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Effect of Yoga Therapy on Disease Activity, Inflammatory Markers, and Heart Rate Variability in Patients with Rheumatoid Arthritis

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Abstract

Background: Rheumatoid arthritis (RA) is an immune-mediated inflammatory disease. Antirheumatoid treatment reduces disease activity and inflammation, but not all patients respond to treatment. Autonomic dysfunction is common in RA leading to frequent cardiovascular complications. Yoga therapy may be useful in these patients, but there are little data on the effect of yoga on disease activity, inflammatory markers, and heart rate variability (HRV).

Objectives: This study assessed the effect of 12-week yoga therapy on disease activity, inflammatory markers, and HRV in patients with RA.

Materials and Methods: This randomized control trial was conducted on newly diagnosed RA patients attending outpatient services at the Department of Clinical Immunology, JIPMER. One hundred and sixty-six participants were randomized into two groups: the control group (CG) ($n = 83$) and yoga group (YG) ($n = 83$). Yoga therapy was administered to participants in the YG for 12 weeks, along with standard medical treatment. The CG received only standard medical treatment. Primary outcomes were disease activity score 28, interleukin-1α (IL-1α), IL-6, tumor necrosis factor-α (TNF-α), cortisol, and HRV parameters. All parameters were measured at baseline and after 12 weeks.

Results: Disease activity significantly decreased in both groups after 12 weeks, but it was reduced more in YG, which was statistically significant ($p < 0.05$). In both YG and CG, IL-1α, IL-6, TNF-α, and cortisol decreased after 12 weeks, but IL-1α and cortisol decreased more significantly in YG than in CG. Low-frequency component expressed as normalized unit (LFnu) and the low-frequency/high-frequency (LF-HF) ratio decreased significantly, and total power and HF component expressed as normalized unit (HFnu) increased significantly in the YG compared with CG.

Conclusion: Twelve-week yoga therapy, if given along with standard medical treatment, significantly reduces disease activity and improves sympathovagal balance in RA patients.

Keywords: autonomic dysfunction, cardiovascular risk, HRV, inflammatory markers, yoga therapy

Introduction

RHEUMATOID ARTHRITIS (RA) is common throughout the world with a prevalence of ~0.5%–1%.[1,2] In India, the prevalence is around 0.7%.[3] RA is more common in women than men. Pharmacologic treatments have improved joint pain, swelling, inflammation, disease activity, and quality of life in the patients of RA. However, not all patients respond effectively to pharmacologic treatment.[4]

Incidences of cardiovascular (CV) morbidity and mortality have been reported to be higher in RA patients than in the general population.[5,6] Cardiac autonomic neuropathy is one of the most common complications of RA and is associated with high mortality resulting from arrhythmia and

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myocardial infarction.[7,8] In previous studies, CV autonomic dysfunction has been reported to be around 61%–75% in RA patients.[9] Furthermore, there was overactivity of the sympathetic nervous system and underactivity of the parasympathetic nervous system.[10] Some studies have reported that increased sympathetic activity stimulates the secretion of tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) and impacts inflammation.[11–13] Other studies observed no such CV autonomic dysfunction in RA.[14] There is paucity of data on the study of sympathetic and parasympathetic activity in RA patients. Heart rate variability (HRV) is the normal phenomenon of beat to beat variation in the cardiac cycle length observed in an innervated heart due to autonomic influences on the sinoatrial node.[15,16] HRV is an established and accepted predictor of CV events[17] and mortality.[18,19]

IL-1, IL-6, and TNF-α are the prime cytokines that drive the inflammatory process in RA.[20] Other reports suggest that IL-1 and TNF-α regulate the expression of adhesion molecules in endothelial cells leading to endothelial dysfunction and an increase in CV atherosclerosis and CV disease events.[21] Furthermore, IL-1 and TNF-α stimulate the recruitment of neutrophils into the joints leading to joint damage.[22]

Yoga consists of a series of mind/body techniques, including breathing practices, physical postures, and meditation, which are beneficial in healthy subjects as well as those suffering from autoimmune disorders such as RA and osteoarthritis. A randomized-controlled trial (RCT) involving RA patients by Zautra et al.[23] reported that meditation reduced daily pain, depression, joint tenderness, and IL-6. Another RCT by Evans et al.[24] from the United States compared a 6-week Iyengar yoga intervention twice weekly with usual care and found a significant decrease in pain disability, but no difference in disease activity. Other studies conducted on RA patients reported improvements in disease activity,[25] hand grip strength,[26] and improvements in psychologic distress and well-being.[27] However, some studies reported no improvement in either disease activity[27] or cortisol levels.[28] This study, therefore, set out to assess the effect of 12 weeks of yoga in patients with RA on disease activity, inflammatory markers, and HRV parameters.

