Pilot randomized, controlled trial of a dyadic yoga program for glioma patients undergoing radiotherapy and their family caregivers

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Abstract

Background. While the use of behavioral medicine in managing glioma patients' symptoms is not well studied, the high symptom burden in patients and their family caregivers is well established. We conducted a pilot randomized, controlled trial to examine the feasibility and preliminary efficacy of a dyadic yoga (DY) intervention as a supportive care strategy.

Methods. Glioma patients undergoing radiotherapy and their caregivers were randomized to a 12-session DY or waitlist control (WLC) group. Prior to radiotherapy and randomization, both groups completed measures of cancer-related symptoms (MD Anderson Symptom Inventory-Brain Tumor module), depressive symptoms (Center for Epidemiological Studies-Depression measure), fatigue (Brief Fatigue Inventory), and overall quality of life (QOL; Medical Outcomes Study 36-item short-form survey). Dyads were reassessed at the last day of radiotherapy.

Results. Twenty patients (mean age: 46 years, 50% female, 80% WHO grade IV) and caregivers (mean age: 50 years, 70% female, 50% spouses) participated in the trial. A priori feasibility criteria were met regarding consent (70%), adherence (88%), and retention (95%) rates. Controlling for relevant covariates, change score analyses revealed clinically significant improvements for patients in the DY compared with the WLC group for overall cancer symptom severity ($d = 0.96$) and symptom interference ($d = 0.74$), depressive symptoms ($d = 0.71$), and mental QOL ($d = 0.69$). Caregivers in the DY group reported clinically significant improvements in depressive symptoms ($d = 1.12$), fatigue ($d = 0.89$), and mental QOL ($d = 0.49$) relative to those in the WLC group.

Conclusion. A DY intervention appears to be a feasible and beneficial symptom and QOL management strategy for glioma patients undergoing radiotherapy and their caregivers. An efficacy trial with a more stringent control group is warranted.

Clinical Trial Number. NCT02481349

Keywords

glioma | patient-caregiver dyads | pilot randomized, controlled trial | quality of life | yoga.

Because of the general poor prognosis of adult glioma, managing patients' symptoms and quality of life (QOL) is highly relevant. Common symptoms include fatigue, sleep

disturbances, and depression as well as cognitive/neurological deficits as a result of the disease and its treatment.¹⁻⁵ More specifically, fatigue and sleep disturbances are

reported in 60%-100% of glioma patients, clinical depression rates in as high as 38%, depressive symptoms in 95%, and neuropsychological deficits in 50%.^{2,4,6-9}

Patients' symptom burden is linked to poor QOL and a need for additional care and support from family caregivers.^{4,10} Although many family members of cancer patients believe that caring for their loved one is a privilege,¹¹ caregiving exerts an emotional and physical toll. For instance, rates of psychological distress are high in cancer caregivers. In fact, the spouses of glioma patients may experience significantly greater levels of anxiety and depression than patients.³ Sleep disturbances and fatigue are also frequently reported among family caregivers at clinical levels similar to those seen in patients.¹²⁻¹⁴ Additionally, many caregivers of patients with brain tumors feel overwhelmed by the changes in patients' cognitive and neurological function, mood, and personality and experience low caregiving efficacy.^{10,15} While symptom burden among caregivers is a clinical problem in itself as it has been associated with morbidity and shorter survival,¹⁶⁻¹⁸ it may have direct implications for patients as distress and QOL are interdependent in families coping with advanced cancer.^{19,20} In contrast, caregivers' perception of mastery, or sense of agency, has been linked to increased survival in patients with glioma.²¹

To address symptom burden, a relatively small yet growing body of knowledge suggests that nonpharmacological interventions (eg, neurocognitive rehabilitation, neurorehabilitation, and exercise) may play a valuable role in the care of glioma patients.²²⁻²⁶ There is also an increasing interest in providing psychoeducation to family caregivers.²⁷ Although these solo interventions show promise, evidence suggests that dyadic interventions may result in better outcomes than delivering supportive care to patients and caregivers separately because dyadic interventions may enhance illness communication and a team approach to symptom management.²⁸ Moreover, dyadic interventions may not only be more efficacious regarding patient and caregiver outcomes but also more feasible regarding participant retention and treatment adherence compared with solo interventions for patients.²⁹⁻³¹ Involving a family caregiver to improve compliance may be particularly beneficial for patients affected by neurocognitive deficits.

