

A randomized controlled bicenter trial of yoga for patients with colorectal cancer

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Abstract

Objective: The aim of this trial was to evaluate the effects of yoga on health-related quality of life in patients with colorectal cancer.

Methods: Patients with non-metastatic colorectal cancer were randomly assigned to a 10-week yoga intervention (90 min once weekly) or a waitlist control group. Primary outcome measure was disease-specific quality of life (Functional Assessment of Cancer Therapy – Colorectal [FACT-C]) at week 10. Secondary outcome measures included FACT-C subscales: spiritual well-being (FACT – Spirituality); fatigue (FACT – Fatigue); sleep disturbances (Pittsburgh Sleep Quality Inventory); depression and anxiety (Hospital Anxiety and Depression Scale); body awareness (Scale of Body Connection); and body-efficacy expectations (Body-Efficacy Expectations Scale). Outcomes were assessed at week 10 and week 22 after randomization.

Results: Fifty-four patients (mean age 68.3 ± 9.7 years) were randomized to yoga ($n=27$; attrition rate 22.2%) and control group ($n=27$; attrition rate 18.5%). Patients in the yoga group attended a mean of 5.3 ± 4.0 yoga classes. No significant group differences for the FACT-C total score were found. Group differences were found for emotional well-being at week 22 ($\Delta=1.59$; 95% CI=0.27,2.90; $p=0.019$), sleep disturbances at week 22 ($\Delta=-1.08$; 95% CI=-2.13, -0.03; $p=0.043$), anxiety at week 10 ($\Delta=-1.14$; 95% CI=-2.20, -0.09; $p=0.043$), and depression at week 10 ($\Delta=-1.34$; 95% CI=-2.61, -0.8; $p=0.038$). No serious adverse events occurred in the yoga group, while liver metastases were diagnosed in one patient in the control group.

Conclusion: This randomized trial found no effects of yoga on health-related quality of life in patients with colorectal cancer. Given the high attrition rate and low intervention adherence, no definite conclusions can be drawn from this trial.

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Background

With more than 1.3 million new cases each year, colorectal cancer is the third most common cancer in men and the second most common cancer in women worldwide [1]. While, due to improved diagnosis and treatment, survival rates are continuously increasing, patients often experience side effects during treatment. These include reduced health-related quality of life, psychological distress, and fatigue [2–5], with substantial psychological distress being present in one out of every three colorectal cancer patients [3]. These symptoms often persist for years after completion of treatment [5].

Rooted in Indian philosophy, yoga has been a part of traditional Indian spiritual and psychological practice

for millennia [6,7]. Nowadays, it is mainly regarded as a means to promote physical and mental well-being through physical postures (asanas), breathing techniques (pranayama), and meditation (dyana), and different yoga schools have emerged that put varying focus on physical and mental practices [7]. Yoga is gaining increased popularity as a therapeutic practice; nearly 14 million Americans (6.1% of the USA's population) reported that yoga had been recommended to them by a physician or therapist [8]. Indeed, about half of the American yoga practitioners (more than 13 million people) reported starting practice explicitly to improve their health [9]. Prior research has shown positive effects of yoga on health-related quality of life and physical and mental health in cancer patients [10–13]. However, only a

minority of research has investigated patients with cancer sites other than breast cancer, and no trial has yet investigated the efficacy of yoga in patients with colorectal cancer [14,15].

The aim of this trial was to evaluate the effects of a 10-week traditional yoga intervention on health-related quality of life in patients with colorectal cancer. It was hypothesized that patients would have higher health-related quality of life assessed by the Functional Assessment of Cancer Therapy – Colorectal Total Score immediately after 10 weeks of yoga than after 10 weeks of no specific treatment.

Materials and methods

Design

This was an open-label randomized controlled bicenter clinical trial conducted at the Departments of Internal and Integrative Medicine and of Surgery, Kliniken Essen-Mitte, Faculty of Medicine, University of Duisburg-Essen, Essen, Germany, and the Tempelhof Colon Centre, St. Joseph's Hospital, Berlin, Germany. The study had been approved by the ethics committees of the University of Duisburg-Essen (approval number: 12-4957-BO) and the Charité University Medical Centre and registered at ClinicalTrials.gov (registration number: NCT01669109) prior to patient recruitment. The study is reported in accordance with the Consolidated Standards of Reporting Trials statement [16].

