

Blood Pressure and Autonomic Changes From 12-Weeks of Yoga-Based Slow Breathing Exercises

Alfredo Gamboa, MD, MSCI¹, Hui Nian, PhD², Emily C. Smith, RN, MPH¹, Sachin Paranjape, BS, MSCI¹, Robert Abraham, MD³, Andre Diedrich, MD, PhD^{1,4}, Chase Bossart, MA⁵, and Gurjeet Birdee, MD, MPH⁶ 

Abstract

Background: Slow breathing exercises have been shown to reduce blood pressure and sympathetic tone acutely, though long-term effects are not well documented.

Objective: Assess changes in blood pressure and autonomic measures from before and after 12 weeks of yoga-based slow breathing.

Methods: We conducted a secondary analysis to assess changes in systolic blood pressure (SBP), diastolic blood pressure (DBP), and autonomic tone as measured by spectral analysis of heart rate variability after 12 weeks of yoga-based slow breathing among 99 healthy participants. Participants were randomized to 2 different slow breathing techniques, length of inhale = exhale (I = E) vs length of inhale < exhale (E > I), to examine if breath ratio produced differential effects.

Results: The baseline average SBP and DBP was 105 ± 11 and 67 ± 8 mmHg respectively. Among the 11 participants with elevated blood pressure, SBP/DBP was $126 \pm 11.0/80 \pm 5$ mmHg. SBP and DBP decreased significantly (-2.4 ± 7.3 and -1.6 ± 5.5 mmHg, respectively) at 12 weeks among all participants. Blood pressure among slow breathing participants with elevated baseline SBP > 120 mmHg and/or DBP > 80 mmHg reduced further (-10.3 ± 7.9 and -3.8 ± 5.5 mmHg, respectively). In our regression model, baseline SBP was associated with further decreases in SBP from baseline to 12 weeks. There were no significant differences in BP changes by breath ratio group. No significant changes were observed from baseline to 12 weeks in autonomic tone as measured with spectral analyses. Nor were there any observed correlations between changes in blood pressure and autonomic tone.

Conclusion: 12-weeks of slow breathing exercises were associated with clinically significant reduction of blood pressure in the absence of statistically significant changes in autonomic tone as measured by heart rate variability. Further research is warranted regarding the mechanisms and clinical efficacy of slow breathing on blood pressure regulation.

Keywords

breathwork, yoga, cardiovascular disease

Received: April 2, 2025; revised: August 19, 2025; accepted: September 2, 2025

¹Division of Clinical Pharmacology, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, USA

²Department of Biostatistics, Vanderbilt University Medical Center, Nashville, TN, USA

³Divisions of Cardiovascular Science, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, USA

⁴Department of Biomedical Engineering, Vanderbilt University, Nashville, TN, USA

⁵Yoga Well, Harbor, WA, USA

⁶Osher Center for Integrative Health, Department of Physical Medicine and Rehabilitation, Vanderbilt University Medical Center, Nashville, TN, USA

Pre-review version available at <https://www.medrxiv.org/content/10.1101/2022.08.30.22279389v1>

Corresponding Author:

Gurjeet Birdee, MD MPH, Osher Center for Integrative Health, Department of Physical Medicine and Rehabilitation, Vanderbilt University Medical Center, 3401 West End Avenue, Nashville, TN 37203, USA.

Email: gurjeet.birdee@vumc.org



Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons

Attribution-NonCommercial 4.0 License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits non-commercial use,

reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and

Open Access pages (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).

Introduction

Almost half the population in the United States has hypertension with only one quarter having their blood pressure under control.¹ Half of hypertensive patients are either not taking or not prescribed antihypertensive medications.² For some patients, pharmacologic treatments are limited by side effects, adherence, and/or efficacy. Lifestyle treatment options for hypertension such as diet and physical activity modifications are recommended but also limited by patient adherence.³ Additional non-pharmacologic treatments for hypertension may augment current therapeutic options and help reduce the burden of this condition.

The cause of hypertension is multifactorial, though one proposed driver are changes in the autonomic nervous system.⁴ Reduced parasympathetic and excessive sympathetic activity contribute to impaired baroreflex, inflammation, and elevated circulating hormones that increase blood pressure.⁵⁻⁹ One potential non-pharmacologic adjunctive treatment for hypertension is slow breathing exercises.^{10,11} Slow breathing exercises are used for health by 12% of adults in the United States¹² with the most common application being for stress reduction. In research, slow breathing has been defined as a respiratory rate less than 10 breaths a minute. Research suggests that slow breathing decreases sympathetic and increases parasympathetic tone.^{13,14} This may be partially mediated through alteration of intra-thoracic pressures,¹⁵⁻¹⁷ stimulation of arterial and cardiopulmonary baroreceptors^{18,19} and afferent pulmonary stretch receptors^{15,16,18,19} or through central interactions between respiratory and cardiovascular centers in the brainstem modulating gating of vagal activity during breathing.²⁰ These afferent signals from baroreceptors and stretch receptors project to the nucleus tractus solitarius in the brainstem, which in turn enhances vagal efferent activity. The resulting increase in vagal tone slows heart rate and facilitates reduced sympathetic outflow via reciprocal inhibition. Additionally, slow breathing enhances respiratory sinus arrhythmia, a marker of vagal modulation, thereby improving autonomic balance. Yoga, a popular form of exercise in the United States, includes an extensive and detailed approach for breathing techniques called *pranayama* of which slow breathing is the predominant technique. Yoga's slow breathing techniques acutely lower blood pressure, which may be mediated through modulation of the autonomic nervous system. In addition to breathing slowly, yoga and other mind-body practices posit that extending the exhale relative to the inhale ($E > I$) produces increases relaxation. There is a lack of data on the long-term effects of yoga-based slow breathing on blood pressure.²¹

