Time spent per day in strenuous activity and total physical activity are inversely associated with mucosal healing but not with clinical remission in patients with ulcerative colitis

Junichi Watanabe[a]*, Shinya Furukawa[b]*, Sen Yagi[c], Kana Shiraishi[d], Masakazu Hanayama[d], Kazuhiro Tange[d], Yu Hashimoto[d], Shogo Kitahata[d], Kenichirou Mori[e], Tomoyuki Ninomiya[e], Seiyuu Suzuki[f], Naozumi Shibata[g], Hidehiro Murakami[c], Katsuhisa Ohashi[h], Aki Hasebe[i], Hideomi Tomida[j], Yasunori Yamamoto[k], Eiji Takeshita[j], Yoshio Ikeda[k], Yoichi Hiasa[d]

Ehime Prefectural Central Hospital, Matsuyama; Ehime University; Saiseikai Matsuyama Hospital, Matsuyama, Ehime; Ehime University Graduate School of Medicine; Sumitomo Besshi Hospital, Niihama; Ehime Prefectural Niihama Hospital, Niihama; Ohashi Clinic participate in Gastro-Enterology and Ano-Proctology, Niihama, Ehime; Shikoku Cancer Center, Matsuyama, Ehime; Ehime University Hospital, Japan

Abstract

Background Epidemiological evidence on the association between physical activity (PA) and ulcerative colitis (UC) is limited, and the effect of PA on the prognosis of UC is currently unknown. We evaluated the association between PA and clinical outcomes, including clinical remission and mucosal healing (MH), in Japanese patients with UC.

Methods The study subjects were 327 Japanese patients with UC. Subjects were asked about the average time spent per day on 4 types of PA (sedentary, standing, walking, and strenuous activity) and metabolic equivalents (METs) using a validated questionnaire. Clinical outcomes were complete MH, MH, and clinical remission. The association between PA, including hours spent on each type of PA and average daily METs, and clinical outcomes was assessed by multivariate logistic regression.

Results Plentiful strenuous activity was significantly inversely associated with MH and complete MH after adjustment (MH: adjusted odds ratio [OR] 0.45, 95% confidence interval [CI] 0.23-0.89; complete MH: adjusted OR 0.24, 95%CI 0.07-0.62; P for trend=0.008). A very high daily MET total was significantly inversely associated with complete MH after adjustment (adjusted OR 0.37, 95%CI 0.16-0.80; P for trend=0.010). In contrast, no association between PA and clinical remission was found (plentiful strenuous activity: adjusted OR 1.10, 95%CI 0.55-2.23; very high daily total METs: adjusted OR 0.74, 95%CI 0.37-1.46).

Conclusion In Japanese patients with UC, time spent per day on strenuous activity and total PA per day may be significantly inversely associated with complete MH, but not with clinical remission.

Keywords Mucosal healing, exercise, clinical remission, ulcerative colitis, metabolic equivalents

Ann Gastroenterol 2021; 34 (6): 796-801

*These authors made an equal contribution to this work and share first authorship

Conflict of Interest: None

Correspondence to: Shinya Furukawa, MD, PhD, Health Services Center, Ehime University, Matsuyama, Bunkyo, Ehime 790-8577, Japan, e-mail: shinya.furukawa@gmail.com

Introduction

The clinical course of ulcerative colitis (UC) is characterized by repeated relapses and remissions [1]. Patients with active UC exhibit endoscopic findings such as erythema, decreased or absent vascular patterns, friability, erosions, spontaneous bleeding, and ulcerations. Mucosal healing (MH) has been associated with clinical remission and lower rates of hospitalization, surgery, and colorectal cancer [2-7]. MH is thus the therapeutic goal for UC.

Several reports have been published regarding the association between physical activity (PA) and UC, with the majority of studies showing that PA has a favorable effect on disease prevention and symptom alleviation. In most case-control and prospective cohort studies, PA was not associated with the onset of UC [8-12]. In one case control study, however, low PA level was a risk factor for UC development [13]. One other study showed a non-significant association between PA and UC disease activity, with higher levels of PA being associated with less frequent relapses [14]. Nevertheless, the effect of PA on the prognosis of UC is currently unknown.

