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Can smoking have an effect on total rectum wall thickness in ulcerative colitis?

Sigara kullanımının ülseratif kolitte total rektum duvar kalınlığı üzerine etkisi olabilir mi?

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Background and Aims: *Ulcerative colitis is an idiopathic, chronic inflammatory disease with a high relapse rate. Smoking contributes to the development and progression of ulcerative colitis. We determined total rectal wall thickness in patients with ulcerative colitis who had a smoking history.* ***Materials and Methods:*** *We included 19 patients with ulcerative colitis (ulcerative colitis group) and 19 controls (control group) and compared total rectal wall thickness among them. Total rectal wall thickness was significantly greater in the ulcerative colitis group. We also compared total rectal wall thickness between patients with and without smoking history in both groups.* ***Results:*** *We included 19 ulcerative colitis patients (4 female/15 male, mean age, y, 46.8±13.3), and 19 control subjects (5 female/14 male, mean age, y, 46.6±11.8). While 9 patients with ulcerative colitis were active, 10 were in remission. The median (interquartile range) total rectal wall thickness was significantly higher in the ulcerative colitis group (4.1 mm [3.1–4.6]) than in the control group (2.5 mm [2.0-3.7]) (p=0.003). The median total rectal wall thickness was significantly higher in patients with ulcerative colitis and a smoking history than in those without (4.6 mm [4.3-4.9] vs. 3.8 mm [2.6-4.1], respectively; p=0.025). Total rectal wall thickness did not differ according to smoking history in the control group.* ***Conclusion:*** *Smoking history is associated with total rectal wall thickness increase in patients with ulcerative colitis on transrectal ultrasonography.*

Key words: *Transrectal ultrasonography, ulcerative colitis, cigarette smoking*

Giriş ve Amaç: *Ülseratif kolit idiyopatik, relapslarla seyreden kronik inflamatuvar bir hastalıktır. Sigara kullanımı ülseratif kolit gelişiminde ve progresyonunda etkilidir. Amacımız sigara kullanım öyküsü olan ülseratif kolitlilerde total rektal duvar kalınlığını değerlendirmekti.* ***Gereç ve Yöntem:*** *Çalışmaya 19 ülseratif kolitli hasta ve 19 kişilik kontrol gurubu alındı. Transrektal ultrasonografi ile total rektal duvar kalınlığı, ülseratif kolit gurubu ile kontrol gurubu arasında karşılaştırıldı. Ülseratif kolit gurubunda total rektal duvar kalınlığını belirgin olarak artmış saptadık. Daha sonra ülseratif kolit ve kontrol gurupları içinde total rektal duvar kalınlığını sigara içme öyküsü olanlarla olmayanlar arasında karşılaştırdık.* ***Bulgular:*** *Çalışmamıza 19 ülseratif kolit li hasta (4 kadın/15 erkek, ortalama yaş 46.8±13.3) ve 19 kontrol (5 kadın/14 erkek, 46.6±11.8) alındı. Ülseratif kolitlilerin 9'unda hastalık aktifken, 10'u remisyondaydı. Total rektal duvar kalınlığını ülseratif kolit'lilerde kontrollere göre artmış olarak saptadık, median sırasıyla [4.1 mm (3.1-4.6)]'ye karşın [2.5 mm (2.0-3.7)] (P=0.003). Ek olarak, total rektal duvar kalınlığı sigara öyküsü olan ülseratif kolit hastalarında sigara öyküsü olmayanlara göre belirgin olarak arttığını saptadık, sırasıyla median [4.6 mm (4.3-4.9)]'ye karşın [3.8 mm (2.6-4.1)] (P=0.025). Kontrol gurubunda ise sigara kullanım öyküsüne göre total rektal duvar kalınlığında farklılık yoktu.* ***Sonuç:*** *Ülseratif kolitlilerde transrektal ultrasonografi değerlendirmesinde sigara kullanım öyküsü ile total rektal duvar kalınlık artışı ilişkilidir.*

Anahtar kelimeler: *Transrektal ultrasonografi, ülseratif kolit, sigara kullanımı*

INTRODUCTION

Ulcerative colitis (UC) is an idiopathic, chronic inflammatory disease with a high relapse rate. It affects primarily colonic mucosa and submucosa. Environmental and genetic factors play crucial roles in the pathogenesis of UC. One of the most influencing UC pathogenesis among environmental factor is smoking (1).

