

ORIGINAL ARTICLE

Acute Effects of Slow, Controlled Breathing Exercises on Arterial Pressure and Autonomic Cardiac Modulation in Hypertensive Patients

Léo José Rubin Neto¹, Gustavo Orione Puntel², Dhayan Quevedo Ferrão³, Mireli Hemann Lamberti⁴, Bruno Cesar Correa Arbiza⁵, Katieli Santos de Lima⁶, Antônio Marcos Vargas da Silva⁷, Luis Ulisses Signori⁸

Highlights:

1. Breathing exercises modify the autonomic cardiac modulation and blood pressure.
2. Slow breathing reduced systolic arterial pressure at approximately 4.5 mmHg.
3. These exercises can be a non-pharmacological tool to control hypertension.

ABSTRACT

The aim of the present study was to evaluate the influence of slow, controlled breathing exercises (SCBE) on arterial pressure and autonomic cardiac modulation in hypertensive patients. 29 hypertensive patients were evaluated in two data collections (period between 1 to 3 days). In each evaluation, data were collected after 10 min of spontaneous breathing (between 12 and 20 breaths per minute – bpm) and 10 min of SCBE (12 bpm, in the rhythm of standardized verbal stimulus). The arterial pressure was evaluated by a multi-parameter monitor and the autonomic cardiac modulation by the rate variability technique. The SCBE reduced systolic arterial pressure (1st evaluation: -4.8 mmHg and 2nd evaluation: -4.3 mmHg), decreased sympathetic activity by 18% and modified autonomic modulation by about 50%. SCBE reduced both systolic arterial pressure and sympathetic activity and can be used in control arterial pressure of hypertensive patients.

Keywords: hypertension; systolic arterial pressure; autonomic nervous system; sympathetic nervous system; breathing exercises.

EFEITOS AGUDOS DE EXERCÍCIOS DE RESPIRAÇÃO LENTA E CONTROLADA SOBRE A PRESSÃO ARTERIAL E MODULAÇÃO AUTÔNOMA CARDÍACA EM PACIENTES HIPERTENSOS

RESUMO

O objetivo do presente estudo foi avaliar a influência de exercícios respiratórios lentos e controlados (SCBE) na pressão arterial e modulação autonômica cardíaca em pacientes hipertensos. Foram avaliados 29 hipertensos em duas coletas de dados (período entre 1 a 3 dias). Em cada avaliação, os dados foram coletados após 10 minutos de respiração espontânea (entre 12 e 20 respirações por minuto – rpm) e 10 minutos de SCBE (12 rpm, no ritmo de estímulo verbal padronizado). A pressão arterial foi avaliada por monitor multiparamétrico e a modulação autonômica cardíaca pela técnica de variabilidade de frequência. O SCBE reduziu a pressão arterial sistólica (1^a avaliação: -4,8 mmHg e 2^a avaliação: -4,3 mmHg), diminuiu a atividade simpática em 18% e modificou a modulação autonômica em cerca de 50%. O SCBE reduziu tanto a pressão arterial sistólica quanto a atividade simpática e pode ser usado no controle da pressão arterial de pacientes hipertensos.

Palavras-chave: hipertensão; pressão arterial sistólica; sistema nervoso autônomo; sistema nervoso simpático; exercícios de respiração.

¹ Universidade Federal de Santa Maria. Santa Maria/RS, Brasil. <https://orcid.org/0000-0003-2682-238X>

² Universidade Federal de Santa Maria. Santa Maria/RS, Brasil. <https://orcid.org/0000-0002-1641-9477>

³ Universidade Federal de Santa Maria. Santa Maria/RS, Brasil. <https://orcid.org/0000-0003-0776-7784>

⁴ Universidade Federal de Santa Maria. Santa Maria/RS, Brasil. <https://orcid.org/0000-0002-4357-427X>

⁵ Universidade Federal de Santa Maria. Santa Maria/RS, Brasil. <https://orcid.org/0000-0003-0514-0857>

⁶ Universidade Federal de Santa Maria. Santa Maria/RS, Brasil. <https://orcid.org/0000-0001-6909-8737>

⁷ Universidade Federal de Santa Maria. Santa Maria/RS, Brasil. <https://orcid.org/0000-0001-8127-6911>

⁸ Universidade Federal de Santa Maria. Santa Maria/RS, Brasil. <https://orcid.org/0000-0001-7784-9940>

INTRODUCTION

Systemic arterial hypertension (SAH) is a severe world health problem since it affects around one billion people and it is estimated that the prevalence of this disease will be superior to 1,5 billion patients around the globe until 2025¹. The autonomic nervous system (ANS) acts on the cardiovascular system through its sympathetic and parasympathetic components, which are responsible for regulating cardiac and circulatory functions, thus modulating the heart rate and the systemic arterial pressure².

Obese patients present ANS alterations, characterized by sympathetic hyperactivity, especially by baroreflex hypersensitivity³. The ANS plays a regulative role in cardiac function through sympathovagal modulation, which can be analyzed using the heart rate variability (HRV)⁴. This method can provide quantitative indicators of both sympathetic (LF) and parasympathetic activity (HF), as well as of the autonomic cardiac modulation (LF/HF ratio)^{5,6}. However, patients breathing control is not always a monitored variable during data collection, which makes it unknown for the data analysis of the HRV.