We have previously conducted a clinical trial among healthy adults ($n = 99$) who performed slow breathing exercises for 12 weeks to examine changes in psychological and physiological stress.²² Participants were randomized to 2 different slow breathing techniques, length of inhale = exhale ($I = E$) vs length of inhale < exhale ($E > I$), to examine if inhale:exhale ratio produced differential effects on stress measures. The study did not

have a non-breathing comparison group. Participants received individual yoga instruction for 30 to 45 min to learn slow breathing techniques that progressively slowed over 12 weeks as tolerated. Participants were asked to practice daily. - Participants demonstrated high adherence to the treatments, with a mean class attendance of 10.7 ± 1.5 out of the 12 provided sessions and an average of 4.8 ± 1.2 home practices reported per week. As previously reported, in week one participants on average achieved a respiratory rate of 6 breaths a minute and by week twelve 3 breaths a minute.²² For all study participants, we observed significant changes in psychological stress as measured by PROMIS-Anxiety, but non-significant changes in physiological stress measured as heart rate variability. There were no significant differences in physiological or psychological stress measures by inhale:exhale ratio.

The objective of the present study is to perform a secondary analysis on changes in blood pressure and cardiovascular autonomic tone after 12-weeks of slow breathing using data from our prior study. We also examined if changes in blood pressure correlate with changes in autonomic tone. In addition, we explored if slow breathing ratios (length of inhale = exhale, $I = E$, vs length of inhale < exhale, $E > I$) produce differential effects on blood pressure. We hypothesized that slow breathing for 12 weeks would be associated with significant reductions in systolic and diastolic blood pressure.^{11,23} Based on our prior study, we hypothesized no significant changes in autonomic tone or associations with autonomic changes and blood pressure or by breathing ratio.²²

Methods

This study was approved by the Vanderbilt University Institutional Review Board. Written consent was obtained from each participant, and the study was registered in [ClinicalTrials.gov](https://clinicaltrials.gov) prior to enrollment (NCT02870868). As shown in [Figure 1](#), the protocol for this trial was previously published.²² We enrolled healthy adults aged 30 to 60 years excluding those with a diagnosis of hypertension or currently taking blood pressure medications and other significant health conditions (heart disease, diabetes, renal disease, anxiety disorder, depression, other psychiatric conditions including schizophrenia or bipolar disorder, attention-deficit-disorder or attention-deficit-hyperactivity disorder, and current cancer other than non-melanoma skin cancer, musculoskeletal condition with chronic pain, pulmonary disease including asthma or chronic obstructive lung disease). Excluding participants with significant medical conditions including hypertension was to accomplish the objective of the primary study which was to examine the effects of slow breathing on stress measures in a generally health population. Patients were also excluded if at baseline their systolic blood pressure ≥ 180 mmHg and/or diastolic blood pressure (DBP) ≥ 120 mmHg. There were 2 consents for this study. The first consent was to participate in baseline assessment and to receive 2 weeks of slow breathing treatments. This initial 2-week period was to ascertain behavioral compliance with breathing protocol.

