Journal of Cardiology (2008) **52**, 79—85

ELSEVIER

JOURNAL of CARDIOLOGY
Official Journal of the Japanese College of Cardiology
www.elsevier.com/locate/jjcc

ORIGINAL ARTICLE

Beneficial effects of Waon therapy on patients with chronic heart failure: Results of a prospective multicenter study

Masaaki Miyata (MD, FJCC)[a], Takashi Kihara (MD)[a], Takuro Kubozono (MD)[a], Yoshiyuki Ikeda (MD)[a], Takuro Shinsato (MD)[a], Toru Izumi (MD, FJCC)[b], Masunori Matsuzaki (MD, FJCC)[c], Tetsu Yamaguchi (MD, FJCC)[d], Hiroshi Kasanuki (MD, FJCC)[e], Hiroyuki Daida (MD, FJCC)[f], Masatoshi Nagayama (MD)[g], Kazuhiro Nishigami (MD)[h], Kumiko Hirata (MD)[i], Koichi Kihara (MD)[j], Chuwa Tei (MD, FJCC)[a,*]

[a] *Department of Cardiovascular, Respiratory and Metabolic Medicine, Graduated School of Medicine, Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima 890-8520, Japan*
[b] *Department of Cardiology, Kitasato University School of Medicine, Sagamihara, Japan*
[c] *Division of Cardiology, Department of Medicine and Clinical Science, Graduate School of Medicine, Yamaguchi University, Ube, Japan*
[d] *Department of Cardiovascular Center Medicine, Toranomon Hospital, Tokyo, Japan*
[e] *Department of Cardiology, Tokyo Women's Medical University, Tokyo, Japan*
[f] *Department of Cardiovascular Medicine, Juntendo University, Tokyo, Japan*
[g] *Department of Cardiology, Sakakibara Heart Institute, Tokyo, Japan*
[h] *Division of Cardiology, Saiseikai Kumamoto Hospital Cardiovascular Center, Kumamoto, Japan*
[i] *Division of Cardiology, Higashisumiyoshi Morimoto Hospital, Osaka, Japan*
[j] *Division of Cardiology, Fujimoto Hayasuzu Hospital, Miyakonojo, Japan*

Received 17 June 2008; accepted 3 July 2008
Available online 27 August 2008

KEYWORDS
Waon therapy;
Heart failure;
Treatment

Summary
Background: We conducted a prospective multicenter case—control study to confirm the clinical efficacy and safety of Waon therapy on chronic heart failure (CHF).
Methods: Patients ($n = 188$) with CHF were treated with standard therapy for at least 1 week, and then were randomized to Waon therapy ($n = 112$) or a control group ($n = 76$). All patients continued conventional treatment for an additional 2 weeks.

* Corresponding author. Tel.: +81 99 275 5316; fax: +81 99 275 5322.
E-mail addresses: miyatam@m3.kufm.kagoshima-u.ac.jp (M. Miyata), tei@m.kufm.kagoshima-u.ac.jp (C. Tei).

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doi:10.1016/j.jjcc.2008.07.009

