


Randomised clinical trial: yoga vs written self-care advice for ulcerative colitis

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Publication data

Submitted 25 January 2017
First decision 12 February 2017
Resubmitted 20 February 2017
Resubmitted 6 March 2017
Accepted 6 March 2017
EV Pub Online 5 April 2017

The Handling Editor for this article was Professor Jonathan Rhodes, and it was accepted for publication after full peer-review.

SUMMARY

Background

Perceived stress seems to be a risk factor for exacerbation of ulcerative colitis. Yoga has been shown to reduce perceived stress.

Aims

To assess the efficacy and safety of yoga for improving quality of life in patients with ulcerative colitis.

Methods

A total of 77 patients (75% women; 45.5 ± 11.9 years) with ulcerative colitis in clinical remission but impaired quality of life were randomly assigned to yoga (12 supervised weekly sessions of 90 min; $n = 39$) or written self-care advice ($n = 38$). Primary outcome was disease-specific quality of life (Inflammatory Bowel Disease Questionnaire). Secondary outcomes included disease activity (Rachmilewitz clinical activity index) and safety. Outcomes were assessed at weeks 12 and 24 by blinded outcome assessors.

Results

The yoga group had significantly higher disease-specific quality of life compared to the self-care group after 12 weeks ($\Delta = 14.6$; 95% confidence interval=2.6–26.7; $P = 0.018$) and after 24 weeks ($\Delta = 16.4$; 95% confidence interval=2.5–30.3; $P = 0.022$). Twenty-one and 12 patients in the yoga group and in the self-care group, respectively, reached a clinical relevant increase in quality of life at week 12 ($P = 0.048$); and 27 and 17 patients at week 24 ($P = 0.030$). Disease activity was lower in the yoga group compared to the self-care group after 24 weeks ($\Delta = -1.2$; 95% confidence interval=-0.1–[-2.3]; $P = 0.029$). Three and one patient in the yoga group and in the self-care group, respectively, experienced serious adverse events ($P = 0.317$); and seven and eight patients experienced nonserious adverse events ($P = 0.731$).

Conclusions

Yoga can be considered as a safe and effective ancillary intervention for patients with ulcerative colitis and impaired quality of life. Trial registration: ClinicalTrials.gov identifier: NCT02043600.

Aliment Pharmacol Ther 2017; **45**: 1379–1389

INTRODUCTION

Ulcerative colitis is a chronic inflammatory bowel disease of uncertain aetiology and pathophysiology.¹ Up to 780 000 persons in North America have ulcerative colitis; between 7000 and 46 000 cases are newly diagnosed with ulcerative colitis each year.² Ulcerative colitis often is associated with marked impairments in all aspects of quality of life. Particularly disease activity and also psychosocial variables can have a strong negative influence on health-related quality of life.^{3–5} However, 31.4% of patients with mucosal endoscopic healing, and 15.1% of patients with mucosal endoscopic healing, normal stool frequency and no rectal bleeding still report impaired quality of life.⁶

Psychosocial stress seems to be an important risk factor for the exacerbation of ulcerative colitis^{7–10}. It has been shown that perceived stress can triple the risk of disease exacerbation, whereas there seems to be no association with life events.¹¹ Thus, perceived stress seems to be more important in disease progression than the presence of objective environmental stressors.⁷

Originally a part of traditional Indian spiritual, philosophical and psychological practice, yoga has been adapted as a method in complementary medicine and is used especially in terms of prevention and therapy of diseases.^{12, 13} Yoga is gaining increased popularity as a therapeutic practice; with about 21 million Americans (9% of the United States of America's population) reporting they used it for health reasons in 2012.¹⁴ From 2002 to 2012, the prevalence of yoga use increased linearly, making it one of the most commonly used complementary and alternative medicine approaches in the United States of America.¹⁵

Yoga has been shown to positively influence subjective stress in both, healthy participants and patient populations,^{16–19} and perceived stress is the main reason for using yoga.¹⁴ Hence, yoga may be efficacious in improving symptoms related to ulcerative colitis. Therefore, this randomised clinical trial aimed to assess the efficacy and safety of yoga compared to self-care advice in patients with ulcerative colitis in remission experiencing impaired quality of life.

METHODS

Design

This was a single-blind randomised controlled trial conducted at a single centre, the Department of Internal and Integrative Medicine, Kliniken Essen-Mitte, Faculty of Medicine, University of Duisburg-Essen,

Essen, Germany. The study had been approved by the University of Duisburg-Essen ethics committee (approval number: 13-5560-BO) and registered at ClinicalTrials.gov (registration number: NCT02043600) prior to patient recruitment. The study was conducted and reported in accordance with the Consolidated Standards of Reporting Trials 2010 guideline.²⁰

Patients

Patients were recruited from the Department of Internal and Integrative Medicine, through local newspaper announcements, and through letters sent to all members of the German Crohn's Colitis Organization residing within a distance of 50 km from the study centre. Patients calling in were screened by a research assistant to assess eligibility. If apparently eligible, patients were invited for an assessment visit where they received detailed written information describing the study. They were assessed by a study physician, and if they met inclusion criteria and did not meet exclusion criteria, they were included in the trial, and written informed consent was obtained.

