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Evaluation of Exhaled Carbon Monoxide Levels, Nicotine Dependence, and Psychosocial Factors in the Process of Smoking Cessation Treatment

Sigara Bırakma Tedavisi Sürecinde Ekspiryum Havası Karbonmonoksit Düzeyleri, Nikotin Bağımlılığı ve Psikososyal Faktörlerin Değerlendirilmesi

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Abstract

Objective: Tobacco use is the most important preventable cause of death and continues to be a major public health problem in our country and the world. Our aim in this study is to examine the changes in Fagerström nicotine dependance test (FNDT) score, depression-anxiety-stress (DASS-21) score, carbon monoxide (CO) levels in expiratory air and ppm level in control in our patients who applied to the smoking cessation clinic during their routine examination.

Method: This retrospective cross-sectional study included all patients with follow-up records at the smoking cessation clinic. The patient files were retrospectively reviewed for information on pack years of smoking, DAS score, and FNDT score obtained during tobacco dependence treatment monitoring system registration, as well as CO levels in expiratory air measured with the piCO Smokerlyzer during their application to our clinic. The SPSS-20 package program was used for statistical analysis. A value of $p<0.05$ was considered statistically significant.

Results: During follow-up, 76% (n=76) of participants quit smoking. Cessation rates did not differ by gender, but men had significantly higher pack-years and admission CO levels ($p<0.05$). In the Pearson correlation test, a significant positive correlation was found between FNDT and stress, depression, and anxiety scores. While there was a strong positive correlation between age and packs/years, a weak negative correlation was found between age and ppm/carboxyhemoglobin levels at admission. The mean pack-year value was found to be higher in the high dependency group.

Öz

Amaç: Tütün kullanımı önlenebilir ölüm nedenlerinden en önemlisi olup, ülkemizde ve dünyada halen büyük bir halk sağlığı problemi olmaya devam etmektedir. Bu çalışmada amacımız; sigara bırakma polikliniğine başvuran hastalarımızın rutin muayenesinde bakmış olduğumuz Fagerström nikotin bağımlılık testi (FNBT) skoru, depresyon-anksiyete-stres (DASS-21) skoru, ekspiryum havasındaki karbonmonoksit (CO) düzeyleri ve kontroldeki ppm düzeyi değişimini incelemektir.

Yöntem: Bu retrospektif kesitsel çalışmaya, sigara bırakma polikliniğine başvurup izlem kaydı bulunan tüm hastalar dahil edildi. Polikliniğimize başvuru esnasında sorgulanan sigara kullanım paket yılı, DAS skoru, tütün bağımlılığı tedavisi izlem sistemi kaydı sırasında elde edilen FNBT skoru, piCO Smokerlyzer ile ölçülen ekspiryum havasındaki CO düzeyleri geriye dönük olarak hasta dosyaları üzerinden taranmıştır. İstatistiksel analizde SPSS-20 paket programı kullanılmıştır. $p<0,05$ değeri istatistiksel olarak anlamlı kabul edilmiştir.

Bulgular: İzlem sürecinde katılımcıların %76'sı (n=76) sigarayı bıraktı. Bırakma oranı cinsiyetle anlamlı fark göstermedi; ancak erkeklerde paket yılı ve başvuru CO düzeyi anlamlı şekilde daha yüksekti ($p<0,05$). Yapılan Pearson korelasyon testinde FNBT ile stres, depresyon ve anksiyete skorları arasında anlamlı pozitif korelasyon bulunmuştur. Yaş ile paket/yıl arasında güçlü pozitif korelasyon olmasına karşın; yaş ile başvuru esnasındaki ppm/karboksihemoglobin düzeyleri

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Abstract

Conclusion: CO is a toxic gas that reduces the amount of oxygen bound to tissues. Exhaled CO can be easily, quickly, and non-invasively used to monitor smoking cessation. Our findings suggest that exhaled CO levels may indirectly reflect nicotine dependence and psychological states. Large multicenter studies are needed to better identify factors influencing smoking cessation success.

Keywords: Carbonmonoxide, cytisine, smoking cessation

Öz

arasında zayıf negatif korelasyon saptanmıştır. Yüksek bağımlı grupta paket-yıl değeri ortalaması daha yüksek bulunmuştur.

