Audiological assessment in patients with chronic obstructive pulmonary disease
Aya M. Abdel Dayem, Iman H. Galala, Fathy Naeem, Maha A. Hassan

Background Chronic obstructive pulmonary disease (COPD), as a multisystemic disease, might have an impact on the auditory function. Thus, this study was designed for the audiological assessment of COPD patients to investigate the effect of smoking, and to further assess its possible correlation with the severity of COPD.

Patients and methods This prospective case–control study was conducted on 100 male patients with COPD with a mean age of 52.8±6.8 years. In addition, 25 healthy nonsmoker male participants with a mean age of 45.5±6.75 years were enrolled as the control group. For all COPD patients and controls, tympanometry and pure-tone audiometry at frequencies 250–8000 Hz were performed by an experienced audiologist.

Results Tympanometry type C was observed in the right ear of 30 COPD patients and in the left ear of 28 COPD patients. All low and high frequency tone audiometry differed significantly between COPD patients and controls (P<0.001), and the cutoff for changes in auditory function was 15 dB at both low and high frequency tones with 96% sensitivity and 100% specificity. Audiometry and tympanometry in COPD patients were not affected by either the smoking status or the type of smoking (P>0.05). Both low and high frequency tone audiometry correlated significantly and inversely with partial pressure of oxygen and forced expiratory volume in the first second, whereas the annual COPD exacerbations correlated significantly and directly.

Conclusion Changes in auditory function but not hearing loss is common in COPD and such audiological changes were not affected by smoking but correlates with the degree of airway obstruction and hypoxia as well as the rate of annual COPD exacerbation.

Introduction Chronic obstructive pulmonary disease (COPD) is a multisystemic disease that often coexists with comorbidities that may have a significant impact on prognosis [1–8]. Some of these comorbidities arise independently of COPD, whereas others may be causally related, either with shared risk factors or by one disease increasing the risk or compounding the severity of the other [9]. Although many risk factors contribute to the development of COPD, cigarette smoking is still considered the most well-studied COPD risk factor [10]. Several studies reported the significant effect of smoking on hearing loss [11,12]. In a previous research, the impact of chronic hypoxemia secondary to COPD on the auditory function of these patients was investigated. The results showed a statistically significant difference for all auditory measures between patients with COPD and controls, but in general hearing impairment to date was not shown to be clinically relevant in patients with COPD [13,14]. Further, in stable patients with COPD and mild-to-moderate airflow obstruction, subclinical abnormalities of brainstem auditory evoked potentials have been observed [15].

In view of the above, this study was designed for the audiological assessment of patients with COPD in an attempt to investigate the effect of smoking on hearing, and to further assess the possible correlation between hearing impairment found with the severity of COPD.

Patients and methods Study design and included patients This prospective case–control study included 100 randomly selected COPD male patients selected from the outpatient clinic or inpatient admitted in the Chest Department at Ain Shams University Hospitals from June 2015 to February 2016. COPD was diagnosed according to the guidelines of the Global Initiative for Chronic Obstructive Lung Diseases [16]. In addition, 25 age-matched and sex-matched healthy nonsmoker male participants were enrolled in the study as the control group. Participants with a history of hearing loss, mental
impairment, intake of ototoxic drugs, diabetes mellitus, hypertension, frequent ear infection, ear surgery, familial deafness, and occupational exposure to noise were excluded from the study. All participants were clinically stable at the time of testing. The study was approved by the institutional ethical committee. Verbal consent was obtained from all included patients.

For all patients, the following were carried out: detailed medical history taking, thorough clinical examination, plain chest radiography, routine laboratory investigations, arterial blood gases, and spirometry.

**Lung function**

Forced expiratory volume in the first second (FEV₁), forced vital capacity (FVC), FEV₁/FVC ratio, and forced expiratory flow over 25–75% part of FVC were measured using the spirometry system (Masterscreen 2001, version 4.5; Erich Jaeger GmbH, Germany). Readings were performed in triplicate, with the highest values recorded and expressed as a percentage of the predicted value according to the guidelines of the American Thoracic Society [17].