Here, we aimed to evaluate the association between PA and UC prognosis, including clinical remission and MH, in Japanese patients with UC. The primary objective of this study was to evaluate the association between total daily metabolic equivalents (METs) in the previous year and UC prognosis. The secondary objective was to evaluate the association between the time spent on each type of PA—namely, sedentary, standing or walking—as well as strenuous activity, and UC prognosis.

Patients and methods

Study population

Between 2015 and 2019, 387 Japanese patients with UC visited the Department of Gastroenterology and Metabology at the Ehime University Graduate School of Medicine, or one of several affiliated hospitals in Ehime Prefecture, as inpatients or outpatients. All patients able to give informed consent and respond to the self-administered questionnaire were considered candidates for the study. Completed questionnaires were available for 84% (327/387) of the patients, accordingly included in the final analysis.

Most UC cases were diagnosed based on endoscopic findings and confirmed through radiological and histological findings. This study was conducted in accordance with the Declaration of Helsinki, and the study protocol was approved by the institutional review board of the Ehime University

[a]Department of Rehabilitation, Ehime Prefectural Central Hospital, Matsuyama (Junichi Watanabe); [b]Health Services Center, Ehime University (Shinya Furukawa); [c]Department of Internal Medicine, Saiseikai Matsuyama Hospital, Matsuyama, Ehime (Sen Yagi, Hidehiro Murakami); [d]Department of Gastroenterology and Metabology, Ehime University Graduate School of Medicine (Kana Shiraishi, Masakazu Hanayama, Kazuhiro Tange, Yu Hashimoto, Shogo Kitahata, Yoichi Hiasa); [e]Department of Gastroenterology, Ehime Prefectural Central Hospital, Matsuyama (Kenichirou Mori, Tomoyuki Ninomiya); [f]Department of Gastroenterology, Sumitomo Besshi Hospital, Niihama (Seiyuu Suzuki); [g]Department of Gastroenterology, Ehime Prefectural Niihama Hospital, Niihama (Naozumi Shibata); [h]Ohashi Clinic participate in Gastro-Enterology and Ano-Proctology, Niihama, Ehime (Katsuhisa Ohashi); [i]Department of Gastroenterology, Shikoku Cancer Center, Matsuyama, Ehime (Aki Hasebe); [j]Department of Inflammatory Bowel Diseases and Therapeutics, Ehime University Graduate School of Medicine (Hideomi Tomida, Eiji Takeshita); [k] Endoscopy Center, Ehime University Hospital (Yasunori Yamamoto, Yoshio Ikeda), Japan

Graduate School of Medicine (#1505011). Trained staff obtained written informed consent from all enrolled patients.

Data collection

To obtain data on habits such as smoking, drinking, and physical activity, we gave patients a self-administered paper-and-pencil questionnaire; we also examined their medical records to obtain information on body mass index (BMI), endoscopic findings, disease extent, clinical remission, and the use of medication for UC. Current smoking was defined as positive if a study subject reported smoking at least one cigarette per day. Current drinking was defined as positive if a study subject reported consuming alcohol, regardless of amount or frequency. Height was measured to the nearest millimeter using a stadiometer with the patient standing completely erect. Weight was measured in light clothing. BMI was calculated as weight in kg divided by height in m^2. All endoscopic findings used in our analysis had been obtained within the last 6 months. In patients without endoscopic findings in the last 6 months, a new endoscopy was performed to assess mucosal status. Certified gastrointestinal endoscopists provided most of the medical reports regarding endoscopic activity.