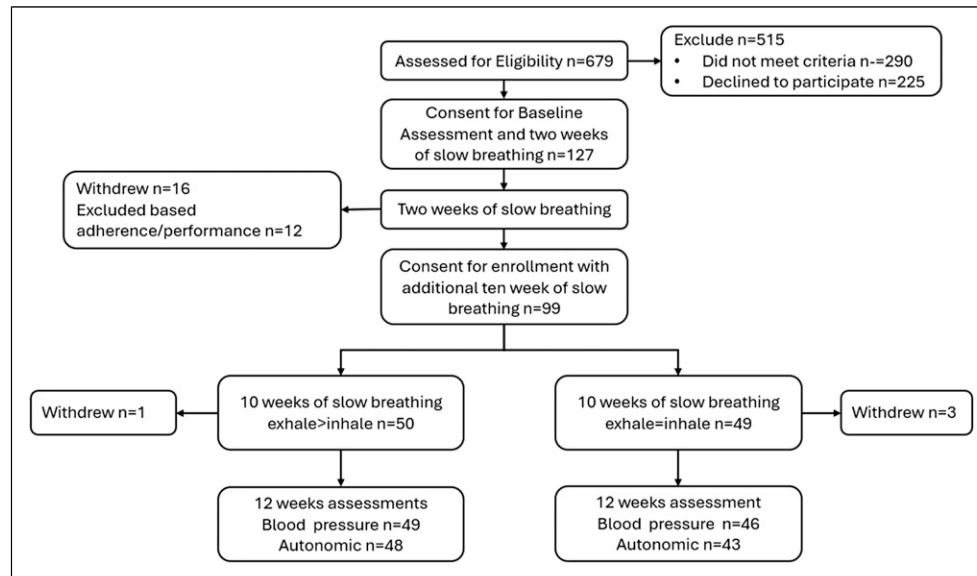


Figure 1. Study Flow Diagram

During this 2-week phase, participants attended 2 private classes with a yoga teacher to learn basic slow breathing and were asked to practice daily. To increase the likelihood of compliance, participants were included if after the first 2 weeks: (1) they practiced 3 times or more a week, and (2) had a breath rate between 3-8 breaths per minute. Participants who were compliant and willing completed a second consent and then randomized to I = E or E > I slow breathing practice for 10 weeks. Participants received individual standardized slow breathing instruction from a yoga teacher at Vanderbilt University Medical Center, Nashville Tennessee. Participants were asked to practice slow breathing at home regularly in addition to in-person instruction. Physiological assessments were performed in the morning after overnight fasting (prior to any breathing treatments) at baseline and at 12 weeks at Vanderbilt's Autonomic Dysfunction Center. Assessments included standard blood pressure measurements and autonomic testing including spectral analysis of heart rate and blood pressure variability. All volunteers were studied in an outpatient setting and asked to abstain from methylxanthine containing products for 3 days prior to each study visit. Subjects were studied after at least 30 min of quiet rest in the supine position, to allow for familiarization with the study procedures and the laboratory environment. While breathing at rest, brachial blood pressure and heart rate were determined at intervals, using an automated cuff-oscillometric sphygmomanometer (VitalGuard 450C, Ivy Biomedical, Branford, CT), and continuously with the finger clamp method (Nexfin, BMEYE, Amsterdam, the Netherlands) and ECG (VitalGuard450 C). Autonomic function was assessed by standardized autonomic testing as previously described.²² Cardiovascular signals were digitized using a Windaq system (DA-220; DATAQ Instruments). Briefly, a customized analysis program written in PV-Wave by one of the authors (A.D.) was used to perform spectral analysis of heart rate and blood

pressure,²⁴ according to Task Force²⁵ recommendations. Linear trends were removed and power spectral density was estimated with the fast fourier transform-based Welch algorithm using segments of 256 data points with 50% overlapping and Hanning window.²⁶ The power in the frequency range of low frequencies (0.04-0.15 Hz) and high frequencies (0.15-0.40 Hz) were calculated. Bivariate power spectral analysis provided useful information about the temporal fluctuations between different hemodynamic parameters, such as HR and blood pressure. We estimated the power spectra, cross spectra, phase, coherence, and transfer function gain of SBP and R-R interval time series using FFT with a segment length of 256 s resampled with 4 Hz.

Survey data was collected and managed using REDCap electronic data capture tools hosted at Vanderbilt University Medical Center.²⁷ REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing (1) an intuitive interface for validated data capture; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for data integration and interoperability with external sources.

Statistical Methods

Descriptive statistics of participant characteristics are presented as mean $\pm$ SD for continuous variables and proportions for categorical variables. Between-group comparisons were conducted using Wilcoxon rank sum test for continuous variables and Pearson's chi-squared test for categorical variables. Analyses followed an intention-to-treat (ITT) framework in which all randomized participants were analyzed in the group to which they were originally assigned to the protocol. We excluded participants with missing baseline and/

Table 1. Baseline Participant Characteristics Including Blood Pressure and Autonomic Assessments

Characteristic	All participants (N = 99)	Elevated blood pressure (N = 11)	Normotensive (N = 88)	P-value
Age	40.3 ± 9.8	47.1 ± 7.5	39.5 ± 9.7	0.006
Female	79%	73%	80%	0.602
BMI	25.7 ± 4.9	29.0 ± 7.0	25.3 ± 4.4	0.029
Systolic blood pressure				
Sitting	109.8 ± 14.0	130.5 ± 9.7	107.4 ± 12.4	<0.001
Standing	111.7 ± 12.0	125.4 ± 9.8	110.1 ± 11.3	<0.001
Standing -sitting	2.3 ± 9.7	−4.3 ± 10.2	3.1 ± 9.4	0.079
Diastolic blood pressure				
Sitting	73.8 ± 9.4	84.5 ± 5.8	72.5 ± 8.9	<0.001
Standing	77.1 ± 8.3	86.4 ± 9.4	76.0 ± 7.5	0.002
Standing -sitting	3.1 ± 6.4	1.9 ± 5.2	3.2 ± 6.6	0.454
Heart rate				
Sitting	66.8 ± 9.2	67.4 ± 8.7	66.7 ± 9.3	0.712
Standing	77.2 ± 10.7	79.2 ± 8.6	76.9 ± 10.9	0.372
Standing-sitting	10.4 ± 6.5	13.2 ± 3.2	10.1 ± 6.7	0.048

Values represent Mean ± S.D.

BMI, Body mass index

or post-intervention BP measurements and performed a complete-case analysis rather than imputing missing values. This approach was chosen because (1) the pattern of missingness was judged to be completely random, and (2) BP was the primary outcome variable. When missingness occurs in the outcome variable only, complete-case approach is equivalent to imputation for more efficient.^{28,29} The main outcome of the present study was the change in systolic blood pressure after 12 weeks of slow breathing training. Based on prior literature, the definition of a minimally clinically important difference (MCID) in systolic blood pressure and diastolic blood pressure is 2 mmHg.³⁰ Within-subject change in blood pressure from baseline to 12 weeks was tested using Wilcoxon signed-rank test. We dichotomized the participants based on baseline blood pressure into normotensive or elevated blood pressure. We defined elevated blood pressure at baseline being a systolic blood pressure higher than 120 mm Hg or diastolic blood pressure greater than 80 mm Hg. A linear regression model was fitted to investigate the effect of baseline SBP as the independent variable on SBP change at 12 weeks of intervention. Correlations between changes in BP and 12-week autonomic measures were evaluated using Spearman's correlation coefficient.