Preliminary findings from one of the two study centers have been presented on the International Research Congress on Integrative Medicine and Health 2014 in Miami, Florida, USA [17].

Participants

Patients were recruited from the Department of Surgery and Centre for Minimal Invasive Surgery, Kliniken Essen-Mitte, Essen, Germany, and the Tempelhof Colon Centre, St. Joseph's Hospital, Berlin, Germany. In order to reduce possible selection bias, patients who had been treated in one of the two centers were approached by a study physician rather than using advertisements.

Patients were included if they were at least 18 years old and had been surgically treated for histologically confirmed non-metastatic colorectal cancer (stage I–III). It was originally planned to include patients that were between 2 and 24 months post-surgery; due to foreseeable problems in patients' recruitment, this was changed to 2 to 48 months post-surgery prior to patient recruitment. This way, patients were able to complete the study within the 5-year survival range. Exclusion criteria included physical disability precluding even light yoga practice, further active oncological diseases, diagnosed and pharmacologically treated psychiatric disorder except for cancer-related

depression or adjustment disorder, pregnancy, and breast-feeding. Patients with regular yoga practice within the prior 12 months were excluded to ensure that potential effects of self-directed yoga did not overlap with the study intervention.

Randomization

Patients were randomly allocated to yoga or waitlist control group by block randomization with randomly varying block lengths that was stratified by (a) study center (two strata: Essen and Berlin) and (b) cancer stage (two strata: stage I or II and stage III). The randomization list was created by the biometrician who was not involved in patient recruitment or assessment using the random allocation software [18]. The randomization list was password secured and no other person than the biometrician had access to 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 group participated in weekly 90-min classes of traditional hatha yoga over a period of 10 weeks [19]. Classes were led by certified hatha yoga instructors with longstanding experience in yoga teaching. It was stressed by the instructors that patients should concentrate on their body with inner involvement during classes while adopting a non-competitive attitude. Besides yoga practices that were thought to activate or relax the body and mind, additional practices were chosen that are traditionally thought to positively influence the intestinal organs [20]. Each class started with low-intensity warm-up exercises and followed by a pre-defined series of yoga postures. Postures in each class built up on the previous ones, and difficulty and intensity levels increased during the course of the program (Supplementary File 1). Starting in study week 3, Surya Namaskar, the Sun Salutation, a traditional flowing sequence of yoga postures (Supplementary File 1) [20], was introduced and, from then on, practiced in each yoga class in addition to the other postures. Each class ended with yogic breathing techniques including 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) [21] and yogic meditation techniques including mantra meditation and yoga nidra (sequentially focusing the attention on different parts of the body, followed by deep relaxation) [21].

In each study center, the yoga intervention was conducted in a single group. The classes were led by a single yoga teacher at each site. The intervention protocol for each session was developed a priori and the instructors were required to adhere to the protocol as close as possible. The participants of each of the two centers did not interact with those of the other study center.

Patients were encouraged to practice yoga at home daily, although no minimal practice time was required. Prior to home practice, practices were introduced in class. The patients indicated their daily home practice time (minutes) in a daily log.

Waitlist control group

Patients in the control group were wait listed and did not participate in any study intervention for the first 22 weeks of the trial. Patients continued their self-directed usual care. After week 22, they were offered the same yoga classes as the yoga group.

Outcome measures

All outcome measures were applied at weeks 1, 10, and 22.

The primary outcome measure, colorectal cancer-specific quality of life, was assessed using the Functional Assessment of Cancer Therapy – Colorectal (FACT-C). Quality of life was calculated as the FACT-C total score (FACT-C total score at week 10 was defined as primary outcome measure) as well as the five sub-dimensions physical, social, emotional, functional well-being, and colorectal cancer-specific concerns [22]. Further, spiritual well-being was assessed on the Functional Assessment of Chronic Illness Therapy – Spiritual well-being [23]. Higher scores indicate higher quality of life.

