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A yoga & exercise randomized controlled trial for vasomotor symptoms: Effects on heart rate variability

Salene M.W. Jones[a,*], Katherine A. Guthrie[b], Susan D. Reed[c], Carol A. Landis[d], Barbara Sternfeld[e], Andrea Z. LaCroix[f], Andrea Dunn[e], Robert L. Burr[d], Katherine M. Newton[a]

[a] Group Health Research Institute, 1730 Minor Ave, Seattle, WA 98101, United States
[b] Fred Hutchinson Cancer Research Center, Seattle, WA, United States
[c] Department of Obstetrics and Gynecology, University of Washington, Seattle, WA, United States
[d] School of Nursing, University of Washington, Seattle, WA, United States
[e] Kaiser Permanente Division of Research, Oakland, CA, United States
[f] University of California San Diego, San Diego, CA, United States

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ABSTRACT

Objectives: Heart rate variability (HRV) reflects the integration of the parasympathetic nervous system with the rest of the body. Studies on the effects of yoga and exercise on HRV have been mixed but suggest that exercise increases HRV. We conducted a secondary analysis of the effect of yoga and exercise on HRV based on a randomized clinical trial of treatments for vasomotor symptoms in peri/post-menopausal women.
Design: Randomized clinical trial of behavioral interventions in women with vasomotor symptoms (n = 335), 40–62 years old from three clinical study sites.
Interventions: 12-weeks of a yoga program, designed specifically for mid-life women, or a supervised aerobic exercise-training program with specific intensity and energy expenditure goals, compared to a usual activity group.
Main outcome measures: Time and frequency domain HRV measured at baseline and at 12 weeks for 15 min using Holter monitors.
Results: Women had a median of 7.6 vasomotor symptoms per 24 h. Time and frequency domain HRV measures did not change significantly in either of the intervention groups compared to the change in the usual activity group. HRV results did not differ when the analyses were restricted to post-menopausal women.
Conclusions: Although yoga and exercise have been shown to increase parasympathetic-mediated HRV in other populations, neither intervention increased HRV in middle-aged women with vasomotor symptoms. Mixed results in previous research may be due to sample differences. Yoga and exercise likely improve short-term health in middle-aged women through mechanisms other than HRV.

1. Background/Introduction

Yoga, a practice that can include physical poses, breathing techniques and meditation, was developed over 5000 years ago in Asia to promote spiritual and physical health.[1] Yoga has been shown to be effective for cardiovascular disease,[2] stress reduction in people with cancer,[3] pain reduction,[4] and treatment of psychiatric disorders.[5] Recent research has also investigated the effects of yoga on physiologic markers of health such as cortisol[6] and immune function.[7] Heart rate variability (HRV) may be another mechanism through which yoga improves health. HRV reflects autonomic nervous system functioning, particularly the parasympathetic branch, and greater HRV is related to better overall and emotional health.[8,9] This study compared HRV changes in women with menopausal symptoms randomized to either yoga, exercise, or a usual activity group.

Few randomized clinical trials (RCTs) have investigated the effect of yoga on HRV. Although several experimental studies have

* Corresponding author.
E-mail addresses: wu.582@osu.edu, salenewu@gmail.com (S.M.W. Jones).

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documented increases in parasympathetic-mediated HRV during the meditative state in yoga,[10–12] evidence of changes in resting, parasympathetic-mediated HRV from RCTs of yoga has been mixed. Some studies have shown increases in resting HRV after yoga interventions, compared to control groups[13–15] but others have not.[16,17] However, most studies were small (no more than 30 individuals). Whether yoga can improve parasympathetic function as reflected by HRV is unknown.

Resting or basal HRV has been shown to increase with exercise training,[18,19] indicating that exercise may improve parasympathetic function. As exercise is beneficial for cardiovascular and other aspects of health[20] HRV may be one mechanism through which exercise affects health. A review of studies in healthy adults comparing yoga and physical activity found that yoga increased HRV to a greater extent than did physical activity while physical activity tended to increase caloric expenditure and other metabolic variables.[21] The effects of yoga and exercise on HRV in menopausal women are unknown. This analysis used data from the second MsFLASH (Menopause Strategies: Finding Lasting Answers for Symptoms and Health) trial[22–24] to investigate whether HRV could be the mechanism through which yoga and exercise improve health in menopausal women.