Male and female patients were included if they were 18–70 years old and suffered from clinical, endoscopic and histological diagnosed ulcerative colitis for at least 12 months. Patients had to be in clinical remission for at least 4 weeks but no longer than 12 months (Rachmilewitz clinical activity index²¹ ≤ 4). They had to report impaired disease-specific quality of life (Inflammatory Bowel Disease Questionnaire⁴ total score < 170). Patients had to be physically and mentally capable to perform yoga exercises.

Exclusion criteria included clinically active disease (Rachmilewitz clinical activity index > 4); complete resection of the colon; acute, infectious or chronic active ulcerative colitis; severe diseases precluding even light yoga exercises; malignancies with a disease-free survival < 5 years; alcohol or drug abuse; dementia; pregnancy; and regular yoga or Pilates use in the previous 12 months.

Randomisation

Patients were randomly allocated to yoga or self-care by block-randomisation with randomly varying block lengths, stratified by the intake/non-intake of immunosuppressive drugs or biologics. The randomisation list was created by the biometrician not involved in patient recruitment or assessment using the Random Allocation Software.²² The list was password-secured and no other person than the biometrician was able to access it. On

this basis, he prepared sealed, sequentially numbered opaque envelopes containing the treatment assignments. After obtaining written informed consent and baseline assessment, the study physician opened the lowest numbered envelope to reveal that patient's assignment.

Interventions

Yoga. The yoga intervention included weekly 90-min traditional hatha yoga group sessions over a period of 12 weeks.²³ The yoga intervention was specifically designed *a priori* in a consensus process by three certified hatha yoga instructors with long-standing experience in teaching yoga (a male physician, a female nutritional scientist and a male with a professional background in adult education) to address the needs, possibilities and limitations of patients suffering from ulcerative colitis with a focus on improving quality of life and reducing bowel symptoms; partly building up on a yoga programme for colorectal cancer survivors.²⁴ The intervention was provided by the three aforementioned yoga instructors; all instructors were required to adhere to the protocol as close as possible; and classes were conducted specifically for this study. It was stressed by the instructors that patients should concentrate on their body with inner involvement during classes while adopting a noncompetitive attitude. Besides yoga exercises that were thought to activate or relax the body and mind, additional exercises were chosen that are traditionally thought to positively influence

the intestinal organs.²⁵ Each class started with low-intensity loosening exercises (20 min for classes 1–3, 10 min for classes 4–12, including movements for each of the major joints: neck, shoulders, elbows, wrists, hips, knees and ankles; further an exercise called “cat-cow” was practised to warm-up the paraspinal muscles), followed by a predefined series of yoga postures over 45 min. Postures in each class built up on the previous ones, and difficulty and intensity levels were carefully increased during the course of the programme (Table 1). Surya Namaskar, the Sun Salutation, a traditional flowing sequence of yoga postures,²⁵ was practised in addition to the other postures for 10 min in classes 4–12. Each class ended with 10 min of yogic breathing techniques including Nadi Shodhana (alternate nostril breathing), Brahmarii Pranayama (a ‘voiced’ breathing technique that includes a meditative focus on the breath) and Kapalabhati Pranayama (a sequence of passive inhalation followed by active forceful exhalation involving the abdominal muscles)²⁶ and 15 min of yogic meditation techniques including mantra meditation and yoga nidra (sequentially focusing the attention on different parts of the body as instructed by the teacher, followed by deep relaxation).²⁶ Patients were provided with a manual and encouraged to daily practice yoga at home although no minimal practice time was required. Prior to home practice, practices were introduced in class. The patients indicated their daily home practice time (min) in a daily log.

Table 1 | Yoga postures (alphabetical order) practised during weekly classes

Yoga posture (English)	Yoga posture (Sanskrit)	Week											
		1	2	3	4	5	6	7	8	9	10	11	12
Cat's pose	Majariasana	x	x	x	x	x	x	x	x	x	x	x	x
Chair pose	Utkatasana	x	x	x	x			x	x	x		x	x
Child's pose	Balasana	x	x	x	x	x	x	x	x	x	x	x	x
Corpse pose	Savasana	x	x	x	x	x	x	x	x	x	x	x	x
Crane pose	Bakasana				x	x	x			x	x	x	x
Legs-up-the-wall pose	Viparita Karani			x	x	x			x	x	x	x	x
Lion pose	Simhasana			x		x				x			
Plow pose	Halasana									x	x	x	x
Seated forward bend pose	Paschimottasana	x		x		x	x		x	x	x	x	x
Side angle pose	Parshvakonasana	x	x	x		x	x		x			x	x
Sitting half spinal twist pose	Ardha Matsyendrasana	x	x	x		x	x	x	x		x	x	x
Staff pose	Dandasana	x	x	x	x	x	x	x	x				
Tree pose	Vrikshasana	x	x	x	x	x	x	x	x	x	x	x	x
Triangle pose	Trikonasana		x		x		x	x		x	x	x	
Upward plank pose	Purvottanasana			x		x	x		x	x	x	x	x
Warrior pose	Virabhadrasana	x	x	x	x	x	x	x	x	x	x	x	x
Wind-Relieving Pose	(Supta) Pawanmuktasana	x	x	x	x	x	x	x	x	x	x	x	x