Natriuretic peptides;
Brain;
Non-pharmacological therapy

The Waon therapy group was treated daily with a far infrared-ray dry sauna at 60 °C for 15 min and then kept on bed rest with a blanket for 30 min for 2 weeks. Chest radiography, echocardiography, and plasma levels of brain natriuretic peptide (BNP) were measured before and 2 weeks after treatment.
Results: NYHA functional class significantly decreased after 2 weeks of treatment in both groups. Chest radiography also showed a significant decrease of the cardiothoracic ratio in both groups (Waon therapy: 57.2 ± 8.0% to 55.2 ± 8.0%, $p < 0.0001$; control: 57.0 ± 7.7% to 56.0 ± 7.1%, $p < 0.05$). Echocardiography demonstrated that left ventricular diastolic dimension (LVDd), left atrial dimension (LAD), and ejection fraction (EF) significantly improved in the Waon therapy group (LVDd: 60.6 ± 7.6 to 59.1 ± 8.4 mm, $p < 0.0001$; LAD: 45.4 ± 9.3 mm to 44.1 ± 9.4 mm, $p < 0.05$; EF: 31.6 ± 10.4% to 34.6 ± 10.6%, $p < 0.0001$), but not in the control group (LVDd: 58.4 ± 10.3 mm to 57.9 ± 10.4 mm; LAD: 46.3 ± 9.7 mm to 46.2 ± 10.1 mm; EF: 36.6 ± 14.1% to 37.3 ± 14.0%). The plasma concentration of BNP significantly decreased with Waon therapy, but not in the control group (Waon: 542 ± 508 pg/ml to 394 ± 410 pg/ml, $p < 0.001$; control: 440 ± 377 pg/ml to 358 ± 382 pg/ml).
Conclusion: Waon therapy is safe, improves clinical symptoms and cardiac function, and decreases cardiac size in CHF patients. Waon therapy is an innovative and promising therapy for patients with CHF.
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Introduction

Chronic heart failure (CHF) is a major and growing public health problem in Japan, as in other developed countries. Drugs that interfere with excessive activation of the rennin—angiotensin—aldosterone system can relieve the symptoms of heart failure in patients with a depressed ejection fraction (EF) by stabilizing and/or reversing cardiac remodeling. Thus, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), and β blockers have emerged as cornerstones of modern heart failure therapy for patients with a depressed EF [1]. Angiotensin II plays an important role in the pathogenesis of CHF, and many large clinical trials have demonstrated the benefits of ACE inhibitors [2,3], and ARBs [4—8] on the morbidity and mortality of CHF. However, the number of heart failure deaths has increased steadily despite advances in treatment, in part, because of increasing numbers of patients with CHF due to better treatment and salvage of patients with acute myocardial infarction earlier in life [9].

We developed a form of thermal therapy that differs from the traditional sauna [10], and have been investigating the effects of thermal therapy since 1989. We discovered that the new thermal therapy offers prominent beneficial effects for patients with CHF [10—13] and peripheral artery disease [14,15]. Thermal therapy at very high temperature was originally used to treat localized cancer. However, the therapy we developed to treat cardiovascular diseases is quite different, in that it consists of systemic soothing warmth that comfortably refreshes the mind and body. Therefore, we have changed the name from thermal, to ''Waon'' therapy, since ''Waon'' in Japanese means soothing warmth [16]. Waon therapy is defined as ''therapy in which the entire body is warmed in an evenly heated chamber for 15 min at a temperature that soothes the mind and body, and after the deep-body temperature has increased by approximately 1.0—1.2 °C, the soothing warmth is sustained by maintaining the warmth at rest for an additional 30 min, with fluids supplied at the end to replace the loss from perspiration'' [16]. We have reported that Waon therapy, the repeated use of a dry sauna at 60 °C, improves hemodynamics and ameliorates symptoms, suppresses ventricular arrhythmias, and improves vascular function in CHF patients [10—13]. We have already performed Waon therapy in several hundred CHF patients in our hospital without any severe adverse effects.

In order to expand the use of Waon therapy, we developed a movable and sitting-position sauna system, in which the temperature at the top and bottom of the chamber is uniformly maintained at the same temperature of 60 °C (Fig. 1). Using this sitting-position sauna system, we conducted a prospective multicenter case—control study to confirm the clinical effect and safety of Waon therapy on CHF at 10 different hospitals.