Drug therapy is the main tool for handling SAH⁷. However, it is estimated that between 10% to 20% of the patients do not respond to anti-hypertensive drug therapy⁸. With drug management effects reduced, studies that investigate complementary therapies are extremely important. Previous researches have demonstrated the efficiency of non-drug therapies in reducing sympathetic hyperactivity and systemic arterial pressure on these patients⁹⁻¹¹.

Previous studies have demonstrated the positive effects of slow breathing on the heart rate, the autonomic modulation^{12,13}, and arterial pressure¹⁴. However, few studies have investigated the influence of slow breathing on arterial pressure and its autonomic cardiac function in hypertensive patients¹⁴⁻¹⁶. In this context, further investigation on the effects of slow, controlled breathing exercises (SCBE) in the management of cardiovascular disorders is needed, especially in patients experiencing hypertensive crises¹⁷. The objective of this study was to evaluate the influence of SCBE on arterial pressure and the heart rate variability of hypertensive patients.

METHODS

Characterization of the study

The present research was conducted in the Evaluation and Function Rehabilitation Laboratories of the Health Sciences Center of the Federal University of Santa Maria (UFSM). The project was approved by the Institutional Ethics Committee (Protocol: 2.180.257) and respects resolution number 510/2016 of the National Health Council and the Declaration of Helsinki. All the patients were previously informed about the study's protocol and signed the Free and Informed Consent Form. Data was collected in the period comprehended between October 2017 and April 2019.

Subjects

The patients were selected in the primary health attention unities of the city of Santa Maria/RS. Inclusion criteria included volunteers who were previously diagnosed with hypertension (SBP \geq 140 mmHg and/or DBP \geq 90 mmHg)¹⁸ and were taking anti-hypertensive drugs for at least three months, of both sexes and aged between 20 and 75 years old, alphabetized, and presenting a body mass index lower than 35 kg/m², non-smokers, without musculoskeletal disorders symptoms, without previously diagnosed rheumatologic, cardiovascular, neurological, cancer, immune, and hematologic diseases or psychiatric and cognitive disorders.

The exclusion criteria included the intake of alcoholic or caffeinated beverages in the 12h preceding the tests and the practice of intense physical exercises in the 48h preceding the evaluation.

Patients who reported experiencing stressful emotional events in the 72h preceding data collection and those presenting dyspnea or tachypnea in the evaluation day were also excluded.

Outcomes

The primary outcome was arterial pressure (systolic and diastolic). Secondary outcomes were the autonomic modulation (LF/HF ratio) evaluated in time and frequency domains. The time-domain involves heart rate (HR), the standard deviation of all RR intervals from normal to normal (SDNN), the square root of the mean of the squares of the RR interval successive differences (RMSSD), the percentage of intervals differing more than 50 ms from the previous interval (PNN50%), and the triangular index. In the frequency domain, the variables were total potency (TP), low frequency (LF), and high frequency (HF), in raw data normalized in percentage form.

Data collection

After the data was collected, for three days all the volunteers adapted to the data collection protocol, which involved training SCBE (12 bpm). In the evaluation days, the participants were in 8-hour fasting and had not taken their drugs, which were taken after the data collection was finished. Both data collection were made within 1 to 3 days. First, the spontaneous breathing data were collected (control), followed by SCBE. During the evaluation, the volunteers remained lying down in a supine position for one hour; in the first 30 minutes (min) they rested, and after that, 10 min of spontaneous breathing were collected, as well as 10 min of slow, controlled breathing. The experimental draw is presented in Figure 1.

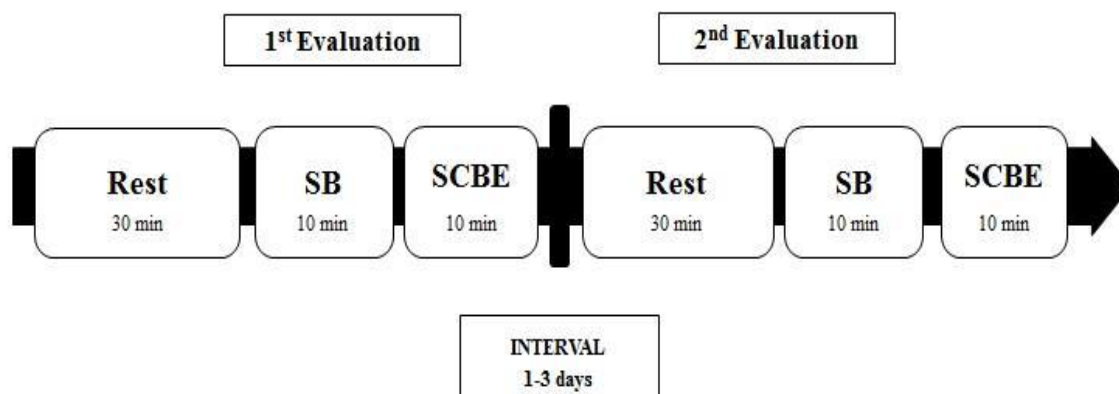


Figure 1 – Experimental design. Rep: Rest; SB: Spontaneous Breathing; SCBE: Slow, Controlled Breathing Exercises

The room temperature was constantly kept between 21 and 24°C. During spontaneous breathing, volunteers did not suffer any interference, and the breathing was monitored between 12 and 20 breaths per minute using visual inspection and a multi-parameter monitor (Dixtral, 2021 model, Manaus, Brazil). During the SCBE (12 bpm; inspiration/expiration: 2/3)^{18,19}, the respiratory frequency was paced by standard verbal stimulus previously recorded in audio.

