TÜBİTAK

Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2016) 46: 1677-1681
© TÜBİTAK
doi:10.3906/sag-1601-140

# Exhaled carbon monoxide is a marker of heavy nicotine dependence

**Elif BABAOĞLU[1,*], Ayşegül KARALEZLİ[2], Mükremin ER[1], Hatice Canan HASANOĞLU[2], Derya ÖZTUNA[3]**

[1]Department of Chest Diseases, Ankara Atatürk Training and Research Hospital, Ankara, Turkey
[2]Department of Chest Diseases, Faculty of Medicine, Yıldırım Beyazıt University, Ankara, Turkey
[3]Department of Biostatistics, Faculty of Medicine, Ankara University, Ankara, Turkey

**Received:** 01.02.2016 • **Accepted/Published Online:** 02.04.2016 • **Final Version:** 20.12.2016

**Background/aim:** Exhaled CO level provides an objective measure of a patient's smoking status. The relationship between CO levels and nicotine dependence is controversial. The aim of this study is to evaluate the relationship between exhaled CO levels and nicotine dependence as well as to demonstrate that exhaled CO levels may be used as a marker of nicotine dependence.

**Materials and methods:** Two hundred eighty-nine patients (132 females, 157 males) were included in the study. Smoking duration, the age of smoking initiation, exhaled CO levels, and Fagerström Test for Nicotine Dependence (FTND) scores were recorded. The relationship between FTND scores and exhaled CO levels was investigated.

**Results:** There was a statistically significant correlation between FTND score and exhaled CO levels ($P < 0.001$). We found that a cut-off score of 7.5 ppm for exhaled CO may be useful as a marker for heavy smoking. The sensitivity and specificity of this cut-off score for exhaled CO was 69.3% and 49.3%, respectively ($P < 0.001$).

**Conclusion:** We found that exhaled CO levels significantly correlated with FTND scores. For patients who are unable to provide reliable answers to questions in the FTND, exhaled CO measurements may be used as an alternative test for estimating the status of heavy smoking.

**Key words:** Carbon monoxide, Fagerström test, nicotine dependence

## 1. Introduction

Smoking is an important global public health concern. It has been classified as a disorder according to the International Classification of Diseases (10th Revision, F.17) and is a dispensable habit according to World Health Organization (1).

The severity of nicotine dependence is important in the evaluation of patient smoking habits in tobacco control programs (1,2). Certain scales for measuring the severity of dependence include the Fagerström Test for Nicotine Dependence (FTND) (3), the Cigarette Dependence Scale (4), and the Nicotine Dependence Syndrome Scale (5). Among these, the FTND scale is most commonly used. It consists of a questionnaire related to the smoking habits of patients in six domains. Although this scale is easy to apply and is noninvasive, the duration of time required to answer all questions is too long to be reliably completed in most clinical settings. Additionally, some patients do not give honest answers to the questions, which is a problem. Another method that has been used for assessing the severity of smoking dependence is simply counting the number of cigarettes smoked within 24 h (cigarettes per day, CPD) (6). This is a quantitative measure that has been used in many population-based studies.

Measurement of exhaled carbon monoxide (CO) levels is commonly performed in smoking cessation programs for the purpose of increasing the motivation of patients. This test obtains information on patient smoking status. CO level in expired air has been used as an indicator of smoking in several studies (7–10). Controversial results persist regarding whether CO measurement can be used as a marker for demonstrating the severity of nicotine dependence. Therefore, we aimed to investigate the relationship between exhaled CO levels and the severity of nicotine dependence.

## 2. Materials and methods

Two hundred eighty-nine patients (132 females, 157 males) who referred to the Smoking Cessation Unit of Ankara Atatürk Training and Research Hospital were included in the study. The study was approved by the Local Ethics Committee of Ankara Atatürk Training and Research

* Correspondence: elifbabaoglu@hotmail.com

Hospital (2011.05.46). The FTND scale was applied to all patients, and exhaled CO levels were measured. For all patients, smoking duration, the age of smoking initiation, exhaled CO levels, and FTND scores were recorded. The relationship between FTND scores and exhaled CO levels was investigated.