Results

Our slow breathing study enrolled 99 healthy adults with 4 withdrawals from the study. There were no serious or moderate adverse events attributed to the breathing treatments. Complete data at baseline and follow-up was available for 95 participants for blood pressure due to the four

withdrawals and 91 participants for autonomic testing due to incomplete data at 12 weeks. Table 1 shows baseline demographics of enrolled subjects. For normotensive participants, baseline seated SBP ranged from 88 to 146 mmHg and seated DBP ranged from 43 to 91 mmHg. For elevated BP participants, they ranged from 119 to 151 mmHg and from 76 to 95 mmHg, respectively. Overall, the mean SBP was 105 ± 11 mmHg and DBP of 67 ± 8 mmHg, with 11 participants having elevated blood pressure with a mean SBP and DBP of 126 ± 11.0 mmHg and 80 ± 5 mmHg, respectively. Table 1 displays baseline autonomic characteristics of our study population. We found that as expected at baseline, the elevated blood pressure group had lower high frequency variability of heart rate, suggesting a relative impairment in cardiac parasympathetic modulation.³¹⁻³³

Changes in blood pressure are shown in Figure 2 with a significant decrease in SBP and DBP (−2.4 ± 7.3 mm Hg and −1.6 ± 5.5 mmHg, respectively) at 12 weeks for all participants who practiced slow breathing. Blood pressure reduced further among slow breathing participants with elevated blood pressure (−10.3 ± 7.9 mmHg and −3.8 ± 5.5 mm Hg, SBP and DBP respectively). Figure 3 displays the regression model with higher SBP associated with greater reduction in SBP from baseline to 12 weeks (slope = −0.28). In the regression mode for DBP, baseline DBP was not associated with changes in DBP. There were no significant differences in blood pressure changes by breathing technique (E>I vs E = I) among all slow breathing participants or by sub-group analyses (normal blood pressure or elevated blood pressure).

Table 2 displays changes in autonomic tone from before and after 12-weeks of slow breathing. No significant

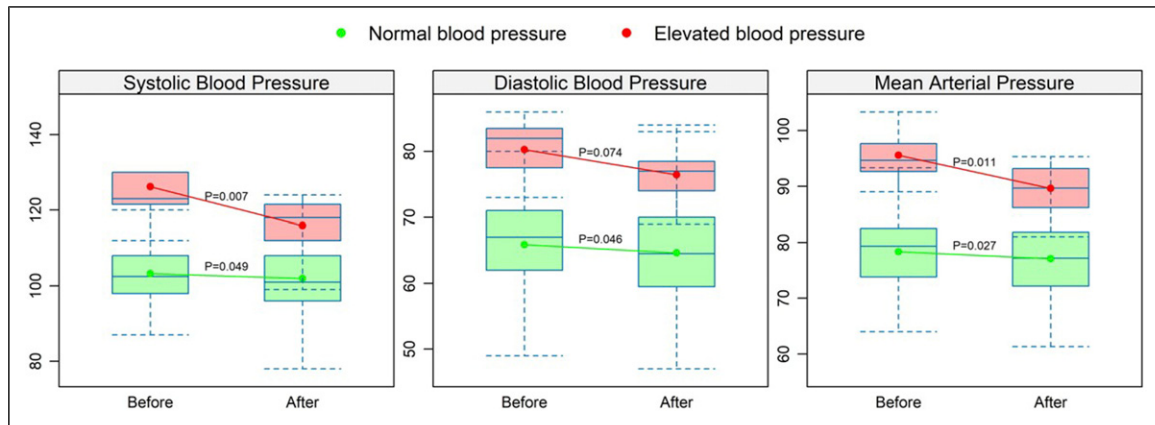


Figure 2. Twelve Weeks of Slow Breathing Training Resulted in a Significant Decrease in Systolic (Panel A), Diastolic (Panel B) and Mean (Panel C) Arterial Blood Pressure Among Participants With Normal and Elevated Blood Pressures. Elevated Blood Pressure is Shown in Red and Normal Blood Pressure is Shown in Green. P-Values are Based on Wilcoxon Signed Rank Test. SBP, Systolic Blood Pressure

differences were observed in spectral analysis changes from baseline to 12 weeks with the intervention. We found poor correlations between changes in blood pressure (SBP, DBP, MAP) and changes in autonomic measures.

Discussion

This study reports changes observed in blood pressure and autonomic function after 12 weeks of regular slow

breathing practice. We defined elevated blood pressure at baseline being a systolic blood pressure higher than 120 mm Hg or diastolic blood pressure greater than 80 mm Hg. Participants demonstrated significant decreases in blood pressure from baseline to 12 weeks with more pronounced decreases among those with elevated baseline blood pressure (SBP >120 and/or DBP >80 mmHg) exceeding the minimum clinically important difference for blood pressure change.³⁴ This confirmed our hypothesis,