Considering the need to address physical and psychological symptoms and overall QOL, mind-body medicine such as a yoga program that integrates gentle physical exercises with relaxation techniques may be an ideal supportive care strategy for patients with glioma and their caregivers. Although yoga has been studied quite extensively in women with breast cancer,³²⁻³⁸ previous investigations have excluded patients with brain tumors. However, it is estimated that 30% of patients with brain tumors use complementary and alternative medicine including mind-body modalities and most often without their providers' knowledge.^{39,40} Moreover, little is known about the benefits of a dyadic approach to mind-body medicine. In our formative research, we developed a dyadic yoga (DY) intervention as a supportive care strategy specifically for patients with brain tumors, and a single-arm trial showed the intervention to be safe and acceptable for patients with high-grade glioma.⁴¹

Building on this earlier study, we sought to examine the feasibility of implementing a pilot randomized, controlled trial (RCT) of this intervention while patients undergo postresection radiotherapy (RT). Incorporating the intervention during RT may buffer against common treatment-related toxicities. Based on previous dyadic interventions in cancer, we hypothesized that at least 60% of dyads would consent to participate, 75% of dyads randomly assigned to the yoga group would attend at least 80% of intervention sessions, and 80% of dyads would be retained at the follow-up assessment.²⁴ Additionally, we hypothesized that the preliminary efficacy of the yoga intervention would be evidenced by clinically significant improvements in patients' cancer-related symptoms and patient and caregiver depressive symptoms and fatigue compared with a waitlist control (WLC) group.

Methods

Participants

Patients were eligible if the following criteria were met: diagnosis of WHO grade I-IV glioma (based on radiographic or pathologic diagnosis) to be treated with a minimum of 20 fractions of RT, a KPS of 80 or higher, and willingness of a family caregiver (eg, spouse, sibling, adult child) to participate. Other inclusion criteria both for patients and caregivers were age 18 years or older, and the ability to read and speak English, and provide informed consent. Exclusion criteria for patients included regular practice (determined by the patient) of yoga in the 12 months preceding the glioma diagnosis and an inability (determined by the clinical team) to complete self-report surveys because of cognitive deficits.

Procedure

Before the trial began enrollment, the MD Anderson Institutional Review Board approved all procedures. Research staff used the institution's electronic medical records database to locate patients who might be eligible. During clinic visits, the staff members approached the patients and caregivers, confirmed their eligibility, and obtained written informed consent prior to data collection. Dyads were randomly assigned to either the DY or WLC group through a form of adaptive randomization called minimization, which ensured a balance of patients' KPS, sex, age, and tumor grade (I and II vs III and IV) between the 2 groups.⁴² Before randomization, patients and caregivers completed survey measures (within 1 week of patients' RT initiation; T1) and on the last day of RT (T2). Each patient and caregiver received a \$20 gift card after each survey (T1 and T2).

DY Program

Patient-caregiver dyads attended jointly 2 or 3 weekly sessions (45 minutes each; 12 sessions in total) of the DY program over the course of RT. This dosage was based

on our previous pilot investigation.⁴¹ Two certified yoga instructors with experience in working with cancer patients led the sessions to reduce therapist-specific effects, but each dyad stayed with 1 instructor once they started the sessions. The DY program was conducted as previously described.⁴¹ Briefly, the program consisted of the following main components: 1) joint loosening with mindfulness training, 2) postures (*asanas*), 3) breathing exercises (*pranayamas*), and 4) meditation/guided imagery. Instructors introduced the program as a team approach to symptom management and stated that the practice is intended to address the needs of patients and caregivers alike. Practices included available modifications based on participants' physical limitations. Participants received printed and electronic support materials to assist with their home practice. All sessions were video-recorded and treatment fidelity was ensured.

WLC Group

The WLC group received the usual care as provided by their health care team and were offered the intervention after they completed the T2 assessment. No additional data were collected.

Measures

Demographic and medical factors

Demographic items (eg, age, marital status, employment) were included in the baseline questionnaires. Patients' medical data were extracted from their electronic medical records.