Fatigue was assessed by the Functional Assessment of Chronic Illness Therapy – Fatigue where higher scores indicate lower fatigue [24]. Sleep disturbance was assessed on the Pittsburgh Sleep Quality Inventory (PSQI). Higher values indicate more severe sleep disturbances [25]. Psychological distress was measured by the Hospital Anxiety and Depression Scale with the two dimensions anxiety and depression. Higher values indicate higher distress with values greater than 8 pointing at potential subclinical anxiety or depressive disorders [26]. Body awareness and bodily dissociation were assessed on the Scale of Body Connection [27], and body-efficacy expectation was measured using the Body-Efficacy Expectation Scale [28]. Patients rated their treatment expectancy before randomization. The single-item instrument asked how much patients believed yoga might increase their well-being on a 4-point Likert-type scale ranging from 1 = 'not at all' to 4 = 'very much'.

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 importance and initiate any necessary response. Open-ended questions were used at week 10 and 22 in order to assess any adverse events not previously mentioned. Participants were required 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 8 points on the FACT-C total score has been recommended as a minimally clinically important difference [29]. Assuming a mean value of 79.9 on the FACT-C and a standard deviation of 11.1 [30], a level 5% *t*-test needs a total of 50 patients to detect an 8-point group difference with a statistical power of 80%. Accounting for a potential loss of power due to a maximum of 10% dropouts, it was planned to include 56 participants in this trial.

Baseline group differences were analyzed using Student *t*-tests for continuous data and chi-square tests for categorical data.

All analyses were based on an intention-to-treat basis, including all patients being randomized, 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 methods [31,32], yielding a total of 50 complete data sets. Colorectal-cancer-specific quality of life, assessed as the FACT-C total score at week 10, was defined as the primary outcome measure and was analyzed by a univariate analysis of covariance (ANCOVA) which modeled the outcome at week 10 as a function of treatment group (classified factor), the patients' expectancy (linear covariate), the stratification factors study center (classified covariate) and cancer stage (classified covariate), and the respective baseline value (linear covariate). Afterwards, the 50 estimates of group differences were combined to produce overall effect size estimates, 95% confidence intervals, and *p*-values. All other outcomes were defined as secondary outcomes and were analyzed exploratively only using comparable models.

Clinical relevance of the findings was assessed by comparing the number of patients who reached a clinically relevant reduction of at least 8 points in the FACT-C total score [29] between groups at weeks 10 and 22 using chi-square tests.

Given the large number of dropouts and the relatively low adherence rates, we post hoc decided to assess associations between intervention adherence and treatment efficacy in a secondary analysis. A variable that indexed all yoga time (minutes of supervised yoga plus minutes of home practice) was calculated. Linear regression analysis was conducted with the primary outcome measure (FACT-C total score at week 10) as dependent variable

and total yoga practice time and the baseline FACT-C total score as independent variables. To control for possible confounding variables, the patients' expectancy, the stratification factors study center and cancer stage, age, and gender were additionally entered as independent variables.

Additionally, potential gender effects were analyzed by repeating the ANCOVA for the primary outcome measure with gender added as another classified covariate and the influence of treatment expectancy by reanalyzing the primary outcome measure without including this covariate.

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

Results

Patients

A total of 292 patients were screened by telephone by a research assistant and 78 completed assessment by a study physician for further assessment of eligibility criteria; a total of 235 patients were not interested or were excluded at screening or assessment because they did not meet the inclusion criteria, had died, or had scheduling problems (Figure 1). Fifty-seven patients fulfilled all inclusion criteria and were enrolled after providing informed consent. However, three patients withdrew before baseline assessment due to scheduling problems. Therefore, 54

patients were randomized. Thirty-six patients (66.7%) patients were recruited from the Essen, Germany, study center and 18 patients (33.3%) from the Berlin, Germany, study center. Six and five patients from the yoga group and the waitlist control group, respectively, dropped out during the course of the study; those patients had provided data at week 1, but not at weeks 10 or 22; missing data were multiply imputed (Figure 1).

Patients' characteristics are given in Table 1. The majority of patients was male (61%), their mean age was 68.26 ± 9.69 years, and patients were 22.76 ± 13.09 months post-surgery on average. Mean treatment expectancy was 2.35 ± 0.68 . Twenty-one patients (38.9%) had lymph node metastases. More patients in the yoga group than in the control group had been treated with colostomy ($p=0.028$). No other group differences in patients' characteristics were found. Patients in the yoga group attended a mean of 5.3 ± 4.0 out of 10 yoga classes; four patients attended all 10 yoga classes, and four patients no classes. Patients in the yoga group practiced 63.8 ± 40.2 min per week on average (range: 0 to 279.5 min) at home; six patients did not practice at home at all or did not indicate their home practice in their daily log (Figure 2).