2. Methods

2.1. Sample and procedures

Details of the study design and methods of the second MsFLASH trial have been described elsewhere.[22–25] Briefly, the 3 × 2 factorial design randomized trial conducted in 2011–2012 tested the efficacy of exercise, and yoga vs. a usual-activity control and omega-3 vs. placebo capsules on the frequency of vasomotor symptoms (see Fig. 1 for CONSORT diagram). Women (n = 355) were recruited from three clinical sites in the United States: Seattle, WA; Indianapolis, IN; and Oakland, CA. Inclusion criteria were: age between 40 and 62 years; 14 or more vasomotor symptoms per week (average over 2 weeks); in the menopausal transition or post-menopausal; and healthy enough to participate in exercise or yoga. We excluded women if they had: body mass index above 37; unstable medical condition; hormone use in the previous month; current use of yoga, meditation or exercise; or a major depressive episode in the previous 3 months. All women provided written informed consent before participating in the study. The coordinating center in Seattle randomized women to the yoga, exercise and usual activity groups using a dynamic allocation in proportions of 3:3:4 respectively. Assessors were blinded to study group assignment. Women with heart disease or taking beta-blockers were excluded from this analysis (excluded n = 11). Nine women were excluded because they did not have HRV measures, leaving a final sample of 335. Of the 20 women excluded, seven were from the yoga group, six from the exercise group and seven from usual activity. HRV and vasomotor symptoms were measured at baseline and at 12-weeks. All study procedures were approved by the institutional review boards at each site and by the Data Coordinating Center for MsFLASH in Seattle.

2.2. Interventions

The yoga intervention consisted of both classes and home practice. Weekly, 90-min classes were conducted for 12 weeks. In each class, women practiced breathing exercises, 11–13 poses, and Yoga Nidra, a deep relaxation practice. Women joined the class as they were recruited. For home practice, participants received written instructions, a DVD of the poses, a CD of the Yoga Nidra practice and yoga equipment (mat, blankets, bolster, and strap). Participants were asked to practice either the poses or Yoga Nidra for 20 min on each day they did not attend class (6 days a week), and it was suggested that they alternate the two practices. Yoga instructors had weekly contact with study investigators and classes were also observed by study staff to reinforce treatment fidelity. Participants weekly turned in diaries, which tracked their home use of poses and Yoga Nidra. The yoga practice was designed to promote relaxation and not necessarily to affect resting breathing rate.

The exercise intervention consisted of three weekly, individual, cardiovascular conditioning sessions for 12 weeks, supervised by a trainer. Trainers tracked heart rate, workload and perceived exertion to help participants maintain appropriate target heart rate during the exercise sessions. Energy expenditure goals were set for each week (ranging from 1000 to 1500 kilocalories per week) based on the results of a baseline graded exercise treadmill test. Sessions lasted from 40 to 60 min depending on time needed to achieve target heart rate and energy expenditure. All trainers underwent centralized training, weekly observation and attended regular conference calls to reinforce treatment fidelity.

Women randomized to the usual activity group were asked to maintain the same level of activity throughout the 12 weeks of the study. They were specifically asked not to increase their level of exercise or yoga and meditation practice from baseline levels until after the 12-week assessment.

2.3. Measures

2.3.1. Heart rate variability

HRV was derived from heart rate measures collected using electrocardiogram (ECG) data from Burdick Vision Holter monitors. Women came into the research clinics at their respective study sites and Holter monitors were placed. Women sat quietly for 25 min while breathing normally. The first 10 min allowed for acclimatization to the monitor and the clinic setting, and monitor calibration. The 15 min of ECG data recording after acclimation was used for the analysis. Interbeat intervals were determined from the R to R spikes on phase plots from the ECGs. Ectopic beats and artifact were removed. The correlations between raters for coding and cleaning the data were high (r's > .97). We calculated both time and frequency domain measures of HRV from the interbeat intervals.

Time domain measures examined in this study included: standard deviation of the R-R (normal to normal) intervals (SDNN); and root mean square of the successive differences (RMSSD) of the R-R intervals. We also examined the SDNN/RMSSD ratio as this is a time domain measure of sympatho-vagal balance. Frequency domain measures examined were: normalized low frequency (0.04–0.15 Hz), normalized high frequency (0.15–0.40 Hz), and the low/high frequency ratio (LF/HF ratio). Parasympathetic nervous system function is indexed by RMSSD and normalized high frequency measures.[26] Some disagreement exists regarding the significance of low frequency and LF/HF ratio HRV, although some argue that low frequency HRV reflects a predominantly sympathetic component with possible contribution from the parasympathetic system.[27] However, normalized LF and LF/HF ratio, due to how they are calculated, may also reflect reductions in parasympathetic output rather than increases in sympathetic output.[28] Normalized LF is the LF power over the total power while LF/HF ratio is the LF power over the HF power. Either can change due to changes in LF power or due to changes in parasympathetic output and hence HF power. SDNN reflects parasympathetic and sympathetic function. The LF/HF and SDNN/RMSSD ratios measure the balance between the sympathetic and parasympathetic nervous systems.

