



1 Article

2 **Work-Related Noise Exposure in a Cohort of Patients** 3 **with Chronic Tinnitus: Analysis of Demographic and** 4 **Audiological Characteristics**

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14 **Abstract:** Work-related noise exposure is one of the major factors contributing to development of
15 adult-onset hearing loss and tinnitus. The aim of this study was to analyze, in patients with chronic
16 tinnitus and long-term occupational noise exposure, A) characteristics of hearing loss, tinnitus,
17 comorbidities, demographic characteristics and history of work-related noise exposure and B)
18 differences among individuals employed in occupations with high and low risk of developing
19 work-related noise induced hearing loss (NIHL). 136 patients with chronic tinnitus and at least 10-
20 year-long working history were divided into two groups based on the risk of their profession to
21 induce NIHL. Individuals employed in jobs at high risk for NIHL were mostly males, and exhibited
22 a poorer hearing threshold, more evident in the left ear. Tinnitus was mostly bilateral; the next
23 largest presentation was left-sided; patients described their tinnitus as buzzing or high-pitched.
24 Correlation between age, length of tinnitus and worse hearing was found. Patients with a higher
25 degree of hearing impairment were mostly males and were more likely to have a family history of
26 hearing loss and at least one cardiovascular comorbidity. Our study shows some differences in
27 individuals with tinnitus and a history of a profession associated with increased exposure to NIHL
28 compared to those without such a history.

29 **Keywords:** noise-induced hearing loss; tinnitus; occupational noise exposure; pure tone audiometry

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31 **Introduction**

32 Noise induced hearing loss (NIHL), commonly defined as a hearing threshold worse than 25 dB
33 HL at the high-frequency range [1], is a major cause of hearing impairment. Workplace noise
34 exposure is an important risk factor of NIHL in workers; 16% of disabling adult-onset hearing loss
35 worldwide is attributed to occupational noise [2,3]. NIHL is the most frequent work-related disorder
36 in the United States [4,5].

37 Chronic exposure to loud noise induces a progressive destruction of inner and outer hair cells
38 in the Organ of Corti, and alterations to the stria vascularis and spiral ganglion neurons. The
39 mechanism of noise-induced hearing loss begins with outer and, to a lesser extent, inner hair cell loss
40 in the high-frequency base of the cochlea, followed by a progression of hair cell loss toward the low-
41 frequency apex of the cochlea [6-8]. Oxidative stress, metabolic exhaustion, ischemia and ionic
42 imbalance in the inner ear fluids play a central role in the pathophysiology of NIHL. Reactive oxygen
43 species and reactive nitrogen species participate in cellular mechanisms that underlie hair cell death
44 after noise exposure, and lead to sensorineural hearing loss [9-14].

45 Tinnitus is defined as the perception of sound without an external auditory stimulus.
46 Approximately 2% of the population in industrialized countries are reported to experience incessant
47 tinnitus [15]. Tinnitus may have audiological, somatic, or psychological bases [16-24]; risk factors for
48 tinnitus include hearing loss, exposure to loud noise, and increasing age [25-27]. Furthermore,
49 patients often report worsening of tinnitus with stress; therefore, workers subject to high job stress
50 may have an increased risk of tinnitus [28-30]. Hearing loss is the most common cause of tinnitus; in
51 patients with NIHL, rates of tinnitus range from 35% to 77% [31,32]. Occupational noise has a role in
52 contributing to development of tinnitus [33].

53 The effects of long-term occupational noise in patients suffering from chronic tinnitus have
54 rarely been studied, and limited information is available for specific occupation groups [34]. The aim
55 of this study was to analyze in a cohort of individuals with chronic tinnitus A) characteristics of
56 hearing loss, tinnitus, comorbidities, demographic variables and history of work-related noise
57 exposure and B) differences among individuals employed in occupations with high and low risk of
58 developing work-related NIHL.

59 **Materials and Methods**

60 In this study, we included 136 patients aged 26-84 years with chronic tinnitus (> 12 months) and
61 anamnestic history of having worked at least 10 years during the previous 20 years, presenting at the
62 Tinnitus Unit of the Sapienza State University Hospital Policlinico Umberto I in Rome, Italy, during
63 a 4-year period from January 2013 to January 2017.

64 Based on working history, patients were divided into two groups: patients with tinnitus and
65 history of employment in one of the professions associated with an increased exposure to
66 occupationally-acquired noise-induced hearing loss (HIGH-RISK, n=68) and patients with tinnitus
67 and history of employment in industries and occupations reported to have lower risks for hearing
68 impairment (LOW-RISK, n=68). Patients were included in the HIGH-RISK group if they had a history
69 of employment in one of the following professions: armed forces [35-42], carpenters [36,38,43],
70 manufacturing workers [5,34,35,43-46], drivers [5,34,38,43,47,48], miners [5,35,38,43,49,50], musicians
71 [38,51-53], railroaders [4,5,34,43,54,55], school teachers [5,34,43], and construction workers
72 [5,34,38,43,55-58]. Patients were included in the LOW-RISK group if they had a history of
73 employment in one of the following occupations: entrepreneurs, hospital workers, office workers,
74 professionals [4,5,29,59,60]. Exclusion criteria were history of prolonged treatment with ototoxic
75 drugs, middle or inner-ear disease (e.g., otosclerosis, chronic suppurative otitis media or
76 endolymphatic hydrops), retrocochlear disease (e.g., vestibular schwannoma), previous ear surgery,
77 psychiatric comorbidities.

78 Informed consent was obtained from each individual participant in the study. The study was
79 conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the
80 Ethics Committee of the Sapienza University, Policlinico Umberto I, Rome. Patients underwent
81 anamnestic interview and hearing evaluation through otoscopy, Pure Tone Audiometry (PTA) and
82 Acoustic Immittance (AI) test. PTA was measured at frequencies of 0.50, 1, 2, 4, and 8 kHz.

83 Detailed work and noise-exposure history data were collected including type of work and family
84 history for hearing loss and tinnitus. The presence of cardiovascular comorbidities such as diabetes,
85 heart disease, and hypertension was investigated.