Subjects and methods

Subjects

Ten hospitals participated in this multicenter study: Kagoshima University Hospital, Kitasato University Hospital, Sakakibara Memorial Hospital, Yamaguchi University Hospital, Juntendo University Hospital, Tokyo Women's Medical University Hospital, Toranomon Hospital, Higashisumiyoshi Morimoto Hospital, Saiseikai Kumamoto Hospital, and Fujimoto Hayasuzu Hospital. We enrolled 188 patients with CHF, aged 26—94 years (mean age: 64.7 ± 13.7 years). 94 patients had idiopathic dilated cardiomyopathy, 45 had ischemic cardiomyopathy, 16 patients had valvular heart disease, and 33 patients had other heart disease (7 hypertensive heart disease, 10 hypertrophic cardiomyopathy, 4 dilated hypertrophic cardiomyopathy, 3 cardiac sarcoidosis, 3 restrictive cardiomyopathy, 2 atrial septal defect, 1 cardiac amyloidosis, 1 drug-induced cardiomyopathy, 1 alcoholic cardiomyopathy, and 1 left ventricular noncompaction).

Inclusion criteria were the presence of symptomatic CHF, left ventricular ejection fraction (LVEF) <50% on echocardiography, and New York Heart Association (NYHA) functional classes II—IV. Exclusion criteria were the presence of severe aortic stenosis, severe obstruction with hypertrophic obstructive cardiomyopathy, and high fever due to infectious disease. Informed consent was obtained from all of the patients before participation. This protocol was approved by the Ethics Committee of the Faculty of Medicine, Kagoshima University.

Design of the study protocol

All patients could receive any kind of medication for CHF and doctors also could change the medication during the study. The subjects were treated with conventional therapy for at least 1 week, and then were randomized to the Waon therapy group or a control group at each hospital. The patients in the Waon therapy group received thermal therapy daily, 5 days a week, for 2 weeks. The patients in the control group continued the conventional treatment for 2 more weeks.

Waon therapy

Waon therapy uses a far infrared-ray dry sauna, which is evenly maintained at 60 °C and differs from traditional sauna. Waon therapy has an absence of hydration pressure, and was performed as previously reported [10]. Briefly, the patients were placed in a sitting-position in a 60 °C sauna system for 15 min, and then after leaving the sauna, they underwent bed rest with a blanket to keep them warm for an additional 30 min. All patients were weighed before and after the therapy, and oral hydration with water was used to compensate for weight lost due to perspiration. Waon therapy was performed once a day, 5 days a week for 2 weeks, for a total of 10 sessions. To rule out any acute effects of Waon therapy, all examinations were performed before the first treatment and on the next day after the last treatment.

Figure 1 Movable and sitting-position sauna system. The temperature at the top and bottom of the chamber is uniformly maintained at the same temperature of 60 °C.

Measurements

Physical examination

The blood pressure (BP), pulse rate, body weight, and body temperature were measured before and 2 weeks after treatment.

Cardiac function

The clinical state of CHF was evaluated by NYHA functional class. Before and 2 weeks after treatment, the cardiothoracic ratio (CTR) was measured by chest radiography and left ventricular diastolic dimension (LVDd), left atrial dimension (LAD), and

Table 1 Baseline clinical characteristics and changes in several variables

	Waon therapy group ($n=112$)			Control group ($n=76$)			Comparison at baseline[a]
	Baseline	After 2 weeks	*p*-Value	Baseline	After 2 weeks	*p*-Value	*p*-Value
Age (years)	63 ± 13			66 ± 14			NS
Gender (male/female)	74/38			51/25			NS
DCM/ICM/VD/other disease	62/29/7/14			32/16/9/19			NS
NYHA functional class (average)	2.61 ± 0.62	1.99 ± 0.60	<0.0001	2.51 ± 0.62	2.23 ± 0.48	<0.01	NS
Body weight (kg)	56.7 ± 11.8	55.9 ± 11.4	<0.0001	54.6 ± 12.0	54.6 ± 12.5	NS	NS
Heart rate (beats/min)	74 ± 15	72 ± 13	NS	74 ± 13	71 ± 11	NS	NS
Systolic BP (mm Hg)	108 ± 21	104 ± 18	<0.01	110 ± 21	106 ± 19	<0.05	NS
Diastolic BP (mm Hg)	64 ± 12	62 ± 11	<0.01	67 ± 12	65 ± 10	<0.05	NS

DCM, dilated cardiomyopathy; ICM, ischemic cardiomyopathy; VD, valvular disease; NYHA, New York Heart Association; BP, blood pressure; and NS, not significant.
[a] Comparison with baseline values. Data are presented as the mean value ± S.D.