Assessment of PA

The main area of interest in the present study was daily total PA level for the past year. We assessed PA using a validated questionnaire that shows a moderately strong correlation (r=0.69) with 24-h self-reported PA records (the gold standard) [15]. In accordance with the Japan Public Health Center-based Prospective Study (JPHC Study) [15], subjects were asked, "How long on average have you engaged in the following activities each day for the past year?"; the activities in question were "sitting", "standing", "walking", and "strenuous". Subjects gave one of the following possible responses about the average duration of each activity type, estimated in h per day: (i) none; (ii) 0-<1; (iii) 1-<3; (iv) 3-<5; (v) 5-<7; (vi) 7-<9; (vii) 9-<11; and (viii) >11. Metabolic equivalents (METs) per day were estimated by multiplying the number of h per day spent at each activity level by that activity level's MET intensity (h of sedentary activity ×1.5, h of walking or standing ×2.0, and h of strenuous activity ×4.5). After summing the METs per day of all activities, subjects were grouped into 4 exposure levels according to quartiles of total METs per day.

Assessment of clinical remission, endoscopic activity and MH

Clinical remission was defined as no rectal bleeding and stool frequency <3 times per day. MH was assessed according to the Mayo endoscopic subscore, which consists of the following 4 categories: 0, normal or inactive disease; 1, mild disease with erythema, decreased vascular patterns, and mild friability; 2,

moderate disease with marked erythema, absence of vascular patterns, friability, and erosions; and 3, severe disease with spontaneous bleeding and ulceration [16]. In this study, complete MH and MH were defined as categories 0 and 0-1, respectively. One endoscopy specialist blinded to patient PA levels was responsible for interpreting the endoscopic findings.

Statistical analysis

To investigate whether different types of PA had different effects on outcome, we analyzed the relationship between MH and frequency of sedentary activity (<3 h [reference], 3-8 h, and ≥8 h), walking and standing (<4 h [reference], 4-8 h, and ≥8 h), and strenuous activity (<1 h [reference], 1-3 h, and ≥3 h). Daily total MET score was divided into quartiles according to its distribution among the study subjects. The resulting 4 categories were as follows: 1) low METs, <14.75 METs/day (reference); 2) moderate METs, 19.36-20.00 METs/day; 3) high METs, 20.00-27.75 METs/da; and 4) very high METs, >27.75 METs/day. Logistic regression analysis was performed to estimate crude odds ratios (ORs) and 95% confidence intervals (CIs) of clinical outcomes for time spent on each type of PA and daily total METs. Multiple logistic regression analysis was employed to adjust for potential confounders. Age, sex, BMI, prednisolone use, anti-tumor necrosis factor (TNF)-α monoclonal antibody use, current drinking, current smoking, and disease extent (proctitis and left-sided colitis vs. extensive colitis, including surgical cases) were selected *a priori* as potential confounding factors. All statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA). All probability values for statistical tests were 2-tailed, and P<0.05 was considered statistically significant.

Results

Table 1 shows the characteristics of this cohort. The rates of clinical remission, complete MH, and MH were 60.6%, 25.1%, and 61.5%, respectively. Prednisolone, thiopurines, and TNF-α monoclonal antibodies were used by 19.6%, 15.6%, and 5.8% of participants, respectively.

The association between PA and clinical remission is shown in Table 2. No association was found between time spent on any one type of PA or total PA and clinical remission.

Table 3 shows the crude and adjusted ORs and 95%CIs for MH in relation to PA. In the crude analysis, the inverse association between plentiful strenuous activity and MH was marginally significant. After adjustment, plentiful strenuous activity was independently inversely associated with MH (adjusted OR 0.45, 95%CI 0.23-0.89). Sedentary activities, walking or standing, and daily total PA were not associated with MH.