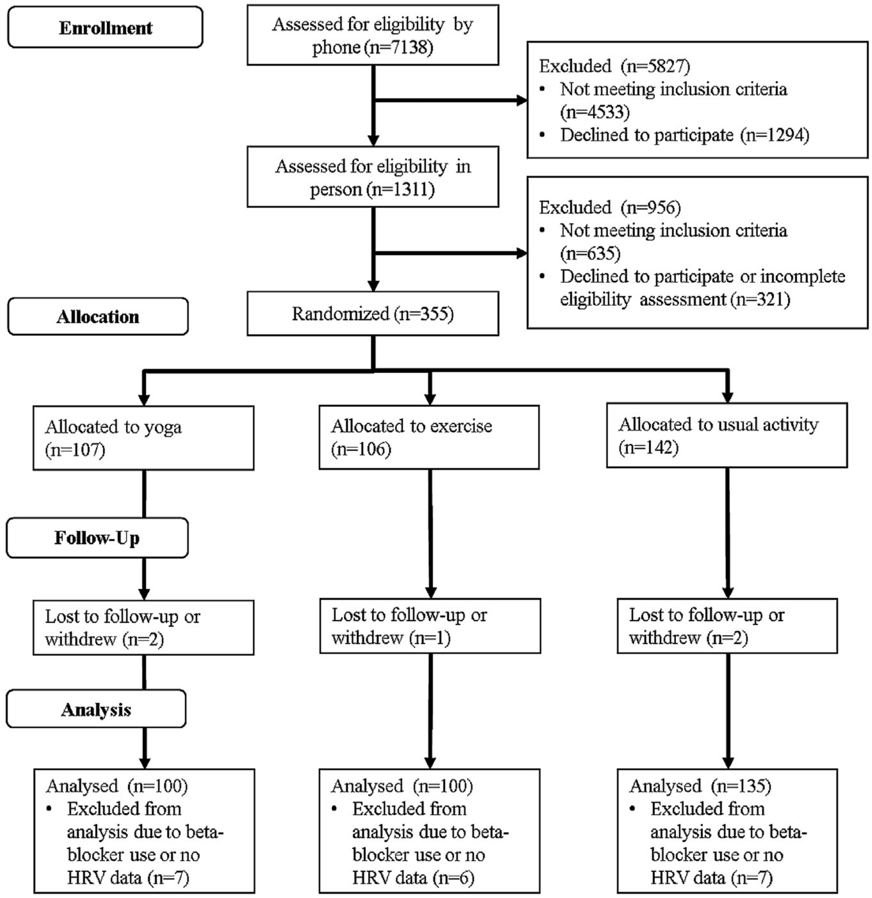

Fig. 1. CONSORT diagram. Please note, due to the statistical technique used, we were able to include women lost to follow-up in our analyses if they provided data at baseline.

2.3.2. Baseline covariates

Perceived stress was measured using the 10-item version of the Perceived Stress Scale (PSS[29]). The PSS has items on perceptions of stress and coping with stress rated on a 0–4 scale. Women also self-reported their alcohol use, smoking behavior, and last menstrual period, which was used to calculate menopausal status. Height (stadiometer) and weight (electronic scale) were measured at clinic visits and were used to calculate body mass index (BMI).

2.4. Statistical analyses

A linear generalized estimating equation model was applied to analyze the HRV data. This method allowed us to include women who were missing baseline HRV but had 12-week HRV (14%) and women who had baseline HRV but were missing 12-week HRV (16%). Analyses compared HRV measures between each intervention group and the usual activity group. HRV was modeled as a function of time (baseline or follow-up) nested within participants, treatment group (usual activity as the reference group) and the interaction of treatment group with time. Each measure of HRV was modeled separately. All analyses adjusted for clinical site and considered the following covariates: menopausal status, age, smoking, alcohol use, race/ethnicity, perceived stress and body mass index (BMI). We first evaluated the associations between the three groups (yoga, exercise and usual activity) and each covariate using analysis of variance (ANOVA) and chi-square tests. If these covariates varied significantly across treatment groups, they were included in the model. As the time domain measures were skewed, they were natural log transformed before conducting analyses. We also ran sensitivity analyses by restricting the sample to just postmenopausal women. Due to the sample size, we were unable to stratify analyses by race/ethnicity.