Arterial pressure evaluation

The evaluation of both systolic arterial pressure (SAP) and diastolic arterial pressure (DAP) was conducted using a multi-parameter monitor (Dixtal, 2021 model, Manaus, Brasil). The cuff was positioned in the right arm, while the participants were lying down in a supine position in the stretcher. Data were collected before and immediately after spontaneous breathing and the SCBE.

Heart rate variability

The autonomic function was evaluated by heart rate variability (HRV). The data were collected through a pulse rate monitor (Polar, 810i model, Kempele – Finland). The measurement of heart rate (sample rate – 1000Hz) was taken in RR interval time series and obtained with continuous intervals (10min) in the spontaneous breathing and the SCBE. The collected data were transferred to a computer equipped with Polar ProTrainer 5 software. RR intervals of 5 min were selected for the analysis, with a stable heart rate, usually between 3 and 8 min. In each RR 5 min series, interferences were fixed (aberrant errors) using the standard software correction algorithm Polar ProTrainer 5 (that is, moderate filter power and minimum protection zone of 6 beats per min). Furthermore, a visual inspection of the RR time series was conducted and all the remaining artifacts were manually removed²⁰.

The data were transferred to the computer and the RR intervals were processed. The analyses of HRV parameter were processed by version 2.1 of Kubios software (Grupo de Análise de Biossinais e Imagens Médicas, Departamento de Física, Universidade de Kuopio, Finlândia, 2012).

The time-domain variables taken into account were the heart rate (HR), the standard deviation of all RR intervals from normal to normal (SDNN), the square root of the mean of the squares of the RR interval successive differences (RMSSD), the percentage of intervals differing more than 50 ms from the previous interval (PNN50%), and the triangular index. In the frequency domain, the variables were total potency (TP), low frequency (LF), high frequency (HF), and the sympathovagal function relationship (LF/HF).

The spectral power analysis was estimated using the fast Fourier transform algorithm. This analysis decomposes the HRV into fundamental oscillatory components, the main ones being: the high frequency (HF) component from 0.15 to 0.4Hz, corresponding to respiratory modulation and the indicator of the vagus nerve's action in the heart; and the low-frequency component (LF) of 0.04 and 0.15 Hz, correlated to the joint action of the vagal and sympathetic components on the heart, with the sympathetic prevailing. The normalized units (n.u) were obtained by dividing the potency of a determined component by the total potency (of which VLF is subtracted) and then multiplying the result by 100 (LF or HF / (Total potency – VLF) x 100). The LF/HF relationship reflects absolute and relative changes among the sympathetic and parasympathetic components of ANS, characterizing sympathovagal influence on the hearth²¹.

Statistical Analysis

The descriptive data are presented as standard mean and standard deviation (SD). The Kolmogorov test was applied to assess the normality of data. The parametric distribution data were compared by the Anova of a route for repeated measures, and those of non-parametric distribution by the Friedman test, then both were submitted to post hoc Tukey test. The meaningful results are presented by the mean differences (MD) and their respective confidence intervals of 95% (CI95%). The effect size differences between breaths (spontaneous breathing vs SCBE) were calculated using the *d* of Cohen and expressed using the following criteria: trivial <0.2, small 0.2-0.49, moderate 0.5-0.79, and large >0.8. All the statistical analyses were made using GraphPad Prism 5.0 software (San Diego, CA, USA). The alpha error rate was of 5% ($p < 0.05$).

RESULTS

This study initially recruited 36 volunteers previously diagnosed with SAH, of which 6 were not present in one of the adaptation to the evaluation protocol days and 1 presented fever in the first evaluation date and was, therefore, excluded (Figure 2). The final sample comprehended 29 patients

with an average age of 54 (± 14) years old, of which 68.9% were female, 41% were sedentary, 55% were overweight, and 31% were obese. The majority of the patients (59%) were taking Angiotensin II receptor blockers. The patient's characterization and the drugs used in the treatment of hypertension are presented in *Table 1*.

Table 1 – Baseline characteristics of patients

Variable	Mean \pm SD
Age (years)	54 \pm 14
Gender (M/F)	9 / 20
Sedentary (%/n)	41% (<i>n</i> = 12)
Body mass index (kg/m²)	29.07 \pm 3.8
Normal weight	14% (<i>n</i> = 4)
Overweight	55% (<i>n</i> = 16)
Grade I obesity	31% (<i>n</i> = 9)
Waist/Hip Ratio (cm)	0.88 \pm 0.06
SBP (mmHg)	128.6 \pm 13.5
DBP (mmHg)	75.0 \pm 7.7
Drugs (%/n)	
Angiotensin II receptor blockers	59% (<i>n</i> = 17)
β -blockers	24% (<i>n</i> = 7)
Calcium channel blockers	24% (<i>n</i> = 7)
Diuretics	17% (<i>n</i> = 5)
ACE inhibitors	17% (<i>n</i> = 5)
Platelet antiaggregants	10% (<i>n</i> = 3)

Data are Data are presented as Mean \pm Standard Deviation (\pm SD); M: male; F: female; *n*: number. SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure.