Table 4 shows the crude and adjusted ORs and 95%CIs for complete MH in relation to PA. Plentiful strenuous activity (crude OR 0.24, 95%CI 0.07-0.63) and very high daily total

Table 1 Clinical characteristics of the 327 study participants

Variable	n (%)
Age, years, median ± IQR, years	48.0±26.0
Male (%)	190 (58.1)
BMI, mean ± SD, kg/m²	22.76±4.63
Current smoking (%)	26 (8.0)
Current drinking (%)	134 (41.0)
Medication	
5-aminosalicylates, n (%)	300 (91.7)
Prednisolone, n (%)	64 (19.6)
Thiopurines, n (%)	51 (15.6)
TNF-α monoclonal antibody, n (%)	19 (5.8)
Disease extent: proctitis/left-sided/ pancolitis/others (including surgical cases)	86/93/143/5
Clinical remission (%)	198 (60.6)
MES, mean ± SD	1.20±0.90
Complete mucosal healing (MES 0) (%)	82 (25.1)
Mucosal healing (MES 0-1) (%)	201 (61.5)
Sedentary activities	
<3 (h/day)	120 (36.7)
3-8 (h/day)	119 (36.4)
≥8 (h/day)	88 (26.9)
Walking or standing	
<4 (h/day)	127 (38.8)
4-8 (h/day)	106 (32.4)
≥8 (h/day)	94 (28.8)
Strenuous activity (heavy physical work or strenuous exercise)	
<1 (h/day)	231 (70.6)
1-3 (h/day)	50 (15.3)
≥3 (h/day)	46 (14.1)
Daily total METs, mean ± SD	23.55±13.13
Low (<14.75)	79 (24.2)
Moderate (14.75-20.00)	85 (26.0)
High (20.00-27.75)	79 (24.2)
Very high (≥27.75)	84 (25.7)

IQR, interquartile range; SD, standard deviation; BMI, body mass index; TNF, tumor necrosis factor; MES, Mayo endoscopic subscore; METs, metabolic equivalents

METs (crude OR 0.40, 95%CI 0.18-0.83) were inversely associated with complete MH, while sedentary activities and walking or standing were not associated with complete MH. After adjustment for confounding factors, plentiful strenuous activity (adjusted OR 0.24, 95%CI 0.07-0.62; P for trend=0.008) and very high daily total METs (adjusted OR 0.37, 95%CI 0.16-0.80; P for trend=0.010) were independently inversely associated with complete MH.

In a sensitivity analysis restricted to patients not using steroids, plentiful strenuous activity (adjusted OR 0.26, 95%CI 0.08-0.70; P for trend=0.021) and very high METs (adjusted OR 0.35, 95%CI 0.15-0.79; P for trend=0.009) were significantly inversely associated with complete MH. Similarly, in another sensitivity analysis restricted to patients in clinical remission, plentiful strenuous activity (adjusted OR 0.20, 95%CI 0.06-

Table 2 Crude and adjusted ORs and 95%CIs for clinical remission in relation to physical activity

Variable	Prevalence (%)	Crude OR (95%CI)	Adjusted OR (95%CI)
Sedentary activities			
<3 (h/day)	74/120 (61.7)	1.00	1.00
3-8 (h/day)	69/119 (60.0)	0.86 (0.51-1.44)	0.76 (0.43-1.32)
≥8 (h/day)	55/88 (62.5)	1.04 (0.59-1.83)	1.11 (0.59-2.07)
P for trend			0.87
Walking or standing			
<4 (h/day)	81/127 (63.8)	1.00	1.00
4-8 (h/day)	59/106 (55.7)	0.71 (0.42-1.21)	0.66 (0.37-1.17)
≥8 (h/day)	58/94 (61.7)	0.92 (0.53-1.59)	0.83 (0.46-1.51)
P for trend			0.49
Strenuous activity			
<1 (h/day)	138/231 (59.7)	1.00	1.00
1-3 (h/day)	31/50 (62.0)	1.10 (0.59-2.09)	1.13 (0.58-2.26)
≥3 (h/day)	29/46 (63.0)	1.15 (0.60-2.25)	1.10 (0.55-2.23)
P for trend			0.73
Total daily PA (METs)			
Low (<14.75)	51/79 (64.6)	1.00	1.00
Moderate (14.75-20.00)	54/85 (63.5)	0.96 (0.50-1.81)	0.92 (0.46-1.83)
High (20.00-27.75)	43/79 (54.4)	0.66 (0.34-1.24)	0.65 (0.32-1.29)
Very high (≥27.75)	50/84 (59.5)	0.81 (0.43-1.52)	0.74 (0.37-1.46)
P for trend			0.25