Materials and Methods

The study was conducted at the Department of Physiology, Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Puducherry, India. It was approved by the JIPMER Scientific Advisory Committee and Institute Ethics Committee before its commencement, and was registered in the Clinical Trials Registry- India (registration number CTRI/2017/07/009132).

Participants

Inclusion criteria. RA patients (diagnosis of RA made as per 2010 ACR/EULAR criteria)[29] of both genders, ages between 30 and 60 years, with nondeforming disease duration of <3 years, and on stable doses of disease modifying antirheumatic drugs (single or combination therapy) with low, moderate, and high disease activity (as per disease activity score [DAS 28] criteria),[30] were included in the study.

Exclusion criteria. RA patients with diabetes mellitus; uncontrolled hypertension; any other neuromuscular or autoimmune disorder; history of alcoholism or drug abuse; and history of yoga therapy or any other biofeedback techniques were excluded from the study.

Sample size

The sample size estimations were done by OpenEpi (open source software for epidemiologic statistics) using the statistical formula for comparing two independent means. The minimum expected difference in DAS 28 between the groups is 0.6[25] with standard deviation (SD) of 1.2. The sample size was estimated for 5% level of significance and 80% power, yielding 75 patients in both the yoga group (YG) and control group (CG), allowing for a 15% dropout rate.

Design and procedures

RA patients fulfilling inclusion and exclusion criteria were recruited from the Department of Clinical Immunology, JIPMER. Written informed consent was obtained from all the participants before initiation of the study. After recruiting participants, baseline assessments of disease activity and short-term HRV were done. Blood samples were collected for IL-1α, IL-6, TNF-α, and cortisol. Then, subjects were randomized to the YG or CG by a computer-generated simple randomization method. Allocation concealment was done using opaque sealed envelopes. An investigator not involved in data collection prepared the assignments in the sealed envelopes, which were then given to participants following the completion of baseline testing. CG participants were given the option of joining yoga sessions after a waitlist period of 3 months.

YG participants underwent yoga therapy for 12 weeks (30 min, 3 times/week), administered in the Advanced Centre for Yoga Therapy, Education & Research (ACYTER), JIPMER, by qualified and experienced yoga instructors as per the yoga therapy schedule (Table 1). During the days when YG participants were not attending yoga sessions, they were advised to practice at home. YG participants were monitored by phone contact during their home practice. Yoga therapy initially consisted of warming up, sukshma vyayama, a few asanas, pranayama, and dhyana (meditation). That was increased to include all the asanas and pranayamas in the yoga therapy schedule when the participants were sufficiently trained in yoga practice. Both YG and CG continued with their standard medical treatment and drugs as prescribed by the department of clinical immunology. After 12 weeks, all the parameters were measured again.

Study assessments

Demographics, anthropometric and blood pressure measurements. Demographic and clinical information (i.e., participant's age, duration of disease) was obtained from the patient or from medical records at the time of entry into the trial. Body weight, height, and blood pressure were measured for all participants.

DAS 28 measurement. DAS 28 was measured by recording 28 tender joint counts, 28 swollen joint counts, patient global assessment, and erythrocyte sedimentation rate.[30]

Table 1. Details of Yoga Therapy Intervention

S. No.	Asanas and pranayama	Duration
1	Warming up	2 Min
2	Sukshma vyayama (1) Purna-bhuja- sakti-vikasaka (exercising muscles controlling the arms) (2) Mani-bandha- sakti-vikasaka (exercising muscles controlling the wrists) (3) Kara-tala- sakti-vikasaka (exercising muscles controlling the palms) (4) Janu- sakti-vikasaka (exercising muscles controlling the knees) (5) Gulpha-pada-prstha-pada-tala- sakti-vikasaka (exercising muscles controlling the ankles and feet)	9 Min
3	Yogasanas (1) Tadasana (mountain pose) (2) Katichakrasana (lateral arc pose) (3) Konasana (angle pose) (4) Urdhwa hastottanasana (upstretched arms posture) (5) Pavanamuktasana (wind removing pose) (6) Bhujangasana (cobra pose) (7) Shavasana (corpse pose, palms up)	8 Min
4	Pranayama (1) Nadishodhana pranayama (alternate nostril breathing) (2) Chandrabhedi pranayama (left nostril breathing) (3) Bhramari (humming bee breathing)	6 Min
5	Dhyana (AUM chanting meditation, i.e., AUM Japa)	5 Min

