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ORIGINAL ARTICLE

The Power of Exhaled Air Carbon Monoxide Levels to Predict Nicotine Dependency and Smoking Cessation

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Main Points

- E-CO levels can distinguish highly dependent smokers.
- Low initial E-CO levels increase the success of smoking cessation at the end of one year.
- It seems that the most effective variable on smoking cessation success is compliance with treatment.

Abstract

The aim of our study was to determine the power of exhaled air CO (E-CO) levels to predict the severity of nicotine dependency and its effect on predicting the one-year smoking cessation success. It also aimed to detect other factors related to smoking cessation success. The smokers who applied to the ADU hospital family medicine and smoking cessation clinic between October 2018 and March 2019 participated in this prospective cohort study, conducted with an analytical design. A significant correlation was found between the E-CO levels and the Fagerstrom Test for Nicotine Dependence (FTND) score, Heaviness of Smoking index (HSI) score, and the amount of smoking per day. The sensitivity of predicting high nicotine dependency based on the FTND score (≥6) at the 8.5 ppm cut-off point for E-CO level was 70.6%, and the specificity was 67.7%. The sensitivity of predicting high nicotine dependency based on the HSI score (≥4) at the 9.5 ppm cut-off point for E-CO level was 68.0%, and specificity was 71.9%. E-CO measurements can be used to determine the level of dependency. Low initial E-CO levels increase smoking cessation success.
Keywords: Carbon monoxide, exhaled air, nicotine dependency, smoking cessation success

Introduction

Tobacco addiction causes many social, economic, medical, and legal problems due to its increasing prevalence, nationally and internationally, and has become an important health problem today (World Health Organization, 2018). On the other hand, the health benefits associated with quitting tobacco use are well known (Kargin & Marakoğlu, 2015). For this reason, stopping smokers from using tobacco is among the most important goals of physicians today.

Smoking constitutes the vast majority of the use of tobacco products. A significant number of smokers want to quit smoking and take initiatives in that direction; however, the success rates are low (Edwards, 2004).

The severity of nicotine dependence in clinical practice is determined by the Fagerstrom Test for Nicotine Dependence (FTND) based on the patient's statement on tobacco use. The Heaviness of Smoking index (HSI), which is the short version of FTND, is also used in clinical practice (Türkcan & Çakmak, 2004).

Another tool used in the diagnosis, treatment, and follow-up of nicotine dependence is the measurement of carbon monoxide (E-CO) level in the exhaled air.

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With the detection of carbon monoxide levels higher in smokers than in non-smokers, E-CO measurement has become the gold standard in objectively determining smoking status. As E-CO is removed from the body at the end of 24 hours of not smoking, the immediate positive effect of quitting motivates patients. The non-invasive technique provides a significant advantage in getting fast results (Middleton & Morice, 2000). However, its suitability is questionable for the detection of low-level smokers.

It is controversial that E-CO measurement can be used as a marker that shows the severity of nicotine dependency and predicts smoking cessation success. Kapusta et al. concluded in 2010 that the E-CO level is a useful predictor of smoking status, but fails to indicate the severity of nicotine dependence (Kapusta et al., 2010). On the other hand, Babaoğlu et al. have found that E-CO levels are significantly associated with the Fagerstrom score. (Babaoğlu et al., 2016).

There is not enough evidence for the level of E-CO, which is an objective determinant of smoking cessation for a long duration, to indicate the severity of nicotine dependency. Knowing such determinants can help family physicians develop effective strategies for smoking cessation of their patients.

The aim of our study was to determine the power of E-CO levels to predict the severity of nicotine dependency and its effect on predicting the one-year smoking cessation success. It also aimed to detect other factors related with smoking cessation success.

Methods

This was a prospective cohort study with an analytical design that was conducted between October 2018 and March 2019 in the smoking cessation outpatient clinic of Aydın Adnan Menderes University Hospital, Department of Family Medicine. Our study consisted of all patients over the age of 18 who applied to the outpatient clinic during the six-month study period. Sample selection was not done.