Outcome measures

No significant group differences for the FACT-C total score were found at week 10 (estimated group difference $\Delta = -0.30$; 95% confidence interval [CI] = $-5.94, 5.35$; $p=0.916$) or at week 22 ($\Delta = 0.59$; 95% CI = $-3.41, 8.66$; $p=0.386$) (Table 2). At week 10, three patients

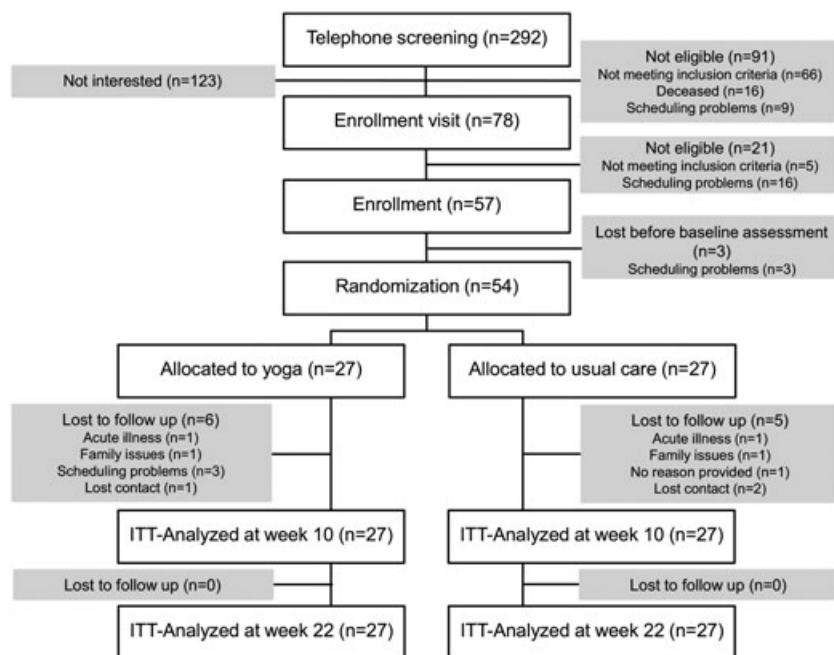


Figure 1. Participant flow diagram. ITT, intention-to-treat

Table 1. Baseline sociodemographic and clinical characteristics (mean \pm standard deviation)