Recording and analysis of HRV. The HRV recording and analysis were performed as per the standard procedures recommended by the task force on HRV.[15] Using Kubios HRV (version 3.0., Bio-signal analysis group, University of Kuopio, Finland), the authors analyzed the frequency domain and time domain components of HRV. Frequency domain indices such as total power (TP) were measured in milliseconds squared (ms^2), low-frequency (LF) component expressed as normalized unit (LFnu), high-frequency (HF) component expressed as normalized unit (HFnu), and LF/HF as a ratio (the ratio between LFnu and HFnu). Time domain indices, such as mean RR, square root of the mean squared differences of successive normal to normal intervals (RMSSD), standard deviation of normal to normal interval (SDNN), the number of interval differences of successive NN intervals greater than 50 ms (NN50), and the proportion derived by dividing NN50 by the total number of NN intervals (pNN50), were recorded.

Estimation of IL-1α, IL-6, TNF-α, and cortisol. Under aseptic precautions, 5-mL venous blood samples were collected between 7.30 and 8.30 AM at both baseline and after 12 weeks for all participants. The blood samples were allowed to clot for ≥30 min, then centrifuged, and then the serum was collected. Serum samples were then aliquoted and stored at −80°C until used for ELISA. Serum concentrations of IL-1α were measured by ELISA with commercial kits from Bioassay Technology laboratory (Korain Biotech Co., Ltd., Shanghai, China) and Diaclone SAS (France). Serum IL-6 and TNF-α were measured by ELISA with commercial kits from Bioassay Technology laboratory (Korain Biotech Co., Ltd.). Serum cortisol was measured by Calbiotech, Inc. (CA).

Statistical analyses

Statistical analyses were performed using Statistical Package for Social Sciences 19 (IBM SPSS Statistics for Windows, Version 19.0.; IBM Corp., Armonk, NY). The data, such as demographic characteristics, disease activity, IL-1α, IL-6, TNF-α, cortisol, and HRV parameters, are expressed as mean ± SD. Paired-samples *t*-test was used to compare the means between baseline and after 12 weeks within the groups. Comparison of disease activity, IL-1α, IL-6, TNF-α, cortisol, and HRV parameters between the groups was carried out using independent Student's *t*-test. Analyses of covariance, with baseline values as a covariate, were used to compare differences between groups after 12 weeks. All the statistical analyses were carried out at 5% level of significance, and so, *p*-values <0.05 were considered statistically significant.

Results

The participant disposition as per CONSORT guidelines is shown in Figure 1. One hundred and sixty-six RA patients were recruited and randomized into the YG ($n = 83$) and CG ($n = 83$). Sixty-eight YG and 75 CG participants completed the 12-week follow-up. Participants in the YG were 63 female participants (92.64%) and 5 male participants (7.35%), and participants in CG were 68 female participants (90.66%) and 7 male participants (9.33%). Participants were South Indian Tamil with a mean age of 41.33 years in YG and 42.59 years in CG. No significant differences were noted between the two groups in the parameters of age, body mass index (BMI), heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP) at baseline (Table 2). BMI, HR, SBP, and DBP were reduced significantly in the YG after 12 weeks compared with CG.

Reduction in disease activity (DAS 28) was statistically significant in both the groups (Table 3) in comparison with baseline values, but the decrease in disease activity was more in the YG compared with the CG; the difference was statistically significant ($p < 0.001$). The authors found that after 12 weeks of yoga therapy, levels of IL-1α and cortisol