During the study period, 86 patients applied to our outpatient clinic for smoking cessation. Of them, 82 smokers volunteered to participate in the study. Four patients were not included in the study because they could not be followed-up for a long duration.

The demographic characteristics and smoking history of the patients in the study were obtained through the smoking cessation outpatient follow-up protocol form. FTND and HSI were used to calculate the smokers' nicotine dependency. E-CO levels were measured with the Bedfont piCO Smokerlyzer (Bedfont Instruments; Kent, UK) device.

Treatment was arranged in line with nicotine dependency levels, comorbid diseases, contraindications of the pharmacotherapeutics used in smoking cessation, and the patient's preferences. E-CO measurement was made on the first day of the interview (initial E-CO level).Those who received pharmacological treatment for at least 8 weeks were considered to have received adequate treatment.

Data analysis was done using the SPSS 25 software program. In addition to descriptive statistics, chi-square and Fisher's exact tests were used for comparison of categorical variables, and the Student's *t*-test and the Mann – Whitney *U*-test were used to compare quantitative data. The relation of E-CO levels with the FTND and HSI scores was evaluated with Spearman's correlation test. The correlation coefficient (*r*) was accepted as weak, at 0.000 – 0.249; medium, at 0.250 – 0.499, strong, at 0.500 – 0.749, and very strong, at 0.750 – 1.000. ROC curve analysis was performed for the ability of E-CO levels to predict nicotine dependency and dependency severity. Sensitivity, specificity, and area under the curve (AUC) were determined for different cut-off points. Multiple logistic regression analysis was performed to determine the effect of E-CO level on one-year smoking cessation success. A value of $p < .05$ was accepted as the level of significance.

Ethical approval was obtained from Aydın Adnan Menderes University School of Medicine Non-Invasive Clinical Research Ethics Committee for the study (date July 5, 2018 and protocol number 20181432).

Results

The mean age of the 82 smokers in our study was 44.2 ± 15.6 years (between 18 and 76 years). Of them, 74.4% (61 people) were male, 68.3% were married, and 40.2% had less than 9 years of education. Most of the smokers (79.3%) had a family income of 1500 – 4500 TL monthly.

The average age at start of smoking was 17.2 ± 5.5 (6 – 35 years). They smoked 24.8 ± 14.0 (1 – 60) cigarettes per day. The mean duration of smoking was 31.5 ± 24.7 (between 1 – 125 packs/year) pack/year. In addition, 30.5% of the smokers consumed alcohol.

The most common reason for starting to smoke was social influence (58.5%) and the most common current reason for smoking was habit (57.3%). Smoking was mostly increased with tea and coffee consumption (61%).

The majority of the smokers (85%) had previously tried to quit. The most common reasons for wanting to quit smoking were fear of illness and current illness (91.5%).

The Power of E-CO Levels to Predict the Severity of Nicotine Dependency

As the amount of cigarettes smoked per day, HSI, and Fagerstrom scores increased, the initial E-CO levels also increased (moderate correlation). The age at start of smoking, the duration of smoking expressed as pack/year, and the presence of nicotine withdrawal symptoms were not associated with the initial E-CO levels ($p > .05$). The relationship between some variables affecting nicotine dependency levels and the initial E-CO levels are shown in Table 1.