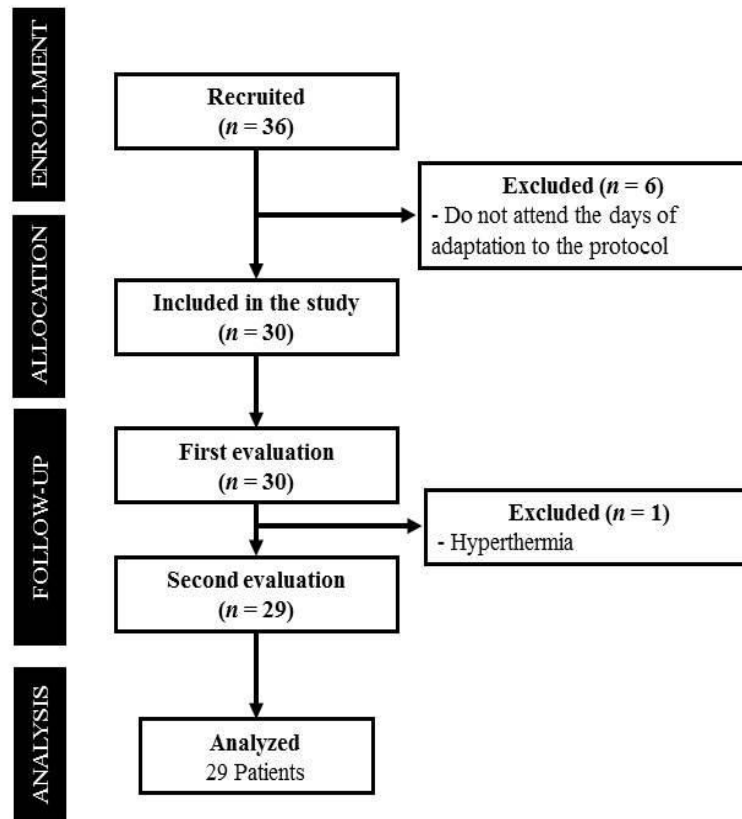


Figure 2 – Study flowchart. n: number

SCBE reduced SAP ($p < 0.001$) in -4.8 mmHg (CI 95%: -1.2 to -8.5) in the first evaluation, and in -4.3 mmHg (CI95%: -0.6 to -7.9) in the second evaluation (Figure 3A). The SAP evaluations comparison in the two days between spontaneous (1st evaluation vs 2nd evaluation) and the SCBE (1st evaluation vs 2nd evaluation) did not present differences. The SAP of spontaneous breathing (SB) measured in the first evaluation was higher (DEM: 3.7 CI95%: 0.01 to 7.3 mmHg) than in the SCBE in the second evaluation, as well as the slow, controlled breathing was smaller than the spontaneous breathing in the second evaluation (DEM: -5.5 CI95%: -1.8 to -9.1 mmHg). The analysis of the effect size of the means for the two evaluated days demonstrate that the SCBE presented a moderate effect (ES= -0.41) on the reduction of SAP. The DAP presented no modification ($p = 0.137$) throughout the study (Figure 3B).

