RESEARCH ARTICLE

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The Relationship between Smoking Status, Carbon Monoxide Levels and Quality of Life, Disease Characteristics in Inflammatory Bowel Diseases

ABSTRACT

Objective: The aim of the study was to analyze the relationship between smoking status and exhaled carbon monoxide (E-CO) levels, quality of life, and disease characteristics in patients with inflammatory bowel disease.

Method: The demographic and disease characteristics and smoking status of 121 patients with inflammatory bowel disease who presented our hospital between 01.12.2020 and 01.03.2021 were investigated. After the first follow-up, the E-CO levels of these participants were measured every four consecutive weeks. The mean of these E-CO readings was accepted as the main E-CO value. After one month after their first application SF-36 Quality of Life Scale was applied. The relationship between these variables was investigated.

Results: The mean age of the participants was 42.06±14.9 years, and 36.3% were active smokers. While patients with Crohn's disease (CD) exhibited a higher smoking rate, smokers with ulcerative colitis (UC) registered significantly higher mean CO ppm readings ($p<0.05$). The general health components of smoker UC patients were higher than those of non-smokers ($p<0.05$). A weak correlation was determined between mean number of cigarettes smoked per day, mean CO ppm, Fagerström Nicotine Dependency Test (FNDT), package year, and the physical and mental components of SF-36 in the UC group ($p<0.05$). There was a weak negative correlation between mental components and mean E-CO in the CD group ($p=0.027$). No difference was observed in the non-smoker group between participants exposed to second-hand smoke and those with no such exposure ($p>0.05$).

Conclusion: Our results revealed that smoking has a weak positive effect on the quality of health in patients with UC, but no effect on patients with CD.

Keywords: Carbon Monoxide, Crohn's Disease, Inflammatory Bowel Disease, SF-36, Smoking, Ulcerative Colitis.

İnflamatuar Bağırsak Hastalıklarında Sigara İçme Durumu, Karbon Monoksit Düzeyleri ile Yaşam Kalitesi ve Hastalık Özellikleri Arasındaki İlişki

ÖZET

Amaç: Bu çalışmada inflamatuar barsak hastalığı olan hastalarda sigara içme durumu ile ekshale edilen karbon monoksit (E-CO) düzeyleri, yaşam kalitesi ve hastalık özellikleri arasındaki ilişkiyi incelenmiştir.

Gereç ve Yöntem: Hastanemize 01.12.2020-01.03.2021 tarihleri arasında başvuran inflamatuar bağırsak hastalığı (İBH) olan 121 hastanın demografik, hastalık özellikleri ve sigara içme durumları araştırıldı. İlk takipten sonra bu katılımcıların (E-CO) seviyeleri birbirini izleyen dört haftada bir ölçüldü. Bu E-CO okumalarının ortalaması, ana E-CO değeri olarak kabul edildi. İlk uygulamadan bir ay sonra SF-36 Yaşam Kalitesi Ölçeği uygulanarak değişkenler arasındaki ilişki araştırıldı.

Bulgular: Katılımcıların yaş ortalaması 42,06±14,9 yıl olup, %36,3'ü aktif olarak sigara içiyordu. Crohn hastalığı (CH) olan hastalar daha yüksek sigara içme oranı sergilerken, ülseratif kolitli (ÜK) sigara içenlerde anlamlı olarak daha yüksek ortalama CO ppm değerleri bulunmuştur ($p<0,05$). Sigara içen ÜK hastalarının genel sağlık bileşenleri içmeyenlere göre daha yüksekti ($p<0,05$). ÜK grubunda günlük içilen ortalama sigara sayısı, ortalama CO ppm, Fagerström Nikotin Bağımlılık Testi (FNBT), paket yılı ile SF-36'nın fiziksel ve mental bileşenleri arasında zayıf korelasyon saptandı ($p<0,05$). CH grubunda mental bileşenler ile ortalama E-CO arasında zayıf negatif korelasyon vardı ($p=0,027$). Sigara içmeyen grupta pasif içiciliğe maruz kalan katılımcılar ile böyle bir maruziyeti olmayanlar arasında fark gözlenmedi ($p>0,05$).