**Audiometry and tympanometry**

Audiometry and tympanometry were performed by an experienced audiologist. All included participants attended one hearing testing session in the audiology laboratory of Ain Shams University Hospitals. The audiologist, who was unaware of the smoking status of the study participant, performed an otoscopic examination. Pure-tone threshold audiometry was conducted in sound-isolated rooms or booths using a clinical audiometer in accordance with the Maximum Permissible Ambient Noise Levels for Audiometric Test Room [18]. Pure-tone audiometric air conduction testing is performed by presenting a pure tone (single frequency) to each ear through an earphone and the participant responding by pressing a button, raising hand, or saying 'yes' when stimuli were heard. Hearing thresholds were measured in each ear for the following frequencies: 250, 500, 1000, 2000, 4000, and 8000 Hz. Hearing threshold is defined as the lowest level in decibels at which a signal (tone) is heard 50% of the time according to standard clinical procedures [19]. Testing should begin with the better ear when identifiable, otherwise it is arbitrary. Test instructions were presented in the Arabic language.

The severity of the hearing loss (HL) was determined as follows: 25±35 dB, mild impairment; 40±60 dB, moderate impairment; and greater than 65 dB, severe impairment.

Impedance tympanometer was used to evaluate the function of the middle ear system by applying the tip of a probe to seal off the entrance to the external ear canal; the air pressure within the enclosed ear canal cavity is gently changed from +200 to -200 mmH₂O, and the change in sound pressure level of a probe tone is graphed to verify the mobility of the eardrum.

**Statistical analysis**

Parametric numerical data were expressed as mean±SD, whereas nonparametric numerical data were expressed as number and percentage. The χ²-test and/or Fisher exact test were applied to examine the comparison between two qualitative variables. The independent sample t-test was used to compare two groups as regards quantitative variables. One-way analysis of variance was used to compare more than two groups as regards quantitative variables. Receiver operating characteristic was plotted to identify the cutoff point for auditory changes. Spearman’s correlation test was used to rank different variables against each other positively or inversely. Linear regression analysis was used to find the relationship between dependent and independent variables. Statistical significance was set at P-value less than 0.05. Statistical analyses were performed utilizing statistical package for the social sciences software (SPSS for Windows, version 20.0; SPSS Inc., Chicago, Illinois, USA).

**Results**

This study included 100 male patients with COPD ranging in age from 35 to 60 years with a mean age of 52.66±6.84 years. The control group comprised 25 healthy nonsmoker male participants ranging in age from 40 to 59 years with a mean age of 45.5±6.75 years. In the COPD group, 40 patients were current smokers, 30 patients were ex-smokers, and the remaining 30 patients were non-smokers. On the basis of the severity of COPD, 66 (66%) patients had moderate COPD, 26 (26%) patients had severe COPD, and the remaining eight (8%) patients had very severe COPD. All low and high frequency tones of audiometry were significantly different between COPD and controls (P<0.001, Table 1).

Among COPD patients, tympanometry results showed type C (normal tympanic membrane mobility and negative middle ear pressure; consistent with Eustachian tube dysfunction) in the right ear of 30 patients and in the left ear of 28 patients (Table 2). In COPD patients, both audiometry and tympanometry of the right and the left ear did not differ statistically (P>0.05, Table 2).
The cutoff point for significant auditory changes in COPD was 15 dB at both low and high frequency tones with 96% sensitivity, 100% specificity, 100% positive predictive value, and 92.3% negative predictive value (Table 3 and Fig. 1).

The cutoff point for significant auditory changes in COPD was 15 dB at both low and high frequency tones with 96% sensitivity, 100% specificity, 100% positive predictive value, and 92.3% negative predictive value (Table 3 and Fig. 1).

Results of audiometry and tympanometry in COPD patients were not affected by either the smoking status or the type of smoking ($P > 0.05$, Tables 4 and 5).