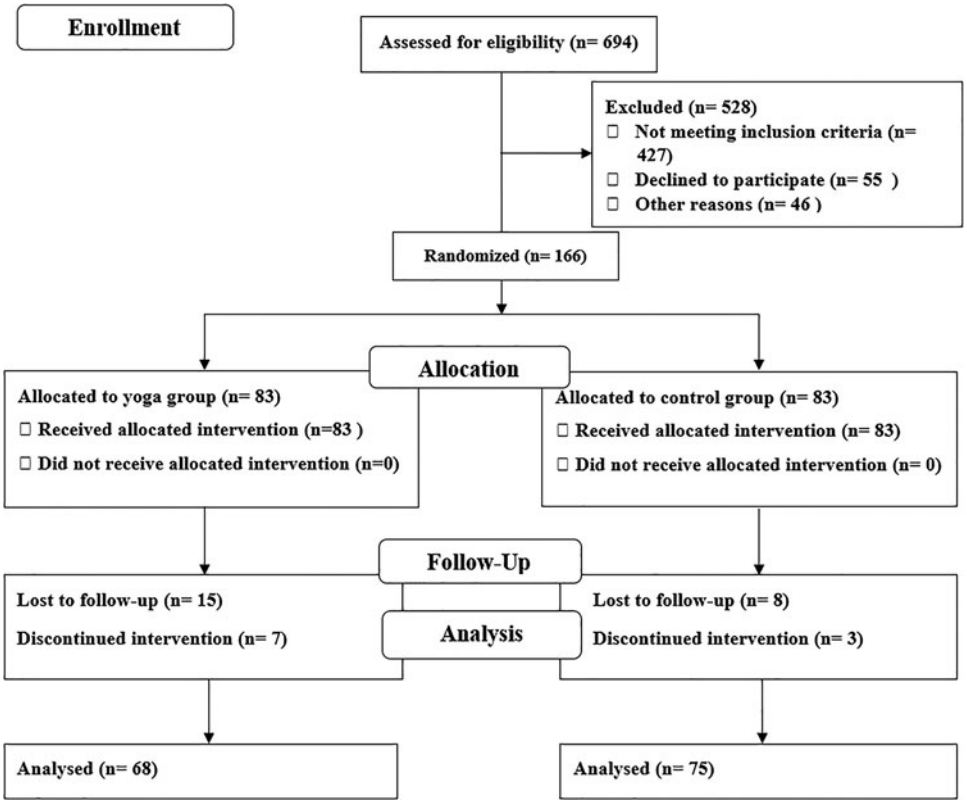

FIG. 1. Study CONSORT (Consolidated Standards of Reporting Trials) flow diagram showing participant flow through each stage of the randomized-controlled trial (enrollment, intervention allocation, follow-up, and data analysis).

reduced more in YG than in CG, that difference also being statistically significant.

Variables of frequency domain indices such as LF, HF, TP, LFnu, HFnu, and LF: HF ratio (Table 4) showed no significant differences ($p > 0.05$) at the baseline. When comparing the two groups after 12 weeks of yoga therapy, TP and HFnu increased more in the YG than the CG, the difference was statistically significant. LFnu and LF: HF ratio reduced more in the YG than the CG, again statistically significant. In comparison with CG, YG showed significant improvement in mean RR, RMSSD, SDNN, NN50, and pNN50 parameters.

Discussion

The study presents novel data regarding the effect of 12-week yoga therapy on disease activity, markers of inflammation, cortisol, and HRV in the patients of RA.

Disease activity was significantly reduced in both YG and CG of RA patients after 12 weeks, but the reduction in disease activity was more in the YG after 12 weeks of yoga therapy compared with CG, which was statistically significant. This finding is consistent with the findings of Badsha et al.,[25] who reported reduction in the counts of tender and swollen joints and disease activity after 8 weeks of yoga

Table 2. Age, Body Mass Index, Blood Pressure at Baseline and After 12 Weeks in Yoga Group and Control Group

Variable	*Group (*n*)*	*Baseline*	*After 12 weeks*	p *(baseline vs. 12 weeks)*	p *(between groups) at baseline*	p *(between groups) after 12 weeks*
Age (years)	YG (68)	41.33 ± 9.51	—	—	0.452	—
	CG (75)	42.59 ± 7.1	—	—		
BMI (kg/m^2)	YG (68)	24.76 ± 4.15	23.62 ± 3.01	0.000	0.307	0.000
	CG (75)	24.07 ± 3.93	23.92 ± 3.74	0.305		
HR (per min)	YG (68)	85.4 ± 8.3	73.88 ± 6.55	0.000	0.475	0.000
	CG (75)	86.52 ± 10.02	81.31 ± 8.72	0.000		
SBP (mmHg)	YG (68)	117.44 ± 10.28	110.06 ± 7.56	0.000	0.597	0.000
	CG (75)	116.6 ± 8.67	113.72 ± 6.95	0.000		
DBP (mmHg)	YG (68)	74.78 ± 11.2	71.68 ± 5.93	0.011	0.922	0.002
	CG (75)	74.93 ± 7.17	74.2 ± 6.2	0.09		

The values are expressed as mean ± SD. The *p*-values <0.05 were considered statistically significant.