Sonuç: Sonuçlarımız, sigara içmenin ÜK tanılı hastalarda sağlık kalitesi üzerinde zayıf bir pozitif etkiye sahip olduğunu, ancak Crohn hastalarında herhangi bir etkisinin olmadığını ortaya koydu.

Anahtar Kelimeler: Crohn Hastalığı, İnflamatuar Barsak Hastalığı, Karbon Monoksit, SF-36, Sigara, Ülseratif Kolit.

INTRODUCTION

Inflammatory bowel disease (IBD), the two most important variants of which are ulcerative colitis (UC) and Crohn's disease (CD), is a chronic inflammatory condition of the gastrointestinal tract. The disease is believed to result from both genetic predisposition and environmental factors leading to an immune response associated with the gut (1). The prevalence of IBD, which peaks most frequently between the ages of 20 and 40 or around the age of 60, has increased worldwide in the last 10 years. Approximately 0.2% of the European population is diagnosed with IBD, while Asia is the continent with the highest number of IBD patients (2). The incidence of UC in a multicenter study from Turkey in 2009 was 4.4 per 100,000, with a reported incidence of CD of 2.2 per 100,000 (3).

One of the most important environmental factors affecting the disease is smoking, the first reports concerning which date back to the 1980s (4). The relationship between smoking and IBD is a complex one. Smoking adversely affects the composition of the lumen (mucus and microbiota), mucosal structure, and the immunological response in the gastrointestinal system (GIS) (5, 6). Some studies have observed a high risk of CD and a low risk of UC in smokers with IBD compared to non-smokers (7, 8). Disease activity, postoperative exacerbation, and first and second surgery requirements in CD are lower among smokers who quit, being almost at the same levels as non-smokers (9). In contrast, the protective effect of smoking on UC is thought to be temporary. An individual who quits smoking has a greater risk of developing UC increased compared to patients who have never smoked. At the same time, smoking may not only protect against the development of UC but may also improve its clinical course. Smokers have been observed to experience fewer disease recurrences, lower steroid or immunosuppressive therapy requirements, fewer hospitalizations, and fewer colectomy procedures (10).

The quality of life of IBD patients is seriously adversely affected in physical, psychological, and social terms. Lengthy and painful disease exacerbation phases (abdominal pain, blood in the stool, etc.) affect most daily GIS functions, but especially nutrition. Blood tests and invasive interventional diagnostic methods such as colonoscopy and sigmoidoscopic biopsy are often needed in these cases to evaluate the exacerbation. Anti-inflammatory therapy used to suppress frequent, severe, and painful GIS symptoms can cause severe side effects (11). Tobacco products (cigarettes, pipe tobacco, etc.) contain more than 4000 toxic and carcinogenic chemicals and produce severe adverse effects on users' quality of life, and smoking will also inevitably impact the quality of life of patients with IBD (12). The deleterious effects on the GIS of numerous harmful chemicals in cigarette smoke have been isolated and reported in published studies. Most of the studies examining the relationship between smoking and IBD so far have focused on daily nicotine intake (13). Nicotine exerts an immunomodulatory effect mediated by the activation of nicotinic receptors of alpha-7 in immune cells such as macrophages and dendritic cells. Recent studies suggest that CO as well as nicotine from cigarettes may have an impact on the clinical features of IBD patients. It was thought that the increase in the CO level had an anti-inflammatory effect and therefore had effective results in the clinic of IBD. CO level affects the maturation of dendritic cells and reduces antigen presentation to the immune system. It also exerts an anti-inflammatory effect by reducing leucocyte migration (14). So far various studies investigated the effect of smoking on quality of life either with self-reports or with cotinine levels (Main nicotine metabolite) in IBD patients. However, there have been no detailed studies investigating the relationship between the quality of life of IBD patients and smoking and CO levels measured in expiratory air, components of cigarette mainstream smoke.

The principal aim of this study is to investigate the relationship between smoking and E-CO measurements, disease characteristics, and quality of life in patients with UC and CD.

MATERIAL AND METHODS

Design of the Study: This case-control study involved 121 patients with IBD who presented to the Ondokuz Mayis Faculty of Medicine between December 2020 and March 2021. Using G-Power analyses before commencement we calculated that a total of 110 cases would be sufficient for the sample.