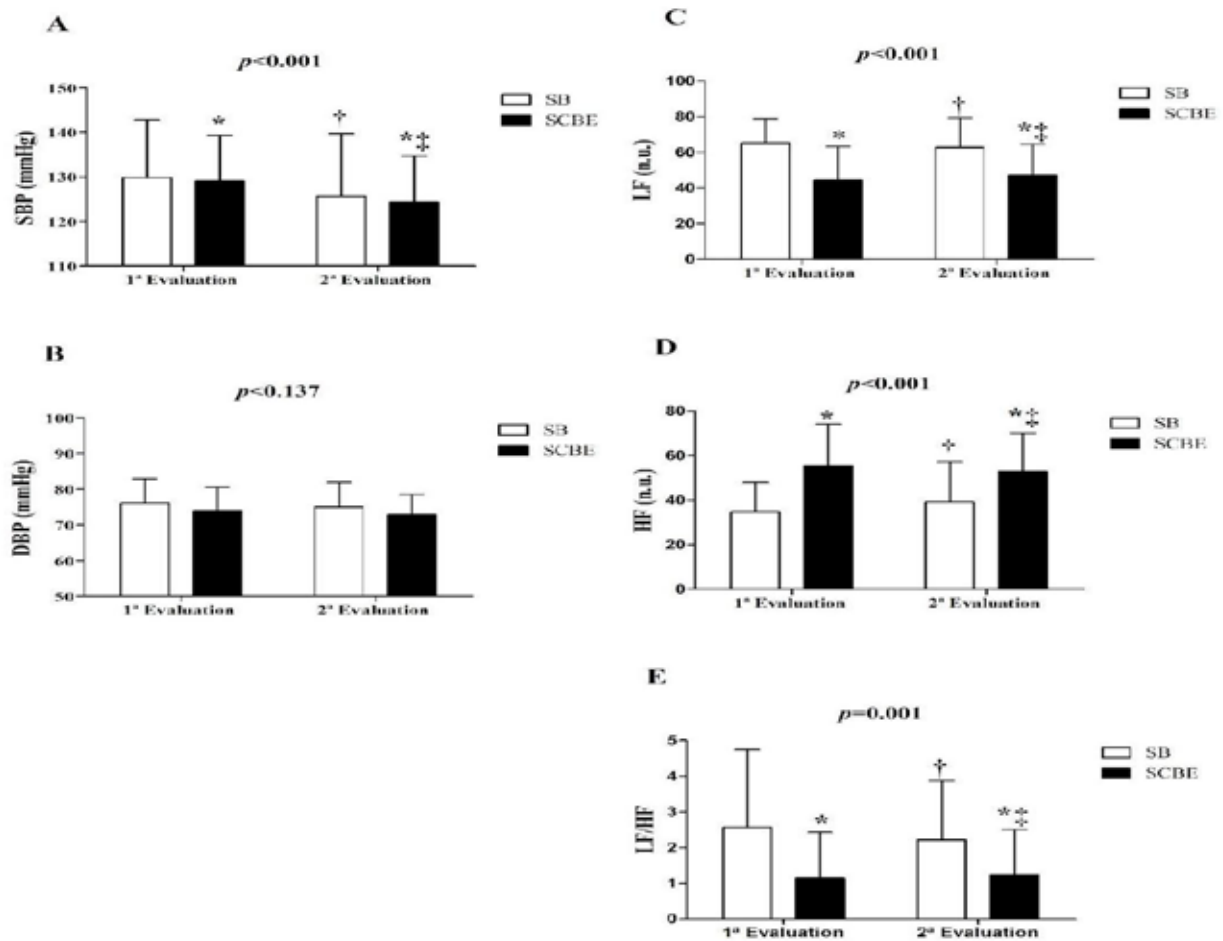


Figure 3 – Results of systolic and diastolic blood pressure and normalized data of heart rate variability in hypertensive patients. SB: Spontaneous Breathing; SCBE: Slow, Controlled Breathing Exercises; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; LF (n.u.) = LF power in standard units; HF (n.u.) = HF power in standard units; LF/HF = Ratio LF (ms^2) / HF (ms^2); * $p < 0.05$ vs Spontaneous Breathing; † $p < 0.05$ vs SCBE 1st Evaluation; ‡ $p < 0.05$ vs Spontaneous Breathing 1st Evaluation

The results for the heart rate variability are presented in *Table 2*. In the time-domain, spontaneous breathing and SCBE did not present differences on any of the analyzed variables (HR, SDNN, RMSSD, and triangular index). The PNN50 presented a difference in the Friedman test that was not confirmed by post hoc Tukey test ($p > 0.05$).

In the frequency domain, non-normalized data presented differences in total power between breaths and between the evaluated days (TP ms^2 : $p = 0.035$) and in high frequency (HF ms^2 : $p = 0.046$), which were not confirmed by *post hoc* Turkey test ($p > 0.05$).

Table 2 – Heart rate variability data analyzed in the time and frequency domain of hypertensive patients

Variable	1 st Evaluation		2 nd Evaluation		p
	Spontaneous Breathing	SCBE	Spontaneous Breathing	SCBE	
Time-Domain					
HR (bpm)	70.3 ± 19.4	68.2 ± 9.5	68.3 ± 8.6	68.5 ± 8.3	0.823
SDNN (ms)	45.9 ± 31.8	42.6 ± 20.5	35.9 ± 18.9	43.2 ± 22.5	0.112
rMSSD	28.2 ± 19.8	33.8 ± 21.7	25.6 ± 15.2	30.8 ± 23.3	0.123
PNN50 (%)	8.5 ± 12.6	13.3 ± 16.4	6.9 ± 11.4	11.7 ± 17.8	0.043
Triangular Index	8.5 ± 3.7	9.3 ± 3.9	8.9 ± 4	10.4 ± 4.8	0.103
Frequency-Domain					
TP (ms ²)	3481 ± 5479	1976 ± 1711	2180 ± 2648	1545 ± 2031	0.035
LF (ms ²)	675.3 ± 1057	432.7 ± 440.1	568.7 ± 1070	475.9 ± 718.2	0.262
HF (ms ²)	306.4 ± 374.4	615.7 ± 873.2	258.4 ± 238.5	637.1 ± 884.2	0.046

Data are presented as mean ± Standard Deviation (SD); SCBE = Slow, Controlled Breathing Exercises; HR = Heart Rate (bpm/min), SDNN = standard deviation of all normal to normal R-R (NN) intervals; rMSSD = Square root of the mean of the squares of successive R-R interval differences; pNN50 = the percentage of intervals differing more than 50ms different from preceding interval; Total power (TP ms²) = The variance of RR intervals over the temporal segment; LF(ms²) = Power in low frequency range (0.04-0.15Hz); HF(ms²) = Power in high frequency range (0.15-0.4Hz); LF(n.u.) = LF power in normalized units; HF(n.u.) = HF power in normalized units; LF/HF = Ratio LF(ms²) / HF(ms²); * p<0.05 vs Slow, Controlled Breathing Exercises.