3. Results

Women were on average, 54.7 (3.7) years old and had, 7.7 VMS per 24 h. The majority was Caucasian and college educated. Few women were current smokers (9.3%) or reported drinking more than 7 alcoholic drinks a week (17.3%; Table 1). The average BMI was in the overweight category, 26.9 kg/m^2 (4.3). The majority was postmenopausal (80.9%). Age was significantly different between intervention groups ($p = 0.003$) but none of the other covariates were significantly related to intervention group assignment (all p's > 0.05). Vasomotor symptom frequency and bother tended to decrease from baseline to 12 weeks later for all groups (Table 2). In this subsample, 85% of women in the exercise group completed 70% or more of the exercise sessions and the mean percentage of exercise sessions completed was 83.7% (SD = 22.0). Among the yoga group, 77% of the women completed 70% or more of the yoga sessions, including home practice, and the mean percentage of sessions completed was 80.0% (SD = 22.9).

3.1. Intervention comparison

Overall, the yoga and exercise interventions did not affect HRV when each was compared with usual activity, and adjusted for site and age (see Table 3). Yoga did not significantly affect any measure of HRV (all p's > 0.07), nor did exercise (all p's > 0.15). The significance of the results did not change when restricted to only women who were post-menopausal (all p's > 0.13). Due to the null results,

Table 1
Participant characteristics.

	Yoga (n = 100)	Exercise (n = 100)	Usual Activity (n = 135)	Total (n = 335)
Age at screening: mean (SD)	54.4 (3.9)	55.7 (3.6)	54.1 (3.5)	54.7 (3.7)
Race/Ethnicity: n (%)				
Caucasian	73 (73.0)	70 (70.0)	93 (68.9)	236 (70.4)
African American	24 (24.0)	26 (26.0)	38 (28.1)	88 (26.3)
Native American	5 (5.0)	1 (1.0)	3 (2.2)	9 (2.7)
Asian	3 (3.0)	1 (1.0)	6 (4.4)	10 (3.0)
Native Hawaiian/Pacific Islander	0 (0.0)	1 (1.0)	1 (0.7)	2 (0.6)
Hispanic	6 (6.0)	2 (2.0)	3 (2.2)	11 (3.3)
Other	3 (3.0)	3 (3.0)	2 (1.5)	8 (2.4)
Education: n (%)				
High school diploma or less	6 (6.0)	6 (6.0)	7 (5.1)	19 (5.7)
Some college or technical school	28 (28.0)	38 (38.0)	38 (28.2)	104 (31.1)
Bachelor's degree or above	66 (66.0)	56 (56.0)	90 (66.7)	212 (63.3)
Employment status: n (%)				
Full time	58 (58.0)	62 (62.0)	86 (63.7)	206 (61.5)
Part time	15 (15.0)	17 (17.0)	16 (11.9)	48 (14.3)
Retired, disable, homemaker	7 (7.0)	10 (10.0)	13 (9.6)	30 (9.0)
Unemployed or other	20 (20.0)	11 (11.0)	20 (14.8)	50 (14.9)
Married or living with partner: n (%)	68 (68.0)	63 (63.0)	92 (68.1)	223 (66.6)
Smoking Status: n (%)				
Never	72 (72.0)	65 (65.0)	84 (62.2)	221 (66.0)
Past	21 (21.0)	27 (27.0)	35 (25.9)	83 (24.8)
Current	7 (7.0)	8 (8.0)	16 (11.9)	31 (9.3)
Alcohol use, drinks per week: n (%)				
0	43 (43.0)	37 (37.0)	52 (38.5)	132 (39.4)
1–6	43 (43.0)	45 (45.0)	57 (42.2)	145 (43.3)
7 or more	14 (14.0)	18 (18.0)	26 (19.3)	58 (17.3)
BMI kg/m^2: Mean (SD)	27.0 (4.6)	26.8 (3.9)	26.8 (4.5)	26.9 (4.3)
Menopausal status: n (%)				
Postmenopausal	75 (75.0)	85 (85.0)	111 (82.2)	271 (80.9)
Perimenopausal	25 (25.0)	15 (15.0)	24 (17.8)	64 (19.1)
Hysterectomy: n (%)	14 (14.0)	23 (23.0)	20 (14.8)	57 (17.0)
Bilateral oophorectomy: n (%)	7 (7.0)	10 (10.0)	13 (9.6)	30 (9.0)
Comorbidities: n (%)				
Diabetes	5 (5.0)	2 (2.0)	5 (3.7)	12 (3.6)
Hypertension	18 (18.0)	17 (17.0)	16 (11.9)	51 (15.2)
Arthritis	13 (13.0)	10 (10.0)	15 (11.1)	38 (11.3)
Medications: n (%)				
Anti-depressants (SSRI, SNRI)	10 (10.0)	14 (14.0)	16 (11.8)	40 (11.9)
Anti-hypertension	15 (15.0)	15 (15.0)	14 (10.4)	44 (13.1)
Baseline Perceived Stress Scale: mean (SD), range 0–40	13.8 (6.9)	14.1 (7.1)	13.5 (7.0)	13.8 (7.0)

