

Blood pressure-lowering effect of repeated Waon therapy in non-smokers with hypertension

Kazuyuki Kominami, MS^{a,*}[®], Etsuko Takahiza^b, Mineko Tabuchi^b, Masatoshi Akino, PhD^{a,c}

Abstract

Waon therapy (WT) has been used as a thermal therapy in chronic heart failure patients. However, its effect in patients with hypertension is unclear. This study aimed to reveal the hypotensive effect of WT in patients with hypertension. WT was performed on 31 patients with hypertension (63.9 ± 11.9 years, male: 17) on standard hypertension treatment focusing on lifestyle modification and medication. Systolic and diastolic blood pressures were measured before and after WT using an upper arm automated sphygmomanometer. We investigated the effect of single and repeated ($1 \tan e/d$, >5 times) WT sessions on blood pressure and further compared its effect between current smoking (n=11, 55.4 ± 6.4 years, 8.5 ± 2.4 times) and non-smoking (n=11, 66.9 ± 8.5 years, 12.2 ± 5.9 times) groups. A total of 370 sessions of WT were conducted. Systolic and diastolic blood pressures significantly decreased after a single WT session (systolic blood pressure: 118.5 ± 10.1 to 115.1 ± 9.0 mm Hg, P < .001; diastolic blood pressure: 70.5 ± 6.4 to 65.9 ± 5.3 mm Hg, P < .001). The blood pressure decrease following repeated WT was not significant when all participants were considered (systolic blood pressure: 122.3 ± 15.2 to 116.9 ± 19.6 mm Hg; diastolic blood pressure: 73.8 ± 16.7 to 68.2 ± 13.2 mm Hg); however, it was significant in the non-smoking group (systolic blood pressure: 124.2 ± 11.3 to 108.8 ± 13.4 mm Hg, P < .001; diastolic blood pressure: 73.6 ± 4.9 to 62.1 ± 7.6 mm Hg, P < .001). Repeated WT (at least 5 sessions) decreased blood pressure in patients with hypertension, especially in non-smokers. WT is a simple method to reduce blood pressure in non-smoking patients with hypertension.

Abbreviations: BP-diff = difference of blood pressure, DBP = diastolic blood pressure, MBP = mean blood pressure, SBP = systolic blood pressure, WT = Waon therapy.

Keywords: blood pressure, antihypertensive effect, blood pressure-lowering effect, smoking, thermal therapy, Waon therapy

1. Introduction

Thermal therapy is one of the oldest forms of physiotherapy. Heat therapy, such as hot baths and saunas, achieves deep heating of the body (i.e., increases the core body temperature), leading to health benefits.^[1] Waon therapy (WT), which was researched and developed in Japan, is one of the most effective ways to increase core body temperature. Its name means "soothing warm therapy," and it is a healing approach in which the entire body is comfortably warmed.^[2] It is characterized

Editor: Neil Patel.

The authors have no funding and conflicts of interest to disclose.

Supplemental Digital Content is available for this article.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Received: 27 January 2021 / Received in final form: 20 May 2021 / Accepted: 21 May 2021

http://dx.doi.org/10.1097/MD.00000000026266

by low cardiac stress and can even be safe to perform in patients with severe heart failure.^[3–5] Repeated dry sauna therapy for 2 weeks has been reported to improve endothelial and cardiac functions,^[6] exercise capacity,^[7] autonomic functions,^[8,9] and prognosis of chronic heart failure.^[10]

In recent years, hypertension, which affects a large number of patients, has been shown to cause heart failure.^[11] Persistent hypertension can lead to deterioration of vascular endothelial,^[12] autonomic,^[13] and cardiac function; development of cardiovas-cular disease; and progression to heart failure.^[14] Smoking is a risk factor for hypertension and arteriosclerosis.^[15]

The general treatment for hypertension is based on medication and lifestyle changes, such as exercise, smoking cessation, and low sodium intake.^[16] Sauna bath has also been shown to prevent hypertension,^[17,18] but tolerance to sauna bath varies from person to person.^[19,20] Some people experience transient increases in cardiac stress, such as rise in blood pressure, heart rate, and sympathetic nerve activity.^[21,22] In addition, cold water immersion after a sauna bath can be problematic.^[22,23] In most cases, there are no adverse health effects, but the few reports of cardiac incidents after sauna bathing underscore the need for caution.^[24]

Previous studies have shown that WT is effective in hemodynamics improvement or symptoms and does not cause exacerbation or high cardiac stress in patients with severe heart failure.^[3–5] Therefore, it may improve cardiovascular dysfunction, such as endothelial dysfunction, which may be comorbid in patients with hypertension.