After data normalization (n.u.), in the frequency domain, the SCBE reduced sympathetic activity ($p<0.001$) represented by the LF component by about 18% (1st evaluation DEM: -20.8; CI95%: -12.5 to -29.1 n.u. and 2nd evaluation DEM: -18.1; CI95%: -9.9 to -26.5 n.u.) (Figure 3C). On the other hand, SCBE ($p<0.001$) the parasympathetic activity evaluated by the HF component in 18% (1st evaluation DEM: 20.7 CI95%: 12.5 to 29.1 n.u. and 2nd evaluation DEM: 18.1 CI95%: 9.8 to 26.4 n.u.) (Figure 3D). The comparison of the first and the second evaluations of the LF and HF components between spontaneous breathing and SCBE did not present differences. In the LF component, spontaneous breathing in the first evaluation was larger than the slow, controlled breathing exercises in the second evaluation, as well as the SCBE in the first evaluation were smaller than the spontaneous breathing in the second evaluation (DEM: -18.2 CI95%: -9.9 to -26.5 n.u.). These results were repeated in the same proportion for the HF component in the comparison of evaluations (1st vs 2nd). The analyses of the effect size of the means of the two evaluated days demonstrates that SCBE presented a large effect (ES=-1.08) in reducing sympathetic activity (LF) and increasing parasympathetic activity.

SCBE reduced ($p<0.001$) autonomic modulation (LF/HF ratio) by about 50% (1st Evaluation DEM: -1.40 CI95%: -0.64 to -2.2; 2nd Evaluation DEM: -0.98 CI95%: -0.22 to -1.74) in both days (1st Evaluation: 45% and 2nd Evaluation: 56%) (Figure 3E). The comparison of the evaluations (1st evaluation vs 2nd evaluation) of LF/HF ratio between spontaneous breaths and SCBE did not present differences. The

spontaneous breathing was smaller (DEM: -1.33 CI95%: -0.57 to -2.08 n.u.) in the first evaluation than the SCBE in the second evaluation, as well as the controlled breathing in the first evaluation was smaller than the spontaneous breathing in the second evaluation (DEM: -1.05 CI95%: -0.29 to -1.81 n.u.). These results were repeated in the same proportion for the HF component in the comparison of the evaluations (1st vs 2nd). The analysis of the effect size of the means of the two evaluated days demonstrates that SCBE presented a moderate effect (ES=-0.74) on autonomic modulation. During and after data collection, the patients did not present and did not report any complications.

DISCUSSION

The present study demonstrates that 10 minutes of SCBE reduces SAP and sympathetic activity, modifying autonomic modulation in hypertensive patients. In SAH, it is observable the imbalance of this modulation agent, which presents an excessively excited sympathetic component and can lead to the emergence of arrhythmia and sudden death^{2,5}. In studies that evaluated normotensive patients, SCBE represented an important increase in the parasympathetic component and autonomic modulation^{12,13,22}. These results with healthy volunteers reinforce the positive benefits of respiratory control over autonomic modulation, which is clinically relevant to the sympathetic hyperactivity of those patients³.

In the present study, the SCBE (12 bpm) reduced the sympathetic activity and increased the parasympathetic activity, which changed the autonomic cardiac modulation in hypertensive patients. These results are due to the respiratory sinus arrhythmia mechanism, which increases parasympathetic activity through SCBE, inducing the sympathetic activity reduction in the cardiac muscle^{23,24}. In such a context, the findings are justified by the feedback mechanism²³, given the modulating effect of ANS on the cardiorespiratory function, especially due to the physiological event of respiratory sinus arrhythmia²⁴, which results in the influence of breathing on cardiac function. During slow, controlled breathing, the expiratory phase excites, and the inspiratory phase inhibits the solitary tract, thus generating stimulus, especially in the X pair of cranial nerves (Vagus), which promotes autonomic cardiac modulation control²². This mechanism occurs mostly in the expiratory phase and, in the present study, that phase was longer than the inspiratory phase (inspiration/expiration: 2/3). This influenced the results for the exercise program on the autonomic modulation and on the SBP reduction found by the present study in a healthy way.

Previous studies with hypertensive patients reinforce the results of the present research²⁵⁻²⁷. Stress control in patients with SAH using slow breathing presents itself as a scientific perspective for the non-pharmacological treatment of this cardiovascular disease^{25,28}. SCBE programs (30 min sessions, 2 times a week for a month) reduced the respiratory frequency (14 bpm to 10 bpm), the SAP (-12 mmHg), the DAP (-7 mmHg), and increased the tidal volume, which is inversely associated with the patients' arterial pressure reduction²⁷. A recent study demonstrated that a SCBE program (10 bpm, during 15 min, 3 times a week, for 8 weeks) with the help of device (Resperate®) reduced SAP (-8,3 mmHg) and DAP (-4.9 mmHg) in patients with SAH²⁶. Li et al, demonstrated that 5 min SCBE (8 bpm), when compared with normal standardized breathing (16 bpm), reduces the heart rate (~5 bpm) and the arterial pressure (SAP: -6 mmHg and DAP: -5 mmHg), as well as modifies the cardiac autonomic modulation of the patients¹⁴. These studies confirm the present study results, demonstrating that SCBE reduce sympathetic activity, restore the sympathovagal balance, and decrease arterial pressure, as well as can serve as a non-pharmacological tool in the management of SAH^{14-16,26,27}. Among this study's limitations, we highlight the lack of measurement of baroreflex sensitivity and the lack of evaluation of the plasma catecholamines levels (norepinephrine, acetylcholine, and epinephrine)²⁹. Another worth considering factor is the lack of microneurography, which is the invasive and direct evaluation of the

autonomic nervous system activity³⁰. However, the techniques employed in this study are widely used in researches, as well as recommended by the TASK Force guidelines⁶.