BMI, body mass index; CG, control group; DBP, diastolic blood pressure; HR, heart rate; SD, standard deviation; SBP, systolic blood pressure; YG, yoga group.

Table 3. Disease Activity, Inflammatory Markers, and Cortisol at Baseline and After 12 Weeks in Yoga Group and Control Group

Variable	*Group (*n*)*	*Baseline*	*After 12 weeks*	p *(baseline vs. 12 weeks)*	p *(between groups) at baseline*	*p (between groups) after 12 weeks*
DAS 28	YG	4.95 ± 0.74	2.99 ± 0.78	0.000	0.128	0.000
	CG	4.77 ± 0.62	3.49 ± 0.78			
Interleukin 1α (pg/mL)	YG	11.97 ± 20.4	6.02 ± 5.31	0.018	0.839	0.017
	CG	12.58 ± 15.4	9.39 ± 10.28	0.97		
Interleukin 6 (ng/L)	YG	114.91 ± 66.98	60.42 ± 62.82	0.000	0.838	0.139
	CG	112.69 ± 62.72	79.35 ± 84.25	0.008		
TNF-α (pg/mL)	YG	91.7 ± 71.8	61.05 ± 46.84	0.001	0.708	0.098
	CG	96.7 ± 81.09	76.6 ± 60.88	0.044		
Cortisol (ng/mL)	YG	132.85 ± 67.92	88.8 ± 61.8	0.001	0.896	0.006
	CG	134.61 ± 89.05	119.7 ± 70.37	0.239		

The values are expressed as mean ± SD. The *p*-values <0.05 were considered statistically significant.
DAS 28, disease activity score 28; SD, standard deviation; TNF-α, tumor necrosis factor-α.

therapy. Evans et al.[24] reported significant improvement in quality of life in the YG, but no significant difference was seen in disease activity in the YG compared with the CG in their study. This difference may be due to duration of yoga therapy given to the RA patients.

Results of the present study demonstrated that IL-1α and cortisol were reduced significantly in the YG compared with the CG. The levels of IL-6 and TNF-α decreased in both groups, but in the YG, reduction was more. These findings are in accordance with findings of the previous studies, which have reported decreases in inflammatory markers such as IL-6,[31] TNF-α,[32] and cortisol[33] after yoga practice.

In the present study, HR, SBP, and DBP decreased significantly in patients of YG compared wiht CG. These are in accordance with Singh et al.,[34] who reported that reduction in HR, SBP, and DBP was more in YG when compared with CG in RA patients. Previous studies of yoga treatment in hypertensive patients also reported the reduction of SBP and DBP.[35–37] Earlier studies have shown that yoga practices,

Table 4. Frequency Domain Indices and Time Domain Indices of Heart Rate Variability at Baseline and After 12 Weeks in Yoga Group and Control Group

Variable	*Group (*n*)*	*Baseline*	*After 12 weeks*	p *(baseline vs. 12 weeks) within groups*	p *(between groups) at baseline*	p *(between groups) after 12 weeks*
LF (ms^2)	YG	224 ± 251.54	261.56 ± 242.33	0.000	0.838	0.47
	CG	203.88 ± 210.34	233.44 ± 228.98	0.047		
HF (ms^2)	YG	146.79 ± 170.56	254.54 ± 264.39	0.004	0.961	0.019
	CG	135.96 ± 185.10	166.11 ± 176.26	0.451		
TP (ms^2)	YG	402.04 ± 411.70	588.5 ± 460.99	0.005	0.99	0.021
	CG	401.13 ± 411.93	425.59 ± 377.33	0.703		
LFnu	YG	63.26 ± 13.72	51.95 ± 10.31	0.000	0.816	0.000
	CG	63.75 ± 11.67	60.40 ± 11.86	0.000		
HFnu	YG	36.31 ± 13.63	47.66 ± 10.27	0.000	0.944	0.000
	CG	36.16 ± 12.75	39.46 ± 11.97	0.002		
LF: HF ratio	YG	2.16 ± 1.29	1.17 ± 0.48	0.000	0.574	0.000
	CG	2.05 ± 0.96	1.76 ± 0.83	0.000		
Mean RR (ms)	YG	731.96 ± 103.51	770.44 ± 101.38	0.04	0.948	0.032
	CG	733.14 ± 110.25	744.63 ± 95.91	0.929		
RMSSD (ms)	YG	22.61 ± 16.67	34.08 ± 20.69	0.001	0.116	0.006
	CG	25.78 ± 16.98	27.87 ± 22.66	0.082		
SDNN (ms)	YG	20.93 ± 10.56	31.85 ± 16.39	0.000	0.494	0.000
	CG	19.61 ± 12.36	22.91 ± 10.84	0.092		
NN50	YG	14.54 ± 24.87	21.29 ± 33.35	0.186	0.263	0.033
	CG	10.17 ± 21.59	11.66 ± 18.74	0.648		
pNN50 (%)	YG	3.78 ± 6.68	5.5 ± 8.88	0.209	0.38	0.041
	CG	2.87 ± 6.52	2.99 ± 5.37	0.827		