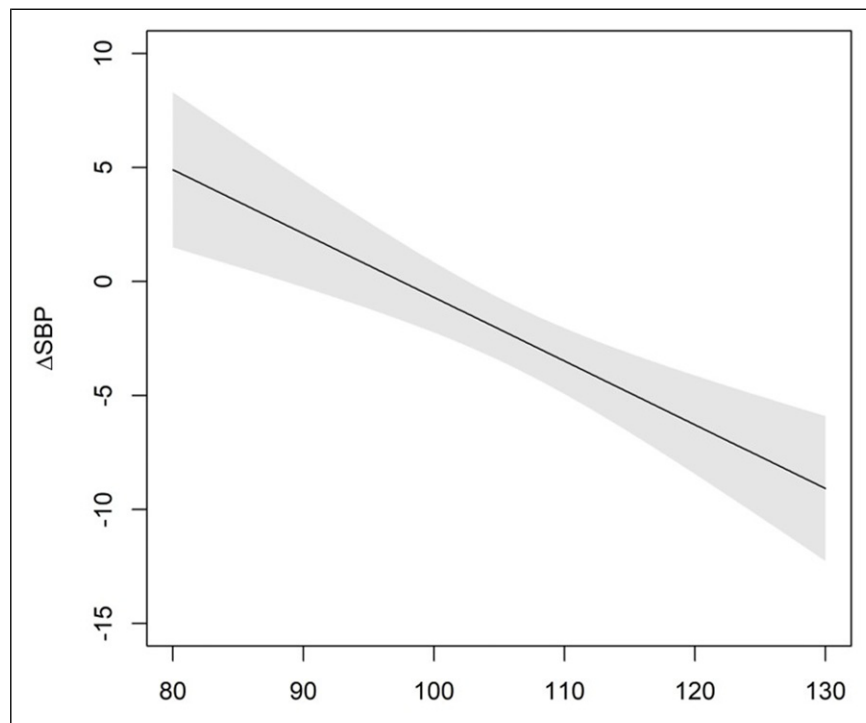


Figure 3. In the Regression Model of Delta of SBP on Baseline SBP, Groups as Well as Interaction Between Baseline SBP and Groups, We Detected a Significant Association Between Baseline SBP and the Predicted Delta of SBP (Based on the Linear Regression Model) SBP, Systolic Blood Pressure

Table 2. Autonomic Assessments at Baseline, 12-Weeks, and Change After 12 weeks of Slow Breathing

	All participants N = 91	Normal BP N = 80	Elevated BP N = 11	P-value
BRS HF (ms/mm Hg)				
Baseline	20.7 ± 17.9	22.1 ± 18.5	10.7 ± 6.4	0.008
12-Week	23.5 ± 23.9	24.9 ± 24.9	13.2 ± 10.1	0.025
Change	2.74 ± 22.64	2.77 ± 24.03	2.51 ± 7.08	0.638
BRS LF (ms/mm hg)				
Baseline	11.7 ± 7.9	12.2 ± 8.2	7.8 ± 3.8	0.049
12-Week	12.7 ± 8.1	13.3 ± 8.3	7.9 ± 4.8	0.01
Change	0.983 ± 7.400	1.107 ± 7.801	0.082 ± 3.335	0.554
SD _{RRI} (ms ²)				
Baseline	55 ± 31	58 ± 32	38 ± 12	0.021
12-Week	61 ± 34	63 ± 36	48 ± 17	0.303
Change	6.07 ± 24.90	5.54 ± 26.16	9.88 ± 12.45	0.39
RMSSD (ms)				
Baseline	47.8 ± 41.1	51.0 ± 42.8	25.1 ± 8.8	0.003
12-Week	51 ± 47	53 ± 49	33 ± 16	0.145
Change	2.959 ± 29.218	2.334 ± 30.832	7.501 ± 12.146	0.135
LF _{RRI} (ms ²)				
Baseline	1034 ± 1639	1103 ± 1727	534 ± 540	0.203
12-Week	1516 ± 2035	1617 ± 2129	782 ± 889	0.148
Change	483 ± 1892	515 ± 2009	247 ± 503	0.791
HF _{RRI} (ms ²)				
Baseline	744 ± 1222	820 ± 1285	190 ± 106	0.029
12-Week	896 ± 1672	985 ± 1763	244 ± 269	0.057
Change	151.5 ± 1323.4	164.9 ± 1409.6	54.5 ± 232.6	0.923
LF _{RRI} /HF _{RRI}				
Baseline	2.50 ± 2.47	2.43 ± 2.49	3.00 ± 2.38	0.199
12-Week	4.37 ± 6.20	4.36 ± 6.46	4.43 ± 3.92	0.595
Change	1.870 ± 6.559	1.931 ± 6.830	1.427 ± 4.287	0.664
LF _{SBP} (mmHg ²)				
Baseline	7.5 ± 5.9	7.2 ± 5.7	9.6 ± 7.1	0.24
12-Week	8.6 ± 6.2	8.3 ± 6.1	11.0 ± 6.4	0.138
Change	1.124 ± 7.150	1.092 ± 7.264	1.354 ± 6.575	0.99
HF _{SBP} (mmHg ²)				
Baseline	1.88 ± 2.28	1.74 ± 2.22	2.91 ± 2.55	0.086
12-Week	1.56 ± 1.50	1.46 ± 1.38	2.29 ± 2.10	0.174
Change	-0.317 ± 2.311	-0.275 ± 2.414	-0.623 ± 1.390	0.371

represent Mean ± S.D.

BRS, baroreflex slope; HF, high frequency; LF, low frequency; SD standard deviation; RMSSD, square root of mean squared successive differences, RRI, R-R interval; SBP, systolic blood pressure

but in the absence of a non-breathing comparison group, it is unclear if changes in blood pressure were a result of slow breathing alone. Changes in blood pressure were independent of specific slow breathing technique (E>I vs E = I). Changes in autonomic tone including spectral analyses of heart rate and blood pressure variability (HF RR and LF sys). Showed poor correlation to changes in blood pressure.