For the performance of the initial E-CO levels in predicting the severity of nicotine dependency (high nicotine dependency), the ROC curve analyses were performed on the basis of FTND and HSI scores. The smokers with an FTND score of 6 and above and a HSI score of 4 and above were considered highly addicted to nicotine. Considering the FTND score of ≥6 at the 8.5 ppm cut-off point, the sensitivity of the E-CO level to predict high nicotine dependency was 70.6%, with a specificity of 67.7%, and AUC of 0.716 (95% CI 0.604 – 0.828; $p = .001$). Considering the HSI score

Table 1.
The Relationship Between Some Variables Affecting Nicotine Addiction Levels and Exhaled Air CO Levels

Independent Variables	Initial CO Level	
The amount of smoking per day	$r = 0.478$*	$p < .001$
HSI score	$r = 0.414$*	$p < .001$
FTND score	$r = 0.440$*	$p < .001$

*Spearman correlation coefficient.
CO, carbon monoxide; HSI, heaviness of smoking index; FTND, Fagerstrom test for nicotine dependence.

of ≥4 at the 9.5 ppm cut-off point, the sensitivity of the E-CO level to predict high nicotine dependency was 68.0%, with a specificity of 71.9%, and AUC of 0.735 (95% CI 0.624 – 0.846; $p < .001$). ROC curves for the performance of E-CO levels in predicting high nicotine dependency according to the FTND and HSI scores are shown in Figure 1 and Figure 2. The sensitivity and specificity of E-CO levels in predicting high nicotine dependency for different cut-off points are shown in Table 2.

The Effect of Initial E-CO Levels on One-Year Smoking Cessation Success

Twenty-one of the 82 patients (25.6%) were still not smoking at the end of one year (smoking cessation success). The E-CO levels measured on the first day of the interview of those who quit smoking were lower than those who did not quit (8.0 ppm vs. 11.3 ppm; $z = -2.352$, and $p = .021$). Smokers who quit smoking had made fewer quit attempts in the past than those who did not quit (1.5 vs. 2.6 times; $t = -2.871$ and $p = .006$). The success of smoking cessation was significantly higher for those who been regular with their medication ($p < .001$) and those who received regular follow-up ($p < .001$). Those who stated that they wanted to quit smoking due to illness or fear of illness ($p = .011$) and those who had previously thought of quitting ($p = .050$) had lower success in quitting.

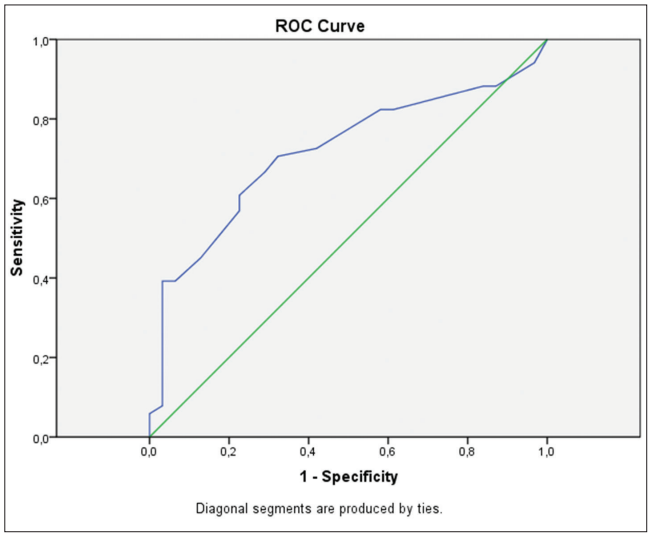

Figure 1. ROC curve for the performance of exhaled CO levels to predicting individuals highly addicted to nicotine, based on the Fagerstrom Test for Nicotine Dependence scores, AUC = 0.716 (95% CI 0.604 – 0.828; p = .001).