	Total (n = 54)	Yoga (n = 27)	Control (n = 27)	p
Age years (range)	68.26 \pm 9.69 (40–87)	68.70 \pm 9.13 (49–87)	67.81 \pm 10.37 (40–84)	0.916
Gender n (%)				0.782
Female	21 (38.9%)	10 (37.0%)	11 (40.7%)	
Male	33 (61.1%)	17 (63.0%)	16 (59.3%)	
Height (cm)	171.59 \pm 9.11	171.11 \pm 7.11	172.02 \pm 10.87	0.798
Weight (kg)	76.59 \pm 12.16	73.94 \pm 11.82	79.37 \pm 12.11	0.126
Marital status n (%)				0.403
Single	1 (1.9%)	0 (0.0%)	1 (3.7%)	
Married	39 (72.2%)	19 (70.4%)	20 (74.1%)	
Living together	4 (7.4%)	3 (11.1%)	1 (3.7%)	
Divorced	4 (7.4%)	3 (11.1%)	1 (3.7%)	
Widowed	4 (7.4%)	1 (3.7%)	3 (11.1%)	
Education n (%)				0.539
No qualification	1 (1.9%)	0 (0.0%)	1 (3.7%)	
Secondary modern school ('Hauptschule') qualification	16 (29.6%)	6 (22.2%)	10 (37.0%)	
High school ('Realschule') qualification	11 (20.4%)	6 (22.2%)	5 (18.5%)	
A level ('Abitur')	6 (11.1%)	4 (14.8%)	2 (7.4%)	
University degree	16 (29.6%)	10 (37.0%)	6 (22.2%)	
Other	3 (5.6%)	1 (3.7%)	2 (7.4%)	
Employment n (%)				0.870
Employed full-time	7 (13.0%)	4 (14.8%)	3 (11.1%)	
Employed part-time	1 (1.9%)	0 (0.0%)	1 (3.7%)	
Homekeeper	4 (7.4%)	2 (7.4%)	2 (7.4%)	
Retired	35 (64.8%)	18 (66.7%)	17 (63.0%)	
Disabled	3 (3.6%)	1 (3.7%)	2 (7.4%)	
Unemployed	1 (1.9%)	1 (3.7%)	0 (0.0%)	
Other	2 (3.7%)	1 (3.7%)	1 (3.7%)	
Cancer stage n (%)				0.933
I	20 (37.0%)	10 (37.0%)	10 (37.0%)	
II	11 (20.4%)	6 (22.2%)	5 (18.5%)	
III	21 (38.9%)	10 (37.0%)	11 (40.7%)	
Affected lymph nodes	1.47 \pm 3.83	2.25 \pm 5.26	0.72 \pm 1.24	0.178
Time since surgery months (range)	22.76 \pm 13.09 (3–46)	21.41 \pm 11.51 (7–43)	24.11 \pm 14.59 (3–46)	0.453
Tumor location n (%)				0.612
Colon	24 (44.4%)	12 (44.4%)	12 (44.4%)	
Rectum	29 (53.7%)	15 (55.6%)	14 (51.9%)	
Colostomy n (%)				0.028
Yes	24 (44.4%)	8 (29.6%)	16 (59.3%)	
No	29 (53.7%)	19 (70.4%)	10 (37.0%)	
Current chemotherapy n (%)				0.491
Yes	2 (3.7%)	0 (0.0%)	2 (7.4%)	
No	52 (96.3%)	27 (100%)	25 (92.6%)	
Prior chemotherapy n (%)				0.586
Yes	25 (46.3%)	11 (40.7%)	14 (51.9%)	
No	29 (53.7%)	16 (59.3%)	13 (48.1%)	
Prior radiotherapy n (%)				0.327
Yes	12 (22.2%)	4 (14.8%)	8 (29.6%)	
No	42 (77.8%)	23 (85.2%)	19 (70.4%)	
Treatment expectancy (range)	2.35 \pm 0.68 (1–3)	2.33 \pm 0.73 (1–3)	2.38 \pm 0.63 (1–3)	0.787

(11.1%) in the yoga group obtained a reduction of at least 8 points on the FACT-C total score compared with five patients (18.5%) in the control group ($p=0.704$). At week 22, four patients (14.8%) in the yoga group and eight patients (29.6%) in the control group obtained a reduction

of at least 8 points on the FACT-C total score ($p=0.327$). Significant group differences in favor of yoga were found for the FACT emotional well-being subscale at week 22 ($\Delta=1.59$; 95% CI=0.27, 2.90; $p=0.019$). No further group differences were found for the FACT

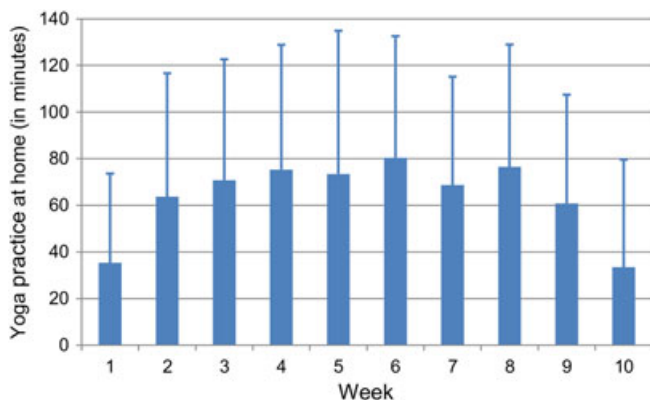


Figure 2. Mean weekly practice time at home (+standard deviation) from week 1 to week 10