Table 2 Comparison between right and left audiometry and tympanometry in chronic obstructive pulmonary disease patients

| Audiometry | Control ($N=25$) [mean±SD (range)] | COPD ($N=100$) [mean±SD (range)] | $P$-value |
|------------|-----------------------------------|----------------------------------|-----------|
| Low-frequency tone (Hz) | | | |
| 250 | 10.20±3.67 (5–15) | 29.40±7.26 (15–45) | 0.000 |
| 500 | 11.20±3.32 (5–15) | 29.08±8.74 (15–50) | 0.000 |
| 1000 | 12.40±2.93 (5–15) | 31.40±10.05 (15–70) | 0.000 |
| Low-frequency tones (250, 500, 1000) | 11.11±2.23 (6.67–15) | 29.96±7.77 (15–48.33) | <0.001 |
| High-frequency tone (Hz) | | | |
| 2000 | 13.00±2.50 (10–15) | 29.90±12.02 (15–70) | 0.000 |
| 4000 | 10.40±3.20 (5–15) | 42.60±12.67 (10–85) | 0.000 |
| 8000 | 11.40±3.39 (5–15) | 45.30±15.99 (10–95) | 0.000 |
| High-frequency tones (2000, 4000, 8000) | 11.67±2.14 (6.67–15) | 39.27±10.54 (15–75) | <0.001 |

COPD, chronic obstructive pulmonary disease.

Table 3 Predictive performance of audiogram in chronic obstructive pulmonary disease

| Cutoff point (dB) | AUC | Sensitivity | Specificity | PPV | NPV |
|------------------|-----|-------------|-------------|-----|-----|
| Low frequency    | >15 | 0.985       | 96          | 100 | 100 |
| High frequency   | >15 | 0.989       | 96          | 100 | 100 |

AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value.
Logistic regression showed that both low and high frequency tone audiometry correlated significantly and inversely with partial pressure of oxygen (PO2) on room air as well as FEV1, whereas the exacerbations of COPD per year correlated significantly and directly (Table 6 and Fig. 2).

### Discussion

On the basis of the above results, our study proved a significant difference in auditory measures but not hearing loss in COPD patients in comparison with normal controls. The cutoff point detected in our study for significant changes in auditory function in COPD was 15 dB at both low and high frequency tones with 96% sensitivity and 100% specificity. This cutoff point is lower than the lower limit for hearing loss identified in our study; thus, the audiological assessment of COPD patients in our study demonstrated changes that were far below the threshold limit for the occurrence of hearing loss. These results are in accordance with several reports documenting that hearing impairment was clinically irrelevant in patients with COPD [13,14,20].

Although smoking is regarded as the main risk factor for the development of COPD, our study

---

### Table 4 Comparison between smoking statuses in chronic obstructive pulmonary disease

| Variables                              | Current smoker (N=40) | Exsmoker (N=30) | Nonsmoker (N=30) | P-value |
|----------------------------------------|-----------------------|-----------------|------------------|--------|
| Age [mean±SD (range)] (years)          | 52.80±7.53 (35–60)    | 55.00±4.61 (47–60) | 50.13±7.28 (36–60) | 0.150 |
| BMI [mean±SD (range)]                  | 26.75±5.72 (17–35)    | 28.35±4.01 (22–35) | 29.4±4.75 (21–37) | 0.292 |
| Comorbidities [n (%)]                  |                       |                  |                  |        |
| No                                     | 28 (70.0)             | 28 (93.3)        | 24 (80.0)        | 0.233 |
| Yes                                    | 12 (30.0)             | 2 (6.7)          | 6 (20.0)         |        |
| FEV1/FVC [mean±SD (range)] (% predicted)| 47.90±16.04 (21–73) | 55.47±18.50 (16–77) | 64.07±15.36 (21–75) | 0.024 |
| Exacerbations/year [mean±SD (range)]  | 4.25±2.12 (1–8)       | 3.80±2.43 (1–8)  | 5.32±2.45 (1–8)  | 0.098 |
| PO2 on RA [mean±SD (range)] (mmHg)    | 59.55±16.03 (42–92)   | 64.53±18.57 (40–93) | 76.87±17.89 (44–98) | 0.018 |
| Low-frequency audiometry [mean±SD (range)] (Hz) | 31.42±8.06 (18.33–48.33) | 29.33±8.97 (18.33–45) | 28.64±6.12 (15–38.33) | 0.550 |
| High-frequency audiometry [mean±SD (range)] (Hz) | 39.25±11.91 (20–75) | 38.56±7.26 (21.67–53.33) | 40.00±11.92 (15–71.67) | 0.935 |

