Waon Therapy Improves Quality of Life as Well as Cardiac Function and Exercise Capacity in Patients With Chronic Heart Failure

Mitsuo Sobajima,[1] MD, Takashi Nozawa,[1] MD, Yasutaka Fukui,[1] MD, Hiroyuki Ihori,[1] MD, Takashi Ohori,[1] MD, Nozomu Fujii,[1] MD, *and* Hiroshi Inoue,[1] MD

Summary

Waon therapy (WT), which in Japanese means soothing warmth, is a repeated sauna therapy that improves cardiac and vascular endothelial function in patients with chronic heart failure (CHF). We investigated whether WT could improve the quality of life (QOL) of CHF patients in addition to improving cardiac function and exercise capacity.

A total of 49 CHF patients (69 ± 14 years old) were treated with a 60°C far infrared-ray dry sauna bath for 15 minutes and then kept in a bed covered with blankets for 30 minutes once a day for 3 weeks. At baseline and 3 weeks after starting WT, cardiac function, 6-minute walk distance (6MWD), flow mediated dilation (FMD) of the brachial artery, and SF36-QOL scores were determined.

WT significantly improved left ventricular ejection fraction (LVEF), B-type natriuretic peptide (BNP), 6MWD, and FMD (3.6 ± 2.3 to 5.1 ± 2.8%, $P < 0.01$). Moreover, WT significantly improved not only the physical (PC) but also mental component (MC) of the QOL scores. WT-induced improvement of PC was negatively correlated with changes in BNP ($r = -0.327$, $P < 0.05$), but MC improvement was not related directly to changes in BNP, LVEF, or 6MWD. WT-induced changes in MC were not parallel to PC improvement.

WT improved QOL as well as cardiac function and exercise capacity in patients with CHF. Mental QOL improved independently of WT-induced improvement of cardiac function and exercise capacity. (Int Heart J 2015; 56: 203-208)

Key words: SF-36, Flow mediated dilation, Natural killer cell, Sauna

Recent studies have shown that repeated sauna therapy called Waon therapy (WT) improves not only cardiac and endothelial function but also prognosis in patients with chronic heart failure (CHF).[1-3] The precise mechanisms of the salutary effects of WT in CHF treatment are not yet fully understood, although WT-induced vasodilation and improvement of endothelial function through up-regulation of endothelial nitric oxide synthase (eNOS) could contribute to the beneficial effects.[4,5]

Depressive symptoms are common in patients with CHF and many CHF patients have impairment of all aspects of their quality of life (QOL) as assessed by SF-36 scores.[6] Moreover, having depressive illness or impaired QOL in CHF patients is linked to a worse prognosis.[7-9] Therefore, QOL would be a more important target for the management of CHF patients. Angiotensin converting enzyme (ACE) inhibitors or β-blockers improve cardiac function and prognosis in patients with CHF.[10-12] However, there have been conflicting results as to whether these drugs also improve QOL.[13,14] Depression was found to be related to reduced heart rate variability,[15] blunted baroreflex sensitivity,[16] and heightened sympathetic nervous activity,[17] while WT restored autonomic imbalance in CHF patients who were associated with sympathetic activation and parasympathetic withdrawal.[18] Mild warming exhibited sedative effects through the sensory nerve endings,[19] and thermal stimulus enhanced plasma levels of β-endorphin.[20,21] Accordingly, the present study aimed to investigate whether WT could improve QOL in CHF patients in addition to improving cardiac function and exercise capacity.

Methods

Subjects and study design: The present study was approved by the ethics committee of Toyama University Hospital and written informed consent was obtained from all patients.

A total of 49 consecutive patients who met the following criteria constituted the study group. First, the patient had CHF-associated symptoms of New York Heart Association (NYHA) functional class ≧ II, previous hospitalization for worsening of heart failure, or both. Second, the patient was in a stable condition and not receiving any intravenous injection drugs at the time of enrollment. WT was performed during hospitalization. No medication was changed during the study period.