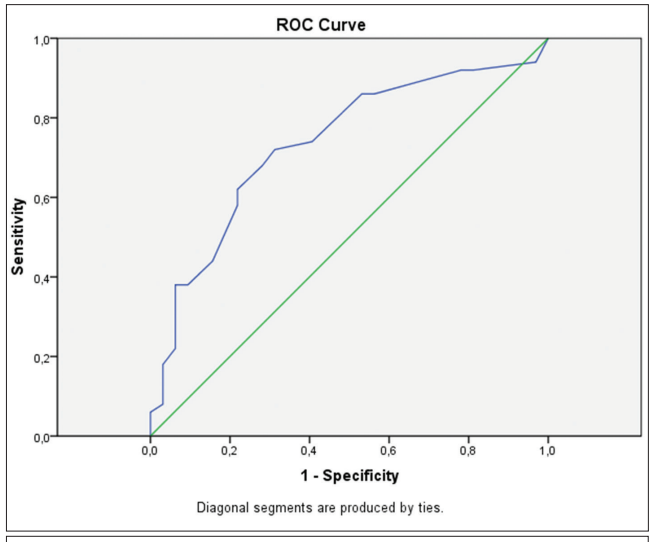

Figure 2. ROC curve for the performance of exhaled air CO levels in predicting high nicotine addiction based on Heaviness of Smoking Index scores. AUC = 0.735 (95% CI 0.624 – 0.846; p < .001).

The demographic characteristics of the patient, the age at start of smoking, reasons for starting, reasons for current smoking, amount of daily smoking, total duration of smoking, factors related to previous quitting experiences, factors that increase smoking, reasons for quitting, alcohol or substance use, presence of chronic disease, and FTND and HSI scores were not effective in smoking cessation success ($p > .05$).

Seven independent variables that were found to be effective on smoking cessation in univariate analyses were included in the logistic regression analysis (Table 3). The variables of "coming to the controls regularly" and "fear of illness or having illness as

Table 2.
Sensitivity and Specificity of CO Levels to Predict High Nicotine Addiction for Different Cut-Off Points (According to FTND and HSI Scores)

	FTND ≥ 6		HIS ≥ 4	
Cut-off point of CO level (ppm)	**Sensitivity (%)**	**Specificity (%)**	**Sensitivity (%)**	**Specificity (%)**
4.5	88.2	16.1	92.0	21.9
5.5	82.4	38.7	86.0	43.7
6.5	82.4	41.9	86.0	46.9
7.5	72.5	58.1	74.0	59.4
8.5	70.6	67.7	72.0	68.7
9.5	66.7	71.0	68.0	71.9
10.5	60.8	77.4	62.0	78.1
11.5	56.9	77.4	58.0	78.1

CO, carbon monoxide; HSI, heaviness of smoking index; FTND, Fagerstrom test for nicotine dependence.

Table 3.
Independent Variables Affecting One-Year Smoking Cessation Success in Smokers (Univariate Analyses)

	Smoking Cessation (1 year)			
Independent Variables	**Successful**	**Unsuccessful**	**Total**	**Statistics**
Initial CO level. M ± SD (Median)	8 ± 5.4 (5)	11.3 ± 5.7 (12)	10.5 ± 5.8 (10)	$Z = -2.430^{*}$
				$p = .015$
Number of attempts to quit M ± SD (Median)	1.5 ± 1.0 (1)	2.6 ± 2.0 (2)	2.3 ± 1.9 (1)	t=-2.871**
				$p = .006$
	n (%)	*n* (%)	*n* (%)	
Compliance with treatment				
No	6 (11.3)	47 (88.7)	53 (64.6)	$\chi^2 = 14.010^{\pm}$
Yes	15 (51.7)	14 (48.3)	29 (35.4)	$p < .001$
Taking prescribed medications				
No	5 (12.5)	35 (87.5)	40 (48.8)	$\chi^2 = 5.766^{\pm}$
Yes	16 (38.1)	26 (61.9)	42 (51.2)	$p = .016$
Coming to follow-up interviews	8 (11.6)	61 (88.4)	69 (84.1)	$p < .001^{\dagger}$
	13 (100)	0 (0)	13 (15.9)	
Reason for quitting- illness/fear of illness				
No	5 (71.4)	2 (28.6)	7 (8.5)	$p = .011^{\dagger}$
Yes	16 (21.3)	59 (78.7)	75 (91.5)	
Have previously thought of quitting				
No	3 (75.0)	1 (25.0)	4 (4.9)	$p = .050^{\dagger}$
Yes	18 (23.1)	60 (76.9)	78 (95.1)	
Total	21 (25.6)	61 (74.4)	82 (100)	