However, the blood pressure-lowering effect of WT in medically managed patients with hypertension has not been elucidated. Additionally, there is no report on the effect of

^a Cardiac Rehabilitation Center, ^b Department of Rehabilitation, ^c Department of Cardiovascular Medicine, Sapporo Ryokuai Hospital, Sapporo, Japan.

^{*} Correspondence: Kazuyuki Kominami, Cardiac Rehabilitation Center, Sapporo Ryokuai Hospital, 6-30, 1-chome, Kitano1-jyo, Kiyota-ku, Sapporo 004-0861, Japan (e-mail: qqae3s4u9@gmail.com).

Copyright © 2021 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Kominami K, Takahiza E, Tabuchi M, Akino M. Blood pressure-lowering effect of repeated Waon therapy in non-smokers with hypertension. Medicine 2021;100:23(e26266).

smoking on the blood pressure-lowering properties of WT. This study aimed to clarify whether the blood pressure-lowering effect of WT differs depending on the presence or absence of smoking in patients with hypertension.

2. Methods

2.1. Participants

A retrospective study was conducted on the records of patients who underwent WT. The participants were 31 inpatients with hypertension $(63.9 \pm 11.9$ years, male: 17) on standard hypertension treatment.^[25] The study period was between Nov 2016 and Feb 2019. None of the participants had cardiovascular, cerebrovascular disease, or irregular arrhythmias such as atrial fibrillation, atrial flutter, or chronic heart failure. The participants' details are shown in Table 1.

2.2. Blood pressure measurement

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured before and after WT using an arm sphygmomanometer (HEM-1020 [cuff size 150 mm; Applicable upper arm diameter; 170–320 mm] Omron Corporation, Kyoto, Japan). Measurements were taken on the right upper arm in a sitting position after a 1-minute rest according to the technique recommended in the guidelines.^[26] The observer practiced the measurement method beforehand so that the patient could measure the blood pressure properly. The sphygmomanometer simultaneously measured the pulse rate.

Mean blood pressure was calculated based on SBP and DBP as follows: mean blood pressure (MBP) = 1/3 SBP + 2/3 DBP. Differential pressure (BP-diff) was calculated as follows: SBP-DBP.

2.3. Waon therapy

WT was conducted according to previously described methods^[27] using far-infrared dry sauna equipment (CTW-5000, Fukuda Denshi, Tokyo, Japan) pre-warmed to 60°C. All sessions were conducted between 3 and 5 pm. The patients sat in the dry sauna for 15 minutes. During the heat-retention phase, they rested supine on a bed for 30 minutes wrapped in a blanket. Body weight was measured before and after each session (HBF-252F-W, Omron Corporation, Kyoto, Japan), and the patients were

_			
		1	

Participants' clinical characteristics.

rehydrated based on the weight lost during the session to prevent dehydration. Sublingual temperature was measured thrice (before and after the session and at the heat-retention phase) using a digital thermometer (MC-681, Omron Corporation, Kyoto, Japan) by placing the tip of the thermometer on the sublingual surface.

2.4. Blood pressure-lowering effect of Waon therapy

The blood pressure-lowering effects of a single (every session, 31 patients) and repeated (at once a day for a total of at least 5 sessions, 22 patients) WT were compared between patients with a history of smoking (current smoking group, 11 patients vs non-smoking group, 11 patients). Of the 31 patients who underwent WT, 9 patients were not included in the group of repeated WT patients because they underwent the WT for less than 5 sessions. The "at least 5 sessions" parameter refers to the fact that the patients could get at least 5 sessions per week, provided they attended daily WT sessions during the weekdays. "Repeated" was set to "at least 5 sessions," as the researchers planned to run these sessions for a period longer than 1 week.

For single WT, blood pressure readings before and after the WT session were used. For repeated WT, blood pressure readings taken before the first and last sessions were used.