From the [1] Second Department of Internal Medicine, Graduate School of Medicine, University of Toyama, Toyama, Japan.

Address for correspondence: Mitsuo Sobajima, MD, The Second Department of Internal Medicine, Graduate School of Medicine, University of Toyama, 2630 Sugitani, Toyama 930-0194, Japan. E-mail: sobajima@med.u-toyama.ac.jp

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Waon therapy: The methods of WT were described previously.[3] Briefly, once a day for three weeks, patients underwent a far-infrared-ray dry sauna therapy at 60°C for 15 minutes and were then kept supine on a bed outside the bath room for 30 minutes with sufficient warmth provided by blankets resulting in an increase in the core temperature by 1.0°C to 1.2°C. Patients were weighed before and after the sauna therapy, and oral hydration with water was given to compensate for the lost weight.

Evaluation of cardiac function and Specific Activity Scale (SAS): We performed echocardiography and also evaluated brain natriuretic peptide (BNP), NYHA, 6-minute walk distance (6MWD) and SAS to determine the state of heart failure. The SAS is based on approximations of the metabolic costs of a variety of personal care, housework, occupational, and recreational activities. SAS was determined from interviews about daily physical activities.[22] Left ventricular end-diastolic and end-systolic dimensions were measured by 2-dimensional echocardiography (Aplio SSA-770A; Toshiba, Ohtawara, Japan). Left ventricular ejection fraction (LVEF) was calculated using the Teichholz method.

Flow-mediated vasodilation: Vascular endothelial function was evaluated by flow-mediated vasodilation (FMD) of the brachial artery.[3] Patients were instructed to fast overnight and to abstain from smoking and consuming any caffeine and medications for at least 12 hours prior to FMD testing. Vasodilation responses of the brachial artery were determined by ultrasound using a semi-automatic device (EF18G; UNEX, Nagoya, Japan). A blood pressure cuff was inflated to 50 mmHg above the systolic blood pressure for 5 minutes. The changes in diastolic diameter were continuously recorded, and FMD was determined as the maximum change in the diameter after cuff release normalized to the baseline diameter (% of baseline diameter).

Natural killer cell activity: Natural killer cells were isolated directly from peripheral blood mononuclear cells. Blood samples were collected in tubes containing citrate phosphate dextrose. Natural killer (NK) cell activity was measured using ^{51}Cr-labeled K562 targets. Effector and target cells were incubated at 37°C for 4.5 hours in plates. A well contained 1×10^4 target cells and 2×10^5 effector cells, and wells with only K562 in the medium or with 1% Triton X were used to evaluate spontaneous and maximum releases. The supernatant was collected and the percentage of cytotoxicity was calculated.

SF-36 QOL scores: Patient self-assessment of health-related QOL was performed using the Japan version of SF-36.[23,24] SF-36 is a generic health survey designed to assess aspects of health that are not specific to disease, treatment, or age. The questionnaire assesses 8 dimensions of physical and mental health: physical functioning (PF, 10 items); role limitations due to physical problems (RP, 4 items); body pain (BP, two items); general perception of health (GH, 5 items); energy and vitality (VT, 4 items); social functioning (SF, two items); role limitations due to emotional problems (RE, 3 items); and mental health (MH, 5 items). Scores for the 8 dimensions were coded, summed and transformed onto a scale from 0 (worst possible health) to 100 (best possible health) using the method described in the user manual. The data are summarized using norm based scores. Norm base scores were calculated by subtracting the adjusted mean scores of the general population sample from the adjusted mean scores of the disease group and dividing this difference by the adjusted standard deviations of the general population. The summarized assessment of each questionnaire was added in areas of physical and mental health; physical (PC) and mental components (MC), respectively.

Statistics: Results are expressed as the mean ± SD. The differences between baseline and post-treatment parametric values were analyzed using the paired Student's *t* test. Non-parametric pair-wise comparisons were made using the Wilcoxon rank sum test. Multiple linear regression analysis was performed to identify the independent determinants of Waon therapy-induced changes in the SF36 score, especially PC and MC. A $P < 0.05$ was considered statistically significant. Statistical analyses were performed with SPSS (SPSS 11.0J; International Business Machines Corporation, Chicago, IL, USA).