The values are expressed as mean ± SD. The *p*-values <0.05 were considered statistically significant.
HF, high frequency; HFnu, normalized high-frequency component; LF, low frequency; LF/HF, ratio of the low-frequency component to the high-frequency component of HRV; LFnu, normalized low-frequency component; mean RR, mean-RR interval; NN50, number of interval differences of successive NN intervals greater than 50 ms; pNN50, proportion derived by dividing NN50 by the total number of NN interval; RMSSD, the square root of the mean of the sum of the squares of differences between adjacent NN intervals; SDNN, standard deviation of the averages of NN intervals in all 5-min segments of the entire recording; TP, total power.

including meditation, pranayamas, and asanas, significantly reduce the levels of SBP and DBP.[38,39]

The LF: HF ratio, a measure of sympathovagal balance,[15,40] was increased in both YG and CG at baseline compared with normal[10] due to increased sympathetic and decreased parasympathetic activity in RA. LFnu, which reflects cardiac sympathetic drive,[15,40] was increased in both YG and CG at baseline compared with normal levels,[10] which further demonstrates increased sympathetic activity in these patients. HFnu, which reflects vagal activity, was decreased in both groups at baseline compared with normal levels,[10] which indicates reduced parasympathetic activity. This was further confirmed by low levels of baseline RMSSD and SDNN, also reflecting decreased vagal tone[15,40] at baseline. These results are consistent with those of the study by Evrengül et al.[41] that reported increased sympathetic activity in the patients of RA, causing ventricular tachyarrhythmia, which may be related to the higher incidence of sudden death in these patients. It has been suggested that increased sympathetic activity causes proinflammatory effects[42,43] and increases the secretion of inflammatory markers such as IL-1 and Il-6.

In this study, reduction of LF: HF ratio and LFnu was more in the YG compared with CG. Furthermore, HFnu increased significantly in the YG compared with CG after 12 weeks. These findings are in conformity with the findings of a previous study by Krishna et al.,[44] who reported decreased LF: HF ratio and LFnu, and increased HFnu after 12 weeks of yoga therapy in heart failure patients. RMSSD and SDNN increased more in YG compared with CG after yoga therapy, which represents vagal tone was increased more in YG than CG.

Thus, a 12-week yoga therapy as an adjunct to standard medical treatment resulted in a significant decrease in the HR, BP, LFnu, and LF/HF ratio, and an increase in HFnu, RMSSD, and SDNN. This represents an overall shift toward parasympathetic predominance as a result of reduction in sympathetic activity and improvement in parasympathetic activity.

Strengths of this study are as follows: the use of inflammatory markers and parameters of HRV in evaluating the efficacy of yoga, while previous studies were based mainly on questionnaires. Sample size, duration of yoga therapy, and inclusion of RA patients with disease duration <3 years also are some of the additional strengths of this study.

Limitations of this study are as follows: observations were taken only at baseline and after 3 months; because the funding was limited, the authors had to restrict their observations at baseline and after 3 months. More time points would have been better. They could not assess the long-term effects of yoga therapy for 6 months or more since compliance posed a major hurdle. Nor could they assess markers such as neuropeptide Y, adrenaline, and noradrenaline. Another limitation was that patients with low-to-severe disease activity were included in the study. Subgroup analysis of low, moderate, and severe disease activity patients was not done because it was underpowered to detect the difference (more patients needed in each subgroup), this may be done in future studies.