*Mann – Whitney *U*-test; **Student *t*-test; ±Chi-square test; †Fisher's exact test.
CO, carbon monoxide.

the main reason for quitting" were excluded from the analysis, as it made it impossible to maintain the regression analysis due to their high correlation with other variables. Only three variables entered the created model. It was found that each 1 ppm increase in E-CO levels measured in the first interview decreased smoking cessation success by 1.2-fold (95% CI: 1.013 – 1.379) and 1.8-fold (95% CI: 1.0 – 3.1) lower for each previous smoking cessation attempt. The success of smoking cessation was 18.0-fold (95% CI: 3.7 – 87.6) higher in those who used their treatment regularly than those who did not. The model formed as a result of the regression analysis is shown in Table 4.

Discussion

Our study results show that E-CO levels are effective in predicting the severity of nicotine dependency, and that as the initial E-CO level increases, one-year smoking cessation success decreases.

Table 4.
Factors Affecting 1-Year Smoking Cessation Success of Smokers in Multiple Logistic Regression Analysis (Forward LR)

Independent Variables	**Odds Ratio**	**95% CI**	*p*
Compliance with treatment			
No (Ref)	1		
Yes	18.043	3.714 – 87.642	.001
Number of attempts to quit			
Increase in success for each reduction in the number of attempts	1.795	1.033 – 3.117	.038
Initial CO level			
Increase in success for each ppm reduction	1.182	1.013 – 1.379	.034

CO, carbon monoxide.

According to our study, there was a positive correlation between initial E-CO levels and daily smoking level, HSI, and FTND scores ($p < .001$). Middleton et al. have reported that there is a significant relationship between the amount of cigarettes smoked in the previous 24 hours and E-CO levels (Middleton & Morice, 2000). There are studies in the literature supporting that FTND scores and initial E-CO levels are interrelated (Groman & Bayer, 2000; Groman et al., 2000). These results support the use of E-CO levels to predict nicotine dependency, instead of tests that measure nicotine dependency by using subjective criteria such as FTND, or with both together.

The initially measured E-CO levels also predicted the severity of nicotine dependency. Based on HSI and FTND scores, the sensitivity and specificity of the E-CO level in detecting high nicotine dependency is about 70%. The performance of E-CO levels in predicting high nicotine addicts is also high (AUC values 0.71 and 0.73, respectively). Kapusta et al. have also found in their study that the performance of E-CO levels in predicting high nicotine dependency was higher based on HSI scores. However, the cut-off value they found was higher (CO cut-off point: 5.5 ppm, AUC: 968) (Kapusta et al., 2010).

The Effect of Initial E-CO Level on One-Year Smoking Cessation Success

As of 2018, in studies conducted to evaluate the smoking cessation success of 476 smoking cessation outpatient clinics (386 of which are within the Ministry of Health and 90 of them are within the university settings) it is seen that the smoking cessation success of 17.8% in 2016 has increased to 25% in 2018 (Halk Sağliği Genel Müdürlüğü, 2020).

The one-year smoking cessation success rate we achieved largely overlaps with the 2018 success average of all smoking cessation centers (25.6%). The one-year success rates of the individual centers that publish their results vary between 34% and 43% (Demir et al., 2004; Solak et al., 2003; Uzaslan et al., 2000; Yaşar et al., 2014).

Three main variables seem to have an effect on the one-year smoking cessation success of smokers. There was no relationship between previous smoking cessation attempts and smoking cessation success. However, the inverse relationship observed between the number of smoking cessation attempts and smoking cessation success is statistically significant ($p = .006$). Success decreased by 1.8-fold (95% CI: 1.0 – 3.1) for each smoking cessation attempt previously made by the smoker. In the literature, there are different results for the relationship between smoking cessation attempts and smoking cessation success. In the study by Raherison et al., an inverse correlation has been found between the number of smoking cessation attempts and smoking cessation success (Raherison et al., 2005). In a study published by Prochaska, it is reported that smoking cessation success increases with increasing smoking cessation attempts (Prochaska et al., 1985).