Results

The characteristics of the study group are summarized in the Table I. Twenty patients had ischemic cardiomyopathy and 29 patients nonischemic cardiomyopathy. More than 60% of the patients were treated with β-blockers and 86% with angiotensin converting enzyme inhibitors or angiotensin receptor blockers.

The effects of 3-week WT are summarized in Table II. No patient exhibited a worsening of clinical symptoms or suffered from complications due to WT. WT significantly improved NYHA functional class, SAS, and 6MWD. LVEF and NK cell activity were slightly but significantly increased, and plasma levels of BNP were reduced after WT. WT improved vascular endothelial function assessed by FMD.

As shown in Figure 1, CHF patients had lower QOL scores in all components of SF-36, compared to the average scores (= 50 points) of the Japanese general population. Three-week WT significantly improved the PF, GH, VT, and MH

Table I. Baseline Characteristics

Variables	
Age (years)	69.1 ± 14.3
Men	31 (63%)
Body mass index (kg/m^2)	21.7 ± 4.2
Cause of heart failure	
Non-ischemic cardiomyopathy	29 (59%)
Ischemic cardiomyopathy	20 (41%)
Co-morbidities	
Hypertension	19 (31%)
Diabetes mellitus	11 (22%)
Dyslipidemia	17 (35%)
Medications	
Digoxin	14 (29%)
β blocker	31 (63%)
ACE inhibitors/ARB	42 (86%)
Statins	20 (41%)
Diuretics	45 (92%)
Non-pharmacological therapy	
Pacemaker	4 (8%)
ICD/CRT	7 (14%)

Data are mean ± SD or number (%) of patients. ACE indicates angiotensin converting enzyme; ARB, angiotensin II receptor blocker; ICD, implantable cardioverter-defibrillator; and CRT, cardiac resynchronization therapy.

Table II. Comparisons of Data Between Before and After Waon Therapy

Variables	Before	After	*P*
Heart rate (beats/minute)	74 ± 12	73 ± 12	0.41
Systolic BP (mmHg)	108 ± 20	107 ± 23	0.13
Diastolic BP (mmHg)	65 ± 10	62 ± 12	0.09
Body weight (kg)	54 ± 16	54 ± 15	0.45
NYHA class			< 0.05
I	6	9	
II	15	18	
III	28	22	
IV	0	0	
SAS (METs)	4.3 ± 1.6	4.7 ± 1.4	< 0.01
6MWD (m)	323 ± 122	366 ± 128	< 0.01
LVEDD (mm)	64 ± 12	62 ± 11	< 0.01
LVESD (mm)	54 ± 13	51 ± 13	< 0.01
LVEF (%)	33 ± 13	37 ± 15	< 0.01
Left atrial dimension (mm)	47 ± 8	44 ± 9	< 0.01
BUN (mg/dL)	27 ± 14	27 ± 15	0.83
Creatinine (mg/dL)	1.2 ± 0.9	1.3 ± 1.3	0.22
LDL cholesterols (mg/dL)	113 ± 29	107 ± 27	0.06
HDL cholesterols (mg/dL)	51 ± 15	49 ± 14	0.08
Triglycerides (mg/dL)	121 ± 58	114 ± 50	0.10
Blood sugar (mg/dL)	97 ± 27	95 ± 21	0.62
BNP (pg/dL)	455 ± 474	354 ± 383	< 0.01
Plasma NE (pg/mL)	386 ± 266	351 ± 217	0.27
NK cell activity (%)*	21.2 ± 14.5	24.1 ± 16.7	< 0.05
FMD (%)	3.6 ± 2.3	5.1 ± 2.8	< 0.01

Data are mean ± SD or number of patients. BP indicates blood pressure; NYHA, New York Heart Association; SAS, specific activity scale; 6MWD, 6-minute walk distance; LVEF, left ventricular (LV) ejection fraction; LVEDD and LVESD, LV end-diastolic and end-systolic dimensions, respectively; BNP, B type natriuretic peptide; NE, norepinephrine; NK cell, natural killer cell; and FMD, flow mediated dilation. *NK cell activity was determined in 32 patients.