2.5. Statistical analysis

Data are presented as means \pm standard deviations. Statistical analyses were performed using Statistics for Excel 2012 (Social Survey Research Information Co., Tokyo). Paired data were analyzed using the paired *t* test. Two-way analysis of variance with post-hoc Bonferroni correction was used for between-group comparisons. The significance level was set at 5%.

2.6. Ethical considerations

This research was conducted in accordance with the code of ethics of Sapporo Ryokuai Hospital and with due consideration for the protection of the participants' personal information. Informed consent was obtained from all participants for their participation in the study and for the publication of this report. The data obtained were de-linked and anonymized. The authors confirm that all participants cannot be identified via the paper and that they have been fully anonymized. Furthermore, the authors affirm that all mandatory health and safety procedures

		Total	Non-smoking (n=11)	Current smoking (n=11)	P value
Sex	Male:Female	21:1	10:1	11:0	.306
Age	(yr)	61.1 ± 9.4	66.9 ± 8.5	55.4 ± 6.4	.002
Height	(cm)	164.5 <u>+</u> 4.9	162.4 ± 4.2	166.6 ± 4.8	.043
Body weight	(kg)	77.8±8.8	72.8 ± 6.8	82.7±7.9	.005
BMI		28.7 ± 2.6	27.6 ± 1.9	29.9 ± 2.8	.040
Antihypertensive medication	n (%)	13 (59.1)	4 (36.4)	9 (81.8)	.030
Ca antagonist	n (%)	12 (54.5)	3 (27.2)	9 (81.8)	.010
ACE/ARB	n (%)	9 (40.9)	4 (36.4)	5 (45.5)	.665
Diuretic	n (%)	1 (4.5)	1 (9.1)	0 (0)	.306
α blocker	n (%)	1 (4.5)	0 (0)	1 (9.1)	.306

Data are presented as mean ± standard deviation. Significant differences in clinical characteristics such as age, body weight, BMI, and details of medication were observed between the 2 groups. ACE=angiotensin converting enzyme inhibitor, ARB=angiotensin II receptor blocker, BMI=body mass index.

were adhered to during the experimental work reported in the paper.

3. Results

A total of 253 WT sessions were conducted. No adverse events such as hypotension or falls as a result of the therapy were reported.

3.1. Participants' characteristics

The participants' characteristics are shown in Table 1. The participants in the current smoking group $(8.5\pm2.4 \text{ times})$ were significantly younger $(55.4\pm6.4 \text{ years} \text{ vs } 66.9\pm8.5 \text{ years}, P = .002)$ and heavier $(71.5\pm5.3 \text{ kg vs } 81.5\pm8 \text{ kg}, P < .001)$ than those in the non-smoking group $(12.2\pm5.9 \text{ times})$. The use of antihypertensive medication, especially calcium antagonists, was more common in the smoking group.

3.2. Blood pressure changes after a single session of Waon therapy

The blood pressure changes after a single session of WT are shown in Table 2. The SBP, DBP, and mean blood pressure were significantly lower after a single WT session (difference in SBP: -3.7 ± 13.8 mm Hg, difference in DBP: -4.5 ± 9.3 mm Hg, difference in MBP: -3.9 ± 9.3 mm Hg). BP-diff was not significantly altered. The blood pressure change after a single session of WT did not differ between the current smoking and non-smoking groups (non-smoking vs current smoking, respectively: SBP: -2.7 ± 13.4 vs -3.1 ± 10.0 mm Hg, P=.837; DBP: -3.9 ± 9.6 vs -5.3 ± 9.0 mm Hg, P=.222; MBP: -3.5 ± 10.0 vs -4.6 ± 8.2 mm Hg, P=.365).

Furthermore, a single session of WT with or without antihypertensive medication had an antihypertensive effect in both groups (Suppl 1, http://links.lww.com/MD/G186).

3.3. Blood pressure changes after repeated Waon therapy (Fig. 1 & Table 3)

Twenty-two patients received repeated WT (at least 5 sessions, once daily; mean, 10.3 ± 4.8 sessions [5–25 sessions]). In these patients, blood pressure before the second session showed a

Table 2				
Effect of a	single	Waon	therapy	sessior

decreasing trend in the non-smoking group compared with the first session, but not in the smoking group (total: SBP: $122.5 \pm 15.2 \rightarrow 122.6 \pm 16.4$ mm Hg, DBP: $73.8 \pm 11.7 \rightarrow 71.5 \pm 12.2$ mm Hg; non-smoking: SBP: $124.2 \pm 11.3 \rightarrow 121.2 \pm 14.6$ mm Hg, DBP: $73.6 \pm 4.9 \rightarrow 68.2 \pm 6.6$ mm Hg; current smoking: SBP: $120.4 \pm 18.8 \rightarrow 123.0 \pm 18.7$ mm Hg, DBP: $74.0 \pm 16.3 \rightarrow 74.2 \pm 15.8$ mm Hg).