ORs were adjusted for age, sex, body mass index, use of prednisolone, use of tumor necrosis factor-α monoclonal antibody, current drinking, current smoking, and disease extent

OR, odds ratio; CI, confidence interval; METs, metabolic equivalents; PA, physical activity

Table 3 Crude and adjusted ORs and 95%CIs for mucosal healing in relation to physical activity

Variable	Prevalence (%)	Crude OR (95%CI)	Adjusted OR (95%CI)
Sedentary activities			
<3 (h/day)	71/120 (59.2)	1.00	1.00
3-8 (h/day)	68/119 (57.1)	0.92 (0.55-1.54)	0.95 (0.55-1.63)
≥8 (h/day)	62/88 (70.5)	1.65 (0.92-2.98)	1.71 (0.91-3.27)
P for trend			0.14
Walking or standing			
<4 (h/day)	83/127 (65.4)	1.00	1.00
4-8 (h/day)	64/106 (60.4)	0.81 (0.47-1.38)	0.75 (0.42-1.32)
≥8 (h/day)	54/94 (57.5)	0.72 (0.41-1.24)	0.67 (0.37-1.21)
P for trend			0.18
Strenuous activity			
<1 (h/day)	145/231 (62.8)	1.00	1.00
1-3 (h/day)	34/50 (68.0)	1.26 (0.67-2.47)	1.47 (0.75-3.02)
≥3 (h/day)	22/46 (47.8)	0.54 (0.29-1.03)	0.45 (0.23-0.89)
P for trend			0.09
Total daily PA (METs)			
Low (<14.75)	50/79 (63.3)	1.00	1.00
Moderate (14.75-20.00)	58/85 (68.2)	1.25 (0.65-2.39)	1.21 (0.61-2.43)
High (20.00-27.75)	45/79 (57.0)	0.77 (0.40-1.45)	0.75 (0.38-1.47)
Very high (≥27.75)	8/84 (57.1)	0.77 (0.41-1.45)	0.68 (0.34-1.34)
P for trend			0.12

ORs were adjusted for age, sex, body mass index, use of prednisolone, use of tumor necrosis factor-α monoclonal antibody, current drinking, current smoking, and disease extent

OR, odds ratio; CI, confidence interval; PA, physical activity; METs, metabolic equivalents

0.57; P for trend=0.005) and very high METs (adjusted OR 0.33, 95%CI 0.13-0.79; P for trend=0.013) were significantly inversely associated with complete MH.

Discussion

The present study demonstrated that plentiful strenuous activity and large amounts of total daily PA were independently inversely associated with complete MH among patients with UC. To the best of our knowledge, this is the first study to show an inverse association between PA and clinical outcome in patients with UC.

Several studies have reported an association between PA and the onset of UC [8-13]. In a Slovakian case control study that included 148 patients with UC, participation in 2 sporting activities per week during childhood was associated with a lower incidence of UC onset compared to control patients [13]. Other studies have found that the amount of PA or exercise does not have a preventive effect on the development of UC. In a Swedish case-control study that included 145 patients

with UC, recreational, outdoor, or sports activities were not associated with the onset of UC [8]. In an Asia-Pacific case-control study that included 256 patients with UC, compared with less-than-daily PA, daily PA was not associated with the onset of UC [9]. In an Israeli case-control study that included 55 patients with UC, PA level—scored according to a system incorporating the number of h per week of sleep, sitting, sedentary activity, and strenuous activity during work and leisure—was similar between UC patients and control participants [10]. In American and European (Denmark, Germany, Italy, the Netherlands, Sweden, and the UK) prospective cohort studies, PA was likewise not associated with the onset of UC [11,12].