Smoking is considered to be protective against UC development. After smoking cessation, UC development and risk of progression may increase (2). It was also determined that active smokers among UCs had a higher risk of developing pouchitis when they quit after the ileal pouch–anal anastomosis (3). To the best of our knowledge, there is no study evaluating the effect of smoking on intestinal wall thickness in UC patients.

Transrectal ultrasonography (TRUS) is a cost-effective instrument that allows the sonographic evaluation of the rectal wall. Cross-sectional imaging did not benefit in early UC patients (4, 5). However, TRUS may distinguish between active UC and those in remission (6,7). Our aim was to evaluate the effects of smoking on total rectal wall thickness (TRWT) in UC patients.

MATERIALS and METHOD

Characteristics of Patients

This study was carried out in a prospective and comparative manner in Trakya University Medicine Faculty Gastroenterology Department between December 2009 and September

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2010. Nineteen UC diagnosed consecutive patients were prospectively enrolled into the study who had been referred for sigmoidoscopy from the inflammatory bowel disease and internal medicine outpatient clinics and 19 controls. Exclusion criteria were 1. Pregnancy, 2. Rectal surgery, 3. Colostomy, 4. Pelvic operation, 5. The ones taking any potential medications to cause or aggravate colitis like nonsteroidal anti-inflammatory drugs, 6. Patients who did not agree to participate in the study.

UC patients were diagnosed according to the clinical history, cross-sectional imaging, endoscopic and histological findings. Macroscopic findings were categorized according to the modified Baron score (MBS), which evaluates the severity of inflammation in sigmoidoscopy (8). Following UC activity scoring with MBS, the patients were divided into two groups as active (MBS ≥1) or in remission (MBS=0).

Control group was included to establish a normal range of rectal wall thickness and as a reference for comparison with patients. In the control group, 19 age and gender matched individuals with nonspecific complaints and normal rectal mucosa in rectosigmoidoscopic evaluation were included. The demographic data of the patients were recorded in the research forms in detail.

Our study has been approved by the local ethics committee (TUTFEK 2009/78). The purpose of the study protocol and the sonographic method to be applied were explained in detail to all of the participants and "Informed Consent Form" was signed, certifying the patient's approval.

TRUS Evaluation

All patients underwent rectosigmoidoscopic evaluation before the TRUS evaluation. TRUS was performed by the same endosonographer by using Siemens Sonoline Sienna (7.5 MHz, Erlangen, Germany) USG device, a rigid linear endorectal probe to examine the rectal wall thickness. In TRUS examination, while the patient was in the left lateral decubitus position, then TRWT measurement was made at a distance of 10 cm from the anal canal. TRWT was defined as the distance between the mucosal hyperechoic layer and the serosal hyperechoic layer.

TRWT measurements were classified as <2.0 mm; below normal thickness, between 2.0-3.0 mm; as normal thickness and >3.0 mm as above normal thickness according to the criteria as reported in the previous studies (6,7,9).

Statistical Analysis

All statistical analyses were performed using SPSS Statistics software version 25 (IBM Corp., Armonk, NY, USA). Since the TRWT was compatible with nonparametric distribution, they were shown as median (Interquartile range- IQR). Kruskal Wallis Test and Mann-Whitney Test were used to compare the averages of the groups. Statistically $p < 0.05$ was considered significant.

RESULTS

Patient Characteristics

Patients who were followed up in Trakya University Medical Faculty Hospital Internal Medicine outpatient clinic and Gastroenterology outpatient clinic with UC diagnoses were included in the study. In this study, 19 UC patients and 19 controls were included. Nine patients had active disease while 10 were in remission in the UC group. Also, there were 8 patients with smoking history in the UC group. Disease was active in 4 of these patients and in remission in 4 of them. In the control group, 11 people had a smoking history. The demographic characteristics of the patients and control group included in the study are shown in Table 1.

Table 1. Demographic features of UC and control group

	UC (n=19)	Controls (n=19)
Age Years mean±SD	46.8±13.3	46.6±11.8
Gender n, F/M	4 /15	5/14
Smoking history n (%)	8 (42.1)	11 (57.8)
UC • Active n (%) • In remission n (%)	9 (47.3) 10 (52.7)	NA

F: Female, M: Male, n: Patient number, SD: Standard deviation, UC: Ulcerative colitis. NA: Non available.

Evaluation of TRWT with TRUS

Table 2 shows TRWT values as median (IQR) in UC and control group. We found TRWT was significantly higher in UC patients than the control group (p=0.003). However, there was no difference in TRWT between active patients and those in remission in the UC group with median (IQR) [4.6 mm (3.9-4.9) vs 3.8 mm (2.9-4.3)] respectively (p=0.085).