Repeated WT did not have a significant blood pressurelowering effect (difference in SBP: -5.4 ± 16.7 mm Hg, effect size d=0.31; difference in DBP: -5.6 ± 10.9 mm Hg, d=0.45; difference in mean blood pressure: -5.6 ± 11.8 mm Hg, d=0.41). On the contrary, the non-smoking group showed significant greater blood pressure-lowering effect compared to the current smoking group (SBP: -15.4 ± 10.0 vs 4.5 ± 16.4 mm Hg, P=.003; DBP: -11.5 ± 4.8 vs 0.3 ± 12.3 mm Hg, P=.008; mean blood pressure: -12.8 ± 5.8 vs 1.7 ± 12.0 mm Hg, P=.002).

Furthermore, the blood pressure-lowering effect of repeated WT with or without antihypertensive medication in the nonsmoking group was similar (Suppl 2, http://links.lww.com/MD/ G187). However, statistical analysis was not performed because the number of cases was not sufficient.

4. Discussion

The present study is a retrospective analysis of the blood pressurelowering effect of WT in patients with hypertension. In all participants, the therapy was relatively safe, and there were no adverse events, such as dizziness or falls due to hypotension, associated with WT.

The results suggest that repeated WT can be safely used to reduce blood pressure in non-smokers with hypertension.

4.1. Differences in participant characteristics

In terms of characteristics, current smokers were found to be younger, weighed heavier, and more likely to be taking antihypertensive medication than non-smokers. Some participants in the non-smoking group had a history of smoking but they made lifestyle changes, alleviating the need for antihypertensive medications. The difference in blood pressure reduction observed in this study may have also been due to the influence of obesity and antihypertensive medication.

		All			Non-smoking			Current smoking		
		Before	After warming	After	Before	After warming	After	Before	After warming	After
Body weight	(kg)	75.9±8.4		75.6±8.3 [*]	71.5 ± 5.3		71.2±5.4 [*]	81.5±8		81.1±7.9 [*]
Sublingual	(°C)	36.6±0.5	37.4±0.4 [*]	$37.2 \pm 0.5^{*}$	36.6 ± 0.5	37.4±0.4 [*]	$37.3 \pm 0.4^{*}$	36.6 ± 0.4	37.5±0.4 [*]	37.1 <u>+</u> 0.5 [*]
temperature										
SBP	(mm Hg)	118.6 ± 14.6		$115.8 \pm 17.4^{*}$	116.2±12.5		$113.5 \pm 15.2^{*}$	122.0 ± 16.6		119.0 ± 19.6
DBP	(mm Hg)	69.8±11.1		$65.3 \pm 12.3^{*}$	67.2±9		$63.3 \pm 10.6^{*}$	73.4±12.7		$68.1 \pm 13.8^{*}$
MBP	(mm Hg)	86.1±11.7		82.1 ± 13.4 [*]	83.5±9.6		$80.1 \pm 11.6^{*}$	89.6±13.5		$85.0 \pm 15.1^{*}$
BP diff	(mm Hg)	48.9±8.4		50.5±10.0	49.0±8.2		50.1 ± 9.0	48.7 <u>±</u> 8.8		50.9±11.3
HR	(bpm)	68.4±8.8		72.1±9.7 [*]	66.4±6.7		$68.6 \pm 7.8^*$	70.6±10.2		$75.8 \pm 10.1^{*}$
DP		8210 ± 1552		$8425 \pm 1897^*$	7749 ± 1369		7843±1768	8572±1481		8975±1674

Data are presented as mean ± standard deviation. Sublingual temperature was measured before and after Waon therapy and immediately after warming.

BP diff=differential pressure, DBP=diastolic blood pressure, DP=double products, HR=heart rate, MBP=mean blood pressure, SBP=systolic blood pressure.

* Significant (P < .01) for before vs after Waon therapy.