Patients older than 18, volunteering to participate, and previously diagnosed with IBD were included in the study (n=125). A questionnaire investigating the cases' sociodemographic characteristics and disease features was completed during face-to-face interviews at the first application. Also, the first E-CO measurement is performed at this time, and rendezvous was given to every participant for the next following three weeks. At these three meetings, the participants' E-CO measurements were repeated and their smoking status is checked. Four subjects who missed their rendezvous were also excluded from the study. The mean of these four E-CO readings is accepted as the main E-CO value for the participants. Quality of life was then evaluated using the SF-36 test. The cases' smoking status was determined, and smokers' addiction levels were graded using the Fagerström Nicotine Dependence Test (FNDT). Pack/year values were also calculated. E-CO levels were measured after all participants had completed the SF-36 quality of life assessment scale.

Individuals who have smoked more than 100 cigarettes over six months or longer are regarded as smokers. Participants who had quit smoking for more than a year were regarded as non-smokers in two-group analyses in the present study. Two groups were established in terms of smoking status (smokers and non-smokers). Individuals who had quit smoking less than one year previously were excluded from the study (n= 6).

Tools

E-CO measurements: All exhaled breath CO measurements were performed using a Tabataba V2 device, an analyzer that measures CO in exhaled breath. This is used to calculate the amount of CO intoxication in both smokers and non-smokers. The CO measurement range for the device is 0-400 ppm, and the accuracy is ±1 ppm. The relationship between ppm and the number of cigarettes smoked is 0-5 ppm – Non-smoker, 5-10 ppm - Passive smoker or light smoker, 10-15 ppm - Frequent smoker, 15-25 ppm - Heavy smoker, and 25-50 ppm - Very heavy smoker.

SF-36: The SF-36 scale was first designed by Ware et al. in 1992 (15). It consists of 36 questions and two main components (Physical and Mental Health) with eight sub-dimensions, which measure the quality of life within the previous month. The Physical component (PC) consists of physical functioning, role limitation due to physical problems, bodily pain, and general health perception sub-dimensions, while the Mental component (MC) consists of social functionality, role limitation due to emotional problems, vitality [energy], and mental health sub-dimensions. We analyzed all of the sub-dimensions individually and then combined them to evaluate the Physical (PC) and Mental Health (MC) components' total scores. Possible scores range from 0-100, with 100 representing the best score for each sub-dimension. The validity and reliability of the SF-36 in Turkish have been previously investigated (16).

Fagerstrom Nicotine Dependency Test (FNDT): The Fagerstrom Nicotine Dependency Test is a self-assessment scale developed by Heatherton et al. consisting of six questions, scored between 0 and 10, used to assess the risk of physical dependence on nicotine (17). The validity and reliability of the FNDT in Turkish were studied by Uysal et al. (18). Scores of 0-2 are interpreted as indicating low-level addiction, 3-7 as medium-level addiction, and 8-10 as high-level addiction.

Statistical Analyses: All the data were uploaded onto Statistical Package for Social Sciences version 22 software. The homogeneity of all the variables was tested using the Kolmogorov-Smirnov test. The SF-36, FNDT, and SF-36 scores were adopted as independent variables. The type of IBD and smoking status were adopted as dependent variables. The statistical relationships between these variables were investigated using the Chi-square, bivariate correlation, and Independent-Samples t-tests. A p level <0.05 was regarded as statistically significant.

Ethics: Approval for the study was granted by the Ondokuz Mayis University Ethical Committee before commencement. The aim of the study was explained to all the participants, and their written consent was obtained before any data were collected.

RESULTS

One hundred twenty-one patients with IBD were included in the study, of whom 39.7% were women (n= 48), 71.9% (n= 34) were married, and 30.7% (n= 36) were educated to the university level or higher. The mean age of the participants was 42.06±14.9 years. Seventy-eight (64.5%) cases were diagnosed with UC and 48 (39.7%) with CD. Participants had been diagnosed with IBD a mean 6.32±5.4 years previously, and their mean age at diagnosis was 35.12±13.08 years. A comparison of the participants' demographic data according to their diagnoses is shown in Table 1.