86 Self-assessment questionnaires regarding tinnitus (Tinnitus Handicap Inventory – THI) [61],
87 hearing loss (Hearing Handicap Inventory – HHI) [62], and hyperacusis (Hyperacusis Questionnaire
88 – HQ [63,64]) were administered during the initial visit. Tinnitus characteristics including side
89 (unilateral, bilateral) and pitch from a predefined set of possibilities including “buzzing”, “whistle”,
90 “high-pitched”, “low-pitched” and “other”, were collected for each patient.

91 *Statistics*

92 Mean and standard deviation (SD) for numeric, and frequency and percentage for categorical
93 demographic characteristics such as sex, age, family history of hearing loss and comorbidities,
94 distribution of tinnitus characteristics and self-administered questionnaire results, and PTA

95 differences between high-risk and low-risk subjects was calculated. Chi-square test of association was
 96 used to analyze differences between the LOW-RISK and HIGH-RISK groups for demographic
 97 variables (age, sex) and tinnitus characteristics; p-values were reported. A multivariate binary logistic
 98 regression analysis was performed to investigate specific variables associated with higher degree of
 99 hearing loss in tinnitus patients according to demographic characteristics such as age and sex,
 100 comorbidities, family history for hearing loss, and self-administered questionnaire scores. The results
 101 of logistic regression were reported in odd ratio scale along with a 95% confidence interval and p-
 102 values. A p-value of 0.05 was used as the cutoff for statistical significance.

103 Results

104 *Demographics, family history and comorbidities*

105 The study included 136 patients: 86 males (63.2%) and 50 females (36.7%). Males were
 106 significantly more prevalent in the HIGH-RISK group (55/68, 80.88% $p < 0.001$). In the LOW-RISK
 107 group, 31/68 were males (45.59%) and 37/68 were females (54.41%) ($p < 0.001$).

108 Mean age was 55.1 years (range 26-84 years). Individuals in the HIGH-RISK group were older
 109 (56.6 years, range 31-81 years, $SD = 12.4$) compared to individuals in the LOW-RISK group (53.5 years,
 110 range 26-84 years, $SD = 13.5$) ($p = 0.08$).

111 Mean time of noise exposure was 18.4 years in the LOW-RISK group and 19.3 years in the HIGH-
 112 RISK group. No statistically significant difference was found between groups ($p = 0.72$).

113 Family history for hearing loss was found in 14/68 (20.6%) individuals in the HIGH-RISK group
 114 and in 9/68 (13.2%) in the LOW-RISK group; difference was not statistically significant ($p = 0.253$).

115 At least one comorbidity among diabetes, heart and vascular diseases and hypertension was
 116 found in 27/68 (39.7%) patients in the HIGH-RISK group and in 24/68 (35.3%) in the LOW-RISK group
 117 ($p = 0.60$); several patients presented more than one comorbidity. The most common comorbidity was
 118 hypertension, followed by heart and vascular diseases. Data are shown in *Table 1*.

119 *Table 1: Demographic Characteristics*

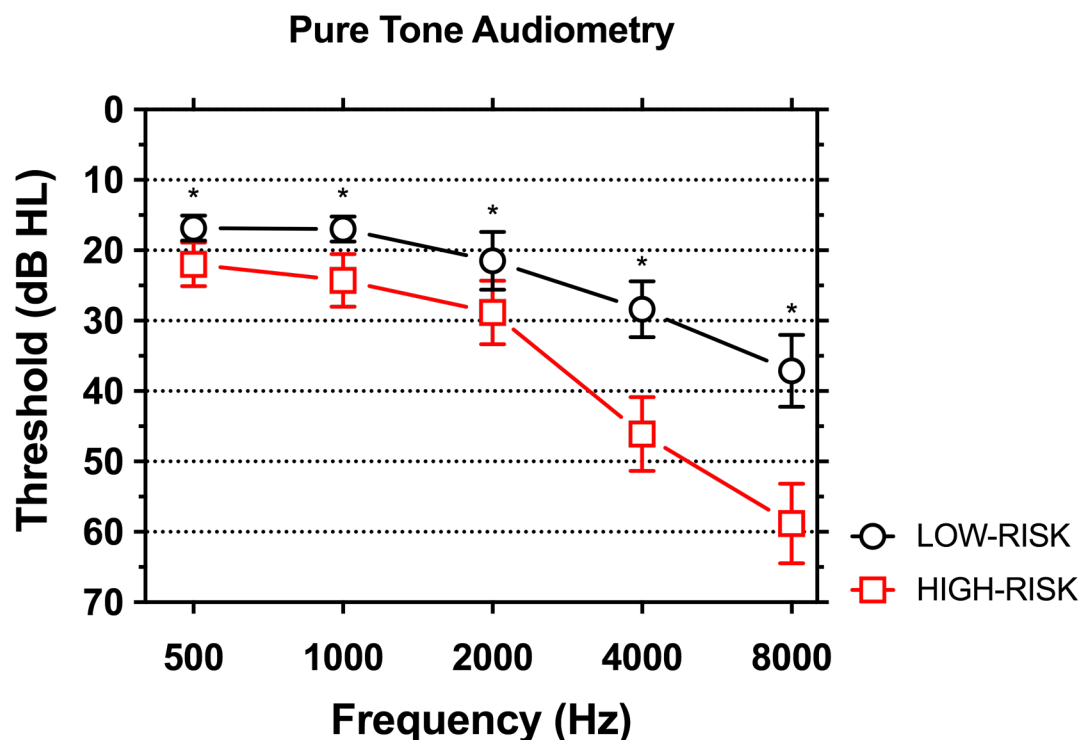
120 **Table 1:** Distribution of demographic characteristics between individuals with tinnitus in the HIGH-
 121 RISK and LOW-RISK groups. A significant prevalence of male gender was found in the HIGH-RISK
 122 group. No significant differences were found for age, time of noise exposure, family history of noise
 123 exposure, and cardiovascular comorbidities between the two groups