Table 2
Vasomotor symptoms and heart rate variability (HRV) at baseline and at 12-week.

	Yoga (n = 100)		Exercise (n = 100)		Usual Activity (n = 135)		Total (n = 335)	
	Baseline	12-weeks	Baseline	12-weeks	Baseline	12-weeks	Baseline	12-weeks
Vasomotor symptoms								
Frequency, #/day	7.6 (3.9)	4.7 (3.6)	7.3 (3.3)	4.9 (3.4)	8.0 (4.2)	5.5 (3.8)	7.7 (3.8)	5.1 (3.6)
Bother	1.9 (0.4)	1.3 (0.6)	1.9 (0.5)	1.5 (0.6)	2.0 (0.5)	1.5 (0.7)	2.0 (0.5)	1.4 (0.6)
HRV								
Average RR interval	860.5 (114.2)	871.0 (104.7)	853.0 (114.3)	900.5 (125.1)	846.2 (115.3)	883.7 (131.8)	852.4 (114.4)	885.0 (122.2)
Ln SDNN	3.4 (0.4)	3.4 (0.4)	3.4 (0.4)	3.4 (0.4)	3.5 (0.4)	3.5 (0.4)	3.4 (0.4)	3.4 (0.4)
Ln RMSSD	3.0 (0.5)	3.1 (0.4)	3.1 (0.5)	3.2 (0.4)	3.2 (0.5)	3.2 (0.5)	3.1 (0.5)	3.2 (0.5)
SDNN/RMSSD	1.9 (0.5)	1.8 (0.5)	1.8 (0.5)	1.7 (0.5)	1.7 (0.5)	1.7 (0.4)	1.8 (0.5)	1.7 (0.5)
Absolute low frequency	379.4 (519.0)	425.8 (475.6)	503.3 (720.9)	414.1 (473.5)	453.2 (579.9)	450.7 (591.9)	446.8 (609.8)	431.9 (522.1)
Normalized low frequency	62.6 (16.5)	62.7 (17.9)	64.8 (17.9)	58.4 (19.6)	61.2 (17.5)	58.2 (16.6)	62.7 (17.4)	59.6 (18.0)
Absolute high frequency	200.5 (187.5)	218.6 (208.7)	237.4 (308.5)	287.4 (331.3)	327.1 (482.8)	336.4 (461.3)	263.1 (368.7)	285.8 (362.7)
Normalized high frequency	37.4 (16.5)	37.3 (17.9)	35.2 (17.9)	41.6 (19.6)	38.8 (17.5)	41.8 (16.6)	37.3 (17.4)	40.4 (18.0)
Ln Low/high ratio	0.6 (0.8)	0.6 (0.8)	0.7 (0.9)	0.4 (0.9)	0.5 (0.8)	0.4 (0.8)	0.6 (0.8)	0.4 (0.8)
Low/high ratio	2.4 (2.0)	2.5 (2.1)	3.0 (3.1)	2.1 (1.9)	2.3 (2.3)	1.9 (1.6)	2.5 (2.5)	2.2 (1.9)

At post-intervention, 322 women had vasomotor frequency data, 317 had vasomotor bother data, and 281 had HRV data.

Table 3
Analyses comparing yoga and exercise to usual activity on HRV (n = 335). The terms for yoga and exercise indicate the interaction of the intervention group with time in the generalized estimating equation.