Table 1. The demographic variables of the patients with UC and CD

Variable	UC	CD n= 45	p
Gender			
Male	44 (58%)	38 (64%)	x^2= 0.922
Female	32 (42%)	17 (36%)	p= 0.203
Mean Age	43.22±12.5	37.68±13.1	t= 2.936 p= 0.004
Marital Status			
Single	12 (19.8%)	14 (34%)	x^2= 8.493 p= 0.003
Married	61 (80.2%)	29 (62%)	
Divorced/Widowed	3 (4.9%)	2 (4%)	
Mean Years of Education	8.12±1.1	8.08±0.9	t= 0.631 p= 0.27

Smoking status, mean E-CO measurements, the mean number of cigarettes smoked per day, FNDT, and pack/year values among the active smokers with UC and CD are shown in Table 2. Analysis showed that 36.3% of the study population were smokers and that 68.2% of the active smokers had previously quit attempts at least once (min= 1, max= 11). Male participants (n= 29, 65.9%) had a

higher smoking rate than women (n= 15, 34.1%) (x^2=17.250, p<0.001). There was no statistical difference between the mean values of each four E-CO readings in both smokers (F=0.235) and non-smokers (F=0.852)

Disease characteristics and features according to smoking status in IBD cases with different diagnoses are shown in Table 3. No statistically significant correlation was observed between gender and diagnosis of IBD. However, patients with CD had a higher proportion of smokers than patients with UC (28.2% versus 44.4%, x^2=6.313, p=0.017).

Table 2. The smoking features and mean E-CO values of the patients with UC and CD

Variables	UC n (%)	CD n (%)	p
Smoking Status			
Smoker	22 (27.2%)	20 (44%)	
Non-Smoker			
Ex-Smoker	27 (37.0%)	17 (38%)	x^2=11.991, p=0.002
Never Smoked	27 (37.0%)	8 (18%)	
FNDT*	3.70±1.3	2.71±2.2	t=3.903, p<0.001
The mean number of cigarettes smoked in a day	8.04±1.3	6.52±14.5	t=6.255, p<0.001
Package/year	7.17±14.6	4.30±0.9	t=1.694, p=0.091
Mean CO ppm	6.7±7.5	4.09±4.8	t=3.453, p=0.001

***FNDT= Fagerström Nicotine Dependency Test**

Table 3. Disease features of the patients with UC and CD according to smoking status

Variable	**UC** n= 76		t, p	**CD** n= 45		t, p
	Smoker n= 22	Non-Smoker n= 54		Smoker n= 20	Non-Smoker n= 25	
Age (years)	40.12±9.9	44.15±13.0	1.587, 0.072	37.06±11.1	38.7±15.2	0.322, 0.462
CO ppm (mean)	12.7±1.2	1.41±0.18	11.746, <0.001	10.4±6.1	1.2±0.25	10.58, <0.001
Duration of the Disease (years)	7.85±4.1	7.23±2.1	1.822, 0.07	3.22±3.1	4.8±3.0	1.125, 0.347
Age at Diagnosis (years)	33.28±10.8	37.98±13.8	5.897, 0.010	34.3±11.1	35.0±15.7	0.227, 0.821
Mean Number of Exacerbations in the Previous Two Years	1.45±2.7	2.6±3.1	1.520, 0.122	3.64±5.9	1.89±2.57	1.928, 0.052
Mean Number of Hospital Admissions in the Previous Two Years	10.7±9.8	7.55±5.6	3.411, <0.001	9.78±1.8	8.06±4.1	2.211, 0.03
Number of Hospitalizations	0.41±0.8	0.76±1.4	1.570, 0.118	1.28±3.6	1.68±2.2	0.177, 0.368
Mean Number of Surgical Operations	0.04±0.6	0.28±1.1	2.735, 0.014	1.09±1.3	0.86±1.2	1.857, 0.058
History of Surgery (n, %)	3, 9.1%	2, 1.7%	4.741, p=0.124	13 (52 %)	12 (48 %)	2.795, 0.061
Treatment (n, %)			x^2, p			x^2, p
Immunosuppressive	6, 27.3%	28, 47.5%	5.655, 0.017	8 (50%)	8 (50%)	0.255, 0.501
Anti-TNF	7, 31.8%	10, 16.9%	4.327, 0.032	12 (57.1%)	9 (42.9%)	5.186, 0.005
Corticosteroid	2, 4.5%	11, 18.6	1.008, 0.152	4 (50%)	4 (50%)	0.511, 0.652
5-ASA	17, 77.3%	51, 86.4%	1.099,0.102	11 (35.5%)	20 (64.5%)	