	LOW-RISK	HIGH-RISK	p-value
Age [mean (SD)]	53.5 (13.5)	56.6 (12.4)	0.08
Male [freq (%)]	37 (54.4)	55 (80.9)	0.001
Female [freq (%)]	31 (45.6)	13 (19.2)	0.001
Family history [freq (%)]			0.253
No Hearing Loss	59 (86.8)	54 (79.4)	
Hearing Loss	9 (13.2)	14 (20.6)	

Time of noise exposure in years [mean (SD)]	18.4 (8.1)	19.3 (6.7)	0.72
			0.60
Comorbidity [freq (%)]	44 (64.7)	41 (60.3)	
No comorbidity	24 (35.3)	27 (39.7)	
At least one comorbidity	7 (29.2)	5 (18.5)	
Heart Disease	4 (16.7)	3 (11.1)	
Diabetes	18 (75)	21 (77.8)	
Hypertension	4 (16.7)	6 (22.2)	
Vascular Diseases			

124 *Hearing Loss*

125 **Figure 1** shows PTA in subjects with high and low risk of work-related NIHL. As expected,
 126 hearing was significantly worse in individuals in the HIGH-RISK group, especially for the
 127 frequencies between 2000 and 8000 Hz.
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130 **Fig.1:** Pure Tone Audiometry in the HIGH-RISK and LOW-RISK groups. Means +/- 95 CI are shown.
 131 A statistically significant worse auditory threshold was found for individuals in the HIGH-RISK
 132 group. Asterisks indicate statistically significant differences.

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134 Frequency-specific hearing thresholds are shown in *Table 2*. In the HIGH-RISK group, mean PTA
 135 thresholds were 22 dB HL for 500 Hz, 24.3 for 1000 Hz, 28.8 for 2000 Hz, 46.1 for 4000 Hz and 58.8 dB
 136 HL for 8000 Hz. In the LOW-RISK group, thresholds were 16.8 dB HL for 500 Hz, 17.0 for 1000 Hz,
 137 21.5 for 2000 Hz, 28.4 for 4000 Hz and 37.1 dB HL for 8000 Hz. Mean PTA thresholds in the HIGH-
 138 RISK exceeded thresholds in the LOW-RISK group by 5.2 dB HL for 500 Hz, 7.3 dB for 1000 Hz, 7.3
 139 dB for 2000 Hz, 17.7 dB for 4000 Hz and 21.7 dB for 8000 Hz. Differences were statistically significant
 140 for each frequency.

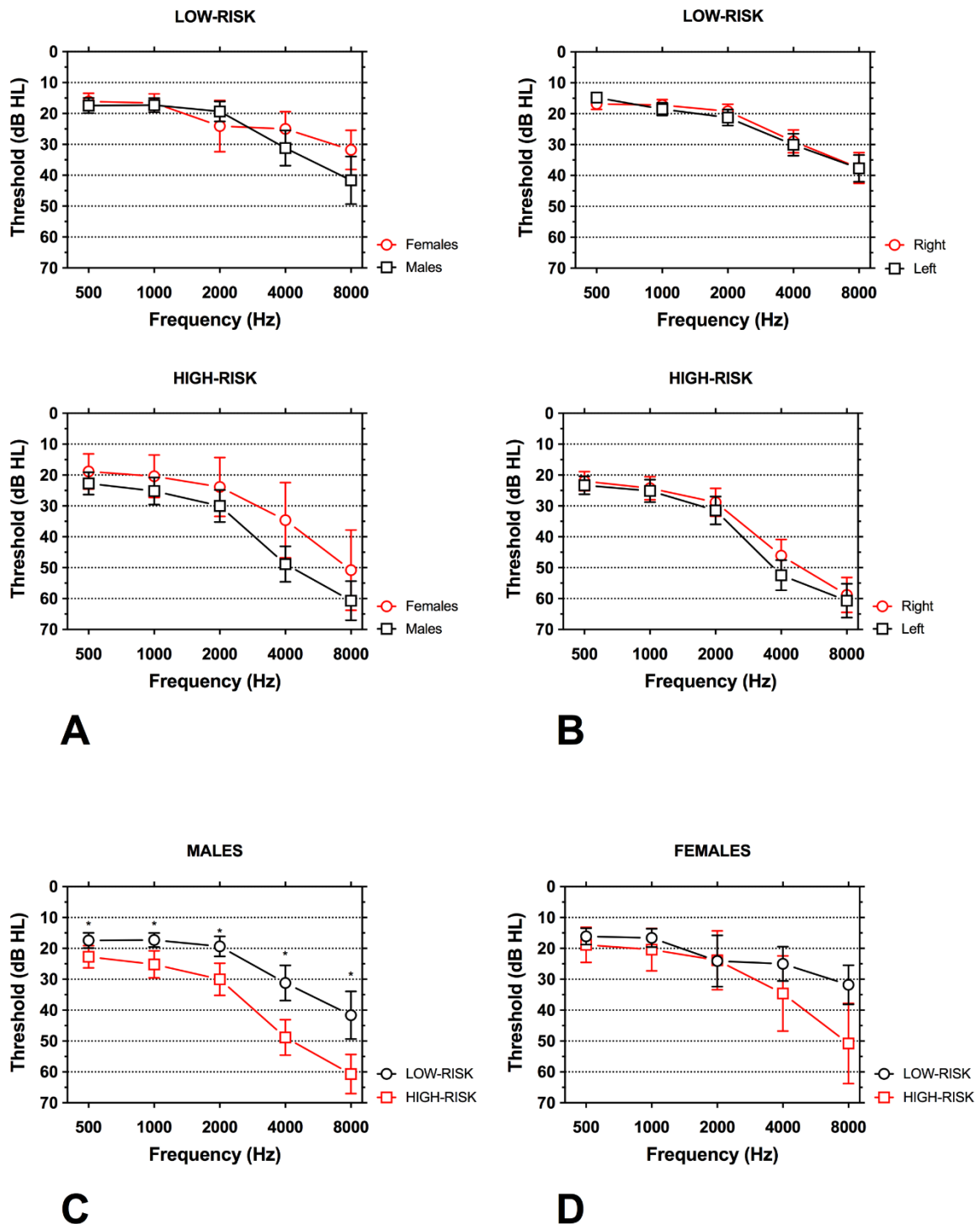
141 Table 2: Pure Tone Audiometry

142 **Table 2:** Pure Tone Audiometry analysis in the HIGH-RISK and LOW-RISK groups. Significant
 143 differences between groups were found for all frequencies for average, right and left ear thresholds.