Sonuç: CO dokulara bağlanan oksijen miktarını azaltan toksik bir gazdır. Sigara bırakma tedavisi, ekspiryumdaki CO ölçümüyle kolay, hızlı ve invaziv olmayan şekilde izlenebilir. Bulgularımız, ekspiryum havasındaki CO düzeyinin nikotin bağımlılığı ve psikolojik durum hakkında dolaylı bilgi verebileceğini göstermektedir. Sigara bırakma tedavisi başarısını etkileyen faktörlerin daha net bir şekilde ortaya konabilmesi için çok merkezli geniş katılımlı araştırmalara ihtiyaç vardır.

Anahtar kelimeler: Karbonmonoksit, sigara bırakma, sitizin

Introduction

Tobacco use is the leading cause of death and remains a major public health problem both in our country and globally. According to the World Health Organization, 1.3 billion people in the world use tobacco products, 80% of whom live in low- and middle-income groups. In Turkey, 150.4 billion cigarettes were consumed in 2024, marking the highest annual cigarette consumption in the Republic (1). Every year, approximately 7 million people die from tobacco use, and an additional 1.2 million die from exposure to tobacco smoke (2,3). More than 83,000 people lose their lives due to tobacco use each year (4).

To prevent the use of tobacco products, which are clearly known to pose a serious threat to public health, the World Health Organization has recommended the monitoring tobacco use; protecting people from tobacco smoke; offering help to quit smoking; warning the public about the harms of tobacco use; enforcing bans on tobacco advertising; raising taxes on tobacco products policy package to all member countries. Turkey was the first country to implement all these components and served as an example for other countries (2). Efforts to combat smoking, which remains the most common form of tobacco use, are ongoing.

Cigarettes contain more than 4.000 antigenic, carcinogenic, cytotoxic, and mutagenic substances (5). The burning of tobacco produces oxidizing chemicals (e.g., nitrosamines and polycyclic hydrocarbons), carcinogens, and toxic substances such as carbon monoxide (CO), metals, and particulate matter. These toxic substances cause various diseases, including cancer (6). CO is a colorless, tasteless, odorless, and non-irritating gas, and its affinity for hemoglobin is greater than that of oxygen. CO binds to hemoglobin, forming carboxyhemoglobin (COHb). The COHb that forms reduces oxygen delivery to the tissues. Normal COHb levels are 0.5-3% in adults, 4-12% in smokers, and 3-7% in newborns (7). The nicotine in cigarettes is addictive to smokers. Considering that addiction has psychological and social aspects, it is not always easy to overcome addiction, and supporting efforts to address addiction is important for both individual and public health.

The Fagerström nicotine dependence test (FNDT) is frequently used to determine the level of nicotine dependence and to plan treatment for individuals who smoke (8). CO levels in exhaled breath are also used as markers for diagnosis, treatment, and monitoring. Since it is directly related to smoking, it helps plan treatment objectively and increase individuals' compliance with treatment. Although no universally established cut-off value exists, studies suggest that exhaled CO levels above 6 ppm are highly indicative of active smoking (9).

Nicotine binds to nicotinic cholinergic receptors in the brain, modulating the activity of neurotransmitter systems such as dopamine, serotonin, and gamma-aminobutyric acid (GABA). This interaction particularly stimulates the reward mechanism within the mesolimbic dopaminergic pathway, forming the neurobiological basis of addiction. In addition, nicotinergic interactions stimulate the release of glutamate, GABA, and endorphins in various brain regions through both direct and indirect mechanisms, thereby mediating the wide range of physiological and behavioral effects of nicotine dependence beyond the reward system (10,11). It is also well established that the process of smoking cessation is influenced not only by biological factors but also by psychosocial determinants. The depression-anxiety-stress (DASS)-21 was employed in this study to simultaneously assess individuals' levels of depression, anxiety, and stress because of its multidimensional structure and well-documented validity and reliability

(12). By integrating psychosocial data with health records from the tobacco dependence treatment monitoring system (TUBATIS) database, the study aimed to provide a more comprehensive evaluation. Several studies have demonstrated an association between smoking behavior and psychological factors such as depression, anxiety, and stress (13-15).

Various methods, such as cognitive-behavioral therapy, nicotine replacement therapy, bupropion, and varenicline, are used in smoking cessation treatment, and the most recently introduced pharmacological agent in our country is cytisine. Cytisine, a plant-based alkaloid, binds to a4b2 nicotinic receptors, reducing nicotine withdrawal symptoms and the person's desire to smoke (16). The treatment protocol lasts approximately 25 days and is completed by gradually decreasing the drug dose.