[†]Significant (P<.01) for non-smoking vs current smoking.

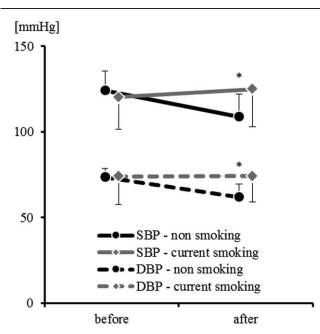


Figure 1. Comparison of blood pressure-lowering effect of repeated Waon therapy between current smokers and non-smokers changes in SBP and DBP before and after repeated Waon therapy in non-smokers (\bigcirc) and current smokers (\bigcirc) with hypertension. Both SBP and DBP are significantly lower in non-smokers. An interaction effect is observed in both groups for SBP and DBP. Data are presented as mean \pm SD. DBP=diastolic blood pressure, SBP=systolic blood pressure. *Significant difference (P<.05) between before and after values.

4.2. Blood pressure-lowering effect of a single session of Waon therapy

Finnish sauna therapy has been shown to lower blood pressure and prevent hypertension in middle-aged adults^[28] but may not have a blood pressure-lowering effect in older adults. WT, which uses a lower temperature than Finnish sauna therapy, has been shown to have a blood pressure-lowering effect in patients with chronic heart failure.^[3]

In the present study, a single session of WT resulted in a significant reduction in both SBP and DBP. This may be due to vasodilation and reduction of peripheral vascular resistance. A previous study reported that WT resulted in significant vasodilation; however, blood pressure reduction was not observed.^[29] The possible reasons for this observation are: the participants were young and healthy; blood pressure was measured in the supine position, which provides

an adaptation to the vasodilation caused by the warm therapy; and the absence of the effects of postural changes and fluid movement due to gravity.^[29] Although the previous study population was different from ours, it is thought that vasodilation also occurred in the participants of the present study.

In the non-smoking group, pre-session blood pressure showed a decreasing trend. WT has been shown to have an inhibitory effect on the sympathetic nervous system,^[29,30] and this effect may have been sustained in the non-smoking group.

4.3. Blood pressure-lowering effect of repeated Waon therapy

When comparing both groups, only the non-smoking group showed a significant decrease in blood pressure after repeated WT. A previous study showed that repeated WT improved endothelial and autonomic nerve function.^[8] This may have led to the blood pressure-lowering effect observed in this study. The smoking group was significantly overweight compared to the non-smoking group and may have contributed to a lack of blood pressure reduction due to physiological changes, such as potential vascular endothelial and vasodilatory dysfunction.^[31–34] Conversely, the non-smoking group had a lower body weight and may not have had as much loss of vascular function as the smoking group. Another reason for the lack of blood pressurelowering effect in the smoking group may be insufficient sympathetic nerve suppression since the blood pressure reduction was not achieved in 1 session of WT, as shown in the results.

This study suggests that current smoking in hypertensive patients counteracts the blood pressure-lowering effect of WT. Alternatively, a greater times may be required to achieve a blood pressure-lowering effect. However, it is thought that blood pressure may fluctuate and gradually decrease among nonsmokers through repeated WT (Fig. 2).

However, there are several unclear aspects of thermal therapy, including WT. First, it is still unclear how long the antihypertensive effect of repeated WT lasts. For example, how long does the effect last after 2 weeks or 1 month of repeated WT, and to what extent is the antihypertensive effect achieved by repeated WT? Secondly, it is not sufficiently clear how often the WT should be repeated to obtain the antihypertensive effect (the recommended frequency is at least twice a week for outpatients with chronic heart failure^[10] and 5 times a week for inpatients with stable symptoms of heart failure,^[4,5] and many studies suggest multiple times a week for Finnish sauna^[18]). In the future, it is desirable to verify the sustained effects and appropriate frequency of thermal therapy, including WT, in various atherosclerotic diseases such as hypertension.

Table 3				
Effect of re	peated Waor	therapy	sessions.	