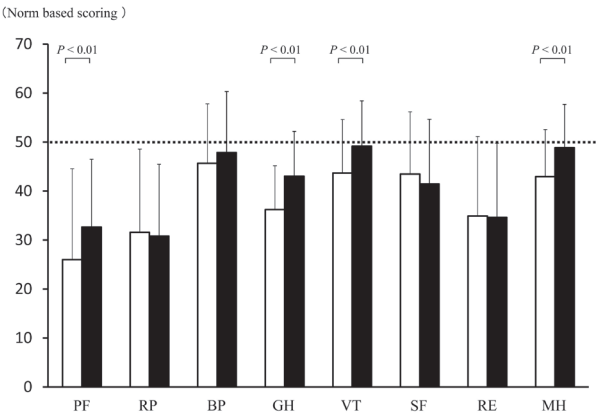

Figure 1. Comparison of SF36-QOL score between before and after 3-week Waon therapy in patients with chronic heart failure. White and black bars indicate the score for before and after Waon therapy, respectively. PF indicates physical functioning; RP, role limitations due to physical problems; BP, body pain; GH, general perception of health; VT, vitality; SF, social functioning; RE, role limitations due to emotional problems; and MH, mental health. Data are mean + SD.

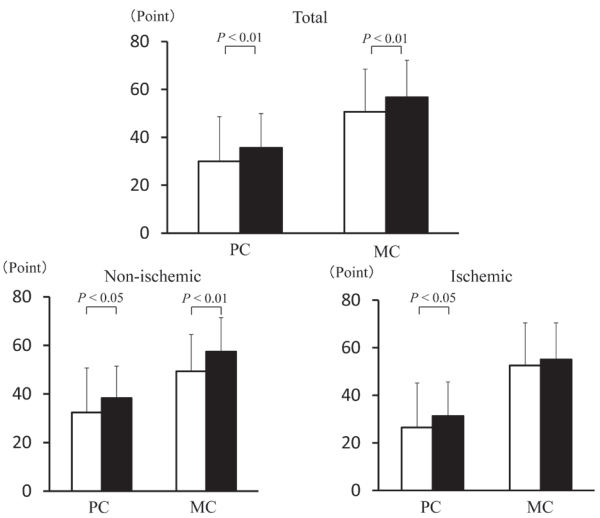

Figure 2. Physical (PC) and mental components (MC) assessed by SF36-QOL scores before (white bars) and after 3-week Waon therapy (black bars) in all patients (top), non-ischemic patients (n = 29, lower light), and ischemic patients (n = 20, lower right). Data are mean + SD.

scores. Both PC and MC, which are summarized assessments of SF-36 questionnaire in each area of physical and mental health, were significantly improved by WT, especially in the nonischemic group (Figure 2). Multivariate analysis revealed that WT-induced changes in PC were independently related to its baseline score before WT, while WT-induced changes in MC were independently related to systolic blood pressure and MC score at baseline (Table III). That is, the improvement of PC and MC was greater in patients with low PC scores before starting WT and in those with low systolic blood pressure and low MC scores before WT, respectively.

WT-induced improvement of PC was not related to changes in LVEF or 6MWD, but was negatively correlated with changes in BNP (r = -0.327, $P < 0.05$), ie, when patients had greater reduction of BNP levels, they had greater improvement of PC scores after WT. However, WT-induced improvement of MC was not related directly to changes in BNP, LVEF, or 6MWD. Thus, WT improved MC scores independently of changes in LV function and exercise tolerance. Moreover, WT-induced improvement of MC was not related to changes in PC (Figure 3).