### 2.1. Statistical analysis

Statistical analyses of the study were performed using SPSS 15.0 (SPSS Inc., Chicago, IL, USA). Means ± standard deviations for metric variables and frequencies as percentages for categorical variables were used. Student's t-test or the Mann–Whitney U test was used to compare two independent groups for metric variables. Spearman's correlation coefficient was used to assess the relationships between two variables. A value of $P < 0.05$ was considered statistically significant. To determine the cut-off score for CO measurements, receiver operating characteristics (ROC) analysis was performed. The area under the ROC curve measures the potential of the ordinal scale for detecting high nicotine dependence with accuracy.

## 3. Results

Demographic features of the 289 patients are summarized in Table 1. According to the variables in Table 1, the mean age of the females (40.1 ± 9.6 years) was similar to that of the males (42.8 ± 13.2 years) ($P = 0.05$). The average smoking duration of the males was significantly longer than that of the females (25.2 ± 13 vs. 20.7 ± 9 years, respectively; $P = 0.001$). In addition, the mean age of smoking initiation was earlier in males than in females (17.3 ± 5.1 vs. 19.2 ± 5.4 years, respectively; $P = 0.002$).

Mean FTND scores and exhaled CO levels are presented in Table 2. FTND scores were significantly higher in females than in males ($P = 0.009$). Exhaled CO levels in both sexes were similar at approximately 11 parts per million (ppm).

We examined whether FTND scores were correlated with CPD numbers and exhaled CO levels. It was observed that FTND scores correlated well with both CPD numbers ($r = 0.668$; $P < 0.01$) and exhaled CO levels ($r = 0.233$; $P < 0.001$; Figure 1).

The patients were classified into five groups according to their FTND scores: 1) very low, 2) low, 3) moderate, 4) high, and 5) very high nicotine dependence, as shown in Table 3. Mean exhaled CO levels were similar in females and males within each group (Table 3).

We compared exhaled CO levels of all patients with their FTND scores using ROC analysis to investigate if a cut-off level for heavy smoking could be determined (Figure 2). ROC analysis yielded that the cut-off score for exhaled CO levels was 7.5 ppm. This value was comparable with the cut-off value of 6 for the FTND. The sensitivity calculated for ROC analysis was 69.3% and the specificity was 49.3% ($P < 0.001$).

## 4. Discussion

In this study, we found that there are some differences between females and males regarding smoking habits and nicotine dependence. As indicated by FTND scores, nicotine dependence of females was higher than that of males, although males started to smoke earlier and had longer smoking duration than females. However, CO levels of females and males were similar in each group of patients. When patients were subgrouped according to smoking levels, CO levels and FTND scores were positively correlated in both females and males.

The FTND is the most commonly used test for the evaluation of nicotine dependence. It takes a long time to ask all of the questions. Some alternative tests are also being investigated. In the study by Charbol et al. (11), the cut-off score for the Heavy Smoking Index (HSI) was found to be useful for the diagnosis of heavy smoking. The

**Table 1.** Demographic features of the patients.

| | Females (n = 132) | Males (n = 157) | P-value |
|---|---|---|---|
| Age (years) | 40.1 ± 9.6 | 42.8 ± 13.2 | 0.05 |
| Smoking duration (years ) | 20.7 ± 9 | 25.2 ± 13 | 0.001 |
| Age of starting smoking (years) | 19.2 ± 5.4 | 17.3 ± 5.1 | 0.002 |

**Table 2.** Mean exhaled CO levels and FTND scores of the patients.

| | Females (n = 132) | Males (n = 157) | P-value |
|---|---|---|---|
| FTND score | 6.0 ± 2.6 | 5.2 ± 2.2 | 0.009 |
| Exhaled CO level (ppm) | 11.5 ± 8.3 | 11.0 ± 7.4 | 0.570 |