		All			Non-smoking			Current smoking		
		Before	After	Effect size (d)	Before	After	Effect size (d)	Before	After	Effect size (d)
Waon therapy sessions		10.3	±4.8		12.2±5.9			8.5±2.4		
SBP	(mm Hg)	122.3 ± 15.2	116.9 ± 19.6	0.31	124.2±11.3	108.8±13.4 [*]	1.24	120.4±18.8	124.9±22	-0.22
DBP	(mm Hg)	73.8±11.7	68.2±13.2	0.45	73.6±4.9	$62.1 \pm 7.6^*$	1.81	74.0±16.3	74.3±15.1	-0.02
MBP	(mm Hg)	90.0±11.8	84.4±14.9	0.41	90.5 ± 4.3	77.7 <u>+</u> 8.5 [*]	1.89	89.5±16.5	91.2±17.1	-0.10
BP diff	(mm Hg)	48.5±11.8	48.7±10.2		50.5 ± 13.3	46.7 ± 10.6		46.4 ± 10.3	50.6 ± 9.8	

Data are presented as mean \pm standard deviation.

BP diff = differential pressure, DBP = diastolic blood pressure, MBP = mean blood pressure, SBP = systolic blood pressure.

* Significant (P < .01) for before vs after repeated Waon therapy.

*Significant (P<.01) for non-smoking vs current smoking.

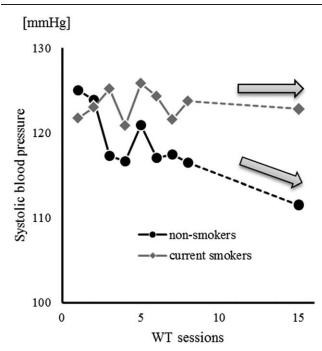


Figure 2. Diagram of the blood pressure changes after repeated Waon therapy. In non-smokers () and current smokers (), predicted changes in SBP are shown in the figure. The results suggest that smoking may create a difference in the blood pressure-lowering effect of Waon therapy.

5. Limitations

The present study has several limitations. First, the primary mechanisms responsible for the blood pressure-lowering effect were unclear since vascular functions (such as vasodilatory response and vascular endothelial function), autonomic and neurohumoral factors based on heart rate variability analysis, and laboratory data were not evaluated. Second, it is unclear how many sessions of Waon therapy are required to achieve the blood pressure-lowering effect. Third, it is unclear how long the blood pressure-lowering effect will last. Furthermore, it was not possible to sufficiently examine the extent to which differences in age, weight, and medication use affected the blood pressurelowering effect or whether other influencing factors were present.

6. Conclusion

After a single session of WT, there was a temporary reduction in blood pressure, but this effect was not sustained. Repeated WT had a blood pressure-lowering effect in non-smokers. Repeated WT for more than 1 week had a blood pressure-lowering effect in non-smokers, but not in smokers, with hypertension.

Acknowledgments

We would like to thank Editage for assistance in English language editing.

Author contributions

Conceptualization: Kazuyuki Kominami, Etsuko Takahiza, Mineko Tabuchi, Masatoshi Akino.

Data curation: Kazuyuki Kominami, Etsuko Takahiza, Mineko Tabuchi.

Formal analysis: Kazuyuki Kominami, Mineko Tabuchi.

Funding acquisition: Masatoshi Akino.

Investigation: Kazuyuki Kominami, Mineko Tabuchi.

Methodology: Kazuyuki Kominami, Etsuko Takahiza, Mineko Tabuchi, Masatoshi Akino.

Project administration: Kazuyuki Kominami, Etsuko Takahiza. Resources: Masatoshi Akino.

Software: Kazuyuki Kominami.

Supervision: Kazuyuki Kominami, Mineko Tabuchi, Masatoshi Akino.

Validation: Kazuyuki Kominami.

Visualization: Kazuyuki Kominami.

- Writing original draft: Kazuyuki Kominami.
- Writing review & editing: Etsuko Takahiza, Mineko Tabuchi, Masatoshi Akino.