The aim of this study is to examine the changes in FNDT scores, DASS-21 scores, and exhaled CO and COHb levels between the initial and follow-up assessments in patients who presented to the Smoking Cessation Outpatient Clinic of Buca Seyfi Demirsoy Training and Research Hospital, which has been providing services since March 2024.

Thus, the study aimed to evaluate the utility of CO and COHb measurements in combating nicotine dependence and to elucidate the bidirectional relationship between dependence levels (as measured by the FNDT) and psychiatric conditions.

Materials and Methods

This study employed a retrospective cross-sectional design. All patients who applied to the smoking cessation clinic, who were treated with cytisine, and who had a recorded follow-up examination were included in the study. Patients without follow-up records, with unknown smoking cessation status, or who were receiving treatment for depression or anxiety were excluded from the study.

The patient files were retrospectively reviewed to extract information on pack-years of smoking, DASS-21 and FNDT scores obtained during TUBATIS registration, as well as CO and COHb levels in exhaled air measured with the piCO Smokerlyzer at the time of their presentation to our clinic. Patients presenting between the opening of the clinic (01.03.2024) and 31.05.2025 were examined.

Ethics committee approval for the study was obtained from the Ethics Committee of Non-Interventional Research of Buca Seyfi Demirsoy Training and Research Hospital (approval number: 2025/457, date: 30 April 2025).

Statistical Analysis

Statistical analysis was performed using SPSS version 20. Descriptive distribution analysis, the chi-square test, and Student's t-test were used to analyze the data. A Pearson correlation test was performed to examine the relationships among variables. A value of $p<0.05$ was considered statistically significant.

Results

When retrospective patient records were examined, data from 100 individuals with control records who had been started on pharmacological treatment were obtained. All patients were started on a drug containing the active ingredient cytisine. 35% of the patients were male (n=35) and 65% were female (n=65). The median age was 42 years (range, 20-76) (Table 1). The average interval between the participants' initial visit and the follow-up assessment was 30 days. During the follow-up period, 76% (n=76) of participants quit smoking, while 24% (n=24) did not. While the smoking cessation rate in men was 65.7% (n=23) positive and 34.3% (n=12)

Table 1. Descriptive statistics

	Mean ± SD	Minimum	Maximum
Age	43.41±13.78	20	76
Pack-years of smoking	27.45±19.40	2	100
FNDT	6.49±2.48	1	12
Depression score	6.26±4.80	0	20
Anxiety score	6.54±4.33	0	20
Stress score	6.85±4.47	0	19
First application ppm	18.10±10.85	3	49
First application COHb	3.50±1.80	1.10	8.50
Control ppm	4.38±6.64	0	33
Control COHb	1.34±1.11	0.00	5.91

SD: Standard deviation

Table 2. The relationship between gender and smoking cessation status

			Smoking cessation status		Total
			Negative	Positive	
Gender	**Male**	**n**	12	23	35
		%	34.3	65.7	100
	Female	**n**	12	53	65
		%	18.5	81.5	100
Total		**n**	24	76	100
		%	24.0	76.0	100

$X^2=3.12$, $p=0.07$

negative, it was 81.5% (n=53) positive and 18.5% (n=12) negative in women (Table 2). There was no statistically significant association between smoking cessation status and gender (Figure 1). Pack-years of smoking, CO (ppm) measured in exhaled air at admission, and COHb levels were significantly higher in men (p<0.05; Table 3). There was a statistically significant difference in ppm change by gender between the ppm measurement at first admission and the ppm value detected at the control assessment; the ppm decrease was greater in men (p<0.05). A significant relationship was observed between the admission ppm value and the decrease in ppm (p<0.001). A significant relationship was observed between admission and control ppm/COHb levels (Table 4). The mean ppm for individuals who quit smoking 16.94 at admission and 1.90 at control; for those who could not quit smoking, it