### Table 5 Comparison of types of smoking in chronic obstructive pulmonary disease

| Variables                              | Cigarette smoker (N=44) | Shisha smoker (N=26) | P-value |
|----------------------------------------|-------------------------|----------------------|--------|
| Audiometry low frequency [mean±SD (range)] (Hz) | 29.24±8.19 (18.33–45) | 32.69±8.62 (20–48.33) | 0.099 |
| Audiometry high frequency [mean±SD (range)] (Hz) | 38.11±8.79 (21.67–56.67) | 40.38±12.16 (20–75) | 0.690 |
| Tympanometry [n (%)]                  |                         |                      |        |
| Type A                                 | 28 (63.6)               | 16 (61.5)            | 0.240 |
| Type C                                 | 16 (36.4)               | 10 (38.5)            |        |

### Table 6 Correlation of audiometry and tympanometry with several variables in chronic obstructive pulmonary disease

| Variables                              | Low frequency | High frequency |
|----------------------------------------|---------------|----------------|
| Age                                    | 0.179         | 0.061          |
| Smoking index (packs/year)             | 0.279         | 0.176          |
| Duration of smoking                    | 0.132         | 0.036          |
| FEV1/FVC                               | -0.152        | -0.109         |
| FEV1                                   | -0.515        | -0.330         |
| Exacerbations/year                     | 0.507         | 0.369          |
| PO2 on RA                              | 0.631         | -0.468         |

FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; PO2, partial pressure of oxygen; RA, room air.
revealed that neither the smoking status nor the type of smoking affected the degree of impairment in auditory measures. On reviewing the literature for studies addressing the possible effect of smoking on hearing, the results were conflicting; some studies reported a significant association between smoking and increased risk for hearing loss [12,21–28], whereas other studies demonstrated no correlation between hearing loss and smoking [29,30].

Auditory changes correlated directly with the rate of COPD exacerbation/year where the increase in the number of these exacerbations significantly increased the degree of auditory changes. Both FEV$_1$ and PO$_2$ also correlated with auditory changes but in an indirect way, wherein the increase in airway obstruction and hypoxia had a significant effect on audiological measures. Several previous studies have documented that the transduction mechanism of the inner ear is highly dependent upon the cochlear oxygen supply, such that hypoxia locally will be accompanied by loss of sensitivity [31–33]. In another study, the results suggested poorer central auditory function in hypoxic patients than in normally oxygenated individuals [34]. One recent study showed a statistically significant difference for all audiological measures between the control group and a COPD subgroup – the presumptive hypoxic patients (partial oxygen tensions, PO$_2$, <75 mmHg). Furthermore, PO$_2$ correlated with the changes observed in all audiological measures [13]. Our results showed no correlation between the changes in audiological measures and several variables, including age, smoking index, and the duration of smoking. In contrast to our results, studies found a significant statistical association between hearing loss and the number of cigarettes smoked and the duration of smoking [11,21,23,24,35–37]. Other studies demonstrated a correlation between age and hearing loss [27,37]. It is worth mentioning that this study has some limitations: smoking was the only risk factor for COPD tested; the included COPD patients were all male, and thus a selection bias cannot be excluded; and the level of
hypoxia was not severe enough to test the possible effect of severe chronic hypoxia on the inner ear.

In conclusion, changes in auditory function but not hearing loss is common in COPD patients in comparison with normal controls and such audiological changes were not affected by smoking but correlates with the degree of airway obstruction and hypoxia as well as the rate of annual exacerbation of COPD.