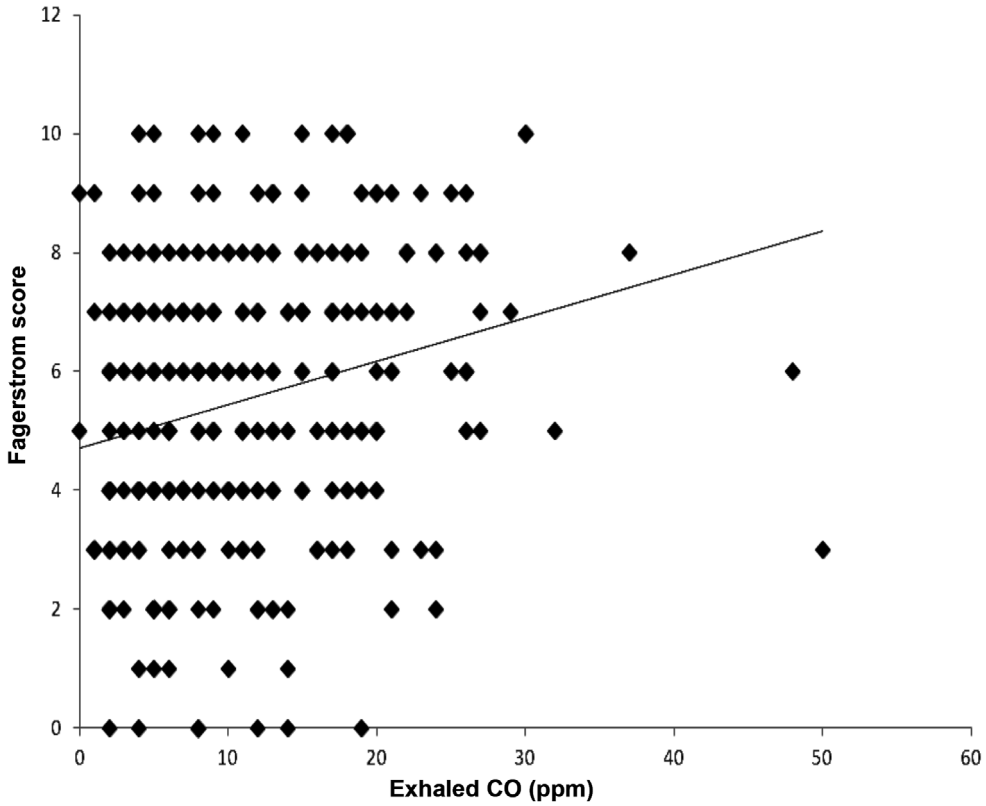


**Figure 1.** Correlation between FTND score and exhaled CO levels (r: 0.233, P < 0.001).

**Table 3.** CO levels and the FTND scores of the patients.

| Nicotine dependence (FTND score) | | n | CO levels (mean ± SD) | P |
|---|---|---|---|---|
| Very low (0–2) | Females | 11 | 11.1 ± 6.8 | 0.12 |
| | Males | 23 | 7.3 ± 4.5 | |
| | Total | 34 | 8.5 ± 5.5 | |
| Low (3–4) | Females | 29 | 9.3 ± 9.6 | 0.86 |
| | Males | 40 | 8.5 ± 6.2 | |
| | Total | 69 | 8.8 ± 7.8 | |
| Moderate (5–6) | Females | 14 | 11.2 ± 8.0 | 0.439 |
| | Males | 19 | 13.1 ± 7.4 | |
| | Total | 33 | 12.3 ± 7.6 | |
| High (6–7) | Females | 40 | 10.1 ± 6.0 | 0.425 |
| | Males | 49 | 12.1 ± 8.8 | |
| | Total | 89 | 11.2 ± 7.7 | |
| Very high (8–10) | Females | 37 | 14.4 ± 8.9 | 0.78 |
| | Males | 26 | 14.2 ± 6.4 | |
| | Total | 63 | 14.4 ± 7.9 | |