Self-care. Patients in the self-care group received two evidence-based self-care books providing general information on pathology and pathophysiology of ulcerative colitis, possible diagnostic procedures and treatments, additional sources of information and self-help groups; and emphasising self-care strategies such as appropriate lifestyle modification, over-the-counter medication, naturopathic and integrative medicine treatment approaches and physical treatments.^{27, 28} No instructions for using the books were provided.

Patients in this group were asked not to initiate a yoga or any other exercise regimen during this period. At week 24, they were offered the same yoga classes as the yoga group.

Outcome measures

Outcomes were assessed at 12 and 24 weeks after randomisation by a blinded outcome assessor who was not involved in patient recruitment, allocation or treatment. Disease-specific health-related quality of life as assessed by the 32-item Inflammatory Bowel Disease Questionnaire total score^{4, 29} at week 12 was defined as the primary outcome measure. The total score ranges from 32 to 224, and higher scores indicate better quality of life. Clinically relevant improvements and normal quality of life are defined as an increase of 16 points or more and an absolute score of 170 points or more respectively.^{4, 30, 31}

Disease activity was assessed on the Clinical Activity Index according to Rachmilewitz taking into account patient-reported clinical as well as laboratory parameters.²¹ Disease activity was categorised as: patients in an acute clinical flare (Clinical Activity Index > 4), patients in clinical remission (CAI ≥ 2 and ≤ 4) and patients in sustained clinical remission (Clinical Activity Index < 2, normal bowel frequency and no blood in stool).

The original protocol, as can be seen in the trial registry (ClinicalTrials.gov, registration number: NCT02043600), contains additional secondary outcomes. The description and results of these secondary outcomes can be found in the Supporting Information.

Safety

All adverse events occurring during the study period were recorded. Patients experiencing such adverse events were asked to see the study physician to assess their import and initiate any necessary response. Open-ended questions were used at week 12 and week 24 in order to assess any adverse events not previously mentioned by the patients. Patients were asked to indicate any adverse

events during the study period regardless of their potential relationship to the study intervention.

Sample size calculation and statistical analysis

The required sample size was calculated *a priori*. A group difference of 16 points on the IBDQ total score has been shown to represent a minimal clinically important group difference.^{4, 30} Assuming a standard deviation of 23.04,²⁹ a two-sided, level 5% *t*-test requires a total of 34 patients per group to detect a respective group difference with a statistical power of 80%. Accounting for a potential loss of power because of a maximum of 10% dropouts, it was planned to include at least 76 patients in this trial.

All analyses were based on an intention-to-treat basis, including all participants being randomised, regardless of whether or not they gave a full set of data or adhered to the study protocol. Missing data were multiply imputed by Markov chain Monte Carlo method;^{32, 33} yielding a total of 50 complete data sets.

Baseline group differences in sociodemographic and weight-related outcomes were analysed using Student's *t*-tests for continuous data and chi-square tests for categorical data.

Linear outcomes were analysed by univariate analyses of covariance which modelled the outcome at week 12 or 24 as a function of the treatment group, the stratum variable and the respective baseline value to produce overall effect size estimates, 95% confidence intervals and *P*-values.

Clinical relevance of the findings was assessed by comparing the number of participants who reached a clinically relevant improvement of 16 points or more on the Inflammatory Bowel Disease Questionnaire total score^{4, 30} between groups at week 12 and at week 24 using chi-square tests. Furthermore, the number of participants with acute clinical flares, in clinical remission and in sustained clinical remission based on Clinical Activity Index was compared between groups at week 12 and at week 24 using a Mann–Whitney *U*-test.

As measures of intervention safety and acceptability, the number of patients experiencing serious adverse events, nonserious adverse events or who were lost to follow-up during the study period were compared between groups using chi-squared tests.

All analyses were performed using the Statistical Package for Social Sciences software (IBM SPSS Statistics for Windows, release 22.0. Armonk, NY, USA: IBM Group).