PTA	LOW-RISK	HIGH-RISK	p-value
<i>Average Right/Left Ear [mean (SD)]</i>			
500 Hz	16.8 (7.2)	22.0 (12.6)	0.002
1000 Hz	17.0 (7.2)	24.3 (15.3)	<0.001
2000 Hz	21.5 (16.8)	28.8 (18.4)	0.008
4000 Hz	28.4 (16.3)	46.1 (21.4)	<0.001
8000 Hz	37.1 (20.9)	58.8 (23.2)	<0.001
<i>Right Ear [mean (SD)]</i>			
500 Hz	16.8 (7.2)	22.0 (12.6)	0.004
1000 Hz	17.2 (7.2)	24.3 (15.3)	<0.001
2000 Hz	19.2 (9.2)	28.8 (18.4)	<0.001
4000 Hz	29.0 (15.1)	46.1 (21.4)	<0.001
8000 Hz	37.6 (20.3)	58.8 (23.1)	<0.001
<i>Left Ear [mean (SD)]</i>			
500 Hz	16.8 (7.2)	23.3 (11.8)	<0.001
1000 Hz	17.0 (7.2)	25.1 (14.9)	<0.001
2000 Hz	18.8 (9.5)	31.5 (18.4)	<0.001
4000 Hz	29.0 (15.9)	52.4 (19.9)	<0.001
8000 Hz	38.2 (20.3)	60.7 (22.3)	<0.001

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145 *Figure 2* shows average PTA for males and females and right and left ear in both groups. No
 146 statistically significant differences between gender ($p=0.086$) and side ($p=0.64$) were found within the
 147 same groups; however, the left ear showed poorer mean auditory thresholds for higher frequencies
 148 in the HIGH-RISK group compared to the right ear. Although worse hearing, especially for high
 149 frequencies, was found in the HIGH-RISK group compared to the LOW-RISK group for both males
 150 and females, a larger and statistically significant difference was found for males ($p<0.001$), not for
 151 females ($p=0.12$).



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Fig. 2: Pure tone audiogram (PTA) in the HIGH-RISK and LOW-RISK groups showing differences between males and females and side. Means +/- 95 CI are shown. A: Worse hearing thresholds were found in males; however, difference within the same group was not significant ($p=0.086$). B: No significant differences were found in hearing threshold between the right and the left ear although thresholds for high frequencies in the left ear were worse compared to the right ear ($p=0.64$). C: PTA for males; individuals in the HIGH-RISK group had a significantly worse hearing threshold than individuals in the LOW-RISK group ($p<0.001$). D: PTA for females; although worse hearing for high frequencies was found in patients in the HIGH-RISK group, difference was not statistically significant ($p=0.12$).

162 *Tinnitus Characteristics and Self-Administered Questionnaires Scores*

163 Average duration of tinnitus at the time of first admission to our center was 10.9 years for the
 164 HIGH-RISK group and 9.2 years in the LOW-RISK group. Difference was not statistically significant
 165 ($p=0.726$). Tinnitus was bilateral in 46/68 (67.6%) patients in the HIGH-RISK group and in 36/68
 166 (52.9%) in the LOW-RISK group ($p=0.05$). Unilateral tinnitus was significantly more prevalent in the
 167 left ear; left-sided tinnitus was found in 18/22 (81.8%) individuals in the HIGH-RISK group and in
 168 19/32 (59.3%) in the LOW-RISK group ($p=0.05$). Tinnitus was described as “Whistle” in 46/136 (33.8%)
 169 patients, “Buzzing” in 30/136 (22.1%), “High-Pitched” in 26/136 (19.1%), “Low-Pitched” in 15/136
 170 (11%), and “Other” in 19/136 (13.9%) ($p=0.06$). “Buzzing” and “High-Pitched” tinnitus sounds were
 171 more common among HIGH-RISK individuals, “Whistle” was more common among patients in the
 172 LOW-RISK group.

173 Mean THI score was 33.1 in the HIGH-RISK group and 30.6 in the LOW-RISK group; mean HHI
 174 score was 18.8 in the HIGH-RISK group and 9.4 in the LOW-RISK group; HQ score was 13.4 in the
 175 HIGH-RISK group versus 11.8 in the LOW-RISK group. Difference was not significant for THI
 176 ($p=0.22$) and HQ ($p=0.12$); a statistically significant difference was found for HHI ($p<0.001$). Table 3
 177 shows detailed data for tinnitus characteristics and questionnaire scores for the HIGH-RISK and
 178 LOW-RISK groups.

179 *Table 3: Tinnitus Characteristics and Questionnaire Scores*

180 **Table 3:** Distribution of tinnitus characteristics and questionnaire scores in the HIGH-RISK and LOW-
 181 RISK groups. A significantly higher number of patients in the HIGH-RISK group had bilateral
 182 tinnitus, followed by unilateral tinnitus in the left ear. “Buzzing” and “High-Pitched” tinnitus sounds
 183 were more common among HIGH-RISK individuals, “Whistle” was more common among
 184 individuals in the LOW-RISK group. Patients in the HIGH-RISK group scored significantly worse at
 185 HHI questionnaire compared to individuals in the LOW-RISK group; no significant differences were
 186 seen for THI and HQ.