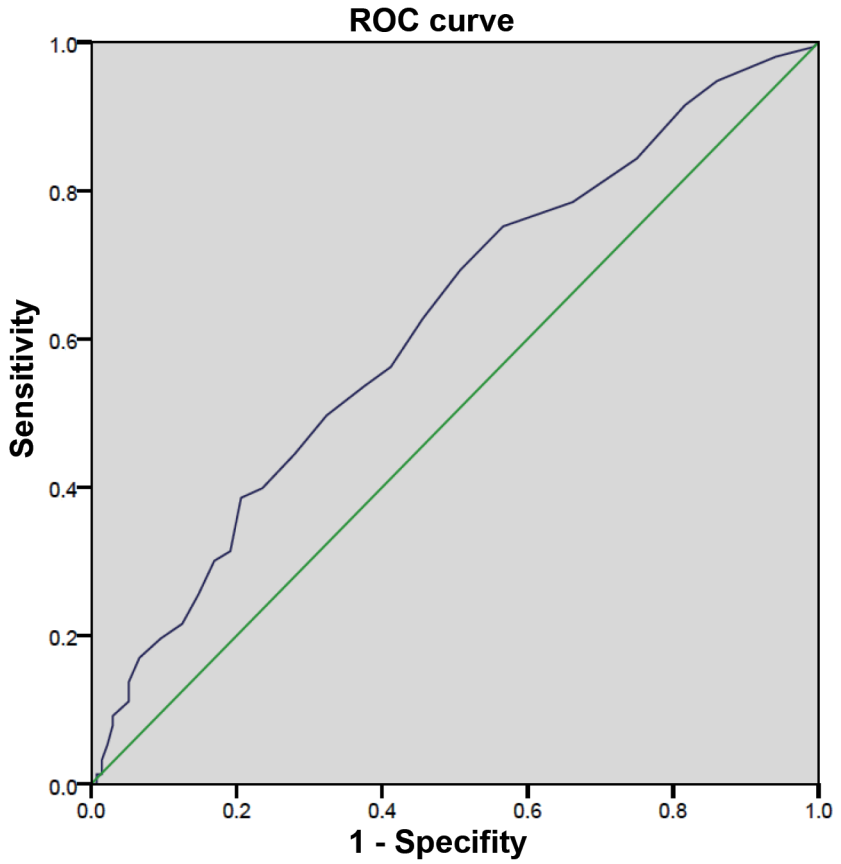


**Figure 2.** The ROC curve for CO cut-off score.

cut-off score for the HSI was 4 with a sensitivity of 80% and a specificity of 97% (10). Lim et al. found that CPD was not a suitable alternative to the FTND (12).

Exhaled CO level has been used as a biological indicator to assess the smoking status of patients (13). It can also be used to show the impact of active smoking and environmental tobacco smoke exposure on nicotine dependence (14,15). Furthermore, it was demonstrated that exhaled CO levels could discriminate between smokers and nonsmokers, yielding an optimal discrimination at a cut-off level of 5.5 ppm with a sensitivity of 95% and a specificity of 83% (8). In addition, exhaled CO was found to be a biomarker that captures aspects of cigarette smoke exposure beyond the CPD number in current smokers (16). Studies on the relationship between exhaled CO and the severity of nicotine dependence yielded controversial results. Kapusta et al. showed that CO levels did not discriminate based on the severity of nicotine dependence (8). On the other hand, Vancelik et al. showed that exhaled CO could be used as an indicator of nicotine dependence in adolescents (17). In the present study, exhaled CO levels positively correlated with FTND scores. In ROC analysis, we found that a cut-off score of 7.5 ppm may be used to predict heavy smoking habits. Exhaled CO levels of >7.5 ppm may be useful to discriminate heavy smokers from others. The sensitivity and specificity of this cut-off score for exhaled CO measurements were 69.3% and 49.3%, respectively. Although the sensitivity and specificity of CO measurements are smaller than those of the HSI for patients who do not provide honest answers to the FTND and HSI or for busy clinicians, CO measurements may be useful to diagnose heavy smoking habits.

As a result, our findings suggest that the measurement of exhaled CO levels is indicative of the severity of smoking. Additionally, CO levels of >7.5 ppm may be useful to determine heavy smoking habits, especially in clinical settings in which the FTND questionnaire cannot be applied because of time limitations of both patients and physicians.