In our study, it has been found that initial E-CO levels are effective on smoking cessation success ($p = .015$). There are other studies showing that the initial E-CO level affects smoking cessation success (Hashimoto et al., 2020). The relationship found in univariate analyses continues in multiple logistic regression analysis. A decrease of 1 ppm in the initial E-CO level increased the smoking cessation success by 1.2-fold. While there is no significant relationship between initial E-CO levels and smoking cessation success in the study conducted by Shie et al., they have shown that there is a relationship between E-CO levels measured on the 8th and 15th days and smoking cessation success (Shie et al., 2017). Onen et al. have also reported that the initial E-CO level has an effect on smoking cessation success (Onen et al., 2010).

Providing prescribed medications and compliance with treatment seem to be effective on smoking cessation success ($p < .05$). The strongest effect on smoking cessation success found in the logistic regression analysis is the compliance with treatment (Odds ratio 18 times). Providing smokers with medicines used in smoking cessation treatment free of charge will increase the access of patients with economic difficulties and thus patient compliance (O.Aksel, personal communication, October 14, 2020).

According to our results, follow-up interviews had a statistically significant effect on smoking cessation success ($p < .001$). In a study similar to our study, it has been found that as the number of follow-up interviews increases, the success of smoking cessation increases (Simon et al., 2003). Considering the fact that those who continue the non-smoking behavior regularly come to follow-up interviews and those who are unable to quit smoking do not attend, it can be thought that the success of smoking cessation and regular attendance at follow-up interviews are similar outcomes, rather than having a cause – effect relationship. This situation has reflected in the regression analysis; this strong association has prevented the continuation of the analysis and this follow-up variable has been excluded from the analysis.

In our study, no statistically significant relationship has been shown between FTND scores and smoking cessation success ($p > .05$). However, there are many studies in the literature showing that smoking cessation success increases in people with low nicotine dependency level (Fai et al., 2016, Yaşar et al., 2014). Górecka et al. have showed in their study that there is an inverse relationship between FTND scores and smoking cessation success (Górecka et al., 2003).

The variables such as the age at start of smoking, the amount of daily smoking, and the duration of smoking did not seem to affect the one-year smoking cessation success ($p > .05$). However, there are studies in the literature that have found that the age at start of smoking (Gaikwad et al., 2017; Khuder et al., 1999), the amount of daily smoking (Monsó et al., 2001; Yaşar et al., 2014), and the duration of smoking (Górecka et al., 2003; Mutlu et al., 2016) are effective on smoking cessation success.

Limitations, Suggestions for Future Research, and Implications for Practice

The most important limitations of our study were the small number of participants and the limited number of regular follow-up interviews.

Another limitation of our study was that treatment options were considered as a single whole. We could not evaluate the effect of different treatment protocols due to the small number of participants.

In this study, factors affecting E-CO levels, the effect of E-CO levels on smoking cessation success, and other factors related to smoking cessation success have been evaluated. E-CO levels can distinguish highly dependent smokers. Therefore, E-CO measurements can be used to determine the level of dependency.

Low initial E-CO levels increase smoking cessation success. It seems that the most effective variable on smoking cessation success is compliance with treatment. In order to increase compliance with treatment, patients should ensure to take their medications and use them regularly, with regular follow-up interviews. Considering the limitations of our study, there is a need for larger studies evaluating the effect of E-CO levels on high nicotine dependency and smoking cessation success.

Ethics Committee Approval: Ethics committee approval was received for this study from the Non-Invasive Clinical Research Ethics Committee of Aydın Adnan Menderes University School of Medicine (date July 5, 2018 and protocol number 20181432).

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