Our study design and intervention differs from prior studies on slow breathing and blood pressure.^{10,11,23} We screened patients to determine if they would be able to adhere

and perform slow breathing. This increased the likelihood that participants would be compliant with the behavioral treatment. There is a predominance of device-guided slow breathing studies, and our study adds to the limited data available regarding effects of yoga-based slow breathing (which is self-guided) on blood pressure.¹⁰ Most other studies used a fixed slow breathing rate (commonly 6 breaths/minute). In contrast, our slow breathing intervention titrated the individual to the slowest comfortable breath over 12-weeks. This is consistent with how slow breathing is taught in traditional yoga. On average, subjects in our study

achieved a respiratory rate less than 3 breaths a minute.²² A majority of slow breathing hypertension studies were of a shorter duration ranging from 4 to 8 weeks. Also, other studies included hypertensive subjects already on medications which may have dampened the observed response to slow breathing. Alternatively, by excluding hypertensive subjects, we have not observed maximal treatment effects. In our study, among participants with elevated baseline blood pressure in our study, the reduction in blood pressure (SBP -10.3 ± 7.9 , DBP -3.8 ± 5.5 mm Hg) was greater than estimated total effects reported in a meta-analysis of slow breathing and blood pressure and equivalent or greater than conventional single antihypertensive therapy.³⁵ Few studies have assessed changes in blood pressure and autonomic tone as a result of slow breathing with contradictory results.^{36,37}

Our results confirm previous studies that show differences in autonomic modulation between groups with normal blood pressure and elevated blood pressure.³⁸ We found that at baseline, high blood pressure groups have lower vagal tone (HF_{RRI}). Prior studies that have found an acute reduction in blood pressure with slow breathing have hypothesized that slow breathing reduces blood pressure through decreases in sympathetic activity and/or increases in vagal tone.^{36,39,40} In our results, spectral analyses did not indicate significant changes or correlation with blood pressure reduction. One possibility for these results is that spectral analyses do not capture changes in autonomic tone sufficiently for the slow breathing intervention and that more sensitive measurements of autonomic function such as direct measurement of muscle sympathetic nerve activity may provide additional information. More likely, our negative results may be explained by the small number of subjects with elevated blood pressure, which prevented us from seeing more dramatic changes that could occur in hypertensive subjects. Another possibility is slow breathing reduces blood pressure by other mechanisms such as endothelial function, oxidative stress, renal mechanisms, or salt metabolism.⁴ Further research into how slow breathing reduces blood pressure is necessary.

Our results have several limitations, the main one being a lack of a non-slow breathing comparison group. Addition of a comparison group would reduce the possibility that reduction of blood pressure was a result of regression to the mean. The results of this study are a secondary analysis of data collected to assess physiological and psychological stress, not blood pressure. We excluded patients with hypertension which may have reduced our power to see potential effects on blood pressure. We used standardized methods to assess blood pressure in the laboratory, but 24-hour ambulatory blood pressure measurement would be a more rigorous method.⁴¹ Another limitation not specific to this study but in general to the current methods to assess autonomic tone have to be acknowledged. Despite popularity of spectral analysis of heart rate and blood pressure due to relative easier data acquisition, valid measurements require strict adherence to measurement guidelines. Even when performed in a

dedicated autonomic laboratory, as the lab at Vanderbilt University Medical Center, results can be affected by artifacts and noise. The signals need to be recorded free of stimuli that can affect the measurements (eg, doors opening or closing, people talking or entering the room, etc.). The recording of the data acquired must be of adequate length and quality and needs to be checked for artifacts. It is noteworthy that though the variability of spectral parameters for the same individual can be very consistent over time, interindividual variability is very high.^{42,43} Finally, there are very few well-done large-scale well studies and therefore we lack normative data.

The large reductions in blood pressure we observed support the need for a larger randomized controlled efficacy trial to further examine slow breathing interventions among hypertensive adults. This study is of public health importance given that small reductions in blood pressure are associated with significant improvement in health outcomes. In pharmacological studies, a 5 mm Hg reduction in SBP reduces risk of major cardiovascular events by 10%.⁴⁴ Yet, anti-hypertensive medications have low adherence and side effects. Whereas our results confirm a high compliance to slow breathing intervention with no adverse effects. Lastly, the absence of changes in autonomic tone as measured by spectral analyses suggest that the cardiovascular mechanisms of slow breathing have yet to be well characterized. Further research into the mechanisms and effectiveness of slow breathing on cardiovascular health is needed.

ORCID iD

Gurjeet Birdee  <https://orcid.org/0000-0001-5776-1095>

Author Contributions

AG: Conceived and designed research, performed experiments, analyzed data, interpreted results of experiments, prepared figures, drafted manuscript, edited and revised manuscript, approved final version of manuscript

HN: Conceived and designed research, analyzed data, interpreted results of experiments, prepared figures, edited and revised manuscript, approved final version of manuscript

ES: Analyzed data

SP: Performed experiments, analyzed data

RA: Analyzed data

AD: Analyzed data

CB: Development of the slow breathing intervention

GB: Conceived and designed research, development of slow breathing intervention, performed experiments, analyzed data, interpreted results of experiments, prepared figures, drafted manuscript, edited and revised manuscript, approved final version of manuscript.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: NIH-NCCIH 5R61AT009340. National Center for Advancing Translational Science, CTSA No. UL1 TR002243

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Clinical Trial Registration

Clinicaltrials.gov identifier: NCT02870868

Disclaimers

The research contents are solely the responsibility of the authors and do not necessarily represent the official views of the National Center for Advancing Translational Sciences, National Center for Complementary and Integrative Health, or the National Institutes of Health.