To date, only one study has shown an association between PA and UC disease activity: in an American cohort study of 515 patients with UC or indeterminate colitis in remission, relapse occurred less frequently in the plentiful exercise group; at 6 months, however, no association between amount of exercise and rate of relapse was found [14]. Compared to our population, these patients had on average a higher BMI, younger age, lower proportion of men, and a higher rate of

Table 4 Crude and adjusted ORs and 95%CIs for complete mucosal healing in relation to physical activity

Variable	Prevalence (%)	Crude OR (95%CI)	Adjusted OR (95%CI)
Sedentary activities			
<3 (h/day)	30/120 (25.0)	1.00	1.00
3-8 (h/day)	29/119 (24.4)	0.97 (0.54-1.74)	0.92 (0.50-1.69)
≥8 (h/day)	23/88 (26.1)	1.06 (0.56-1.99)	1.18 (0.60-2.34)
P for trend			0.68
Walking or standing			
<4 (h/day)	34/127 (26.8)	1.00	1.00
4-8 (h/day)	31/106 (29.3)	1.13 (0.642.01)	1.06 (0.58-1.94)
≥8 (h/day)	17/94 (18.1)	0.60 (0.31-1.15)	0.55 (0.27-1.06)
P for trend			0.10
Strenuous activity			
<1 (h/day)	65/231 (28.1)	1.00	1.00
1-3 (h/day)	13/50 (26.0)	0.90 (0.44-1.76)	0.98 (0.46-1.99)
≥3 (h/day)	4/46 (8.7)	0.24 (0.07-0.63)	0.24 (0.07-0.62)
P for trend			0.008
Total daily PA (METs)			
Low (<14.75)	25/79 (31.7)	1.00	1.00
Moderate (14.75-20.00)	25/85 (29.4)	0.90 (0.46-1.75)	0.84 (0.42-1.69)
High (20.00-27.75)	19/79 (24.1)	0.68 (0.34-1.37)	0.68 (0.33-1.41)
Very high (≥27.75)	13/84 (15.5)	0.40 (0.18-0.83)	0.37 (0.16-0.80)
P for trend			0.010

ORs were adjusted for age, sex, body mass index, use of prednisolone, use of tumor necrosis factor-α monoclonal antibody, current smoking, current drinking, and disease extent

OR, odds ratio; CI, confidence interval; METs, metabolic equivalents

treatment with biologics; in addition, PA was assessed using different indices in these 2 studies, which may explain the different results.

Although the mechanism underlying the link between PA and disease activity remains unclear, there are several biologically plausible possibilities. An association between proinflammatory cytokines (such as interleukin [IL]-6, IL-17, and TNF-α) and mucosal injury has been reported in patients with UC [17,18]. There is some evidence that intestinal ischemia is triggered by strenuous exercise [19]. In humans, high PA may cause mucosal ischemia and elevate the proinflammatory response [20,21]. Thus, high PA may cause mucosal injury via elevated inflammatory cytokines and mucosal ischemia. If this is the case, then the mild mucosal ischemia and proinflammatory responses caused by standing, walking, and low to high total MET might be more easily suppressed by treatment than the more severe responses induced by plentiful strenuous exercise. Although exercise habits and higher PA levels have favourable effects on health in general, the present study suggests that patients with UC may need to refrain from strenuous exercise. Strenuous activity was not associated with clinical remission. The mean PA level in this cohort was lower than that in the

Japanese general population [22]. Thus, plentiful strenuous activity and high daily total PA levels may have been too rare in this cohort to interfere with clinical remission.