CONCLUSION

SCBE (12 breaths per minute; Inspiration / Expiration: 2/3) modify the autonomic cardiac modulation and reduce hypertensive patients' arterial pressure. These alterations are demonstrated by the decrease of the sympathetic activity, the increase of the parasympathetic activity, and the reduction of the SBP. The present research findings show the importance of considering the role of breathing control, even if in physiological values, on the autonomic cardiac function during scientific studies data collection. Clinically, SCBE can be a non-pharmacological tool in the reduction of the arterial pressure of hypertensive patients.

REFERENCES

- ¹ Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart Disease and Stroke Statistics'2017 Update: A Report from the American Heart Association. *Circulation* 2017;135(10):146-603. DOI: 10.1161/CIR.0000000000000485
- ² Vaseghi M, Shivkumar K. The Role of the Autonomic Nervous System in Sudden Cardiac Death. *Prog Cardiovasc Dis* 2008;50(6):404-419. DOI: 10.1016/j.pcad.2008.01.003
- ³ Merino-Jiménez C, Miguel F, Feria Pliego JA, et al. Sympathetic Hyperactivity and Age Affect Segregation and Expression of Neurotransmitters. *Front Cell Neurosci* 2018;12. DOI: 10.3389/fncel.2018.00411
- ⁴ Shaffer F, McCraty R, Zerr CL. A healthy heart is not a metronome: an integrative review of the heart's anatomy and heart rate variability. *Front Psychol* 2014;5(1.040):1-19. DOI: 10.3389/fpsyg.2014.01040
- ⁵ Rizas KD, Nieminen T, Barthel P, et al. Sympathetic activity-associated periodic repolarization dynamics predict mortality following myocardial infarction. *Journal of Clinical Investigation* 2014;124(4):1.770-1.780. DOI: 10.1172/JCI70085
- ⁶ Task Force of TES of C and TNAS of P and E. Heart rate variability: Standards of measurement, physiological interpretation, and clinical use. *Eur Heart J* 1996;17(x):354-381. DOI: <https://doi.org/10.1161/01.CIR.93.5.1043>
- ⁷ Whelton PK, Carey RM. The 2017 Clinical Practice Guideline for High Blood Pressure. *Jama – Journal of the American Medical Association* 2017;318(21):2.073-2.074. DOI: 10.1001/jama.2017.18209
- ⁸ Dudenbostel T, Siddiqui M, Oparil S, et al. Refractory hypertension: A novel phenotype of antihypertensive treatment failure. *Hypertension* 2016;67(6):1.085-1.092. DOI: 10.1161/HYPERTENSIONAHA.116.06587.
- ⁹ Gkaliagkousi E, Gavriilaki E, Douma S. Effects of acute and chronic exercise in patients with essential hypertension: Benefits and risks. *Am J Hypertens* 2015;28(4):429-439. DOI: 10.1093/ajh/hpu203
- ¹⁰ Hering D, Narkiewicz K. Sympathetic Nervous System and Arterial Hypertension: New Perspectives, New Data. *Kardiologia Pol* 2013;71(5):441-446. DOI: 10.5603/KP.2013.0089
- ¹¹ do Amaral Sartori S, Stein C, Coronel CC, et al. Effects of Transcutaneous Electrical Nerve Stimulation in Autonomic Nervous System of Hypertensive Patients: A Randomized Controlled Trial. *Curr Hypertens Rev* 2018;14(1):66-71. DOI: 10.2174/15734021146666180416155528
- ¹² Chang Q, Liu R, Li C, et al. Effects of slow breathing rate on blood pressure and heart rate variabilities in essential hypertension. *Int J Cardiol* 2015;185:52-54. DOI: 10.1016/j.ijcard.2015.02.105
- ¹³ Levin CJ, Swoap SJ. The impact of deep breathing and alternate nostril breathing on heart rate variability: a human physiology laboratory. *Adv Physiol Educ* 2019;43(x):270-276. DOI: 10.1152/advan.00019.2019
- ¹⁴ Li C, Chang Q, Zhang J, et al. Effects of slow breathing rate on heart rate variability and arterial baroreflex sensitivity in essential hypertension. *Medicine (United States)* 2018;97(18). DOI: 10.1097/MD.00000000000010639
- ¹⁵ Melo HM, Martins TC, Nascimento LM, et al. Ultra-short heart rate variability recording reliability: The effect of controlled paced breathing. *Annals of Noninvasive Electrocardiology* 2018;23(5):1-9. DOI: 10.1111/anec.12565
- ¹⁶ Sasaki K, Maruyama R. Consciously controlled breathing decreases the high-frequency component of heart rate variability by inhibiting cardiac parasympathetic nerve activity. *Tohoku Journal of Experimental Medicine* 2014;233(3):155-163. DOI: 10.1620/tjem.233.155
- ¹⁷ Zou Y, Zhao X, Hou YY, et al. Meta-Analysis of Effects of Voluntary Slow Breathing Exercises for Control of Heart Rate and Blood Pressure in Patients With Cardiovascular Diseases. *American Journal of Cardiology* 2017;120(1):148-153. DOI: 10.1016/j.amjcard.2017.03.247