Feasibility data

Tracking data regarding consent rates, session attendance, and completion of survey instruments were kept throughout the study. Participants in the DY group completed the 0-10 Borg Rating of Perceived Exertion Scale⁴³ as well as an evaluation of the intervention to assess their satisfaction (ie, perceived benefit of each component and overall program usefulness) using Likert scale items (range, 0-4) and 1 open-ended question. The frequency of home yoga practice and whether the participants practiced together or individually was assessed weekly.

At T1 and T2, the patients and caregivers filled out the self-report symptom and QOL measures described below.

Cancer-related symptoms

Patients completed the MD Anderson Symptom Inventory-BrainTumor module (MDASI-BT) consisting of 13 core items and 9 brain tumor items assessing symptom severity and 6 additional items assessing interference with daily life.⁴⁴ The 22 symptoms of the MDASI-BT measure 6 underlying factors pertaining to affective, cognitive, focal neurologic deficit, generalized disease, and treatment-related and gastrointestinal (GI)-related symptoms.⁴⁴ The interference items factor into activity-related and mood-related

interference. These 6-symptom factor and 2-interference factor subscales along with the overall symptom and interference scores are presented here. The minimal clinically important difference (MCID) for each factor is 1 point difference. Caregivers completed the MDASI-BT as they perceived patients' symptom severity and interference.

Depressive symptoms

Depressive symptoms were assessed with the Center for Epidemiological Studies-Depression measure (CES-D) consisting of 20 items. Scores of 16 or higher are indicative of further evaluation for a depressive disorder "caseness."⁴⁵

Fatigue

Fatigue was measured with the Brief Fatigue Inventory (BFI),⁴⁶ a 10-item questionnaire designed to rapidly assess the severity and impact of cancer-related fatigue. The tool defines MCID of 1 point difference.

Overall QOL

The Medical Outcomes Study 36-item short-form survey (SF-36) assesses 8 distinct domains: physical functioning, physical impediments to role functioning, pain, general health perceptions, vitality, social functioning, emotional impediments to role functioning, and mental health. The SF-36 yields mental and physical composite summaries (Mental Component Summary [MCS] and Physical Component Summary [PCS], respectively), which are presented here.⁴⁷ The MCID difference for each subscale is 5 points.

Statistical Analyses

The main objectives of this pilot trial were to establish the feasibility and preliminary efficacy of a DY program by comparing the patient cancer-related symptoms and patient and caregiver depressive symptoms, fatigue, and QOL between the DY and WLC groups. To characterize the study sample, we performed descriptive analyses (eg, means, SDs) as well as dyadic analyses (eg, paired sample *t* tests). To examine feasibility, we calculated descriptive statistics for consent, session attendance, completion of survey instruments, and program satisfaction. We calculated change scores from baseline (T2-T1) and controlled for participants' sex and age and patients' tumor grade and KPS when performing general linear modeling (GLM) using PROC GLM (SAS, version 9.4) to examine preliminary efficacy. All randomized dyads were included in the analyses. We used separate analyses for patients and caregivers. Because the current study is a pilot trial and not adequately powered, we interpreted least squares mean (LSM) of the change scores (ie, T2-T1) based on clinical relevance (ie, MCID) as opposed to inferential significance testing when examining between-group differences. As these group differences are interpreted as *preliminary evidence* for efficacy, we did not perform Bonferroni adjustments to control

for multiple comparisons. We also calculated the effect size (Cohen's d) associated with each between-group comparison using pooled SDs and interpreted the effect size in terms of Cohen's taxonomy (small effect, $d = 0.2$; medium effect, $d = 0.5$; and large effect, $d = 0.8$).⁴⁸

Results

Participant Characteristics

Baseline demographic and medical data are shown in Table 1 by group and role. Briefly, most patients were white, educated with at least some college credits, middle aged, and had a WHO grade IV tumor. Half the patient sample were women. Most caregivers were women, educated with at least some college credits, and middle aged, and about half of them were spouses of the patient. CES-D caseness was high for patients (50%) and moderate for caregivers (35%). There were no significant group differences for patients and caregivers on these baseline characteristics except that caregivers in the yoga group had significantly greater CES-D caseness scores compared to those in the control group ($P < .05$).