References

- Laukkanen JA, Laukkanen T, Kunutsor SK. Cardiovascular and other health benefits of sauna bathing: a review of the evidence. Mayo Clin Proc 2018;93:1111–21. doi: 10.1016/j.mayocp.2018.04.008. PMID: 30077204.
- [2] About Waon therapy; n.d. Available at: http://www.waon-therapy.com/ en/about.html [access date January 22, 2021].
- [3] Tei C, Horikiri Y, Park JC, et al. Acute hemodynamic improvement by thermal vasodilation in congestive heart failure. Circulation 1995;91:2582–90. doi: 10.1161/01.cir.91.10.2582. PMID: 7743620.
- [4] Miyata M, Kihara T, Kubozono T, et al. Beneficial effects of Waon therapy on patients with chronic heart failure: results of a prospective multicenter study. J Cardiol 2008;52:79–85. doi: 10.1016/j. jjcc.2008.07.009. Epub August 27, 2008. PMID: 18922381.
- [5] Tei C, Imamura T, Kinugawa K, et al. Waon therapy for managing chronic heart failure – results from a multicenter prospective randomized WAON-CHF study. Circ J 2016;80:827–34. doi: 10.1253/circj.CJ-16-0051. Epub March 18, 2016. PMID: 27001189.
- [6] Källström M, Soveri I, Oldgren J, et al. Effects of sauna bath on heart failure: a systematic review and meta-analysis. Clin Cardiol 2018;41:1491–501. doi: 10.1002/clc.23077. Epub November 21, 2018. PMID: 30239008; PMCID: PMC6489706.
- [7] Sobajima M, Nozawa T, Fukui Y, et al. Waon therapy improves quality of life as well as cardiac function and exercise capacity in patients with chronic heart failure. Int Heart J 2015;56:203–8. doi: 10.1536/ihj.14-266. Epub February 27, 2015. PMID: 25740582.
- [8] Kihara T, Biro S, Ikeda Y, et al. Effects of repeated sauna treatment on ventricular arrhythmias in patients with chronic heart failure. Circ J 2004;68:1146–51. doi: 10.1253/circj.68.1146. PMID: 15564698.
- [9] Kuwahata S, Miyata M, Fujita S, et al. Improvement of autonomic nervous activity by Waon therapy in patients with chronic heart failure. J Cardiol 2011;57:100–6. doi: 10.1016/j.jjcc.2010.08.005. Epub September 29, 2010. PMID: 20884178.
- Kihara T, Miyata M, Fukudome T, et al. Waon therapy improves the prognosis of patients with chronic heart failure. J Cardiol 2009;53:214– 8. doi: 10.1016/j.jjcc.2008.11.005. Epub January 18, 2009. PMID: 19304125.
- [11] Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol 2020;16:223–37. doi: 10.1038/s41581-019-0244-2. Epub February 5, 2020. PMID: 32024986.
- [12] Mordi I, Mordi N, Delles C, Tzemos N. Endothelial dysfunction in human essential hypertension. J Hypertens 2016;34:1464–72. doi: 10.1097/HJH.00000000000965. PMID: 27203578.
- [13] Kishi T. Regulation of the sympathetic nervous system by nitric oxide and oxidative stress in the rostral ventrolateral medulla: 2012 Academic Conference Award from the Japanese Society of Hypertension. Hypertens Res 2013;36:845–51. doi: 10.1038/hr.2013.73. Epub July 18, 2013. PMID: 23864055.
- [14] Messerli FH, Rimoldi SF, Bangalore S. The transition from hypertension to heart failure: contemporary update. JACC Heart Fail 2017;5:543–51. doi: 10.1016/j.jchf.2017.04.012. Epub July 12, 2017. Erratum in: JACC Heart Fail. 2017 Dec;5(12):948. PMID: 28711447.