Seventeen (38.6%) active smokers stated that they wished to quit smoking within the following six months. No significant relationship was found between willingness to quit smoking and disease diagnosis (x^2=1.014). Twenty-three non-smokers (29.9%) reported being exposed to second-hand smoke during the day; 9.2% of the participants reported being exposed to second-hand smoke at home, 16.8% at work, and 29% in their social environment. The mean E-CO measurements (1.77±0.88 ppm) of these non-smokers who reported exposure to second-hand smoke did not differ significantly from those of the other non-smokers (1.75±0.6) (t=0.087).

The Quality of Life of the Patients with UC and CD: A comparison of the SF-36 sub-dimensions between the patients with UC and CD patients is presented in Table 4. No difference was observed between the groups' mean scores from the eight SF-36 sub-dimensions except for general health perception, on which the patients with UC registered better results than those with CD. There was no significant difference in mean total SF-36 MC and PC scores between the UC and CD groups.

Analysis of the SF-36 sub-dimensions among the patients with UC showed that male patients achieved better physical functioning subdimension scores than women (86.5±20.6 vs

77.9±23.9, respectively, t=2.406, p=0.015). Men with CD also registered better physical functioning sub-dimension scores than women (87.6±20.9 vs 78.0±20.9, respectively, t=2.340, p=0.021).

Table 4. A comparison of the SF-36 sub-dimensions of SF-36 between the UC and CD groups

SF-36 Subdimensions (mean)		UC (n=76)	CD (n=45)	t, p
Physical Component	Physical Functioning	82.9±22.4	84.2±20.1	0.451, 0.653
	Physical Role Limitations	63.2±47.4	58.7±48.7	0.741, 459
	General Health Perceptions	61.6±24.9	54.8±28.1	2.045, 0.042
	Bodily Pain	64.5±31.3	72.6±84.8	1.091, 0.276
	Total Physical Component Score	272.4±102.5	270.4±121.7	0.104, 0,917
Mental Component	Mental Health	59.9±16.0	59.6±16.4	0.137, 0.891
	Social Function	68.9±27.3	65.4±26.4	1.206, 0.306
	Energy/Vitality	50.1±20.3	47.3±18.1	1.108, 0.269
	Emotional Role Limitations	69.1±46.3	72.6±44.2	0.608, 0.544
	Total Mental Score	248.0±83.1	245±84.5	0.201, 0.841

Relationships between Quality of Life, Mean Number of Cigarettes Smoked in Day FNDT, Package/Year, and E-CO Measurements: The SF-36 general health sub-dimension scores of smokers with UC (71.36±24.7) were significantly higher than those of the non-smoker UC group (58.7±24.2) (t=2.052, p=0.042). The mean total SF-36 PC scores were significantly higher among the smoker UC patients compared to the non-smokers (296.4±107.1 vs. 241.52±100.2, t=1.285, p=0.002). The mean total SF-36 MC scores were significantly higher in the smoker UC patients compared to the non-smokers (285.1±87.4 vs. 231.81±101.2, t=1.665, p=0.005). Correlations between mean number of cigarettes smoked per day, FNDT, package/year, and E-CO measurements, and the PC and MC of the SF-36 in patients with UC are presented in Table 5. A weak correlation was observed between E-CO ppm, the mean number of cigarettes smoked per day, FNDT, and package year, and the mean total SF-36 MC and PC scores ($p<0.05$).