This study has some limitations. First, because a cross-sectional design was employed, we cannot conclude that there is a causal relationship between PA and complete MH. Thus, longitudinal and interventional studies should be performed to confirm the present findings. Second, this study utilized a self-administered questionnaire, introducing the possibility that participants may have misreported their own levels of PA. However, previous epidemiological studies have relied on similar questionnaires to assess PA [8-13]. Although our questionnaire's accuracy has been validated, some misclassification may have been unavoidable [15]. Changes in PA over time may also have caused misclassification, which might have led to an underestimation of the association. Third, given that the rates of MH and complete MH were 61.5% and 25.1%, respectively, it is likely that most of the patients in this cohort had been receiving long-term treatment. A long duration of treatment might have affected both PA and MH. Fourth, we asked participants to assess their PA over the previous year. The distance in time between the earlier parts of that year and the assessment of clinical outcomes may have resulted in a misclassification. However, the non-differential misclassification was towards the null. Fourth, although fecal calprotectin is a reliable marker for MH, we did not measure it in this cohort. We also did not collect data regarding any recent changes in medication, although these might have masked the association between PA and clinical outcomes. However, a similar association was found in patients who did not use steroids, indicating that medication status did not make a difference to the association. Finally, selection bias could have influenced our results. According to the large-scale JPHC Study, the mean METs per day among the Japanese general population in 2005 were 33.5 in men and 33.4 in women [22], but the corresponding value in the current study was 23.55. For this and other reasons, the subjects of the current study were probably not representative of all Japanese patients with UC. Nevertheless, the median age and the percentage of males in the present study (48.0 years and 58.1%, respectively) were similar to those in a Japanese national study based on UC claims data (44.0 years and 63.9%, respectively) [23].

The treat-to-target strategy is widely accepted as a means of improving clinical outcomes in patients with UC. Achieving complete MH (Mayo endoscopic subscore 0) is the ideal therapeutic goal [24]. In a treat-to-target approach, histological remission is also considered a significant outcome for UC patients. In the present study, however, information regarding the association between PA and histological remission is missing and further research is warranted.

In conclusion, plentiful strenuous activity and high daily total PA levels might be significantly inversely associated with complete MH but not with clinical remission in Japanese patients with UC.

Acknowledgments

Summary Box

What is already known:

- Most studies have found no association between physical activity and the onset of ulcerative colitis (UC)
- An association between low physical activity levels and UC relapse rate has been reported
- Although physical activity has favorable effects on health, the relationship between physical activity and disease activity in UC patients is still unclear

What the new findings are:

- Physical activity levels were assessed using a validated questionnaire
- Plentiful strenuous activity and high daily total physical activity were significantly inversely associated with mucosal healing
- No association between physical activity and clinical remission of UC was found

---

References

1. Langholz E, Munkholm P, Davidsen M, Binder V. Course of ulcerative colitis: analysis of changes in disease activity over years. *Gastroenterology* 1994;**107**:3-11.

2. Colombel JF, Rutgeerts P, Reinisch W, et al. Early mucosal healing with infliximab is associated with improved long-term clinical outcomes in ulcerative colitis. *Gastroenterology* 2011;**141**:1194-1201.

3. Frøslie KF, Jahnsen J, Moum BA, Vatn MH; IBSEN Group. Mucosal healing in inflammatory bowel disease: results from a Norwegian population-based cohort. *Gastroenterology* 2007;**133**:412-422.

4. Lichtenstein GR, Rutgeerts P. Importance of mucosal healing in ulcerative colitis. *Inflamm Bowel Dis* 2010;**16**:338-346.

5. Peyrin-Biroulet L, Ferrante M, Magro F, et al; Scientific Committee of the European Crohn's and Colitis Organization. Results from the 2nd scientific workshop of the ECCO. I: Impact of mucosal healing on the course of inflammatory bowel disease. *J Crohns Colitis* 2011;**5**:477-483.

6. Sandborn WJ, Panés J, Zhang H, Yu D, Niezychowski W, Su C. Correlation between concentrations of fecal calprotectin and outcomes of patients with ulcerative colitis in a phase 2 trial. *Gastroenterology* 2016;**150**:96-102.