- [15] Virdis A, Giannarelli C, Neves MF, Taddei S, Ghiadoni L. Cigarette smoking and hypertension. Curr Pharm Des 2010;16:2518–25. doi: 10.2174/138161210792062920. PMID: 20550499.
- [16] Valenzuela PL, Carrera-Bastos P, Gálvez BG, et al. Lifestyle interventions for the prevention and treatment of hypertension. Nat Rev Cardiol 2021;18:251–75. doi: 10.1038/s41569-020-00437-9. Epub 2020 Oct 9. PMID: 33037326.
- [17] Zaccardi F, Laukkanen T, Willeit P, Kunutsor SK, Kauhanen J, Laukkanen JA. Sauna bathing and incident hypertension: a prospective cohort study. Am J Hypertens 2017;30:1120–5. doi: 10.1093/ajh/ hpx102. PMID: 28633297.
- [18] Laukkanen T, Khan H, Zaccardi F, Laukkanen JA. Association between sauna bathing and fatal cardiovascular and all-cause mortality events. JAMA Intern Med 2015;175:542–8. doi: 10.1001/jamainternmed.2014.8187. PMID: 25705824.
- [19] Leppo JA. If you can't stand the heat, get out of the kitchen. Am J Med 1999;107:290–2. doi: 10.1016/s0002-9343(99)00230-2. PMID: 10492326.
- [20] Hannuksela ML, Ellahham S. Benefits and risks of sauna bathing. Am J Med 2001;110:118–26. doi: 10.1016/s0002-9343(00)00671-9. PMID: 11165553.
- [21] Taggart P, Parkinson P, Carruthers M. Cardiac responses to thermal, physical, and emotional stress. Br Med J 1972;3:71–6. doi: 10.1136/ bmj.3.5818.71. PMID: 4114377; PMCID: PMC1785579.
- [22] Radtke T, Poerschke D, Wilhelm M, et al. Acute effects of Finnish sauna and cold-water immersion on haemodynamic variables and autonomic nervous system activity in patients with heart failure. Eur J Prev Cardiol 2016;23:593–601. doi: 10.1177/2047487315594506. Epub July 7, 2015. PMID: 26152773.
- [23] Ahmad M, Dubiel JP, Haibach H. Cold pressor thallium-201 myocardial scintigraphy in the diagnosis of coronary artery disease. Am J Cardiol 1982;50:1253–7. doi: 10.1016/0002-9149(82)90458-1. PMID: 7148699.
- [24] Giannetti N, Juneau M, Arsenault A, et al. Sauna-induced myocardial ischemia in patients with coronary artery disease. Am J Med 1999;107:228–33. doi: 10.1016/s0002-9343(99)00220-x. PMID: 10492315.
- [25] Shimamoto K, Ando K, Fujita T, et al. The Japanese Society of Hypertension guidelines for the management of hypertension (JSH)

2014). Hypertens Res 2014;37:253-390. doi: 10.1038/hr.2014.20. PMID: 24705419.

- [26] Pickering TG, Hall JE, Appel LJ, et al. Recommendations for blood pressure measurement in humans and experimental animals, part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Hypertension 2005;45:142–61. doi: 10.1161/01.HYP.0000150859.47929.8e.
- [27] Miyata M, Tei C. Waon therapy for cardiovascular disease: innovative therapy for the 21st century. Circ J 2010;74:617–21. doi: 10.1253/circj. cj-09-0939. Epub February 13, 2010. PMID: 20154403.
- [28] Ketelhut S, Ketelhut RG. The blood pressure and heart rate during sauna bath correspond to cardiac responses during submaximal dynamic exercise. Complement Ther Med 2019;44:218–22. doi: 10.1016/j. ctim.2019.05.002. Epub May 2, 2019. PMID: 31126559.
- [29] Kominami K, Noda K, Takahashi N, Izumi T, Yonezawa K. Cardiovascular reactions for whole-body thermal therapy with a hot pack and Waon therapy. Int J Hyperthermia 2020;37:184–91. doi: 10.1080/02656736.2020.1723719. PMID: 32046537.
- [30] Imamura T, Kinugawa K, Nitta D, Komuro I. Real-time assessment of autonomic nerve activity during adaptive servo-ventilation support or Waon therapy. Int Heart J 2016;57:511–4. doi: 10.1536/ihj.16-014. Epub July 7, 2016. PMID: 27385607.
- [31] Butler R, Morris AD, Struthers AD. Cigarette smoking in men and vascular responsiveness. Br J Clin Pharmacol 2001;52:145–9. doi: 10.1046/j.0306-5251.2001.01434.x. PMID: 11488770; PMCID: PMC2014533.
- [32] Lanza GA, Spera FR, Villano A, et al. Effect of smoking on endotheliumindependent vasodilatation. Atherosclerosis 2015;240:330–2. doi: 10.1016/j.atherosclerosis.2015.03.041. Epub April 1, 2015. PMID: 25875383.
- [33] Messner B, Bernhard D. Smoking and cardiovascular disease: mechanisms of endothelial dysfunction and early atherogenesis. Arterioscler Thromb Vasc Biol 2014;34:509–15. doi: 10.1161/ATV-BAHA.113.300156. PMID: 24554606.
- [34] Toda N, Okamura T. Obesity impairs vasodilatation and blood flow increase mediated by endothelial nitric oxide: an overview. J Clin Pharmacol 2013;53:1228–39. doi: 10.1002/jcph.179. Epub September 30, 2013. PMID: 24030923.