well-being subscales (Table 2). Also, no significant group differences were found for fatigue. On the PSQI, no significant group differences occurred at week 10 ($\Delta = -0.62$, 95% CI = $-1.70, 0.46$; $p = 0.256$), while significantly lower sleep disturbance was found in the yoga group compared with the control group at week 22 ($\Delta = -1.08$; 95% CI = $-2.13, -0.03$; $p = 0.043$). Conversely, significant group differences favoring the yoga group occurred on both Hospital Anxiety and Depression Scale subscales at week 10 (anxiety: $\Delta = -1.14$; 95% CI = $-2.20, -0.09$; $p = 0.043$; depression: $\Delta = -1.34$; 95% CI = $-2.61, -0.8$; $p = 0.038$) but not at week 22 (anxiety: $\Delta = -0.08$; 95% CI = $-1.71, 1.01$; $p = 0.878$; depression: $\Delta = -0.55$; 95% CI = $-1.81, 0.71$; $p = 0.384$). No significant group difference occurred regarding body awareness or body dissociation on the Scale of Body Connection or regarding body-efficacy expectations on the Body-Efficacy Expectation Scale (Table 2).

In secondary analysis, no association of the primary outcome measure with total yoga practice time was found ($p = 0.545$). Likewise, the results of the ANCOVA did not change substantially, when gender was entered as a covariate ($p = 0.998$) or when treatment expectancy was not used as a covariate ($p = 0.889$).

Safety

No serious adverse event occurred in the yoga group. Seven patients (25.9%) in the yoga group reported minor adverse events, including transient abdominal pain ($n = 1$), muscle soreness ($n = 3$), neck pain ($n = 1$), and minor vertigo ($n = 1$). All patients recovered without treatment. Another patient in the yoga group reported hip pain ($n = 1$) after yoga and recovered with the use of analgesic drugs. One patient (3.7%) in the waitlist control group experienced a serious adverse event that was probably not causally related to the study intervention. He was diagnosed with liver metastasis; anticancer treatment was still ongoing at the end of the study. No other adverse events occurred in the control group.

Discussion

In this randomized controlled trial, a 10-week yoga intervention did not improve health-related quality of life as assessed by the primary outcome measure in patients with colorectal cancer who had completed surgery within 4 years prior to the start of the study. This finding, however, should be interpreted in the light of the relatively low intervention adherence; on average, patients in the yoga group attended only about half of the available yoga sessions and practiced only about 1 h per week at home. This renders conclusions about yoga's helpfulness difficult. Although total yoga practice time was not associated with the intervention's effect, it cannot be ruled out that yoga would have been effective in this patient group if adherence rates could have been increased. Future research should investigate methods to increase patients' adherence to the intervention. It has been shown that a Tele-Yoga intervention, that is, a home-based intervention with video instructions, is feasible and acceptable for cardiologic patients [33]. A home-based intervention might also lead to a better adherence in patients with colorectal cancer, especially because about 10% of yoga participants in the current trial dropped out of the study due to scheduling problems. Overall, drop-out rates in the present study were considerably high. In the a priori sample size calculation, a drop-out rate of up to 10% was anticipated. While considerably more patients (20.4%) were lost to follow-up, the intention-to-treat analysis using multiple imputations should have statistically preserved sample size and, thus, statistical power of the analysis [34]. The inclusion of noncompliant patients and those who dropped out before the intervention started in the analysis might, however, reduce the confidence in the intention-to-treat analysis. There are a number of further potential explanations for the lack of effects on health-related quality of life. While colorectal cancer patients are reported to often suffer from symptoms that persist for several years post-surgery [5], the sample in the present study had a considerable good health-related quality of life profile. Thus, the lack of effects on the FACT total score might be due to a ceiling effect. In qualitative interviews that were conducted with patients in the yoga group, the program was perceived as helpful; patients reported improved back pain, body awareness, and flexibility. However, little benefit was perceived for cancer-related physical symptoms. The patients assumed that yoga might be a valuable adjunct intervention especially during earlier phases of anticancer treatment when symptoms and impairments are more pronounced [17]. Thus, it might be worthwhile for future studies to investigate the effects of yoga in patients with newly diagnosed colorectal cancer, metastatic colorectal cancer, and/or persisting symptoms. On the other hand, the findings of this trial are in line with those of a recent meta-analysis

Table 2. Effects (mean \pm standard deviation) of yoga and waiting on health-related quality of life, fatigue, sleep, and mental health