LVEF were evaluated by conventional echocardiography.

Laboratory measurements

A fasting blood sample was obtained in the morning to measure the plasma concentrations of the brain natriuretic peptide (BNP) with radioimmunoassay, before and 2 weeks after treatment.

Statistical analysis

All data are expressed as the mean value ± S.D. Differences in baseline characteristics were evaluated by a χ^2 test and unpaired *t*-test. The data before and 2 weeks after treatment were compared using a paired *t*-test. A *p*-value of <0.05 was considered statistically significant.

Results

Baseline clinical characteristics

The baseline clinical characteristics are summarized in Table 1. There were no significant differences in age, gender, causative heart disease, NYHA functional class, body weight, heart rate, systolic BP (SBP), or diastolic BP (DBP) at baseline between the two groups.

Clinical findings and physical examinations

During the study, none of the patients treated with Waon therapy had worsened clinical symptoms. The changes in the clinical findings and variables after 2 weeks are summarized in Table 1. NYHA functional class, SBP, and DBP significantly decreased in both groups. Body weight significantly decreased in the Waon therapy group, but not in the control group. There were no significant changes in heart rate in either group.

Chest radiography and echocardiography

Fig. 2 shows the results of chest radiography and echocardiography. Chest radiography showed a significant decrease of the CTR after 2 weeks of treatment in both groups (Waon therapy group: 57.2 ± 8.0% to 55.2 ± 8.0%, $p < 0.0001$; control group: 57.0 ± 7.7% to 56.0 ± 7.1%, $p < 0.05$). In addition, echocardiography demonstrated that LVDd, LAD, and LVEF significantly improved after Waon therapy (LVDd: 60.6 ± 7.6 mm to 59.1 ± 8.4 mm, $p < 0.0001$; LAD: 45.4 ± 9.3 mm to 44.1 ± 9.4 mm,