## References


1. Breslau N, Johnson EO, Hiripi E, Kessler R. Nicotine dependence in the United States: prevalence, trends, and smoking persistence. Arch Gen Psychiatry 2001; 58: 810-816.
2. Sağlam L. Investigation of the results of a smoking cessation clinic and the factors associated with success. Turk J Med Sci 2012; 42: 515-522.
3. Heatherton TF, Kozlowoski LT, Frecker RC, Fagerström KO. The Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. Br J Addict 1991; 86: 1119-1127.
4. Etter JF. A comparison of the content-, construct- and predictive validity of the cigarette dependence scale and the Fagerström test for nicotine dependence. Drug Alcohol Depend 2005; 77: 259-268.
5. Shiffman RN, Michel G, Essaihi A, Marcy TW. Using a guideline-centered approach for the design of a clinical decision support system to promote smoking cessation. Stud Health Technol Inform 2004; 101: 152-156.
6. De Leon J, Diaz FJ, Becona E, Gurpegui M, Jurado D, Gonzalez-Pinto A. Exploring brief measures of nicotine dependence for epidemiological surveys. Addict Behav 2003; 28: 1481-1486.
7. Fritz M, Wallner R, Grohs U, Kemmler G, Saria A, Zernig G. Comparable sensitivities of urine cotinine and breath carbon monoxide at follow-up time points of three months or more in a smoking cessation trial. Pharmacology 2010; 85; 234-240.
8. Kapusta ND, Pietschnig J, Plener PL, Blüml V, Lesch OM, Walter H. Does breath carbon monoxide measure nicotine dependence? J Addict Dis 2010; 29: 493-499.
9. Guan NC, Ann AY. Exhaled carbon monoxide levels among Malaysian male smokers with nicotine dependence. Asian Pac J Cancer Prev 2012; 13: 343-346.
10. Politis A, Ioannidis V, Daniil Z, Hatzoglou C, Gourgoulianis K. Smoking cessation in hospitalized patients with comorbidities. J Thorac Dis 2015; 7: AB052.
11. Charbol H, Niezborala M, Chastan E, de Leon J. Comparison of the Heavy Smoking Index and Fagerström Test for Nicotine Dependence in a sample of 749 cigarette smokers. Addict Behav 2005; 30: 1474-1477.
12. Lim KH, Idzwan MF, Sumarni MG, Kee CC, Amal NM, Lim KK, Gurpreet K. Heaviness of smoking index, number of cigarettes smoked and the Fagerstrom test for nicotine dependence among adult male Malaysians. Asian Pac J Cancer Prev 2012; 13: 343-346.
13. Deveci SE, Deveci F, Acik Y, Ozan AT. The measurement of exhaled carbon monoxide in healthy smokers and non-smokers. Resp Med 2004; 98: 551-556.
14. Brimkulov NN, Vinnikov DV, Cholurova RA. Complex assessment of nicotine dependence using questionnaires and measurement of carbon monoxide concentration in exhaled air. Ter Arkh 2004; 76: 53-58.
15. Nakayama T, Yamamoto A, Ichimura T, Yoshiike N, Yokoyama T, Fujimoto EK, Tanaka H. An optimal cut-off point of expired-air carbon monoxide levels for detecting current smoking: in the case of a Japanese male population whose smoking prevalence was sixty percent. J Epidemiol 1998; 8: 140-145.
16. Bloom AJ, Hartz SM, Baker TB, Chen LS, Piper ME, Fox L, Martinez M, Hatsukami D, Johnson EO, Laurie CC et al. Beyond cigarettes per day. A genome wide association study of the biomarker carbonmonoxide. Ann Am Thorac Soc 2014 ; 11: 1003-1010.
17. Vançelik S, Beyhun NE, Acemoğlu H. Interactions between exhaled CO, smoking status and nicotine dependency in a sample of Turkish adolescents. Turk J Pediatr 2009; 51: 56-64.