RESULTS

Patients

A total of 203 patients completed telephone screening and 124 of them were excluded due to lack of interest, scheduling problems, or not meeting inclusion criteria, mainly due to not having had an acute flare in the past 12 months (Figure 1). Seventy-nine patients completed assessment by a study physician and two were excluded. Seventy-seven patients were enrolled after providing informed consent, and were randomised to the yoga group ($n = 39$) or the self-care group ($n = 38$). A total of 12 patients in the yoga group (30.8%) and 6 patients in the control group (15.8%) were lost to follow-up ($P = 0.120$) (Figure 1). Four patients in the yoga group were lost to follow-up due to adverse events including three self-reported acute flares and one case of a newly diagnosed colorectal cancer; as were two patients in the self-care group, including one self-reported acute flare and one case of a newly diagnosed spinal canal stenosis. Missing data were multiply imputed and all randomised patients were included in the analyses.

There were no group differences in sociodemographic or clinical characteristics (Table 2).

Patients in the yoga group attended 7.3 ± 3.3 (60.8%) yoga classes on average (Figure 2); 71.8% attended at least half of the 12 yoga classes. Patients additionally practised a mean of 38.7 ± 16.1 min per week at home (median = 30 min, range = 7.5–176.9 min).

Health-related quality of life

From week 1 to week 12, the primary outcome measure Inflammatory Bowel Disease Questionnaire total score increased from 143.5 ± 22.3 to 159.8 ± 32.2 in the yoga group and from 146.3 ± 24.6 to 147.1 ± 36.0 in the self-care group (Figure 2), resulting in a significant group difference at week 12 ($\Delta = 14.7$; 95% confidence interval = 2.4–26.9; $P = 0.018$). Group differences were sustained at week 24 ($\Delta = 16.4$; 95% confidence interval = 2.5–30.3; $P = 0.022$); the total score further increased to 167.8 ± 29.2 in the yoga group and to 153.1 ± 35.9 in the self-care group (Figure 3). Comparable group differences favouring yoga over self-care at week 12 and week 24 were found for the IBDQ subscales bowel symptoms (Δ at week 12 = 4.9; 95% confidence interval = 1.9–8.7; $P = 0.014$; Δ at week 24 = 5.7; 95% confidence interval = 1.1–10.3; $P = 0.015$), systemic symptoms (Δ at week 12 = 2.5; 95% confidence interval = 0.5–4.6; $P = 0.016$; Δ at week 24 = 2.8; 95% confidence interval = 0.8–4.8; $P = 0.006$) and emotional function (Δ at week 12 = 5.4; 95% confidence interval = 0.8–10.1; $P = 0.023$; Δ at week 24 = 5.8; 95% confidence interval = 0.6–11.1; $P = 0.030$); all subscales increased across the three time points in the yoga group. No group differences occurred for social function (Figure 4).

Disease activity

During the course of the study, disease activity assessed on the Clinical Activity Index decreased from 2.5 ± 1.4 to 2.4 ± 2.2 and to 1.7 ± 2.1 in the yoga group and

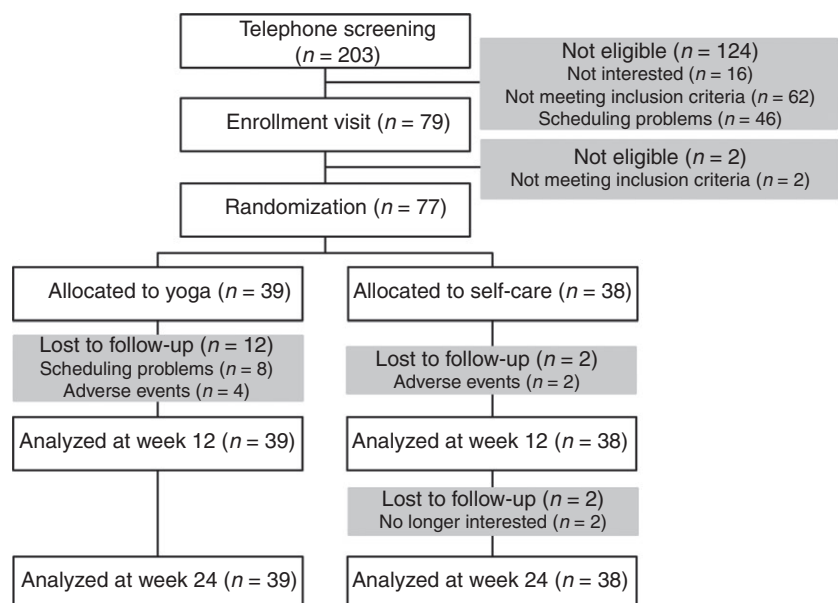


Figure 1 | Participant flow diagram.