Conclusion

Since yoga therapy proved to be beneficial for RA patients due to reduction in disease activity, IL-1α, cortisol levels, and improvement in sympathovagal balance, appropriate yoga therapy can be given to RA patients as an adjunct to standard medical treatment.

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Author Disclosure Statement

No competing financial interests exist.

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References

1. Carmona L, Cross M, Williams B, et al. Rheumatoid arthritis. Best Practice Res Clin Rheumatol 2010;24:733–745.
2. Scott DL, Wolfe F, Huizinga TW. Rheumatoid arthritis. Lancet 2010;376:1094–1108.
3. Malaviya AN, Kapoor SK, Singh RR, et al. Prevalence of rheumatoid arthritis in the adult Indian population. Rheumatol Int 1993;13:131–134.
4. Daul P, Grisanti J. Monitoring response to therapy in rheumatoid arthritis—Perspectives from the clinic. Bull NYU Hosp Jt Dis 2009;67:236–242.
5. Amaya-Amaya J, Montoya-Sánchez L, Rojas-Villarraga A. Cardiovascular involvement in autoimmune diseases. Biomed Res Int 2014;2014:367359.
6. Wright K, Crowson CS, Gabriel SE. Cardiovascular comorbidity in rheumatic diseases: A focus on heart failure. Heart Fail Clin 2014;10:339–352.
7. Mutru O, Laakso M, Isomaki H, Koota K. Ten year mortality and causes of death in patients with rheumatoid arthritis. Br Med J (Clin Res Ed) 1985;290:1797–1799.
8. Prior P, Symmons DP, Scott DL, et al. Cause of death in rheumatoid arthritis. Br J Rheumatol 1984;23:92–99.
9. Stojanovich L, Milovanovich B, de Luka SR, et al. Cardiovascular autonomic dysfunction in systemic lupus, rheumatoid arthritis, primary Sjögren syndrome and other autoimmune diseases. Lupus 2007;16:181–185.
10. Yadav RK, Gupta R, Deepak KK. A pilot study on short term heart rate variability and its correlation with disease activity in Indian patients with rheumatoid arthritis. Indian J Med Res 2012;136:593–598.
11. Pöyhönen-Alho MK, Manhem K, Katzman P, et al. Central sympatholytic therapy has anti-inflammatory properties in hypertensive postmenopausal women. J Hypertens 2008; 26:2445–2449. DOI: 10.1097/HJH.0b013e328311cf37
12. Bernstein IM, Damron D, Schonberg AL, Shapiro R. The relationship of plasma volume, sympathetic tone, and proinflammatory cytokines in young healthy nonpregnant women. Reprod Sci 2009;16:980–985. DOI: 10.1177/1933719109338876
13. Straub RH, Kalden JR. Stress of different types increases the proinflammatory load in rheumatoid arthritis. Arthritis Res Ther 2009;11:114. DOI: 10.1186/ar2712
14. Javady Nejad J, Jamshidi AR, Qorbani M. Cardiovascular autonomic neuropathy in rheumatoid arthritis assessed by