	LOW-RISK	HIGH-RISK	p-value
<i>Tinnitus side [freq (%)]</i>			
Left	19 (27.9)	18 (26.5)	0.05
Right	13 (19.1)	4 (5.9)	
Bilateral	36 (52.9)	46 (67.6)	
<i>Tinnitus Sound [freq (%)]</i>			
Buzzing	11 (16.2)	19 (27.9)	0.06
High-pitched	9 (13.2)	17 (25.0)	
Low-pitched	7 (10.3)	8 (11.8)	
Other	12 (17.6)	7 (10.3)	
Whistle	29 (42.6)	17 (25.0)	
<i>Questionnaire scores [mean (SD)]</i>			
THI	30.6 (18.1)	33.1 (18.8)	0.22
HHI	9.4 (13.4)	18.8 (20.3)	<0.001
HQ	11.8 (7.9)	13.4 (8.3)	0.12

187 *Differences among occupations*

188 Differences in demographics, tinnitus onset and laterality, self-administered questionnaire
189 responses, and hearing loss were found in relation to the different occupations reported by patients.

190 In the HIGH-RISK group, female gender was more prevalent among manufacturing workers
191 and school teachers, while the male gender prevailed among all other occupations. Tinnitus was
192 mostly bilateral in school teachers (91.6%), miners (75%), construction workers (73.3%) and armed
193 forces (72.7%); unilateral in railroaders (66.6%) and musicians (100%). Worst THI scores were found
194 for school teachers (50.5), best among musicians (21) and armed forces (24.1). Manufacturing workers
195 (23.5) and construction workers (23.4) scored worst at HHI. Surprisingly, railroaders had the best
196 HHI score (2.6). Worst hearing thresholds were found in miners (47.5 dB for 0.5-2 kHz and 78.1 dB
197 for 4-8 kHz) and railroaders (31.6 dB for 0.5-2 kHz and 65.8 dB for 4-8 kHz). Musicians had the best
198 hearing threshold among individuals in the HIGH-RISK group (11.6 dB for 0.5-2 kHz and 33.7 dB for
199 4-8 kHz).

200 In the LOW-RISK group, bilateral tinnitus was more prevalent among entrepreneurs (63.6%)
201 and office workers (54.2%), unilateral among hospital workers (75%). Worst THI score was found
202 among office workers (33.7); worst HHI score among entrepreneurs (13.18). Worst hearing thresholds
203 were found for professionals (23.2 dB for 0.5-2 kHz and 40.9 dB for 4-8 kHz); hospital workers had
204 the best hearing among individuals in the LOW-RISK group (13.3 dB for 0.5-2 kHz and 15 dB for 4-8
205 kHz). Data sorted by type of work are shown in *Table 4*.

206 *Table 4: Demographics and Audiological Characteristics Sorted by Occupation*

207 **Table 4.** Demographics, Tinnitus characteristics, Questionnaire scores, and Hearing Loss metrics
208 among job types. A) Upper part of the table: jobs of patients in the HIGH-RISK group; B) Lower part
209 of the table: jobs of individuals in the LOW-RISK group.

Occupation	Male (%)	Age (y)	Work (y)	Bilateral Tin (%)	Tin onset (y)	THI	HHI	HQ	PTA (0.5-2 kHz)	PTA (4-8 kHz)
<i>HIGH-RISK</i>										
Armed Forces (n=11)	100	54.8	19.9	72.7	9.8	24.1	11	9.7	16.8	44.5
Carpenters (n=8)	100	54.2	14.7	62.5	9.7	29.7	21.7	15.1	24.7	52
Manufacturing Workers (n=4)	0	44.5	11.2	50	8	50.5	23.5	16.2	25.4	46.2
Drivers (n=9)	100	61.1	16.5	55.5	12.6	29.1	17.1	10.6	31.2	60
Miners (n=4)	100	55	20.7	75	8.5	38	47	14.2	47.5	78.1
Musicians (n=2)	100	47.5	13	0	6.5	21	30	22	11.6	33.7
Railroaders (n=3)	100	61.3	21	33.3	15.3	42	2.6	8	31.6	65.8
School Teachers (n=12)	33.3	63.7	21	91.6	16.6	33.6	15.1	17.4	22.3	45.6