Baseline Dyadic Results

Patient and caregiver CES-D scores were not different (mean = 16.49, SD = 7.58 and mean = 16.25, SD = 5.30, respectively; $t = 0.13$, $P = .90$). Patient-reported and caregiver-perceived MDASI-BT scores did not clinically or statistically significantly differ for the overall symptom and overall interference subscales or any of the symptom factors. Intraclass correlation for each MDASI-BT subscale or factor was significant (at $P = .007$ to $P = .0001$), ranging from .51 to .82. Although the BFI scores of patients were higher than those of caregivers, the scores were not clinically or statistically different (mean = 3.35, SD = 2.74 and mean = 2.65, SD = 2.32, respectively; $t = 1.00$, $P = .33$).

Feasibility Results

We approached 30 eligible patient-caregiver dyads for study participation, 21 of whom (70%) consented. Refusal reasons included a busy schedule ($n = 6$) or lack of interest ($n = 3$). Prior to randomization, 1 dyad became ineligible (the patient had discontinued treatment). Of the remaining 20 dyads, 19 (95%) completed T2 assessments; 1 dyad in the DY group withdrew consent because of a lack of time after the first session (see Consolidated Standards of Reporting Trials diagram, Fig. 1). Dyads in the DY group attended a mean of 10.60 sessions (SD = 3.44; range: 1-12; 90% of dyads attended 83.3% of all sessions) and practiced a mean of 2.33 times (SD = 1.18; range: 0-4 times) per week outside class. All participants in the DY group rated each component of the intervention as either "beneficial" or "very beneficial" and the overall program as "useful" or "very useful" (0-4 scales; means = 3.49-3.88). All participants would recommend the program to a friend undergoing RT. On the Borg Exertion 0-10 Scale, patients rated the yoga sessions as "moderate"

(mean = 2.61; SD = 0.96; range: 1-4) and caregivers as "easy" (mean = 1.83; SD = 0.41; range: 1-2). Open-ended comments were very encouraging regarding acceptability (eg, "I feel so much better after a session, I have more energy and feel more clarity in my brain. I love it and will encourage others to do yoga"). Three patients mentioned they would like the program to last longer than 6 weeks. Patients also mentioned that they used the DY relaxation skills while receiving RT, "which made the treatment bearable." Regarding modifications, one patient developed weakness over the course of RT so that all aspects of the program were performed in a seated position.

Preliminary Efficacy Results

Raw means for each measure for patients and caregivers at T1 and T2 are presented in Table 2.

Cancer-related symptoms

Controlling for the above-mentioned covariates, GLM analyses revealed clinically significant between-group effects for change scores of the MDASI-BT overall symptom severity (LSM: DY = -1.09; WLC = 0.50, $F = 5.17$, $P = .04$, $d = 0.96$) and interference (LSM: DY = -1.88; WLC = -0.04, $F = 2.37$, $P = .11$, $d = 0.74$) subscales. Patients in the yoga group reported less symptom burden and interference compared with those in the control group. More specifically, clinically significant between-group differences of change scores were found in each of the 6 symptom factors: affective ($F = 4.90$, $P = .04$, $d = 0.90$); cognitive ($F = 2.24$, $P = .16$, $d = 0.49$); neurologic ($F = 3.28$, $P = .09$, $d = 0.78$); treatment-related ($F = 6.87$, $P = .02$, $d = 1.22$); general disease ($F = 2.85$, $P = .11$, $d = 0.79$); and GI-related ($F = 3.35$, $P = .09$, $d = 0.80$) symptoms. Clinically significant between-group differences were also found on both of the interference factors: activity-related ($F = 2.24$, $P = .33$, $d = 0.45$) and mood-related ($F = 6.27$, $P = .02$, $d = 1.01$) interference. LSMs of difference scores for each factor are presented in Fig. 2A).

Caregivers' perceptions of patient symptoms and interference mirrored the patient findings in overall symptom severity (LSM: DY = -1.00; WLC = 0.16, $F = 2.18$, $P = .16$, $d = 0.60$) and interference (LSM: DY = -.87; WLC = 0.18, $F = 1.04$, $P = .32$, $d = 0.51$) so caregivers in the yoga group perceived that patients had less symptom burden and interference compared to caregivers in the control group. Clinically significant group differences for change scores were found only in the areas of affective ($F = 2.02$, $P = .18$, $d = 0.59$), cognitive ($F = 3.05$, $P = .10$, $d = 0.76$), and general disease ($F = 1.29$, $P = .28$, $d = 0.47$) symptoms and mood-related interference ($F = 2.09$, $P = .17$, $d = 0.68$). LSMs of difference scores for each factor are presented in Fig. 2B).