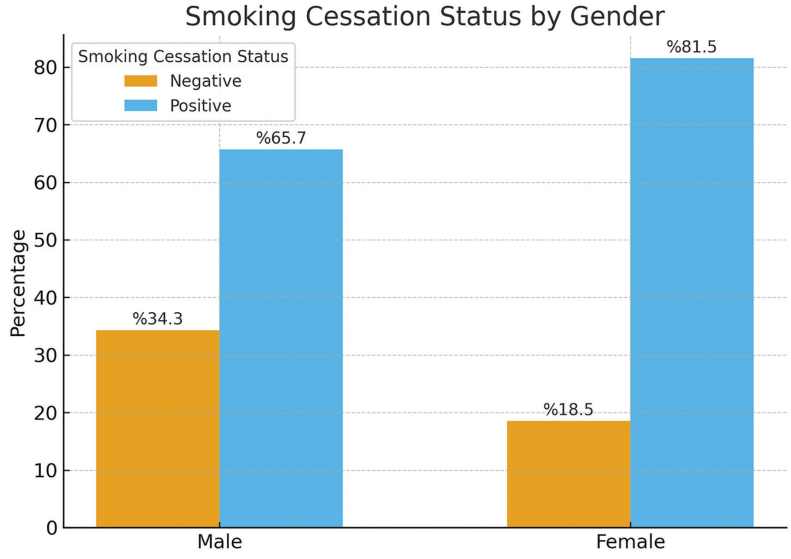

Figure 1. Smoking cessation status according to gender

Table 3. Comparison of clinical and psychological variables according to gender

	Gender	n	Mean	SD	p-value
Age	**M**	35	40.34	16.28	0.10
	F	65	45.06	12.04	
Pack-years of smoking	**M**	35	33.44	26.15	**0.02***
	F	65	24.22	13.74	
FNDT	**M**	34	6.71	2.53	0.54
	F	63	6.38	2.46	
Depression score	**M**	25	4.80	4.10	0.07
	F	56	6.91	4.97	
Anxiety score	**M**	25	5.76	3.90	0.28
	F	56	6.89	4.50	
Stress score	**M**	25	5.80	3.75	0.16
	F	56	7.32	4.71	
First application ppm	**M**	31	22.26	11.74	**0.01***
	F	56	15.80	9.69	
First application COHb	**M**	31	4.12	1.96	**0.02***
	F	56	3.16	1.62	
Control ppm	**M**	29	7.28	9.09	**0.003***
	F	55	2.85	4.25	
Control COHb	**M**	29	1.80	1.46	**0.004***
	F	55	1.09	0.78	

T-test, SD: Standard deviation, *: p<0.05, FNDT: Fagerström nicotine dependence test, COHb: Carboxyhemoglobin

was 22.53 at admission and 12.89 at control. There were statistically significant differences between the ppm levels at first admission and at control in both groups (p<0.001 for those who quit smoking; p=0.001 for those who could not quit). Using Pearson correlation analysis, significant positive correlations were found between FNDT and stress, depression, and anxiety scores (r=0.379, p<0.001; r=0.487, p<0.001; and r=0.386, p<0.001, respectively). While there was a strong positive correlation between age and pack-years, a weak negative correlation was found between age and ppm and COHb levels at admission (Table 5). When those with FNDT scores between 0-2 were classified as low dependency, those between 3-7 as moderate dependency, and those between 8-10 as highly dependent, 7 individuals had low, 48 individuals had moderate, and 42 individuals had high dependency. Since 3 patients had a TUBATIS record in the past, a new record could not be created, and their FNDT scores were not noted. According to the FNDT scores of the individuals, significant differences were found in some variables in low, moderate, and high dependency levels. No significant differences were found between the groups in terms of age, first application/control ppm, and COHb levels. On the other hand, a significant difference was found among the low-, moderate-, and high-dependency groups with respect to the cigarette pack-year variable (p=0.005). The mean pack-year value was higher in the high-dependency group. A significant difference was found between dependency groups for depression, anxiety, and stress scores (psychological variables) (p<0.05; Table 6).

Table 4. Comparison of baseline and follow-up exhaled CO values

	n	Mean ± SD	p-value
First application ppm	82	18.23±10.99	**<0.001***
Control ppm	82	4.45±6.71	
First application COHb	82	3.52±1.82	**0.001***
Control COHb	82	1.35±1.12	

Paired Samples t-test; SD: Standard deviation, *: p<0.001, COHb: Carboxyhemoglobin