Table 5. Correlations between FNDT, Package/year, and E-CO measurements and the SF-36 Physical and Mental dimensions in the UC group

Variable	PC-SF-36	MC-SF-36	CO ppm	FNDT	The mean number of cigarettes smoked per day	Package/year
PC-SF-36	1					
MC-SF-36	0.713*, 0.001**	1				
Mean CO ppm	0.163*, 0.038**	0.164*, 0.037**	1			
FNDT	0.237*, 0.002**	0.219*, 0.005**	0.754*, 0.001**			
The mean number of cigarettes smoked per day	0.314* 0.001**	0.298* 0.002**	0.785* 0.001**	0.755* 0.001**	1	
Package/year	0.185*, 0.019**	0.187*, 0.017**	0.603*, 0.001**	0.575*, 0.001**	0.561* 0.001**	1
r=* **p=****						

The mean scores of the eight SF-36 sub-dimensions in the smoker CD group did not differ significantly from those of the non-smokers ($p>0.05$). There was a weak negative correlation between MC and E-CO in the CD group (p=0.027). Correlations between the mean number of cigarettes smoked per day, FNDT, package/year, and E-CO measurements and the Physical and Mental dimensions of the SF-36 in the CD group are shown in Table 6.

Table 6. Correlations between FNDT, Package/year, and E-CO measurements and SF-36 Physical and Mental dimensions in the CD group

Variable	PC-SF-36	MC-SF-36	CO ppm	FNDT	The mean number of cigarettes smoked in a day	Package/year
PC-SF-36	1					
MC-SF-36	0.582*, 0.001**	1				
Mean CO ppm	0.175*, 0.081**	-0.199*, 0.027**	1			
FNDT	-0.145*, 0.150**	-0.139*, 0.169**	0.810*, 0.001**	1		
The mean number of cigarettes smoked in a day	-0.122 0.087	-0.250 0.090	0.658 0.001	0.712 0.001	1	
Package/year	-0.060*, 0.551**	-0.023*, 0.818**	0.521*, 0.001***	0.670*, 0.001**	0.590*, 0.001**	1
r=* **p=****						

DISCUSSION

Our study is the first in the literature to investigate the mean E-CO level and quality of life and clinical characteristics of IBD patients as far as we know. In this context, some striking results have been achieved. Smoking rates were quite high in our sample (34.7%), with 44.4% of patients with CD and 29.3% of those with UC being active smokers. Although smoking rates were higher among the patients with CD, the UC group exhibited higher FNDT, pack/year, and mean CO ppm measurement values. Smokers with UC and CD both had much higher mean E-CO measurements than non-smokers (9-fold and 8.9-fold, respectively). A study of 1098 cases of IBD reported a smoking rate of 10%, 88.2% of these being patients with CD (Scoville et al., 2020). Also similar to our results, a cohort study of 1203 participants by Lunney et al. reported a higher frequency of smoking in patients with CD (19).

The results of this study indicate that GIS symptoms commenced four years later in non-smoker patients with UC. Smokers with UC also experienced less frequent disease exacerbation, had fewer hospital admissions, and needed fewer surgical operations in the previous two years. However, they also had greater immunosuppressive requirements and received more anti-TNF therapies. There are conflicting reports regarding the clinical course in patients with UC who smoke. One meta-analysis study concluded that smoking is a protective factor in terms of clinical outcomes of UC (20). However, this positive effect disappears when a smoker with UC quits, and symptoms peak within one year (21). It has also been emphasized that this clinical deterioration is dose-dependent and that heavier smokers are more susceptible to the risk of disease exacerbation after cessation compared to light smokers (22). We, therefore, excluded patients who had quit smoking one year previously so that they would not affect our results. There are also conflicting reports concerning the effect of smoking on the frequency of surgical procedures and the risk of postoperative complications. Some studies have reported a significant decrease in the number of surgical procedures, while some have observed no effect, and others have shown a significant increase (23-25).

The results of this study indicate no significant difference in terms of clinical outcomes. Like smoker participants of UC, smoker CD patients had higher numbers of hospital visits in the previous two years compared to non-smokers. Previous studies have described smoking as the most potent environmental factor in the development and clinical manifestation of CD (26, 27). Studies have estimated that smoking increases the incidence of CD 1.8 to 4.6-fold (28, 29). Smoking cessation has therefore been recommended as the primary therapeutic approach in CD (30). Despite inconsistent reports having been published (27), the risk of exacerbation and clinical symptom severity decreases two-fold after quitting among smokers with CD patients in the following years (31). A smoking cessation intervention study by Cosnes et al. reported that the clinical course improved in the 474 smokers with CD (with a quit rate of 14%) who had quit smoking for more than one year, while the number of attacks was significantly lower (12). Other follow-up studies of the improvement in the clinical course of CD in patients who quit smoking have confirmed these data (32, 33).