Depressive symptoms

GLM analyses of change scores revealed a medium effect size for improved depressive symptoms for patients in the DY group compared with those in the WLG group (LSM: DY = -5.26 vs WLC = 1.73; $F = 3.19$, $P = .09$; $d = 0.71$). For caregivers, a large effect size was found to the extent that caregivers in the DY group reported significantly improved

Table 1 Baseline Patient and Caregiver Demographics and Patient Medical Factors by Group Assignment

Characteristic	Patient (n = 20)		Caregiver (n = 20)	
	Yoga (N = 10)	Control (N = 10)	Yoga (N = 10)	Control (N = 10)
Gender, n (%)				
Female	5 (50)	5 (50)	7 (70)	6 (60)
Age, y, mean $\pm$ SD, (range)	47.91 $\pm$ 14.66 (27-75)	44.73 $\pm$ 12.23 (24-61)	52.36 $\pm$ 16.00 (34-74)	48.27 $\pm$ 11.88 (28-66)
Relationship to Patient, n (%)				
Spouse			6 (60)	5 (50)
Other family member			4 (80)	5 (50)
Ethnicity, n (%)				
Non-Hispanic/White	9 (90)	8 (45)	8 (80)	7 (70)
Latino/Hispanic	1 (10)	2 (10)	1 (10)	2 (20)
African American			1 (10)	
More than 1 race				1 (50)
Highest Level of Education, n (%)				
Some college or higher	10 (100)	9 (90)	8 (80)	8 (80)
Household income, n (%)				
\$50 000 or more	10 (100)	10 (100)	10 (100)	10 (100)
Employment Status, n (%)				
Full-time	3 (30)	2 (20)	4 (40)	6 (60)
Retired	2 (20)	2 (20)	2 (20)	2 (20)
Part-time	1 (10)	1 (10)	1 (10)	1 (10)
Medical leave	3 (30)	4 (40)	0 (0)	0 (0)
Homemaker	1 (10)	1 (10)	3 (30)	1 (10)
WHO grade, n (%)				
II	1 (10)	1 (10)		
III	1 (10)	1 (10)		
IV	8 (80)	8 (80)		
KPS, n (%)				
80	3 (30)	3 (30)		
90	6 (60)	4 (80)		
100	1 (10)	3 (30)		
Tumor Location, n (%)				
Temporal	5 (50)	3 (30)		
Frontal	3 (30)	5 (50)		
Parietal	2 (20)	2 (20)		
Lateralization, n (%)				
Right	5 (50)	5 (50)		
Chemotherapy, n (%)	10 (100)	10 (100)		
Surgery, n (%)	10 (100)	10 (100)		
Time since diagnoses, wk, mean $\pm$ SD, (range)	4.75 $\pm$ 1.31 (3.00-6.75)	6.89 $\pm$ 1.56 (4.12-6.85)		
Medications, n (%)		9 (90)		
Anticonvulsants	9 (90)			
Corticosteroids	10 (100)	10 (100)		
Caseness on CES-D ^a , n (%)	6 (60)	4 (80)	6 (60)	1 (10)

Abbreviation: CES-D, Centers for Epidemiological Studies-Depression. ^aCES-D score $\geq$ 16.

Fig. 1 Consolidated Standards of Reporting Trials Flow Diagram. GI indicates gastrointestinal; Int, interference; WLC, waitlist control.

depressive symptoms compared with those in the WLC group (LSM: DY = -5.40 vs WLC = 3.60; $F = 6.14$, $P = .03$; $d = 1.12$).

Fatigue

GLM analyses revealed a marginally clinically significant between-group difference for BFI change scores for patients (LSM: DY = -0.88, WLC = 0.07; $F = 0.72$, $P = .41$; $d = 0.28$) and a clinically significant difference for caregivers (LSM: DY = -1.76, WLC = 2.5; $F = 3.96$; $P = .07$; $d = 0.89$).