	Yoga (n = 27)				Control (n = 27)				Group difference (95% CI) Week 10	p	Group difference (95% CI) Week 22	p	
	Week 1	Week 10	Week 22	Week 1	Week 10	Week 22	Week 1	Week 10					Week 22
	FACT-C												
Physical well-being	25.07 \pm 3.12	24.52 \pm 3.04	24.64 \pm 2.79	23.41 \pm 3.68	22.99 \pm 3.75	22.92 \pm 3.80	0.53 (-1.04;2.10)	0.500	0.70 (-0.89;2.29)	0.379			
Social well-being	23.02 \pm 3.61	21.86 \pm 4.26	22.30 \pm 3.89	21.75 \pm 4.58	22.41 \pm 4.13	22.08 \pm 3.89	-1.13 (-3.28;1.02)	0.297	-0.33 (-2.36;1.71)	0.748			
Emotional well-being	20.22 \pm 3.23	20.15 \pm 2.90	20.60 \pm 2.40	19.58 \pm 3.38	19.33 \pm 3.50	18.77 \pm 3.06	0.54 (-0.99;2.07)	0.484	1.59 (0.27;2.90)	0.019			
Functional well-being	21.63 \pm 4.99	21.23 \pm 4.96	20.94 \pm 4.77	20.86 \pm 4.16	20.47 \pm 5.45	19.46 \pm 5.55	0.15 (-1.69;1.98)	0.871	0.89 (-0.97;2.75)	0.342			
Colorectal cancer-specific	22.04 \pm 4.35	21.95 \pm 3.67	22.05 \pm 3.72	21.45 \pm 4.20	21.37 \pm 4.28	20.95 \pm 4.29	0.15 (-0.92;1.22)	0.777	0.59 (0.84;2.03)	0.410			
Total	111.98 \pm 14.83	110.66 \pm 13.26	111.16 \pm 14.81	106.65 \pm 14.53	106.44 \pm 18.46	104.10 \pm 16.78	-0.30 (-5.94;5.35)	0.916	2.62 (-3.41;8.66)	0.386			
FACT-Sp	32.84 \pm 7.67	33.67 \pm 5.83	34.17 \pm 6.57	32.49 \pm 6.02	31.87 \pm 7.96	32.07 \pm 7.38	1.57 (-1.33;4.47)	0.281	1.75 (-1.13;4.62)	0.228			
Spiritual well-being													
FACT-F	42.70 \pm 9.19	43.02 \pm 6.52	43.12 \pm 7.28	40.13 \pm 7.72	40.45 \pm 8.04	40.10 \pm 9.46	0.84 (-2.12;3.81)	0.571	1.18 (-2.44;4.80)	0.514			
Fatigue													
PSQI	9.11 \pm 3.27	9.21 \pm 2.14	9.00 \pm 2.11	9.88 \pm 2.58	10.34 \pm 2.87	10.57 \pm 2.96	-0.62 (-1.70;0.46)	0.256	-1.08 (-2.13; -0.03)	0.043			
HADS													
Sleep disturbance													
Anxiety	5.00 \pm 2.08	4.74 \pm 1.70	5.28 \pm 2.15	5.88 \pm 2.78	6.45 \pm 3.30	5.86 \pm 2.48	-1.14 -2.20; -0.09)	0.034	-0.08 (-1.71;1.01)	0.878			
Depression	3.19 \pm 3.01	2.83 \pm 2.81	3.49 \pm 3.32	3.92 \pm 2.94	4.78 \pm 3.66	4.72 \pm 3.13	-1.34 (-2.61; -0.08)	0.038	-0.55 (-1.81;0.71)	0.384			
SBC													
Body awareness	2.15 \pm 0.70	2.31 \pm 0.60	2.34 \pm 0.64	2.10 \pm 0.65	2.22 \pm 0.59	2.18 \pm 0.69	0.06 (-0.18;0.30)	0.621	0.12 (-0.18;0.42)	0.426			
Body dissociation	0.82 \pm 0.49	0.78 \pm 0.38	0.88 \pm 0.47	0.88 \pm 0.37	0.80 \pm 0.32	0.94 \pm 0.34	0.01 (-0.15;0.18)	0.871	-0.03 (-0.23;0.17)	0.757			
BEE													
Body-Efficacy Expectation	2.93 \pm 0.80	3.10 \pm 0.55	3.14 \pm 0.60	2.97 \pm 0.69	2.87 \pm 0.53	2.95 \pm 0.69	0.26 (-0.01;0.53)	0.060	0.20 (-0.10;0.49)	0.189			