Table 2 | Baseline sociodemographic and clinical characteristics. Values are expressed as means \pm s.d. if not otherwise denoted

	Yoga (<i>n</i> = 39)	Self-care (<i>n</i> = 38)	<i>P</i> -value
Sociodemographic characteristics			
Age, years	45 \pm 13.3	46.1 \pm 10.4	0.679
Gender, female <i>n</i> (%)	28 (71.8%)	30 (78.9%)	0.467
Marital status <i>n</i> (%)			0.624
Single	10 (25.6%)	5 (13.2%)	
In relationship	3 (7.7%)	6 (15.8%)	
Married	20 (51.3%)	20 (52.6%)	
Divorced	5 (12.8%)	5 (13.2%)	
Education, <i>n</i> (%)			0.718
Secondary modern school ('Hauptschule') qualification	5 (12.8%)	4 (10.5%)	
High school ('Realschule') qualification	8 (20.5%)	12 (31.6%)	
A level ('Abitur')	11 (28.2%)	9 (23.7%)	
University degree	12 (30.7%)	12 (31.6%)	
Other	3 (7.7%)	1 (2.6%)	
Employment, <i>n</i> (%)			0.142
Employed full-time	15 (38.5%)	15 (39.5%)	
Employed part-time	9 (23.1%)	12 (31.6%)	
Homekeeper	3 (7.7%)	0 (0.0%)	
Student	2 (5.1%)	2 (5.3%)	
Retired	3 (7.7%)	5 (13.2%)	
Disabled	5 (12.8%)	0 (0.0%)	
Unemployed	0 (0.0%)	2 (5.3%)	
Others	2 (5.1%)	2 (5.3%)	
Smoking status, <i>n</i> (%)			0.666
Current smoker <i>n</i> (%)	3 (7.7%)	3 (7.9%)	
Former smoker <i>n</i> (%)	5 (12.8%)	3 (7.9%)	
Clinical characteristics			
Time since diagnosis months	160.3 \pm 112	160.2 \pm 100	0.996
Age at diagnosis years	29.8 \pm 14	31.6 \pm 11.2	0.521
Time since last flare months	6.0 \pm 2.9	6.0 \pm 3.6	0.939
Clinical activity index Rachmilewitz	2.5 \pm 1.4	2.0 \pm 1.5	0.214
Pancolitis <i>n</i> (%)	14 (35.9%)	11 (28.9%)	0.320
Current biologics intake <i>n</i> (%)	4 (10.3%)	6 (15.8%)	0.589
Current intake of other immunosuppressive drugs <i>n</i> (%)	0 (0.0%)	1 (2.6%)	0.494
Current thiopurines intake <i>n</i> (%)	10 (25.6%)	10 (26.3%)	1.000
Current mesalazine intake <i>n</i> (%)	30 (76.9%)	28 (73.7%)	0.589
Current probiotics intake <i>n</i> (%)	5 (12.8%)	1 (2.6%)	0.082

increased from 2.0 ± 1.5 to 2.6 ± 2.6 and to 2.8 ± 2.7 in the self-care group. This resulted in a significant group difference at week 24 ($\Delta = -1.2$; 95% confidence interval = -0.1 – -2.3 ; $P = 0.029$) (Figure 3).

Clinical relevance

Twenty-one patients in the yoga group reached a clinical relevant increase of at least 16 points on the Inflammatory Bowel Disease Questionnaire total score at week 12 compared to 12 in the self-care group ($P = 0.048$); and a total of 27 patients in the yoga group compared to 17 in the self-care group at week 24 ($P = 0.030$). A total of 19,

13 and 7 patients in the yoga group were in sustained clinical remission, clinical remission and in acute flares at week 12 based on the Clinical Activity Index, respectively, compared to 15, 19 and 4 in the self-care group ($P = 0.756$). In week 24, a total of 23, 14 and 2 patients in the yoga group were in sustained clinical remission, clinical remission and in acute flares, respectively, compared to 14, 19 and 5 in the self-care group ($P = 0.042$).

Safety

Three patients in the yoga group and one patient in the self-care group reported one serious adverse event each

Figure 2 | Compliance to the study intervention: Number of participants attending a given number of yoga sessions.