QOL

Clinically significant between-group differences for change scores were found for patients (LSM: DY = 3.60 vs WLC = -3.99; $F = 1.92$; $P = .19$; $d = 0.69$) and caregivers (LSM: DY = 6.76 vs WLC = 0.49; $F = 0.76$; $P = .4$; $d = 0.49$) for the MCS of the SF-36 to the extent that dyads in the DY group reported better mental QOL than did those in the WLC group. No clinically significant differences for change scores were found for patients or caregivers' physical QOL (PCS).

Conclusions

The purpose of this pilot RCT was to examine the feasibility of a DY program for glioma patients undergoing RT and their family caregivers. We also sought to examine preliminary evidence for treatment efficacy according to changes in self-reported cancer-related symptoms, depressive symptoms, fatigue, and overall QOL. Our findings support our hypothesis that an RCT of a dyadic behavioral intervention while patients undergo standard RT is feasible with acceptable rates of consent, retention, and adherence. In addition, the intervention was well received and rated useful and beneficial by all participants.

Our findings also revealed evidence supporting preliminary intervention efficacy. For patients, we found a clinically significant decrease in overall cancer-related symptom severity and interference as measured by the MDASI-BT. This reduction in overall symptom severity and interference was also noticeable to caregivers based on their perception ratings. Regarding individual factors, large effect sizes were revealed in the areas of affective, treatment-related, and GI-related symptom severity as well as mood-related symptom interference. Medium effect sizes were observed in the areas of cognitive, neurologic, and general disease-related symptom severity and activity-related symptom interference. Moreover, we revealed a medium and large effect for reductions in patient and caregiver depressive symptoms, respectively. Also encouraging were our findings of clinically significant improvements in patient and caregiver mental QOL. Likewise, we found clinically significant improvements in fatigue for caregivers and marginally significant improvements for patients in the DY relative to those in the WLC group. These clinically significant between-group differences fell into the medium to large effect size range. Thus, this pilot RCT suggests that a DY program may be an effective approach to symptom and QOL management for glioma patients and their caregivers.

Despite these exciting findings, we caution against a firm interpretation of group differences because the current study was a pilot RCT. Specifically, the relatively small sample size limits the robustness of reported means and SDs, thus affecting effect size calculations. Other study limitations include patients in our sample having a high performance status (ie, KPS was mainly 90 or 100 at study entry), and it is unknown how patients with a lower status would tolerate the intervention. Considering the high tolerability, we will include patients with a lower performance status (ie, 70) in the next, larger trial. Although the current sample was relatively ethnically and racially diverse, our participant population had a high level of education and household income, and thus it is unclear whether our findings can be generalized to patients of

Table 2 Raw Means of Outcomes at Each Assessment Point for Patients and Caregivers in the Dyadic Yoga and Waitlist Control Groups

Measure	Dyadic Yoga						Waitlist Control					
	Patient			Caregiver			Patient			Caregiver		
	Baseline		Postprogram	Baseline		Postprogram	Baseline		Postprogram	Baseline		Postprogram
	Mean	SD	Mean	Mean	SD	Mean	Mean	SD	Mean	Mean	SD	Mean
BFI	3.76	3.19	3.02	2.12	2.26	2.40	2.24	2.84	3.39	2.500	1.93	1.83
CES-D	17.53	12.15	13.20	10.58	7.85	12.45	8.38	10.85	12.42	7.92	8.91	5.91
Overall Sx	2.5	2.12	1.65	1.15	2.55	1.90	1.98	1.49	1.92	1.31	1.53	1.15
Affective Sx	3.67	2.64	2.42	2.11	2.56	2.87	2.04	2.25	2.83	1.87	2.33	1.68
Cognitive Sx	2.34	2.58	1.53	1.27	3.33	2.00	2.65	2.14	2.23	2.53	2.05	2.83
Neurolog. Sx	1.91	2.44	.64	.54	1.94	.94	1.38	1.19	1.32	1.03	1.20	1.35
Treatment Sx	3.18	2.22	2.93	2.03	3.11	2.59	2.58	1.36	2.48	1.4	1.48	1.32
General Disease Sx	1.92	2.26	1.38	1.33	2.88	1.60	2.23	1.00	1.54	1.34	.95	1.02
GI Sx	1.54	1.94	.60	.61	1.66	.89	2.13	.05	.14	.15	.45	1.51
Overall Interfer.	3.18	2.73	1.52	1.34	3.22	2.20	2.75	2.98	2.83	2.77	2.70	1.94
Interfer.-Activity	3.15	2.85	1.73	1.36	3.42	2.14	2.93	3.39	2.94	2.97	3.42	2.46
Interfer.-Mood	3.18	2.85	1.30	1.60	3.17	2.22	2.62	2.50	2.73	2.70	1.97	1.83
SF 36-MCS	41.79	12.38	46.71	12.30	34.63	42.29	9.50	49.14	44.20	9.28	43.63	11.71
SF 36-PCS	41.38	9.10	42.09	10.67	56.45	54.30	7.18	38.84	43.94	11.448	54.21	7.69