Discussion

Expiratory CO measurement is used in many countries to objectively assess smoking because it is non-invasive, delivers rapid results, and is easy to perform. In studies conducted in Brazil in 2001 and 2007, expiratory CO values of smokers were significantly higher than those of non-smokers, and these values were reported to be useful for determining the probability that an individual is still smoking during smoking cessation treatment (17,18). Two recent studies in India have similarly found higher ppm concentrations among smokers (19,20). Similarly, in our study, the CO levels in the exhaled air of individuals who had quit smoking were significantly lower than those in smokers. A study conducted in 2018, similar to our study, showed a significant correlation between FNDT and pack-years of smoking (r=0.304, p<0.000). Although a positive correlation was found between FNDT and both age and ppm levels in the same study, no significant correlation was found in our study (21). In the study conducted by Kutlu et al. (22), the mean FNDT was 6.13±2.39 and the mean CO was 13.33±6.31 ppm; a statistically significant decrease was observed between the level at the time of application and that at the control, which is similar to our study. Babaoğlu et al. (23) showed that exhaled CO levels were higher in individuals with high addiction levels according to FNDT, consistent with our study. However, in the study, the FNDT scores of women (6±2.6) were significantly higher than those of men (5.2±2.2) (p=0.009). In contrast, no significant difference in nicotine addiction levels was found between genders in our study (23). In another study conducted by

Table 5. Relationship between age, pack-years of smoking, FNDT and psychological assessment results and CO measurement values

		Age	Pack-years of smoking	FNDT	Depression	Anxiety	Stress	First application ppm	First application COHb	Control ppm	Control COHb
Age	**r**	1	**0.57****	-0.0004	0.04	-0.04	-0.069	**-0.263***	**-0.271***	-0.083	-0.086
	p		**0.000****	0.97	0.76	0.75	0.540	**0.014**	**0.011**	0.452	0.439
Pack-years of smoking	**r**		1	**0.323***	0.102	0.048	0.019	0.059	0.036	0.039	0.017
	p			**0.001***	0.366	0.670	0.869	0.586	0.738	0.722	0.880
FNDT	**r**			1	**0.487****	**0.386****	**0.379****	0.155	0.120	0.148	0.116
	p				**0.000**	**0.000**	**0.001**	0.159	0.276	0.187	0.303

r: Pearson correlation coefficient; p: Significance level, **: Correlation is significant at the 0.001 level (2-tailed), *: Correlation is significant at the 0.05 level (2-tailed), CO: Carbon monoxide, FNDT: Fagerström nicotine dependence test, COHb: Carboxyhemoglobin

Table 6. Comparison of variables according to dependency level

		n	Mean	SD	p-value			Minimum	Maximum
					Low-moderate dependency	Moderate-high dependency	Low-high dependency		
Age	**Low dependency**	**7**	47.00	18.24	0.56	0.82	0.42	20	66
	Moderate dependency	**48**	43.35	14.87				20	76
	High dependency	**42**	42.71	11.87				20	66
	Total	**97**	43.34	13.80				20	76
Pack-years of smoking	**Low dependency**	**7**	28.43	21.0	0.31	**0.005***	0.58	2	50
	Moderate dependency	**48**	22.21	14.07				2	60
	High dependency	**42**	33.64	22.99				4	100
	Total	**97**	27.61	19.56				2	100
Depression	**Low dependency**	**6**	2.50	3.83	0.12	**0.008***	**0.001****	0	10
	Moderate dependency	**38**	5.21	3.93				0	16
	High dependency	**34**	8.03	4.85				1	20
	Total	**78**	6.23	4.63				0	20
Anxiety	**Low dependency**	**6**	3.33	2.66	0.1	**0.05***	**0.04***	1	8
	Moderate dependency	**38**	5.74	3.34				0	15
	High dependency	**34**	7.79	5.12				0	20
	Total	**78**	6.45	4.34				0	20
Stress	**Low dependency**	**6**	3.67	3.01	0.16	**0.03***	**0.03***	0	9
	Moderate dependency	**38**	6.08	3.99				0	15
	High dependency	**34**	8.32	4.77				0	19
	Total	**78**	6.87	4.48				0	19
First application ppm	**Low dependency**	**7**	17.29	12.66	0.82	0.15	0.60	5	35
	Moderate dependency	**39**	16.36	9.66				7	41
	High dependency	**38**	19.92	11.90				3	49
	Total	**84**	18.05	10.97				3	49
First application COHb	**Low dependency**	**7**	3.33	2.09	0.92	0.23	0.61	1.15	6.23
	Moderate dependency	**39**	3.26	1.57				1.25	7.20
	High dependency	**38**	3.76	2.01				1.10	8.50
	Total	**84**	3.49	1.82				1.10	8.50
Control ppm	**Low dependency**	**6**	3.50	3.02	0.98	0.32	0.66	1	9
	Moderate dependency	**38**	3.45	4.71				1	26
	High dependency	**37**	4.86	7.30				0	29
	Total	**81**	4.10	5.94				0	29
Control COHb	**Low dependency**	**6**	1.28	0.53	0.79	0.40	0.82	0.79	2.10
	Moderate dependency	**38**	1.19	0.77				0.43	4.79
	High dependency	**37**	1.39	1.25				0.00	5.67
	Total	**81**	1.29	1.0				0.00	5.67