Hopefully, this study might pave the way for large-scale studies investigating thoroughly the effect of various risk factors for COPD on auditory function in an attempt for early detection of any hearing impairment among COPD patients to further carry out a timely intervention for its correction.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References
1. Barnes PJ, Celli BR. Systemic manifestations and comorbidities of COPD. *Eur Respir J* 2009; 335:1165–1185.
2. Soriano JB, Visick GT, Muellerova H, Payvandi N, Hansell AL. Patterns of comorbidities in newly diagnosed COPD and asthma in primary care. *Chest* 2005; 128:2099–2107.
3. Mannino DM, Thom D, Swensen A, Holguin F. Prevalence and outcomes of diabetes, hypertension and cardiovascular disease in COPD. *Eur Respir J* 2008; 32:962–969.
4. Sin DD, Anthonisen NR, Soriano JB, Agusti AG. Mortality in COPD: Role of comorbidities. *Eur Respir J* 2006; 28:1245–1257.
5. Iversen KK, Kjærgaard J, Akkan D, Kober L, Torp-Pedersen C, Hassager C, et al. The prognostic importance of lung function in patients admitted with heart failure. *Eur J Heart Fail* 2010; 12:685–691.
6. Almagro P, Soriano JB, Cabrera FJ, Boixeda R, Alonso-Ortiz MB, Barreiro B, et al. Short- and medium-term prognosis in patients hospitalized for COPD exacerbation: the CODEX index. *Chest* 2014; 145:972–980.
7. Miller J, Edwards LD, Agusti A, Bakke P, Calverley PM, Celli B, et al. Comorbidity, systemic inflammation and outcomes in the ECLIPSE cohort. *Respir Med* 2013; 107:1376–1384.
8. Campo G, Napoli N, Serenelli C, Tekbald M, Ferrari R. Impact of a recent hospitalization on treatment and prognosis of ST-segment elevation myocardial infarction. *Int J Cardiol* 2013; 167:296–297.
9. Global Initiative for Chronic Obstructive Lung Diseases. *Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease, 2017*. Available at: http://www.goldcopd.com
10. Lamprecht B, McMunie MA, Vollmer WM, Gudmundsson G, Welle T, Nizankowska-Mogilnicka E, et al. COPD in never smokers: results from the population-based burden of obstructive lung disease study. *Chest* 2011; 139:752–763.
11. Kumar A, Gurali R, Singhal S, Hasan A, Khan A. The effect of smoking on the hearing status – a hospital based study. *J Clin Diagn Res* 2013; 7:210–214.
12. Sharabi Y, Reshef-Haran I, Burstein M, Eldad A. Cigarette smoking and hearing loss: lessons from the young adult periodic examinations in Israel (YAPEIS) database. *Int Med Assoc J 2002; 4:1118–1120.
13. el-Kady MA, Durrant JD, Tawfik S, Abdel-Ghany S, Moussa AM. Study of auditory function in patients with chronic obstructive pulmonary diseases. *Hear Res* 2006; 212:109–116.
14. Atis S, Ozge A, Sevim S. The brainstem auditory evoked potential abnormalities in severe chronic obstructive pulmonary disease. *Respirology* 2001; 6:225–229.
15. Gupta PP, Sood S, Areuja A, Agarwal D. Evaluation of brain stem auditory evoked potentials in stable patients with chronic obstructive pulmonary disease. *Ann Thorac Med* 2008; 3:128–134.
16. Global Initiative for Chronic Obstructive Lung Diseases. *Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease, 2015*. Available at: http://www.goldcopd.com. [Last accessed 2017 Jan 10].
17. Miller MR, Crapo R, Hankinson J, Brusasco V, Burgos F, Casaburi R, et al. ATS/ERS task force: standardisation of lung function testing. General considerations for lung function testing. *Eur Respir J* 2005; 26:153–161.
18. Frank T. ANSI update: maximum permissible ambient noise levels for audiometric test rooms. *Am J Audiol* 2000; 9:3–8.