References

- Osthega Y, Fryar CD, Nwankwo T, Nguyen DT. Hypertension Prevalence Among Adults Aged 18 and Over: United States, 2017-2018. *NCHS Data Brief*. 2020;364:1-8.
- Muntner P, Hardy ST, Fine LJ, et al. Trends in blood pressure control among US adults with hypertension, 1999-2000 to 2017-2018. *JAMA*. 2020;324(12):1190-1200. doi:10.1001/jama.2020.14545
- Tam HL, Wong EML, Cheung K. Effectiveness of educational interventions on adherence to lifestyle modifications among hypertensive patients: an integrative review. *Int J Environ Res Publ Health*. 2020;17(7):2513. doi:10.3390/ijerph17072513
- Harrison DG, Coffman TM, Wilcox CS. Pathophysiology of hypertension: the mosaic theory and beyond. *Circ Res*. 2021;128(7):847-863. doi:10.1161/circresaha.121.318082
- Grassi G, Seravalle G, Cattaneo BM, et al. Sympathetic activation in Obese normotensive subjects. *Hypertens Dallas Tex*. 1995;25(4 Pt 1):560-563. doi:10.1161/01.hyp.25.4.560
- Mancia G, Grassi G. The autonomic nervous system and hypertension. *Circ Res*. 2014;114(11):1804-1814. doi:10.1161/CIRCRESAHA.114.302524
- Lohmeier TE, Iliescu R. The sympathetic nervous system in obesity hypertension. *Curr Hypertens Rep*. 2013;15(4):409-416. doi:10.1007/s11906-013-0356-1
- Gamboa A, Okamoto LE, Diedrich A, et al. Sympathetic activation and nitric oxide function in early hypertension. *Am J Physiol Heart Circ Physiol*. 2012;302(7):H1438-1443. doi:10.1152/ajpheart.01020.2011
- Hall JE, do Carmo JM, da Silva AA, Wang Z, Hall ME. Obesity-induced hypertension: interaction of neurohumoral and renal mechanisms. *Circ Res*. 2015;116(6):991-1006. doi:10.1161/CIRCRESAHA.116.305697
- de Freitas Gonçalves KS, Queiroz Godoy Daniel AC, Tatagiba LJJ, et al. Device and nondevice-guided slow breathing to reduce blood pressure in hypertensive patients: a systematic review and meta-analysis. *Health Sci Rep*. 2022;5(3):e636. doi:10.1002/hsr2.636
- Herawati I, Mat Ludin AF, M M, Ishak I, Farah NMF. Breathing exercise for hypertensive patients: a scoping review. *Front Physiol*. 2023;14:1048338. doi:10.3389/fphys.2023.1048338
- Barnes PM, Bloom B, Nahin RL. Complementary and alternative medicine use among adults and children: united States, 2007. *Natl Health Stat Rep*. 2008;(12):1-23.
- Bernardi L, Porta C, Gabutti A, Spicuzza L, Sleight P. Modulatory effects of respiration. *Auton Neurosci*. 2001;90(1-2):47-56. doi:10.1016/S1566-0702(01)00267-3
- Sevoz-Couche C, Laborde S. Heart rate variability and slow-paced breathing: when coherence meets resonance. *Neurosci Biobehav Rev*. 2022;135:104576. doi:10.1016/j.neubiorev.2022.104576
- Triedman JK, Saul JP. Blood pressure modulation by central venous pressure and respiration. Buffering effects of the heart rate reflexes. *Circulation*. 1994;89(1):169-179. doi:10.1161/01.cir.89.1.169
- Toska K, Eriksen M. Respiration-synchronous fluctuations in stroke volume, heart rate and arterial pressure in humans. *J Physiol*. 1993;472:501-512. doi:10.1113/jphysiol.1993.sp019958
- Dornhorst AC, Howard P, Leathart GL. Respiratory variations in blood pressure. *Circulation*. 1952;6(4):553-558. doi:10.1161/01.cir.6.4.553
- Eckberg DL, Nerhed C, Wallin BG. Respiratory modulation of muscle sympathetic and vagal cardiac outflow in man. *J Physiol*. 1985;365(1):181-196. doi:10.1113/jphysiol.1985.sp015766
- deBoer RW, Karemaker JM, Strackee J. Hemodynamic fluctuations and baroreflex sensitivity in humans: a beat-to-beat model. *Am J Physiol*. 1987;253(3 Pt 2):H680-689. doi:10.1152/ajpheart.1987.253.3.H680
- Eckberg DL. Point:Counterpoint: respiratory sinus arrhythmia is due to a central mechanism vs. respiratory sinus arrhythmia is due to the baroreflex mechanism. *J Appl Physiol*. 2009;106(5):1740-1742. doi:10.1152/jappphysiol.91107.2008
- Mahtani KR, Beinortas T, Bauza K, Nunan D. Device-guided breathing for hypertension: a summary evidence review. *Curr Hypertens Rep*. 2016;18(4):33. doi:10.1007/s11906-016-0631-z
- Birdee G, Nelson K, Wallston K, et al. Slow breathing for reducing stress: the effect of extending exhale. *Compl Ther Med*. 2023;73:102937. doi:10.1016/j.ctim.2023.102937
- Chaddha A, Modaff D, Hooper-Lane C, Feldstein DA. Device and non-device-guided slow breathing to reduce blood pressure: a systematic review and meta-analysis. *Compl Ther Med*. 2019;45:179-184. doi:10.1016/j.ctim.2019.03.005
- Diedrich A, Jordan J, Tank J, et al. The sympathetic nervous system in hypertension: assessment by blood pressure variability and ganglionic blockade. *J Hypertens*. 2003;21(9):1677-1686. doi:10.1097/00004872-200309000-00017
- Force ST. 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*. 1996;Published online.
- Oppenheim AV, Schaffer RW. *Digital Signal Processing*. 23. Prentice-Hall; 1975.
- Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software platform partners. *J Biomed Inf*. 2019;95:103208. doi:10.1016/j.jbi.2019.103208