T-test, SD: Standard deviation *: p<0.05, COHb: Carboxyhemoglobin

Çelepkolu (24), as in our study, no significant association was found between FNDT scores and age or gender. In the study conducted by Bohadana et al. (25), FNDT scores in men were reported to be significantly higher than those in women (6.44 and 5.99, respectively; p=0.018). In another study investigating the relationship between CO levels in exhaled air and FNDT, the average CO concentration was 13.2 ppm in smokers and 2.8 ppm in non-smokers. It was thought that ppm levels did not provide direct information about addiction severity, but were valuable for distinguishing smokers from non-smokers (26). In the literature, various scales have been employed to assess mental health status. In a study conducted among medical students, depression and anxiety scores, evaluated using the Beck depression inventory and the Beck anxiety inventory, respectively were higher in smokers than in non-smokers (13). Another study reported improvements in DASS-21 scores in patients with chronic obstructive pulmonary disease as their cigarette consumption decreased (27). Similarly, a study using the general health questionnaire-12 found that smokers exhibited higher levels of depression and anxiety than non-smokers. High nicotine dependence was associated with elevated depression and anxiety scores, consistent with the findings of our study (28).

The conflicting results in the literature regarding the relationship between FNDT scores and gender indicate that further studies are needed. The positive correlation between age and the pack-year value, which indicates cigarette consumption, is an expected consequence of longer smoking duration with increasing age. On the other hand, the smaller decrease in CO (ppm) levels in older age groups compared with younger age groups may be due to the adverse effects of long-term smoking on lung function. The significant decrease in the control CO levels among those who cannot quit smoking can be explained by increased awareness during the treatment process, increased motivational support, or decreased frequency of use.

Study Limitations

The limitations of our study include its retrospective design based on patient records, its single-center setting, and the lack of long-term follow-up for the patients. Since only patients who were initiated on cytisine and who attended regular check-ups were included, our study reports the success rate among cytisine-treated patients who attended follow-up. The fact that drug support can be provided free of charge may explain why individuals who apply to our smoking cessation clinic primarily seek drug treatment. In addition, non-attendance at follow-up appointments by individuals who have not been started on medication may be related to this situation. Three patients FNDT scores were not noted. Another limitation of our study is the higher proportion of female participants, which can be attributed to the inclusion only of individuals with follow-up records and to the generally greater tendency of women to seek healthcare services (29).

Conclusion

CO is a toxic gas that reduces the amount of oxygen bound to tissues. It binds to hemoglobin during smoking, forming the COHb complex and impairing tissue oxygenation. Smoking cessation treatment can be monitored easily, non-invasively, and rapidly by measuring CO levels in exhaled breath. Although the literature does not provide a clear-cut distinction between CO levels in smokers and non-smokers, the change in ppm from admission to follow-up indicates treatment response to both patient and physician and provides motivational support. In our study, significant relationships were found among addiction level, stress, anxiety, depression, and exhaled CO level; these findings suggest that exhaled CO measurement can provide indirect clues about nicotine addiction and individuals' psychological states. Multicenter studies with substantial participation are needed to better elucidate the factors affecting the success of smoking cessation treatment. In addition, cytisine requires a shorter treatment course than other therapies, which may increase patient compliance. However, since it has only recently been used in our country, a limited number of studies are available, and more comprehensive data on this subject are needed.

Ethics

Ethics Committee Approval: Ethics committee approval for the study was obtained from the Ethics Committee of Non-Interventional Research of Buca Seyfi Demirsoy Training and Research Hospital (approval number: 2025/457, date: 30 April 2025).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.G., K.E., Concept: H.G., K.E., Design: H.G., K.E., Data Collection or Processing: H.G., K.E., Analysis or Interpretation: H.G., K.E., Literature Search: H.G., K.E., Writing: H.G., K.E.

Conflict of Interest: No conflict of interest was declared by the authors.

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