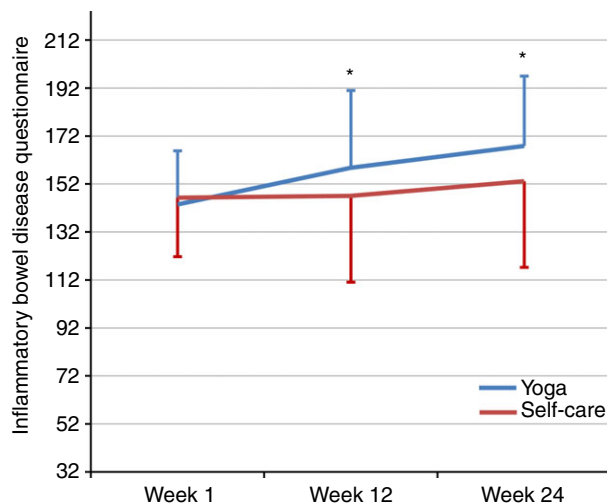
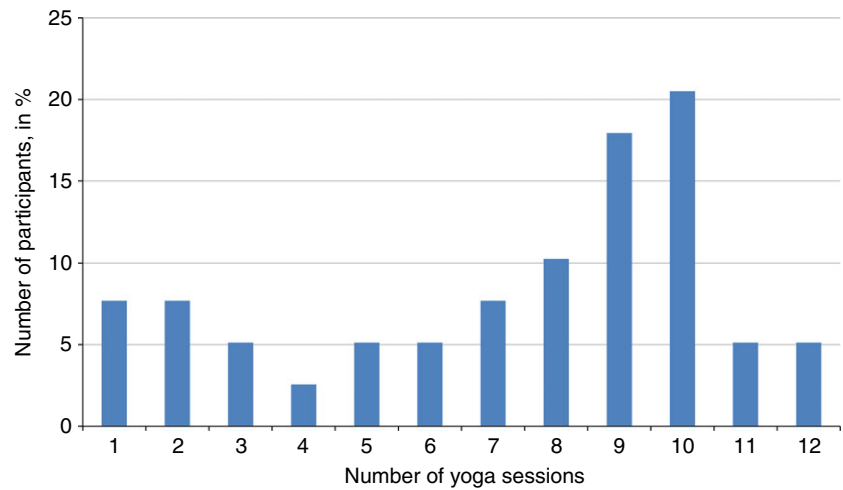


Figure 3 | Effects of yoga and self-care on the primary outcome measure disease-specific quality of life assessed using the Inflammatory Bowel Disease Questionnaire at weeks 1, 12 and 24. Values are expressed as mean \pm s.d.; asterisks indicate significant group differences.

($P = 0.317$). Serious adverse events included a case of a newly diagnosed colorectal cancer and two cases of hospital stays due to acute flares in the yoga group, and a case of a newly diagnosed spinal canal stenosis in the self-care group.

Seven patients in the yoga group reported a total of seven nonserious adverse events and eight patients in the self-care group reported a total of nine nonserious adverse events ($P = 0.731$). Two nonserious adverse events in the yoga group (one case of a self-reported acute flare and one case of a transient increase in ulcerative colitis symptoms without experiencing an acute flare) were not temporarily related to the yoga

intervention. A further five nonserious adverse events in the yoga group (transient musculoskeletal pain) were temporarily and probably causally related to the yoga intervention. None of the adverse events in the self-care group (one case of a self-reported acute flare, seven cases of transient increases in ulcerative colitis symptoms without experiencing an acute flare and one case of increased emotional distress) were apparently related to the intervention.

DISCUSSION

In this randomised clinical trial, a 12-week yoga intervention induced a stronger increase in quality of life in patients with ulcerative colitis compared to written self-care advice. The intervention also reduced disease activity; and less patients in the yoga group reported disease flare-ups 6 months after randomisation when compared to the self-care group. While serious adverse events occurred, they were equally balanced between groups, as were nonserious adverse events.

To the best of our knowledge, only one randomised trial so far has investigated the effects of yoga in patients with ulcerative colitis.³⁴ However, while it also assessed disease-related symptoms, the study's main focus was on cardiovascular autonomic functions. Moreover, the study had a number of major flaws including unclear methods of random sequence generation and lack of *a priori* sample size calculation. Further trials have investigated the effects of multimodal interventions (including yoga among others) and found effects partly in line with those of the current study: in a randomised trials on mindfulness-based stress reduction and another trial on a multimodal mind-body therapy which incorporated elements of the Harvard mind-body programme as well as mindfulness-based stress reduction,³⁵ positive short-term