BEE, Body-Efficacy Expectation Scale; CI, confidence interval; FACT-F, Functional Assessment of Chronic Illness Therapy – Fatigue; FACT-Sp, Functional Assessment of Chronic Illness Therapy – Spiritual well-being; FACT-C, Functional Assessment of Cancer Therapy – Colorectal; HADS, Hospital Anxiety and Depression Scale; PSQI, Pittsburgh Sleep Quality Index; SBC, Scale of Body Connection.

that found no evidence for effects of exercise interventions on health-related quality of life or fatigue in patients with colorectal cancer [15]. Thus, while exercise has been shown to improve quality of life and fatigue in patients with different cancer sites [35–39], evidence is insufficient to evaluate whether patients with colorectal cancer in particular gain benefit from exercising or not. This might also apply to yoga, even though yoga also encompasses breathing techniques, relaxation, and meditation in addition to exercise. Contrary to many other studies, patients in the present study were approached by the study physician rather than self-selected, therefore, the study sample does not represent the typically yoga users (and yoga trial participants). It has been shown that yoga is mainly used by young well-educated women [40–42]. In contrast, the study sample was predominantly male, older, and had a medium level of education. However, at least gender had no significant influence on the intervention's effect. Because yoga's efficacy as a supportive cancer therapy has mainly been investigated in women with breast cancer [12,14] that are likely to have a more positive attitude towards the intervention, the apparent differences in efficacy could also be at least partly explained by differences in treatment-efficacy expectations. This is also reflected in the somewhat moderate expectancy of efficacy in the present study. However, treatment expectancy also did not influence the treatment's effect. Although in line with studies on yoga for patients with other cancer sites [10,43], it can also not be ruled out that the intervention length of 10 weeks was too short to induce substantial improvements.

In a number of secondary outcome measures, positive effects of the intervention occurred. Immediately after the end of the intervention, depression and anxiety decreased; however, because the baseline levels of both variables were considerably below the recognized cut-off values for potential psychiatric disorders [26], these improvements might not be clinically relevant. Specifically, three, two, and four patients in the yoga group were above the proposed cut-off of 8 points for subthreshold or threshold anxiety [26] at week 1, 10, and 22, respectively, compared with 7, 9, and 8 in the control group. Two, two, and three patients in the yoga group and four, five, and five patients in the control group were above the proposed

cut-off of 8 points for subthreshold or threshold depression [26] at week 1, 10, and 22, respectively. In contrast, because baseline PSQI scores were above the proposed cut-off [25], the improvement in sleep disturbances at week 22 might well be of clinical relevance. All group differences in psychological distress should, however, be regarded as preliminary because there were no effects on the primary outcome measure.

Strengths of the study include the randomized study design and the use of different interventionists and outcome assessors at the two study centers. There are several limitations in this study. First, the waitlist control group did not control for unspecific effects of the intervention. Future studies should use an attention control group that controls for unspecific effects by, for example, applying educational classes of the same duration and attention by therapists as the yoga intervention. Second, there was no follow-up beyond 22 weeks. Third, as the patients were not required to have a reduced health-related quality of life to be eligible, there was a ceiling effect for the primary outcome measure, reducing the likelihood of finding significant group differences. Future trials should employ impaired health-related quality of life and/or emotional distress as an inclusion criterion. Finally, as acknowledged earlier, the low adherence and high attrition rate might mean that even an intention-to-treat analysis is unable to produce valid effect estimates of the study treatment. Future trials should explore whether different forms of delivering the intervention, for example, ehealth approaches, can improve adherence and reduce attrition.

In conclusion, this trial found no evidence for effects of yoga on health-related quality of life in patients with colorectal cancer as assessed by the FACT total score. Given the high attrition rate and low intervention adherence, any conclusions of this randomized trial remain preliminary.

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Trial registration

ClinicalTrials.gov (NCT01669109).

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