Evaluation of TRWT in UC and Control Group with Smoking History

In Table 3, UC and control groups were compared separately between those with and without smoking history from the aspect of TRWT.

UC patients with smoking history had a thicker rectal wall than the ones with no smoking history (p=0.025). In the

Table 2. TRWT measurement in UC and control group

	UC (n=19)	Control (n=19)	p
TRWT mm, median (IQR)	4.1 (3.1-4.6)	2.5 (2.0-3.7)	0.003

UC vs control. Mann-Whitney Test.
n: Number of cases, TRWT: Rectum wall thickness, UC: Ulcerative colitis.

Table 3. TRWT comparison between UC and control group according to smoking history

	TRWT, mm, median (IQR)	p
UC;		
1. Smoking hist. n=8	4.6 (4.3-4.9)	***0.025****
2. Non smoking hist. n=11	3.8 (2.6-4.1)*	
Control;		
1. Smoking hist. n=11	3.0 (1.9-3.2)	0.935
2. Non smoking hist. n=8	2.3 (2.0-3.8)	

Hist: History, n: Number, UC: Ulcerative colitis, TRWT: Rectal wall thickness.

control group, we did not find any difference between those who had a history of smoking in TRWT and those who did not (Table 3).

Also, in considering UC activity, 4 out of 8 UC patients with smoking history had active disease while the other 4 were in remission (median TRWT were 5.2, 4.6, 4.3, and 3.1 mm, respectively).

DISCUSSION

Our study included 19 UC patients (4 female/15 male, mean age, y, 46.8±13.3), and 19 control subjects (5 female/14 male, mean age, y, 46.6±11.8). At first, we found that median [interquartile range (IQR)] TRWT in control group was 2.5 mm (2.0-3.7) which is in agreement with other reports from the literature (7,10-12). We also found that; median (IQR) TRWT in UC patients [4.1mm (3.1-4.6)] was significantly higher than the control group (p =0.003). However, we did not find a significant difference in median (IQR) TRWT between the active and in remission groups [4.6 (3.9-4.9) vs 3.8 (2.9-4.3)], respectively (p=0.085). Finally, TRWT was significantly higher in UC patients with smoking history than the nonsmokers median (IQR) [4.6 mm (4.3-4.9) mm] vs [3.8 mm (2.6-4.1)], (p =0.025). However, we did not find any difference in TRWT between those with and without smoking history in the control group (p=0.935) (Table 3).

Hurlstone, et al. and Ellrichmann, et al. stated that there was a marked difference in TRWT between active and in remission UC patients (13,14). In subsequent studies where the rectum wall can be evaluated in more detail with EUS and miniprobe, it was shown that wall thickness increase was significant in the active period of UC (15-17). However, in this study, the reason for this distinction cannot be made clearly it might be due to the fact that the hypoechoic area of the mucosal edema in the rectum wall cannot be fully limited. Also, in another study, Rustemovic et al similarly did not find any significant difference in TRWT between active and in remission UC patients (18).

There are many contradictory studies on the emergence, remission and exacerbation of UC related with smoking. Smoking might have a positive effect on UC's remission (19,20). In this study, 8 (42.1%) UC patients with a history of smoking had higher TRWT than the 11 UC patients with no smoking history. In UC patients with a history of smoking, the increase in TRWT may be considered to be due to activation in UC, however, among the 8 patients with smoking history, the disease was active only in 4 (50%) patients, while the remaining 4 patients were in remission. When we compared the TRWT of these two groups, we did not find a significant TRWT difference between the active and in remission UC subgroups (p=0.266) with smoking history. Therefore, we cannot explain TRWT increase with disease activity in UC patients with smoking history. To the best of our knowledge, there are no studies evaluating the relationship between smoking and TRWT. Increased TRWT in UC patients with smoking history can be considered hypothetically that smoking may affect the bowel wall via vascular pathogenesis other than inflammatory response. However, we cannot attribute this finding to the hypothesis that there is a disease activation after smoking cessation.

The limitations of the study is that our study was single-centered with relatively fewer patients. The second limitation was rectosigmoidoscopic evaluation and TRUS evaluations of the patients and control subjects were made by the same endoscopist. The third limitation was the TRUS device used is not as sensitive as echoendoscopes.

In conclusion, we found that TRWT was increased in UC group compared to control group. TRWT was not associated with disease activity in UCs. Interestingly, TRWT was significantly higher in UC patients with smoking history than the ones with no smoking history.

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