Type C tympanogram.

In Table 2, the low/middle- and high-frequency PTAs (means and SD) are shown by sex, BE/WE and age group for the two case groups and controls. As expected, age and sex were strongly associated with PTAs in both the low/middle (PTA_{512})- and high (PTA_{3468})-frequency ranges. Hearing threshold levels (e.g. average PTA for the better ear) increase (hearing is poorer) as individuals get older; also PTAs are usually higher (worse) for males than females (Table 2).

Unadjusted multivariable regression analysis suggested worse hearing for those 75-79 year old with XFS, particularly for the higher frequencies, PTA_{3468} (model 1, Table 3). After adjusting for age and sex, however, multivariable linear regression results showed no significant association of HLs for cases as compared to controls (Table 3; model 2), except possibly in for WE PTA_{512} in persons 80 years and older with XFS/XFG, although due to small numbers of cases and controls the power to detect true differences was low. After adjustment for additional covariates including education level, health status, hypertension, tinnitus, repeated ear infections, noise exposure and smoking (Table 3; model 3), the multivariable linear regression results continued to demonstrate no significant association of HLs for XFS cases as compared to controls, although the regression estimate associated with individuals aged 80 years and older strengthened, but the p-value remains unchanged. There was no evidence from these analyses in any model that HLs of XFS/XFG individuals and controls aged 80 years or older were different in the high-frequency range. In all three models, there was no statistical difference in the HLs of individuals with POAG compared to controls, for all frequencies tested.

Discussion

Results from our study, involving the largest number of XFS/XFG cases assembled to date, do not show any significant difference in low- or high-frequency hearing in the better or worse ear compared to controls after considering age, sex and other possible confounders. Although there have been a number of non-controlled studies reporting that patients with XFS/XFG have worse hearing than some comparison group, most studies have been small in size with the number of cases ranging from 41 to 83 and did not consider sufficient numbers of suitable age- and sex-matched controls (Paliobei et al. 2011).

Cahill et al. (2002) in a non-controlled study examining hearing thresholds 1, 2, 3 kHz concluded that most XFS/XFG individuals seemed to have worse hearing when compared to the age- and sex-matched ISO 7029 standard. Yazdani et al. (2008) in the second largest published study with 83 cases and 83 controls examining the same HLs suggested that hearing thresholds of XFS/XFG cases may be around 10 dB HL worse for both lower (1 kHz) and middle/higher frequencies (2 and 3 kHz) compared to controls. Papadopoulos et al. (2010) examined 47 persons with XFS and 22 controls and found, contrary to the above-mentioned studies, the strongest association at the highest frequency, 8 kHz, and no association with thresholds at frequencies of 0.25, 0.5, 1 and 2 kHz.

Paliobei et al. (2011) published on hearing and exfoliation syndrome, including 110 patients with XFG as well as 85 patients with POAG, mean age 66 years, range 50–70 years, examining auditory thresholds of 0.5, 1, 2, 4 and 8 kHz. They showed poorer hearing in the XFG group for all frequencies compared with the ISO 7029 standard. They also studied an

auditory brainstem response whose results indicated increased latency in the exfoliation group and also other morphologic variants that they described as 'abnormal' (including absent waveforms) suggesting possible retrocochlear pathology.

A possible reason why our study yielded basically null findings is that our population was older than those in previous studies. The mean age of the 158 XFS/XFG participants in the present study was 77 years, an older mean age than any of the studies reported in the literature. Additionally, two-thirds of participants in this study were ≥75 years old, reflecting common age for patients with glaucoma in Iceland. Our results clearly show age and sex differences in hearing among older individuals, with females having better hearing than males of the same age, a finding confirmed in studies from numerous countries (Stevens et al. 2013). Lack of adjustment for age and sex and other confounding factors in some of the previous studies may have biased their results. Additionally, there may have been other well-designed studies which, like our study, yielded null results and therefore may have been unpublished, due to publication bias.

In addition to hearing in older adults with XFS/XFG, persons with POAG were studied as a separate case group in the present study. Older studies examining this association are rather vague on the type of glaucoma under consideration and short on suitable controls. We could only identify two more recent articles in the literature examining the association of hearing and POAG. The study by Shapiro et al. (1997) compared patients with POAG 60 years and younger with age- and sex-matched controls and found no difference in HLs. The study by Paliobei et al. (2011) compared 50- to 70-year-old POAG patients with age- and sex-matched controls and found worse hearing for cases than for controls. Both studies examined cohorts younger than the present study and this may affect results. A small study on normal tension glaucoma (NTG), a variant of POAG and hearing, however, did find a high coincidence of hearing loss and NTG in participants aged 31–81 years (Kremmer et al. 2004).

Although the present study includes larger number of cases and controls than all previous studies, its main limitation may be a rather small sample. Large epidemiologic studies including both detailed slit-lamp examination of the eye for XFS and assessment of hearing are scarce.

We have shown that hearing difficulty increases with age, is highly prevalent in this older population and is more common among men than women. In our case–control study, adjusting for age and sex, and in a further model adjusting additionally for education level, health status, smoking, hypertension, tinnitus, noise exposure and repeated ear infections, we did not find conclusive evidence of worse hearing among persons with XFS/XFG or persons with POAG compared to a carefully selected control group. Therefore, these data do not lend support to the suggestion (Paliobei et al. 2011) that a multidisciplinary approach involving the ear, nose and throat specialist is indicated when managing patients with XFS/XFG or POAG.

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