- ¹⁸ Stein C, Dal Lago P, Ferreira JB, et al. Transcutaneous electrical nerve stimulation at different frequencies on heart rate variability in healthy subjects. *Auton Neurosci* 2011;165(2):205-208. DOI: 10.1016/j.autneu.2011.07.003
- ¹⁹ de Nardi AT, Hauck M, Franco OS, et al. Different frequencies of transcutaneous electrical nerve stimulation on sympatho-vagal balance. *Acta Scientiarum – Health Sciences* 2017;39(1):9-16. DOI: 10.4025/actascihealthsci.v39i1.32854
- ²⁰ Franco OS, Júnior AOS, Signori LU, et al. Cardiac autonomic modulation assessed by heart rate variability in children with asthma. *Pediatr Pulmonol* 2020;55(6):1.334-1.339. DOI: 10.1002/ppul.24714
- ²¹ McCraty R, Shaffer F. Heart rate variability: New perspectives on physiological mechanisms, assessment of self-regulatory capacity, and health risk. *Glob Adv Health Med* 2015;4(1):46-61. DOI: 10.7453/gahmj.2014.073
- ²² Russo MA, Santarelli DM, O'Rourke D. The physiological effects of slow breathing in the healthy human. *Breathe* 2017;13(4):298-309. DOI: 10.1183/20734735.009817
- ²³ Berntson GG, Cacioppo JT, Quigley KS. Respiratory sinus arrhythmia: Autonomic origins, physiological mechanisms, and psychophysiological implications. *Psychophysiology* 1993;30(x):183-196. DOI: <https://doi.org/10.1111/j.1469-8986.1993.tb01731.x>
- ²⁴ Mestanik M, Mestanikova A, Langer P, et al. Respiratory sinus arrhythmia – testing the method of choice for evaluation of cardiovagal regulation. *Respir Physiol Neurobiol* 2019;259:86-92. DOI: 10.1016/j.resp.2018.08.002
- ²⁵ Lipp MEN. Stress management training and systemic hypertension. *Rev Bras Hipertens* 2007;14(2):89-93.
- ²⁶ Lopes DA da C, Souza ALT de, Gusmão JL de. Effect of slow and guided breathing exercise on blood pressure in institutionalized hypertensive elderly. *Saúde e Pesquisa* 2021;14(4):1-12. DOI: 10.17765/2176-9206.2021v14n4e9025
- ²⁷ Pinheiro CH da J, Medeiros RAR, Pinheiro DGM, et al. Spontaneous Respiratory Modulation Improves Cardiovascular Control in Essential Hypertension. *Arq Bras Cardiol* 2007;88(6):576-583. DOI: <https://doi.org/10.1590/S0066-782X2007000600005>
- ²⁸ Signori LU, Rubin Neto LJ, Lima KS de, et al. Influence of Controlled Breath on Healthy Adult Autonomic Heart Modulation. *Acta Scientiarum Health Sciences* 2022; 45(1):1-17. DOI: <https://doi.org/10.4025/actascihealthsci.v45i1.60429>.
- ²⁹ Sun BB, Maranville JC, Peters JE, et al. Genomic atlas of the human plasma proteome. *Nature* 2018;558(7708):73-79. DOI: 10.1038/s41586-018-0175-2
- ³⁰ Wehrwein EA, Orer HS, Barman SM. Overview of the Anatomy, Physiology, and Pharmacology of the Autonomic Nervous System. *Compr Physiol* 2016;6(3):1.239-1.278. DOI: 10.1002/CPHY.C150037

Received: January 17, 2023

Accepted: November 30, 2023

Published: February 21, 2024

Authors' Contributions:

Léo José Rubin Neto: Data curation; Investigation; Writing – review & editing

Gustavo Orione Puntel: Conceptualization; Investigation; Methodology; Resources; Supervision; Validation

Dhayan Quevedo Ferrão: Data curation; Formal analysis; Investigation; Writing – original draft

Mireli Hemann Lamberti: Data curation; Formal analysis; Investigation; Writing – original draft

Bruno Cesar Correa Arbiza: Data curation; Investigation; Writing – original draft

Katieli Santos de Lima: Data curation; Formal analysis; Writing – original draft

Antônio Marcos Vargas da Silva: Conceptualization; Investigation; Methodology; Resources; Validation

Luis Ulisses Signori: Conceptualization; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Writing – review & editing

All authors have approved the final version of the text.

Conflict of interest: There are no conflicts of interest.

Financing: Does not have financing.

Corresponding Author:

Luis Ulisses Signori

Universidade Federal de Santa Maria – UFSM

Avenida Prefeito Evandro Behr, nº 4400, AP. 203. Bloco: A. Bairro: Pé de Platano. Santa Maria/RS.

CEP: 97110-800.

E-mail: l.signori@hotmail.com

Editor: Dra. Eliane Roseli Winkelmann

Editor-in-chief: Dra. Adriane Cristina Bernat Kolankiewicz

This is an open access article distributed under the terms of the Creative Commons license.