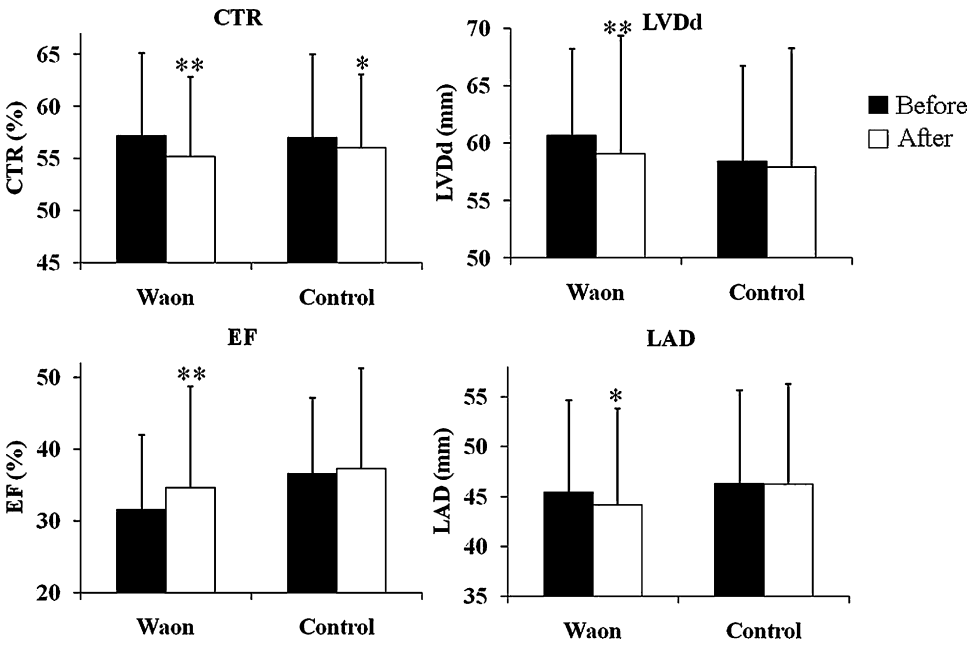

Figure 2 Data from chest radiography and echocardiography. Chest radiography showed a significant decrease of the cardiothoracic ratio (CTR) after 2 weeks of treatment in both groups. Echocardiography demonstrated that left ventricular diastolic dimension (LVDd), left atrial dimension (LAD), and left ventricular ejection fraction (LVEF) significantly decreased after 2 weeks of Waon therapy, but did not change after 2 weeks of conventional therapy in the control group. *$p < 0.05$ vs. baseline; **$p < 0.0001$ vs. baseline. Closed bars show baseline and open bars indicate values after 2 weeks of treatment.

$p < 0.05$; LVEF: $31.6 \pm 10.4\%$ to $34.6 \pm 10.6\%$, $p < 0.0001$), but did not change in the control group (LVDd: 58.4 ± 10.3 mm to 57.9 ± 10.4 mm, not significant; LAD: 46.3 ± 9.7 mm to 46.2 ± 10.1 mm, not significant; LVEF: $36.6 \pm 14.1\%$ to $37.3 \pm 14.0\%$, not significant).

Plasma levels of BNP

Fig. 3 shows the changes in plasma concentration of BNP. The plasma concentration of BNP significantly decreased after 2 weeks of Waon therapy, while it did not change in the control group (Waon therapy group: 542 ± 508 pg/ml to 394 ± 410 pg/ml, $p < 0.001$; control group: 440 ± 377 pg/ml to 358 ± 382 pg/ml, not significant).

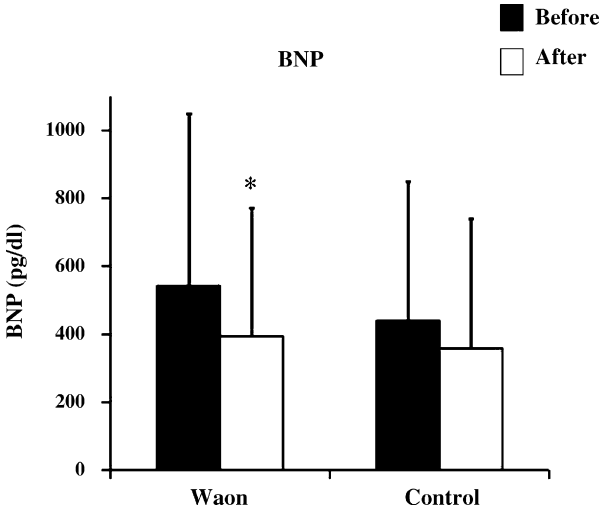

Figure 3 Changes in plasma concentration of BNP. The plasma concentration of BNP significantly decreased after 2 weeks of Waon therapy, but did not change in the control group. *$p < 0.001$ vs. baseline. Closed bars show baseline and open bars indicate values after 2 weeks of treatment.

Discussion

We developed the sitting-position sauna system, and conducted a prospective multicenter case–control study to confirm the clinical efficacy and safety of Waon therapy on CHF at 10 hospitals. In this study, we confirmed that Waon therapy improved clinical symptoms and cardiac function evaluated by echocardiography and BNP concentrations, and decreased cardiac size on chest radiography and echocardiography after 2 weeks of Waon therapy in patients with CHF. We also demonstrated that our movable and sitting-position sauna system is effective and safe for patients with CHF.