19. American Speech Language Hearing Association. Guidelines for manual pure-tone audiometry. *Asta* 1978; 20:297–301.
20. Kameski G, Bendova J, Fink W, Sönichsen A, Spiegel W, Zehetmayer S. Does COPD have a clinically relevant impact on hearing loss? A retrospective matched cohort study with selection of patients diagnosed with COPD. *BMJ Open* 2015; 5:e008247.
21. Cruickshanks KJ, Tweed TS, Wiley TL, Klein BE, Klein R, Chappell R, et al. The 5-year progression and the progression of hearing loss: the epidemiology of the hearing loss study. *Arch Otolaryngol Head Neck Surg* 2003; 129:1041–1046.
22. Itoh A, Nakashima T, Arah H, Waki K, Tamakoshi A, Ohno Y. Smoking and drinking habits as the risk factors for hearing loss in the elderly: an epidemiological study on subjects who were undergoing routine health checks in Aichi, Japan. *Public Health* 2001; 115:192–196.
23. Uchida Y, Nakashima T, Ando F, Niino N, Shimokata H. Is there a relevant effect of noise and smoking on hearing? A population-based aging study. *Int J Audiol* 2005; 44:86–91.
24. Nakashima N, Okamoto M, Nakamura K, Suzuki K, Tatsuruta K. Cigarette smoking and the risk for hearing impairment: a longitudinal study in Japanese male office workers. *J Occup Environ Med* 2000; 42:1045–1049.
25. Drettnr B, Hedsbrand H, Klockhoff I, Svedberg A. The cardiovascular risk factors and hearing loss. A study on 1000 fifty-year-old men. *Acta Otolaryngol* 1975; 79:366–371.
26. Siegelbaum AB, Friedman GD, Addor K, Seltzer CC. The hearing loss in adults: the correlation with age, sex, exposure to loud noise, and cigarette smoking. *Arch Environ Health* 1974; 29:107–109.
27. Melgarejo Moreno PJ, Latorre Lopez JF, Fuentes Botargues A, Melgarejo Moreno C. Prevalence of age-related hearing loss in a primary care clinic. *Acta Otorrinolaringol Esp* 1996; 47:213–215.
28. Cruickshanks KJ, Klein R, Klein BE, Wiley TL, Nondahl DM, Tweed TS. Cigarette smoking and hearing loss: the epidemiology of hearing loss study. *JAMA* 1998; 279:1715–1719.
29. Gates GA, Cobb JL, D’Agostino RB, Wolf PA. The correlation of the hearing in the elderly to the presence of cardiovascular diseases and cardiovascular risk factors. *Arch Otolaryngol Head Neck Surg* 1993; 119:56–161.
30. Brant LJ, Gordon-Salant S, Pearson JD, Klein LL, Morrell CH, Metter EJ, et al. The risk factors which were related to the age-associated hearing loss in speech frequencies. *J Am Acad Audiol* 1996; 7:152–160.
31. Lawrence M, Nuttall AL, Burgio PA. Cochlear potentials and oxygen in hypoxia. *Ann Otol Rhinol Laryngol* 1975; 84:499–512.
32. Gafni M, Sohmer H. Intermediate endocochlear potential levels induced by hypoxia. *Acta Otolaryngol (Stockh)* 1976; 82:354–358.
33. Sohmer H, Freeman S, Gafni M, Goiten K. The depression of the auditory nerve-brainstem evoked response in hypoxemia. Mechanism and site of effect. *Electroencephalogr Clin Neurophysiol* 1986; 64:334–338.
34. Cunningham DR, Cunningham CA, Vise LK. The effects of chronic hypoxia on central auditory processing in patients with chronic obstructive pulmonary disease. *Ear Hear* 1985; 6:297–303.
35. Nomura K, Nakao M, Morimoto T. The effect of smoking on the hearing loss: the quality assessment and meta-analysis. *Prev Med* 2005; 40:136–144.
36. Mizoue T, Miyamoto T, Shimizu T. The combined effect of smoking and the occupational exposure to noise on the hearing loss in steel factory workers. *Occup Environ Med* 2003; 60:56–59.
37. Noorhassim I, Rampal KG. The multiplicative effect of smoking and age on the hearing impairment. *Am J Otolaryngol* 1998; 19:240–243.