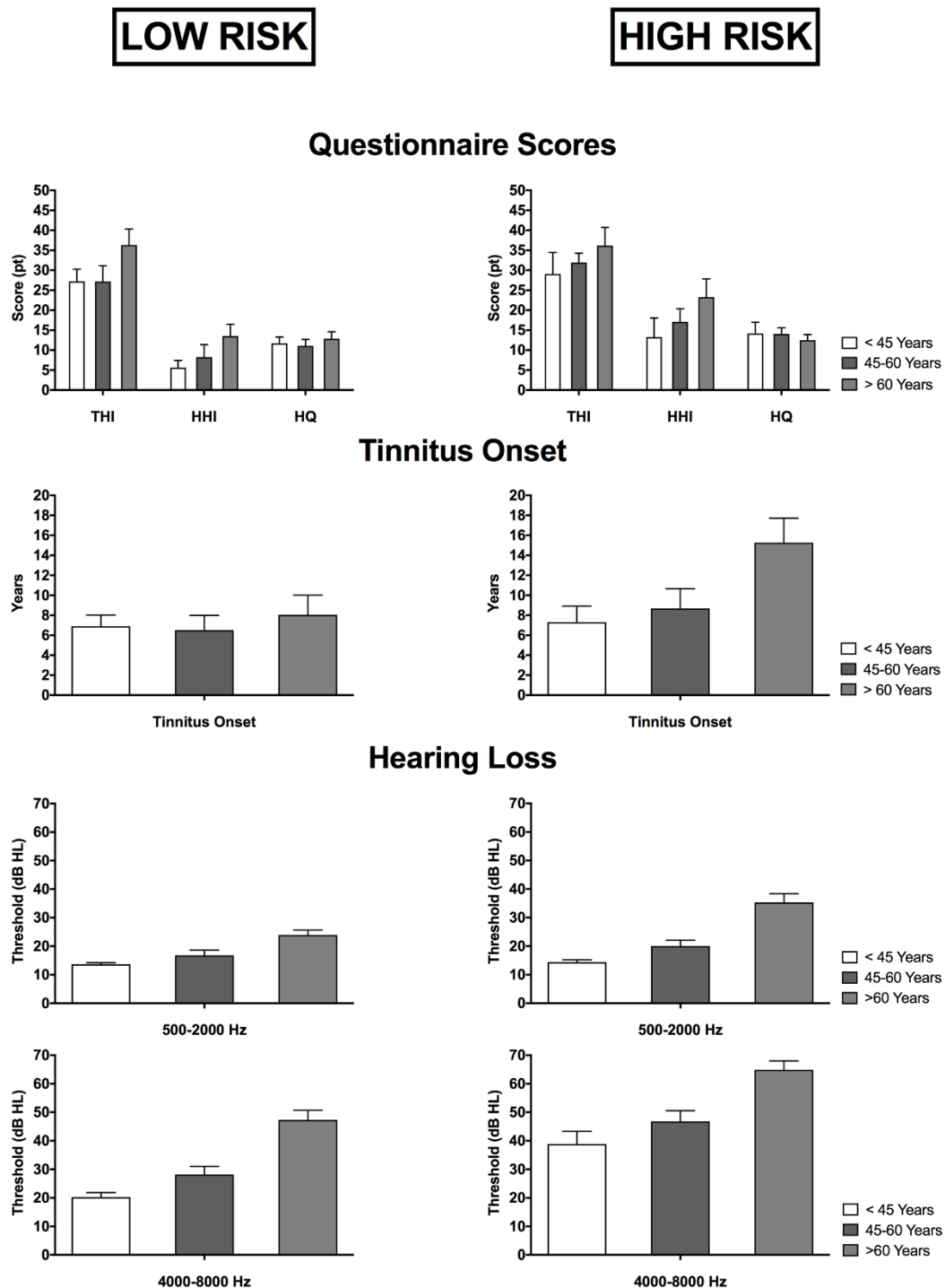
Construction Workers (n=15)	93.3	54.8	23	73.3	8.8	37	23.4	12.6	23.8	54.5
<i>LOW-RISK</i>										
Entrepreneurs (n=11)	81.8	48.7	18.5	63.6	11.6	28	13.1	13.8	16.1	31.8
Hospital Workers (n=4)	50	38.7	16.7	25	6.2	21	1.5	10	13.3	15
Office Workers (n=35)	51.4	53.7	19.2	54.2	6.6	33.7	8.9	11.1	17.2	31.4
Professionals (n=18)	44.4	59.5	21.8	33.7	9.5	27.8	11.9	9.6	23.2	40.9

210 *The role of age in relation to tinnitus, hearing characteristics, and questionnaire scores*

211 The role of age in relation to tinnitus onset, hearing threshold, and THI, HHI and HQ scores was
 212 evaluated for both groups. In the LOW-RISK group, younger patients (<45 years) showed
 213 significantly lower THI and HHI scores ($p=0.001$) and PTA for the 0.5-2 kHz ($p=0.05$) and the 4-8 kHz
 214 frequency range ($p<0.001$) compared to older subjects (>60 years). No significant differences were
 215 found for HQ score and tinnitus length. In the HIGH-RISK group, compared to participants older
 216 than 60 years, patients younger than 45 years showed a significant lower length of tinnitus ($p=0.02$),
 217 PTA for the 0.5-2 kHz ($p<0.001$) and the 4-8 kHz frequency range ($p<0.001$). No significant differences
 218 were found for THI, HHI and HQ scores (Figure 3).

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Role of Age in Hearing, Tinnitus and Questionnaires



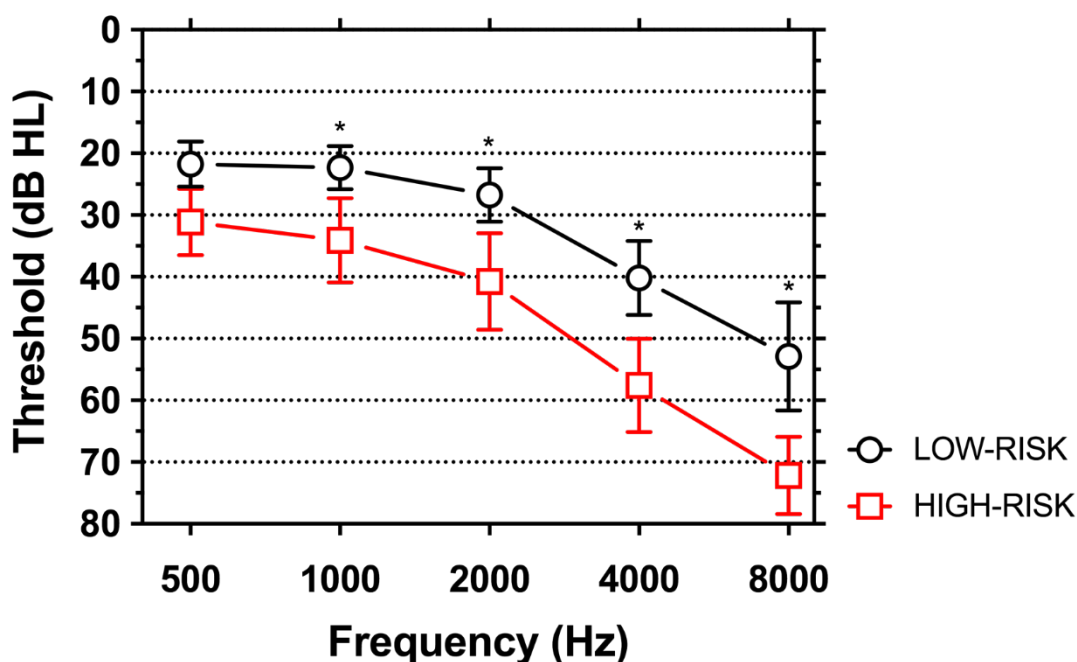
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221 **Fig.3:** Relationship between age of the patient and hearing loss (PTA), tinnitus onset, and self-
 222 administered questionnaire scores (HHI, THI, HQ) sorted by HIGH-RISK and LOW-RISK groups.

223 When analyzing hearing loss for single frequencies, older (> 60 years) individuals showed a
 224 significantly worse hearing in the HIGH-RISK group compared to the LOW-RISK group for all
 225 frequencies above 500 Hz ($p < 0.001$) (Figure 4).