Regarding the acute effect of Waon therapy, we have reported that 60 °C sauna therapy for 15 min improved acute hemodynamics in patients with CHF, including cardiac index, mean pulmonary wedge pressure, systemic and pulmonary resistance, and cardiac function [10]. Subsequently, we examined the chronic effects of repeated Waon therapy on clinical symptoms and cardiac function in patients with CHF and have reported that 4 weeks of Waon therapy significantly improved clinical symptoms, increased ejection fraction, and decreased cardiac size on the echocardiogram and chest X-ray [10,11]. Furthermore, we demonstrated that daily Waon therapy for 2 weeks decreased ventricular premature contractions and increased heart rate variability (SDNN, standard deviation of normal-to-normal beat interval) in patients with CHF, suggesting that Waon therapy decreased sympathetic nervous activity and improved ventricular arrhythmias [13].

We then investigated the vascular endothelial function to clarify the mechanisms of the effect of Waon therapy on CHF, since vascular endothelial function had been reported to be impaired in CHF. We have reported that 2 weeks of Waon therapy significantly reduced BNP concentrations and improved endothelial function in patients with CHF. There was a significant correlation between the change in %FMD (flow-mediated dilatation) and the percent improvement in BNP concentrations in the Waon therapy group [12].

In order to confirm the effect of Waon therapy on CHF and clarify its mechanism, we performed experimental studies using TO-2 cardiomyopathic hamsters with heart failure. We reported that the repeated Waon therapy improved survival in TO-2 cardiomyopathic hamsters with heart failure [17]. We clarified that one of the molecular mechanisms by which repeated Waon therapy improved endothelial function was an increase in mRNA and protein of endothelial nitric oxide synthase (eNOS) in Syrian golden hamsters [18] and TO-2 cardiomyopathic hamsters [19]. We believe that eNOS up-regulation induced by repeated Waon therapy is caused by an increase in cardiac output and blood flow, which in turn results in increased shear stress, although thermal stimulation might up-regulate arterial eNOS directly.

Compared to pharmacological vasodilator therapy and other non-pharmacological therapy, such as cardiac resynchronization therapy and physical therapy, there are several advantages of Waon therapy for CHF. First, it is quite safe and has no adverse effects. Second, it is less expensive and more cost-effective. Third, unlike physical therapy, patients who are elderly or have severe congestive heart failure, uncontrolled ventricular arrhythmias, and orthopedic limitations are not exempt from undergoing Waon therapy. Fourth, this treatment promotes mental and physical relaxation. Waon therapy may thus be a valuable adjunct to pharmacological or non-pharmacological intervention in the management of CHF.

We have treated many CHF patients with Waon therapy, and none of the patients so far has shown any deterioration in their condition. However, Waon therapy does not appear to be indicated for CHF patients with severe aortic stenosis or obstructive hypertrophic cardiomyopathy, because the pressure gradient might be increased during Waon therapy. Patients with infectious disease are also excluded from Waon therapy.

Study limitations

We have already reported that repeated Waon therapy improved the prognosis of TO-2 cardiomyopathic hamsters with CHF, suggesting a new potential non-pharmacologic therapy for CHF [17]. The ultimate goal of treatment is the improvement of prognosis and quality of life. Therefore, we must evaluate the effect of Waon therapy on prognosis, as well as quality of life, in patients with CHF. We are conducting a prospective clinical randomized study to assess the impact of Waon therapy on the rate of cardiac death or re-hospitalization in patients with CHF.

Conclusion

In this prospective multicenter study, we confirmed that Waon therapy is quite safe, improved clinical symptoms and cardiac function, and decreased cardiac size in patients with CHF. Therefore, Waon therapy is an innovative and promising therapy for patients with CHF.

Acknowledgements

We appreciated Dr. Tsuyoshi Fukudome, Dr. Shoji Fujita, and Dr. So Kuwahata in Kagoshima University, Dr. Chiharu Noda in Kitasato University, Dr. Shigeki Kobayashi in Yamaguchi University, Dr. Katsuyuki Masaki in Juntendo University, Dr. Kazue Watanabe in Tokyo Women's Medical University, and Dr. Minoru Ohno in Toranomon Hospital for collecting data at each hospital.

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