Abbreviations: BFI, Brief Fatigue Inventory; CES-D, Centers for Epidemiological Studies-Depression; Overall Sx, MD Anderson Symptom Inventory (MDASI)-Brain Tumor (BT) symptoms (22 items); Affective Sx, MDASI-BT affective factor (fatigue, sleep, distress, sad, irritability items); Cognitive Sx, MDASI-BT cognitive factor (remembering, understanding, speaking, concentrating items); GI Sx, gastrointestinal factor; Neurolog. Sx, MDASI-BT neurologic factor (pain, numbness, weakness, seizures items); Treatment Sx, MDASI-BT treatment-related factor (appetite, drowsy, dry mouth items); General Disease Sx, MDASI-BT general disease factor (shortness of breath, vision, change in appearance, change in bowel pattern items); Overall Interfer, MDASI-BT overall interference (6 items); Interfer.-Activity, MDASI-BT activity-related interference (activity, work, walking items); Interfer.-Mood, MDASI-BT mood-related interference (mood, relations, enjoyment items); MCID, minimal clinically important difference; SF-36 MCS, Mental Component Summary; SF-36 PCS, Physical Component Summary.

For BFI, MDASI, and CES-D scores, higher scores denote greater symptomology/symptom severity or symptom interference. For SF-36 MCS and PCS scores, higher scores denote better quality of life. The MCID for BFI and MDASI score is 1 point difference (including subscales). The MCID for SF-36 MCS and PCS is a 5-point difference.

Fig. 2 Least Square Mean Difference Scores for MD Anderson Symptom Inventory-Brain Tumor Factors for the Yoga Group and Waitlist Control Group Controlling for Participants' Sex and Age and Patients' Performance Status and Tumor Grade. A, Patients. B, Caregivers. GI indicates gastro-intestinal; Int, interference; WLC, waitlist control. Difference scores were calculated T2-T1 so that a negative score indicates a greater reduction in symptom severity and interference. The minimal clinically important difference for each factor is 1 point difference.

lower socioeconomic status. Given our promising findings regarding feasibility, a future, larger trial is warranted that not only is adequately powered to examine efficacy but also includes greater participant diversity, which would allow us to analyze subgroups to better understand the intervention's effects. Moreover, a future efficacy trial with a more stringent comparison group that controls for nonspecific treatment effects such as attention and expectational biases is needed to establish intervention efficacy. Selecting a dose-match comparison group that would allow for blinding participants to study the hypotheses would be ideal to control for expectational biases. It is also important to design a future trial that includes a longer follow-up period to examine whether the intervention buffers against long-term toxicities (eg, fatigue, memory deficits, steroid myopathy). Future research may also examine the timing of the intervention delivery as later phases in patients' treatment trajectory

may reveal a differential treatment response compared to delivering the intervention while patients undergo RT. Trials that include biomarkers of inflammation (eg, interleukin 6, corticoprotein-releasing factor) and objective measures of cognitive and physical function may provide further support of intervention efficacy and shed light on underlying mechanisms by which the DY program may improve outcomes. Last, although there is a convincing theoretical rationale that a dyadic approach optimizes intervention outcomes, a head-to-head comparison between a dyadic and a patient-solo intervention is needed to establish empirical evidence.²⁹

In conclusion, a DY program delivered to glioma patients undergoing RT and their caregivers is feasible and potentially effective. This initial pilot RCT has laid the foundation for studying the role of dyadic behavioral interventions in symptom and QOL management in this population. Based on these findings, a larger efficacy trial is warranted.

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