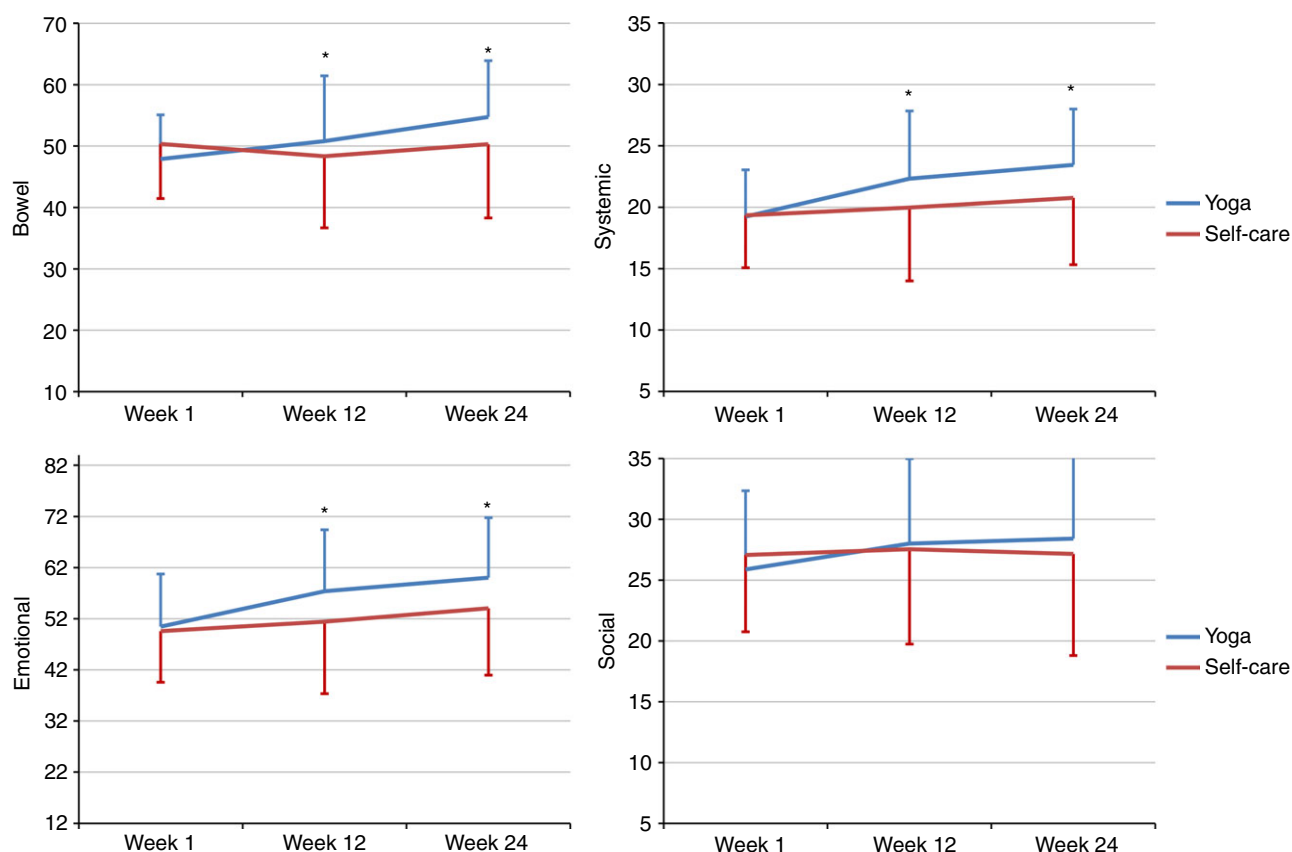


Figure 4 | Effects of yoga and self-care on subdimensions of disease-specific quality of life assessed using the Inflammatory Bowel Disease Questionnaire at weeks 1, 12 and 24. Values are expressed as mean \pm s.d.; asterisks indicate significant group differences.

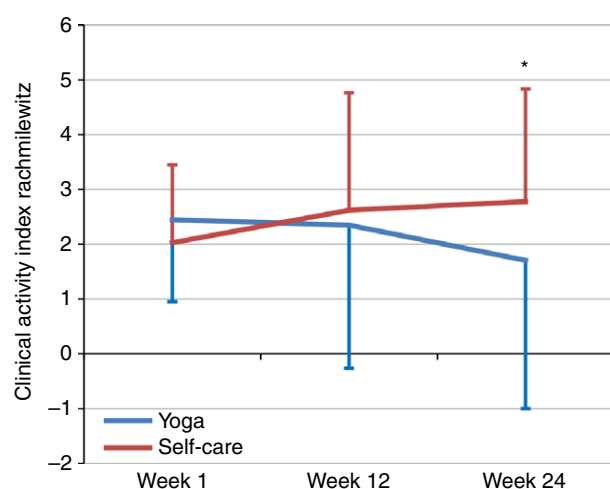


Figure 5 | Effects of yoga and self-care on the Clinical Activity Index according to Rachmilewitz at weeks 1, 12 and 24. Values are expressed as mean \pm s.d.; asterisks indicate significant group differences.

effects on health-related quality of life but not on disease activity or laboratory markers were found.^{36–38}

A major determinant of the impact of ulcerative colitis on quality of life is disease activity.^{39–41} While disease activity was comparable between group at baseline and directly after the end of the interventions, clinically relevant group differences were found 6 months after randomisation. These potential positive effects of yoga on disease activity might be an important factor for its effects on quality of life. Prior studies have shown that yoga can reduce inflammatory responses in healthy participants and those with other inflammatory diseases, probably via a reduced stress response.^{42–44} Stress has been shown to be a potential modifying factor for course of disease in ulcerative colitis.^{45, 46} No effects of yoga on inflammatory biomarkers were found in this study, most likely due to the fact that patients were in clinical remission. However, yoga's preventive effect with regard to disease exacerbation hints at a potential anti-inflammatory mechanism. These

findings on effects of yoga on disease activity are partly in contrast to those in a recent trial on mindfulness-based stress reduction that demonstrated effects on the prevention of flare-ups only in the subgroup with the highest perceived stress.³⁸ This might be explained by the stronger focus on physical activity in the current study; physical activity has been argued to induce anti-inflammatory effects and might thus reduce the risk of flare-ups.^{47, 48} Given that the yoga intervention included physical postures as well as breathing and meditation techniques, physical activity might thus be an important factor for the positive effects of yoga on quality of life and disease activity in patients with ulcerative colitis in the current study besides stress reduction.