28. Von Hippel PT. 4. Regression with missing ys: an improved strategy for analyzing multiply imputed data. *Sociol Methodol.* 2007;37(1):83-117. doi:[10.1111/j.1467-9531.2007.00180.x](https://doi.org/10.1111/j.1467-9531.2007.00180.x)
29. White IR, Carlin JB. Bias and efficiency of multiple imputation compared with complete-case analysis for missing covariate values. *Stat Med.* 2010;29(28):2920-2931. doi:[10.1002/sim.3944](https://doi.org/10.1002/sim.3944)
30. Stamler J, Rose G, Stamler R, Elliott P, Dyer A, Marmot M. INTERSALT study findings. Public health and medical care implications. *Hypertens Dallas Tex.* 1989;14(5):570-577. doi:[10.1161/01.hyp.14.5.570](https://doi.org/10.1161/01.hyp.14.5.570)
31. Schroeder EB, Liao D, Chambless LE, Prineas RJ, Evans GW, Heiss G. Hypertension, blood pressure, and heart rate variability: the atherosclerosis risk in communities (ARIC) study. *Hypertens Dallas Tex.* 2003;42(6):1106-1111. doi:[10.1161/01.hyp.0000100444.71069.73](https://doi.org/10.1161/01.hyp.0000100444.71069.73)
32. Singh JP, Larson MG, Tsuji H, Evans JC, O'Donnell CJ, Levy D. Reduced heart rate variability and new-onset hypertension: insights into pathogenesis of hypertension: the framingham heart study. *Hypertens Dallas Tex.* 1998;32(2):293-297. doi:[10.1161/01.hyp.32.2.293](https://doi.org/10.1161/01.hyp.32.2.293)
33. Guzzetti S, Piccaluga E, Casati R, et al. Sympathetic predominance an essential hypertension: a study employing spectral analysis of heart rate variability. *J Hypertens.* 1988; 6(9):711-717. doi:[10.1097/00004872-198809000-00004](https://doi.org/10.1097/00004872-198809000-00004)
34. Ritchey MD, Gillespie C, Wozniak G, et al. Potential need for expanded pharmacologic treatment and lifestyle modification services under the 2017 ACC/AHA hypertension guideline. *J Clin Hypertens.* 2018;20(10):1377-1391. doi:[10.1111/jch.13364](https://doi.org/10.1111/jch.13364)
35. Paz MA, de-La-Sierra A, Sáez M, et al. Treatment efficacy of anti-hypertensive drugs in monotherapy or combination: ATOM systematic review and meta-analysis of randomized clinical trials according to PRISMA statement. *Medicine (Baltim).* 2016; 95(30):e4071. doi:[10.1097/MD.00000000000004071](https://doi.org/10.1097/MD.00000000000004071)
36. Oneda B, Ortega KC, Gusmão JL, Araújo TG, Mion D. Sympathetic nerve activity is decreased during device-guided slow breathing. *Hypertens Res.* 2010;33(7):708-712. doi:[10.1038/hr.2010.74](https://doi.org/10.1038/hr.2010.74)
37. de Barros S, da Silva GV, de Gusmão JL, et al. Effects of long term device-guided slow breathing on sympathetic nervous activity in hypertensive patients: a randomized open-label clinical trial. *Blood Press.* 2017;26(6):359-365. doi:[10.1080/08037051.2017.1357109](https://doi.org/10.1080/08037051.2017.1357109)
38. Parati G, Saul JP, Rienzo MD, Mancia G. Spectral analysis of blood pressure and heart rate variability in evaluating cardiovascular regulation: a critical appraisal. *Hypertension.* 1995; 25(6):1276-1286. doi:[10.1161/01.hyp.25.6.1276](https://doi.org/10.1161/01.hyp.25.6.1276)
39. Cottin F, Papelier Y, Escourrou P. Effects of exercise load and breathing frequency on heart rate and blood pressure variability during dynamic exercise. *Int J Sports Med.* 1999;20(04): 232-238. doi:[10.1055/s-2007-971123](https://doi.org/10.1055/s-2007-971123)
40. Pal GK, Velkumary S, Madanmohan. Madanmohan. Effect of short-term practice of breathing exercises on autonomic functions in normal human volunteers. *Indian J Med Res.* 2004; 120(2):115-121.
41. Wei W, Tölle M, Zidek W, van der Giet M. Validation of the mobil-O-Graph: 24 h-blood pressure measurement device. *Blood Pres Monit.* 2010;15(4):225-228. doi:[10.1097/MBP.0b013e328338892f](https://doi.org/10.1097/MBP.0b013e328338892f)
42. Lischke A, Lemke D, Neubert J, Hamm AO, Lotze M. Inter-individual differences in heart rate variability are associated with inter-individual differences in mind-reading. *Sci Rep.* 2017;7(1):11557. doi:[10.1038/s41598-017-11290-1](https://doi.org/10.1038/s41598-017-11290-1)
43. Jíra M, Závodná E, Nováková Z, Fiser B, Honzíkova N. Reproducibility of blood pressure and inter-beat interval variability in man. *Physiol Res.* 2010;59(Suppl 1):S113-S121. doi:[10.33549/physiolres.932002](https://doi.org/10.33549/physiolres.932002)
44. Collaboration TBPLTT, Adler A, Agodoa L. Pharmacological blood pressure lowering for primary and secondary prevention of cardiovascular disease across different levels of blood pressure: an individual participant-level data meta-analysis. *Lancet Lond Engl.* 2021;397(10285):1625-1636. doi:[10.1016/s0140-6736\(21\)00590-0](https://doi.org/10.1016/s0140-6736(21)00590-0)