cardiovascular autonomic function tests: A cross sectional survey. Anatol J Cardiol 2015;15:722–726.
15. Heart rate variability: Standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Circulation 1996; 93:1043–1065.
16. Lahiri MK, Kannankeril PJ, Goldberger JJ. Assessment of autonomic function in cardiovascular disease: Physiological basis and prognostic implications. J Am Coll Cardiol 2008;51:1725–1733. DOI: 10.1016/j.jacc.2008.01.038
17. Tsuji H, Larson M, Venditti F, et al. Impact of reduced heart rate variability on risk for cardiac events. The Framlingam heart study. Circulation 1996;94:2850–2855.
18. Tsuji H, Venditti F, Manders E, et al. Reduced heart rate variability and mortality risk in an elderly cohort. The Framingham heart study. Circulation 1994;90:878–883.
19. Nolan J, Batin PD, Andrews R, et al. Prospective study of heart rate variability and mortality in chronic heart failure: Results of the United Kingdom heart failure evaluation and assessment of risk trial (UK-heart). Circulation 1998;98: 1510–1516.
20. Choy EH, Panayi GS. Cytokine pathways and joint inflammation in rheumatoid arthritis. N Engl J Med 2001; 344:907–916.
21. Manzi S, Wasko MC. Inflammation-mediated rheumatic diseases and atherosclerosis. Ann Rheum Dis 2000;59:321–325.
22. Moore AR, Iwamura H, Larbre JP, et al. Cartilage degradation by polymorphonuclear leucocytes: In vitro assessment of the pathogenic mechanisms. Ann Rheum Dis 1993; 52:27–31.
23. Zautra AJ, Davis MC, Reich JW, et al. Comparison of cognitive behavioral and mindfulness meditation interventions on adaptation to rheumatoid arthritis for patients with and without history of recurrent depression. J Consult Clin Psychol 2008;76:408–421.
24. Evans S, Moieni M, Lung K, et al. Impact of Iyengar yoga on quality of life in young women with rheumatoid arthritis. Clin J Pain 2013;29:988–997.
25. Badsha H, Chhabra V, Leibman C, et al. The benefits of yoga for rheumatoid arthritis: Results of a preliminary, structured 8-week program. Rheumatol Int 2009;29:1417–1421.
26. Dash M, Telles S. Improvement in hand grip strength in normal volunteers and rheumatoid arthritis patients following yoga training. Indian J Physiol Pharmacol 2001;45: 355–360.
27. Pradhan EK, Baumgarten M, Langenberg P, et al. Effect of mindfulness-based stress reduction in rheumatoid arthritis patients. Arthritis Rheum 2007;57:1134–1142.
28. Bosch PR, Traustadottir T, Howard P, Matt KS. Functional and physiological effects of yoga in women with rheumatoid arthritis: A pilot study. Altern Ther Health Med 2009; 15:24–31.
29. Aletaha D, Neogi T, Silman AJ, et al. 2010 rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis 2010;69:1580–1588.
30. Anderson J, Caplan L, Yazdany J, et al. Rheumatoid arthritis disease activity measures: American College of Rheumatology recommendations for use in clinical practice. Arthritis Care Res (Hoboken) 2012;64:640–647.
31. Pullen PR, Nagamia SH, Mehta PK, et al. Effects of Yoga on inflammation and exercise capacity in patients with chronic heart failure. J Card Fail 2008;14:407–413.
32. Bandi HK, Pravati P, Pal GK, et al. Yoga training in heart failure (NYHA I–II) reduces oxidative stress and inflammation. J Exerc Physiol Online 2014;17:10–18.
33. Naveen GH, Varambally S, Thirthalli J, et al. Serum cortisol and BDNF in patients with major depression-effect of yoga. Int Rev Psychiatry 2016;28:273–278.
34. Singh VK, Bhandari RB, Rana BB. Effect of yogic package on rheumatoid arthritis. Indian J Physiol Pharmacol 2011; 55:329–335.
35. Schneider R, Alexander C, Staggers F, et al. A randomized controlled trial of stress reduction in African Americans treated for hypertension for over one year. Am J Hypertens 2005;18:88–98.
36. Selvamurthy W, Sridharan K, Ray US, et al. A new physiological approach to control essential hypertension. Indian J Physiol Pharmacol 1998;42:205–213.
37. Murugesan R, Govindarajulu N, Bera TK. Effect of selected yogic practices on the management of hypertension. Indian J Physiol Pharmacol 2000;44:207–210.
38. Pramanik T, Sharma HO, Mishra S, et al. Immediate effect of slow pace bhastrika pranayama on blood pressure and heart rate. J Altern Complement Med 2009;15:293–295.
39. Sudsuang R, Chentanez V, Veluvan K. Effect of Buddhist meditation on serum cortisol and total protein levels, blood pressure, pulse rate, lung volume and reaction time. Physiol Behav 1991;50: 543–548.
40. Alberto M. Heart rate variability: From bench to bedside. Eur J Intern Med 2005;16:12–60.
41. Evrengül H, Dursunoğlu D, Çobankara V, et al. Heart rate variability in patients with rheumatoid arthritis. Rheumatol Int 2004; 24: 198–202.
42. Straub RH, Harle P. Sympathetic neurotransmitters in joint inflammation. Rheum Dis Clin North Am 2005;31:43–59, viii. DOI: 10.1016/j.rdc.2004.09.003
43. Härle P, Möbius D, Carr DJ, et al. An opposing time-dependent immune-modulating effect of the sympathetic nervous system conferred by altering the cytokine profile in the local lymph nodes and spleen of mice with type II collagen-induced arthritis. Arthritis Rheum 2005;52:1305–1313.
44. Krishna BH, Pal P, Gopal KP, et al. Effect of yoga therapy on heart rate, blood pressure and cardiac autonomic function in heart failure. J Clin Diagn Res 2014;8:14–16.

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