The findings of this study revealed no difference between the quality of life of patients with UC and CD in terms of the eight sub-dimensions of the SF-36. However, other studies have observed a higher quality of life in patients with UC than in those with CD (34, 35). Our results indicated a weak and positive relationship between

the Physical and Mental components of the SF-36 and the mean number of cigarettes smoked per day, FNDT scores, pack/year values, and mean E-CO measurements in the UC group. Among the SF-36 sub-dimensions, only the mean General Health Perception was higher in the patients with UC who smoked than in the non-smokers. We also determined a weak negative correlation between E-CO measurements and MC of the SF-36 in the CD group patients. Other studies have observed significantly lower quality of life in active smokers with CD (21, 36). Our results may have been affected by the demographic and smoking features of the study population. The CD cases in our sample were on average five years younger and smoked less than the UC cases. In addition, the SF-36, a common clinical scale, was used to evaluate the quality of life in the present study. This scale is also affected by other comorbid chronic diseases. The effects of other chronic diseases in our cases could not, therefore, be eliminated in the analyses. Other quality-of-life questionnaires are available for clinical follow-up of IBD patients, and studies using these surveys may produce different results (37).

The study results revealed no relationship between second-hand smoking and quality of life in patients with IBD. The World Health Organization notes that there is no safe range for exposure to secondhand smoke (38). Our scan of the literature revealed no randomized controlled trials showing a direct relationship between passive exposure to cigarette smoke and IBD. While nearly 40% of smokers in the present study stated that they were considering quitting, no difference was found between the two diseases in terms of motivation. Similarly, a study conducted with CD patients emphasized that although nearly 90% of the patients had thought about quitting smoking, less than 30% were willing to participate in a free smoking cessation program (39).

Limitations and Directions/Suggestions for Future Research: There are several strengths and weaknesses to this investigation of the effect of smoking on the quality of life and disease characteristics of patients with IBD. Although our university is the most important reference center in the region, this research is not a descriptive study aimed at determining the true proportion of smokers among patients with IBD in our region. As described above, the two most important agents in smoke that affect the clinical outcomes of IBD are believed to be nicotine and CO (40, 41). Patients' exposure to nicotine was evaluated using the mean number of cigarettes smoked per day, FNDT, and pack/year criteria. However, these are declarative parameters that do not directly reflect total plasma nicotine levels. Cigarettes smoked per day provide a crude estimation of the nicotine consumed in a day as the nicotine amount of each cigarette brand differs (light cigarettes etc.). In contrast to this phenomenon, E-CO measurements provide an objective variable for determining exposure to smoke which can be measured very easily. However, it is a disadvantageous situation that E-CO measurements provide short-term information about the level of cigarettes smoked as the mean half-life of exhaled CO in smokers is approximately five hours (42). Also, E-CO measurements can be affected by numerous different environmental factors (indoor smoking, being in well-ventilated areas, etc.). To minimize this disadvantageous situation, we performed four measurements each week to monitor these readings for a longer period. In this way, we had the advantage of evaluating average measures of CO ppm in every participant. Our results showed us that there was no difference in the E-CO levels of the study participants during these four weeks, regardless of their smoking status. Also, the clinical features of UC and CD can differ significantly, depending on the anatomical site of the inflammatory process in the GIS (43). However, since colonoscopy was not applied during the study, these sites of involvement could not be determined exactly. These factors may have influenced our results. In addition, one of the most important limitations of our study is that the disease activity of patients, which may affect the quality of life, has not been evaluated. Therefore, we believe that it will be useful to evaluate this factor in future studies.

In conclusion, a weak, positive correlation was found between quality of life in patients with UC and the mean number of cigarettes smoked per day, FNDT, pack/year, and E-CO levels, also there was a negative correlation between E-CO measurements and MC in patients with CD.

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