Strengths of the study include the randomised study design; the inclusion of a well-defined patient population; the use of different interventionists reducing the influence of therapist effects; and the use of subjective patient-reported outcomes as well as objective laboratory parameters. There are a number of limitations in this study. Particularly, compliance was lower than expected. In the *a priori* sample size calculation, a drop-out rate of up to 10% was anticipated. While considerably more patients (23.4%) were lost to follow-up during the 6-month study course, the intention-to-treat analysis using multiple imputations statistically preserved sample size and thus statistical power of the analysis;⁴⁹ and drop-out rates not exceeding 30% in the long-term are generally regarded as acceptable.⁵⁰ A considerable number of patients in the yoga group was lost to follow-up due to scheduling problems; mainly because the weekly sessions proved to be too time-consuming. Future studies should investigate strategies to make yoga interventions more acceptable for patients with ulcerative colitis. This could, e.g. include the offer of e-health or tele-yoga solutions.⁵¹ While patients attended only a mean of less than two-thirds of the available yoga sessions, this low adherence would most likely have reduced the effect of the yoga intervention and cannot negate the positive findings of this study. Nevertheless, future research should investigate methods to increase patients' adherence to the intervention. Patients practised only an average of 38.7 min per week. It has been shown that symptoms of ulcerative colitis limit adherence to physical activity interventions.⁵² However, providing a minimal required home practice time might increase home practice and might compensate for the relatively low attendance at yoga classes. Finally, only the yoga group received personal treatment while the self-care group did not get personal treatment. Given that most outcome measures

in this study were self-reported, it cannot be ruled out that the differences between groups were at least in part due to unspecific effects and therapists' attention. Future research should try to develop an **adequate attention-control condition for yoga interventions**.

Future studies should try to address the above-mentioned problems. Beyond that, it might be worthwhile to investigate efficacy and safety of yoga as an adjunct to medical therapy in patients with active ulcerative colitis and to investigate additional biomarkers.

In conclusion, a 12-week yoga intervention induced statistically significant and clinically relevant improvements in quality of life, mental health and disease activity in patients with ulcerative colitis compared to written self-care advice. The effects persisted and even increased for at least 3 months after the end of the intervention. The intervention appeared relatively safe with adverse events and serious adverse events being equally balanced between groups. **Yoga can thus be discussed as a safe, acceptable and effective ancillary intervention for patients with ulcerative colitis and impaired quality of life.**

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Data S1. Methods and results.

Table S1. Effects of yoga and self-care on patient-reported outcomes. Values are expressed as mean \pm s.d. Bold *P*-values indicate significant group differences ($P < 0.05$).

Table S2. Effects of yoga and self-care on laboratory parameters. Values are expressed as mean \pm s.d.

AUTHORSHIP

Guarantor of the article: Dr Holger Cramer.

Author contributions: Dr Holger Cramer was responsible for conception and design of the work, the analysis and interpretation of the data, participated in acquisition of the data and drafted the work. Miriam Schäfer, Dr Margarita Schöls and Janina Köcke were responsible for the acquisition of the data and critically revised the work for important intellectual content. Dr Sigrid Elsenbruch and Dr Harald Engler participated in the conception and design of the work, the acquisition and interpretation of the data, and critically revised the work for important intellectual content. Dr Romy Lauche participated in the conception and design of the work, analysis of the data and critically revised the work for important intellectual content. Dr Gustav Dobos participated in the conception and design of the work, and critically revised the work for important intellectual content. Dr Jost Langhorst was responsible for conception or design of the work, the interpretation of the data, participated in acquisition of the data and critically revised the work for important intellectual content. All authors approved the final version of the work and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ACKNOWLEDGEMENTS

The authors thank Dr Bijay Pokhrel, Matthias Scheffel and Dania Schumann for designing and providing the yoga intervention; and Annette Tengelmann for participating in patient recruitment and data assessment.

Declaration of personal interests: All authors declare that they have no potential conflicts of interest to disclose that are relevant to the manuscript.

Declaration of funding interests: This work was supported by a grant from the Deutsche Morbus Crohn/Colitis ulcerosa Vereinigung e.V. (DCCV; German Crohn's Colitis Organization), Germany. The

DCCV had no influence on the design and conduct of the study; the collection, management, analysis and interpretation of the data; the preparation, review or approval of the manuscript; or the decision to submit the manuscript for publication.

LINKED CONTENT

This article is linked to Andrews and Cramer et al papers. To view these articles visit <https://doi.org/10.1111/apt.14115> and <https://doi.org/10.1111/apt.14141>.

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