7. Shah SC, Colombel JF, Sands BE, Narula N. Mucosal healing is associated with improved long-term outcomes of patients with ulcerative colitis: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 2016;**14**:1245-1255.

8. Persson PG, Leijonmarck CE, Bernell O, Hellers G, Ahlbom A. Risk indicators for inflammatory bowel disease. *Int J Epidemiol* 1993;**22**:268-272.

9. Ng SC, Tang W, Leong RW, et al; Asia-Pacific Crohn's and Colitis Epidemiology Study ACCESS Group. Environmental risk factors in inflammatory bowel disease: a population-based case-control study in Asia-Pacific. *Gut* 2015;**64**:1063-1071.

10. Klein I, Reif S, Farbstein H, Halak A, Gilat T. Preillness non dietary factors and habits in inflammatory bowel disease. *Ital J Gastroenterol Hepatol* 1998;**30**:247-251.

11. Khalili H, Ananthakrishnan AN, Konijeti GG, et al. Physical activity and risk of inflammatory bowel disease: prospective study from the Nurses' Health Study cohorts. *BMJ* 2013;**347**:f6633.

12. Chan SS, Luben R, Olsen A, et al. Body mass index and the risk for Crohn's disease and ulcerative colitis: data from a European prospective cohort study (the IBD in EPIC Study). *Am J Gastroenterol* 2013;**108**:575-582.

13. Hlavaty T, Toth J, Koller T, et al. Smoking, breastfeeding, physical inactivity, contact with animals, and size of the family influence the risk of inflammatory bowel disease: A Slovak case-control study. *United European Gastroenterol J* 2013;**1**:109-119.

14. Jones PD, Kappelman MD, Martin CF, Chen W, Sandler RS, Long MD. Exercise decreases risk of future active disease in patients with inflammatory bowel disease in remission. *Inflamm Bowel Dis* 2015;**21**:1063-1071.

15. Fujii H, Yamamoto S, Takeda-Imai F, et al. Validity and applicability of a simple questionnaire for the estimation of total and domain-specific physical activity. *Diabetol Int* 2011;**2**:47-54.

16. Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. *N Engl J Med* 1987;**317**:1625-1629.

17. Scheller J, Garbers C, Rose-John S. Interleukin-6: from basic biology to selective blockade of pro-inflammatory activities. *Semin Immunol* 2014;**26**:2-12.

18. Lee SH, Kwon JE, Cho ML. Immunological pathogenesis of inflammatory bowel disease. *Intest Res* 2018;**16**:26-42.

19. Camus G, Deby-Dupont G, Duchateau J, Deby C, Pincemail J, Lamy M. Are similar inflammatory factors involved in strenuous exercise and sepsis? *Intensive Care Med* 1994;**20**:602-610.

20. Ashton T, Young IS, Davison GW, et al. Exercise-induced endotoxemia: the effect of ascorbic acid supplementation. *Free Radic Biol Med* 2003;**35**:284-291.

21. Phillips RA. The relationship between proinflammatory mediators and heat stress induced rhabdomyolysis in exercising marines. *Crit Care Nurs Clin North Am* 2003;**15**:163-170, vii.

22. Inoue M, Iso H, Yamamoto S, et al; Japan Public Health Center-Based Prospective Study Group. Daily total physical activity level and premature death in men and women: results from a large-scale population-based cohort study in Japan (JPHC study). *Ann Epidemiol* 2008;**18**:522-530.

23. Matsuoka K, Igarashi A, Sato N, et al. Trends in corticosteroid prescriptions for ulcerative colitis and factors associated with long-term corticosteroid use: analysis using Japanese claims data from 2006 to 2016. *J Crohns Colitis* 2021;**15**:358-366.

24. Turner D, Ricciuto A, Lewis A, et al; International Organization for the Study of IBD. STRIDE-II: An update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) initiative of the International Organization for the Study of IBD (IOIBD): determining therapeutic goals for treat-to-target strategies in IBD. *Gastroenterology* 2021;**160**:1570-1583.