Outcome	Predictor	Coefficient (Confidence Interval)	p-value
Ln SDNN	Usual activity (reference)		
	Yoga	0.001 (−0.100, 0.101)	0.992
	Exercise	0.004 (−0.090, 0.097)	0.941
Ln RMSSD	Usual activity (reference)		
	Yoga	−0.034 (−0.149, 0.080)	0.558
	Exercise	0.063 (−0.047, 0.174)	0.264
SDNN/RMSSD	Usual activity (reference)		
	Yoga	−0.007 (−0.147, 0.134)	0.923
	Exercise	−0.071 (−0.214, 0.072)	0.931
nu LF	Usual activity (reference)		
	Yoga	3.823 (−1.145, 8.791)	0.131
	Exercise	−3.407 (−8.735, 1.920)	0.210
nu HF	Usual activity (reference)		
	Yoga	−3.823 (−8.791, 1.145)	0.131
	Exercise	3.407 (−1.920, 8.735)	0.210
Ln LF/HF	Usual activity (reference)		
	Yoga	0.569 (−0.060, 1.198)	0.076
	Exercise	−0.553 (−1.307, 0.201)	0.151

Analyses adjusted for age and clinical site.

we calculated post-hoc power. With our sample size and a two-tailed significance level of 0.05, we had more than 90% power to detect a moderate effect size (Cohen's d of 0.43).

4. Discussion

Yoga and exercise did not have a significant effect on HRV in a randomized trial that evaluated the effects of these interventions on vasomotor symptoms. To the best of our knowledge, this was the first study to examine the effect of yoga on HRV in peri- and post-menopausal women. Studies showing significant effects of yoga on basal, resting HRV examined people with heart failure,[13] older adults who had already completed some yoga classes,[14] pregnant women[15] and adults employed at a university.[30] However, several of those studies[14,30] only showed significant change on some measures of HRV, both sympathetic and parasympathetic mediated, while other measures did not improve. Studies of women with asthma[17] and men following a natural disaster[16] also did not show significant differences. The only other study comparing women in a similar age group (40–60 years of age) did not report post-yoga intervention comparisons of HRV.[31] Methods of these studies varied but were not as strongly controlled as the current study. Although a previous meta-analysis of the effect of exercise on parasympathetic measures of HRV showed the effect was strongest in the middle-aged compared to younger and older adults, samples of only women tended to show smaller effects.[18] It is possible that in our sample of relatively healthy women, the effects of exercise were too small to detect.

The study has strengths and limitations that should be considered when interpreting the results. First, this was a rigorously designed and conducted randomized controlled trial. The sample size was relatively large compared to other studies[14,16,30,31] and was adequately powered. By design, the MsFLASH trials are limited to middle-aged women who are in the menopause transition or early postmenopause and generalizability is limited to similar groups. We also did not have a long-term follow-up assessment of HRV in this study and did not have 24-h HRV data collection. However, previous studies of yoga and HRV have also used brief (5–20 min) resting HRV measures rather than 24-h measures.[13,30,31] Both 24-h and brief, resting HRV have been linked to cardiovascular outcomes[32] and a brief, resting HRV measurement of four to five minutes is sufficient for the measures used in our study.[33,34] One limitation in this study, particularly relevant for our measures of HRV, is the lack of resting breathing rate as a covariate. Future studies on resting HRV and either yoga or exercise should include breathing rate as this can affect HRV, particularly frequency measures.[35,36] HRV was also measured outside of the intervention in this study and not immediately following a yoga or exercise session. It is possible that HRV would improve immediately following a yoga or exercise session, as has been shown previously,[10–12] and that more than 12 weeks may be needed to see an effect on HRV outside of intervention sessions.

5. Conclusions

Given the rigorous nature of the reported trial, it seems that neither yoga practice nor an aerobic exercise program in peri- and post-menopausal women affects HRV, although previous trial results suggested these interventions can improve quality of life and sleep problems related to menopausal symptoms.[23,24] This implies that beneficial effects of yoga and exercise[2,4,34] may not be mediated through the ANS as measured by HRV at least in middle-aged women. Future research should continue to investigate the mechanisms through which yoga and exercise improve health in this population.

Conflict of interest

Dr. Newton has received research support from Otsuka Pharmaceutical Co., Ltd. and Integrated Diagnostics Inc for unrelated projects. Dr. LaCroix has been supported by Sanofi-Aventis for an unrelated project. The remaining authors do not have any conflicts of interest to report.

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