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Pure Tone Audiometry for older patients (>60 years)



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Fig.4: Comparison of Pure Tone Audiometry thresholds in subjects older than 60 years in the HIGH-RISK and LOW-RISK groups. Significantly worse hearing was found in individuals in the HIGH-RISK group for all frequencies above 500 Hz ($p < 0.001$). Asterisks indicate statistically significant differences.

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A multivariate binary logistic regression analysis was used to investigate specific variables associated with higher degree of hearing loss in tinnitus patients according to demographic characteristics such as age and sex, comorbidities, family history for hearing loss, and HHI self-administered questionnaire score. Analysis indicated that patients with a higher degree of hearing loss: A) were 3.54 times more probable to come from male populations; B) were 1.7 times more likely to have family history of hearing loss; and C) were 1.2 times more likely to have at least one comorbidity (Table 5).

240 *Table 5: Binary Logistic Regression Analysis*

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Table 5. Binary logistic regression analysis for demographic characteristics such as age and sex, comorbidities, family history for hearing loss, and HHI questionnaire score in patients with a higher degree of hearing loss. Statistically significant results are shown in bold.

	Odds ratio	Confidence interval	p-value
Age	1.02	0.99-1.05	0.16
Male	3.54	1.64-7.66	0.001
Family history	1.70	0.68-4.24	0.26
Comorbidity	1.20	0.6-2.42	0.60
HHI	1.03	1.01-1.06	0.003

244

245 **Discussion**

246 The association between hearing loss, tinnitus and occupation has been previously
247 demonstrated [34,43,65-71]. The aim of this study was to survey patients with chronic tinnitus with
248 and without history of long-term work-related noise exposure, comparing demographic variables,
249 tinnitus and hearing loss characteristics, and self-administered questionnaire responses for tinnitus,
250 hearing loss and hyperacusis. Significant differences were found between groups for gender,
251 auditory threshold, and tinnitus laterality. Individuals employed in jobs with high-risk of noise
252 exposure were mostly males and had a poorer hearing threshold, more evident in the left ear
253 although difference with the right ear was not significant; tinnitus was mostly bilateral, followed by
254 left-sided, described as buzzing or high-pitched. Correlation between age, length of tinnitus and
255 worse hearing was found. Patients with a higher degree of hearing loss were mostly males and were
256 likelier to have a family history of hearing loss and at least one cardiovascular comorbidity.

257 *Main differences for gender, age, family history and comorbidities*

258 The main demographic difference found among our groups was for the male gender. The larger
259 prevalence of males found between individuals in the HIGH-RISK group compared to the LOW-
260 RISK group (80.8% vs 45.6%) is in accordance with other studies that show that men are mostly
261 involved in jobs with elevated noise exposure [68,72,73]. Within different professions, females were
262 more prevalent among school teachers and manufacturing workers in the HIGH-RISK group and
263 among hospital workers and professionals in the LOW-RISK group.

264 Mean age did not differ between groups; however, a significant difference was found between
265 patients younger than 45 years and older than 60 years for auditory thresholds and length of tinnitus.
266 Older individuals had worse hearing thresholds and experienced tinnitus for a longer time. This is
267 consistent with literature that reports greater incidence of tinnitus and hearing loss with age [24-
268 26,68,69,74]. When comparing older (> 60-year-old) individuals in the two groups, significantly worse
269 hearing was found in patients in the HIGH-RISK group, suggesting that such a trend is accelerated
270 in patients exposed to noise in general and, more specifically, to noisy working environments [68,69].

271 Although the degree of NIHL has been shown to be significantly influenced by environmental
272 factors, strong evidence has been gathered through various animal and human studies about the role
273 of genetic predisposition [75-77]. In our study, family history for hearing loss did not seem to be
274 statistically different between groups. However, a larger percentage of patients in the HIGH-RISK
275 group reported a positive history (20.6%) compared to the LOW-RISK group (13.2%). Furthermore,
276 by binary logistic regression analysis, patients with a higher degree of hearing loss were 1.7 times
277 more likely to have a family history of hearing loss.

278 The presence of cardiovascular comorbidities in individuals with NIHL has been previously
279 described [78-81]. In our sample, 27/68 (39.7%) patients in the HIGH-RISK group had at least one
280 comorbidity, predominantly hypertension and vascular diseases. Although we could not find a
281 statistical difference with patients in the LOW-RISK group, our findings are in accordance with
282 literature that shows a well-established relationship between hearing loss, diabetes and heart disease
283 [82]. Diabetes represents a risk factor for early-onset NIHL, as high blood sugar may cause reduction
284 in caliber of blood vessels in the inner ear and especially in the stria vascularis [83-85]. Similarly,
285 cardiovascular diseases have been shown to increase the risk of hearing loss [86]. In addition,
286 exposure to loud noise has been shown to have non-auditory long-term effects that may include
287 elevated blood pressure, loss of sleep, and increased heart rate [82,87].

288 *Characteristics of hearing loss in subjects at high- and low-risk for work-related hearing loss*

289 Among individuals with chronic tinnitus, hearing thresholds were significantly worse in
290 patients in the HIGH-RISK group compared to those in the LOW-RISK group. This finding is in
291 accordance with the literature [3-5,34-39,41-45,47-51,54-58,68,70,74,88]. Our results showed worse –

292 although not significant - hearing threshold for high frequencies in the left ear compared to the right
293 among individuals in the HIGH-RISK group; no side difference was found in the LOW-RISK group.
294 Occupational noise was demonstrated to induce asymmetric hearing loss with higher impact on the
295 left side compared to the right [70,88], with an incidence between 4.7% and 36% [70]. Asymmetries
296 are usually inferior to 5 dB and tend to increase at higher frequencies [89]. Such higher vulnerability
297 of the left ear could be attributed to ambient exogenous noise-exposure factors, such as the
298 “handedness” of noise source for different occupations [70], or by endogenous factors such as
299 neuroanatomic differences between the left and right parts of the auditory system, with involvement
300 of the protective role of the efferent pathways to cochlea [69]. Tinnitus was also reported to be more
301 frequent in the left ear than the right ear [70,72].

302 One possible explanation for this phenomenon is the different shielding of the right ear from
303 noise in specific occupations. An example of a work environment resulting in asymmetrical noise
304 exposure are tractor drivers, in which the left ear is more frequently affected than the right ear, as
305 these operators monitor equipment mounted on the rear side looking over their right shoulder and
306 therefore exposing their left ear to the noise while their right ear is shielded by head shadow. The
307 acoustic shielding of the head is also usually found in right-handed shooters, that have a more severe
308 hearing loss in the left ear. The handedness of the subject could thus be of relevance; however, studies
309 assessing the impact of handedness on hearing loss showed no correlation between the ear with the
310 asymmetry and the individual’s handedness [88]. To date, the reasons for asymmetric hearing loss
311 following noise exposure are still unclear and need further research.

312 *Tinnitus characteristics: laterality, pitch, annoyance*

313 The main difference in tinnitus characteristics among individuals in the HIGH-RISK and LOW-
314 RISK groups was laterality. A significantly higher number of individuals in the HIGH-RISK group
315 had bilateral tinnitus. Among patients with unilateral tinnitus, a strong prevalence of left ear tinnitus
316 was found in patients in the HIGH-RISK group (81.8% vs 59.3%). Our findings are in accordance with
317 other studies [32,68-70,88] and consistent with the auditory asymmetry generally documented in
318 NIHL [69,70,72,88,89] and in our study.

319 Consistent with findings in a recent paper by Flores [68], no association between pitch of tinnitus
320 and frequency of hearing loss could be found in our sample. However, our results are in
321 disagreement with those by Schecklmann, who analyzed the relationship between audiometric slope
322 and tinnitus pitch in 286 patients and reported that the pitch of tinnitus was associated with the
323 frequency of the greatest hearing loss [73]. Our relatively small cohort could explain the missed
324 statistical significance for our data.

325 No significant differences were found for mean THI questionnaire scores between our groups,
326 in contrast to other authors who showed a higher tinnitus discomfort in individuals with NIHL
327 [69,90]. When looking at THI in specific working categories, a direct relationship with hearing
328 threshold was found for miners and railroaders, two categories in which patients reported poor
329 hearing thresholds and relatively elevated THI scores. However, the worst THI scores were found
330 among manufacturing workers, a category of workers that showed limited hearing loss in our study.
331 This may be due to non-auditory elements, such as the psychological factors, that affect the self-
332 perception of the disorders. Higher tinnitus loudness, discomfort and annoyance in this category
333 could be therefore explained by the involvement of emotion-related neural circuits [91,92].

334 *Study limitations*

335 This is one of the few studies on work-related noise exposure to include only individuals with
336 chronic tinnitus and a long working history. Accurate audiological and tinnitus evaluation was
337 uniformly performed among groups, although it was limited to PTA and did not investigate outer
338 hair cell functions with otoacoustic emissions. Acuphenometry for pitch and loudness of tinnitus was
339 not performed; pitch was investigated through anamnestic interview; psychometric scores were used
340 to assess the degree of tinnitus severity instead of investigating its psychoacoustic characteristics.
341 Studies report that mood disorder comorbidity among individuals with tinnitus can be as high as

342 60% to 80% and can lead to increases in measures of tinnitus annoyance [93,94]. Therefore, extra-
343 auditory characteristics must be considered when evaluating tinnitus annoyance and its relationship
344 to hearing loss.

345 A limitation of this study is the lack of information about the loudness of noise exposure and
346 about the degree to which workplace prophylaxis might have been used to mitigate the work-related
347 hazard for individuals included in the study. However, assignment to the HIGH-RISK or LOW-RISK
348 groups was done according to extensive evidence reported in large demographical studies
349 [5,34,38,43] and recommended by the US National Institute for Occupational Safety and Health
350 (NIOSH).

351 Hearing loss in the range of 10-16 kHz was not investigated in the present study. Such high-
352 frequency hearing loss can be found in many individuals above the age of 40 and is common in noise-
353 exposed subjects [8,9]. Hearing loss above the clinical range has been studied with high-frequency
354 audiometry in occupational-noise-exposed individuals. High-frequency hearing loss has been
355 suggested as an early indicator of NIHL and high-frequency audiometry has been proposed for
356 assessing susceptibility to noise damage [95-97].

357 The relatively small size of our study cohort did not allow a uniform distribution of individuals
358 among the different job categories. A large heterogeneity of noise exposure levels and timing of
359 exposure can be found in our sample and may have biased results. A larger sample size may have
360 improved the significance of our data, and allowed us to examine a larger number of occupations.
361 Also, although no significant differences for length of noise exposure between groups were found,
362 correlation between time of occupational noise exposure and audiological and tinnitus characteristics
363 in exposed subjects was not performed in our sample and could be further explored in future studies.

364 No historical audiological data were collected for patients, preventing us from differentiating
365 hearing losses due to noise exposure, ototoxic agents, or a combination of exposures, and therefore
366 to correlate the degree of hearing loss found in our study exclusively with work-related noise
367 exposure.

368 Conclusions

369 Our study shows some differences in individuals with tinnitus and a history of a profession
370 associated with an increased exposure to occupationally-acquired noise-induced hearing loss
371 compared to those who had no such history. Individuals employed in jobs at high risk for NIHL were
372 mostly males and had a poorer hearing threshold, more evident in the left ear; tinnitus was mostly
373 bilateral, followed by left-sided, described as buzzing or high-pitched. Correlation between age,
374 length of tinnitus and worse hearing was found. Patients with a higher degree of hearing loss were
375 mostly males and were more likely to have family history of hearing loss and at least one
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381 conceived the experiments, Giancarlo Altissimi and Pasquale Ricci analyzed the data, Rosaria Turchetta
382 performed the experiments, Marco de Vincentiis supervised the work and provided experimental insights,
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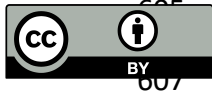
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