Discussion

The major findings of the present study were as follows. Firstly, 3-week WT improved exercise tolerance, and cardiac and endothelial function in patients with CHF, a finding consistent with previous studies.[3,4] Secondly, WT improved both the PC and MC scores of patients' self-assessment of health-related QOL. Moreover, CHF patients with severely impaired MC and PC at baseline gained greater improvement of both components by WT. Finally, WT improved mental QOL independently of its effects on cardiac function and exercise tolerance, and the improvement of MC was not related directly to changes in PC.

The prognosis of patients with CHF was very poor and QOL was severely restricted in CHF patients.[6,25] Symptoms of depression were common and associated with an adverse prog-

Table III. Determinants of Waon Therapy-Induced Changes in SF-36 Components

Variables at baseline	Univariate		Multivariate	
	r	*P*	β coefficient	*P*
I. Changes in physical component				
BNP	0.31	0.017	0.001	0.995
Baseline PC	-0.54	0.000	-0.492	0.000
II. Changes in mental component				
Systolic blood pressure	-0.35	0.013	-0.327	0.019
BNP	0.31	0.028	0.177	0.171
Baseline MC	-0.49	0.000	-0.383	0.006

Univariate and multivariate analyses were performed to identify the determinants of Waon therapy-induced changes in physical and mental components (PC and MC) assessed by SF-36. The following variables at baseline were included in these analyses; age, systolic blood pressure, heart rate, flow-mediated vasodilation, B type natriuretic peptide (BNP), plasma norepinephrine, left ventricular ejection fraction, 6-minute walk distance, and physical and mental components before Waon therapy.

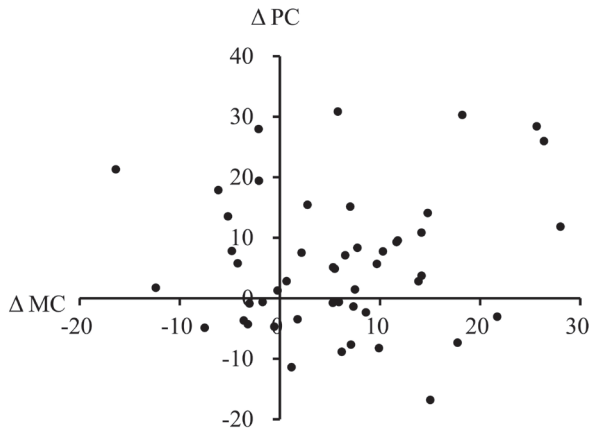

Figure 3. Relation between Waon therapy-induced changes in physical (PC) and mental components (MC) assessed by SF-36 scores (n = 49). There was no relation between changes in these components.

nosis in patients with CHF.[7-9] In a large clinical trial,[26] activities of daily living, general health, and heart failure symptoms were the independent and strongest predictors of mortality and hospitalization after adjustment for LVEF, age, NYHA functional class, and type of treatment. Thus, QOL would be a more important target for the management of CHF patients.

Angiotensin converting enzyme (ACE) inhibitors or β-blockers improve cardiac function and prognosis in patients with CHF.[10-12] However, there have been conflicting results as to whether these drugs improve QOL.[13,14] The SOLVD study[27] revealed a limited effect of enalapril on QOL, while there were no significant improvements in somatic symptoms, emotions, or physical limitations after 12 weeks in ramipril treatment.[28] Among studies of the effects of β-blockers on health-related QOL assessed by the Quality of Life Questionnaire in Severe Heart Failure and the Minnesota Living with Heart Failure Questionnaire, only a few studies reported significant improvements in QOL scores.[14] Jenkinson, *et al*[29] reported little difference of QOL assessed by SF-36 between before and after 4-week treatment with an ACE inhibitor in elderly patients with CHF. By contrast a sub-study of the COMPANION trial[30] showed patients treated with cardiac resynchronization therapy had a significant improvement of QOL assessed by the Minnesota Living with Heart Failure Questionnaire in association with improvements of 6MWD and NYHA functional class, as compared to those treated with optimal medical therapy. In the present study, 3-week WT improved both physical and mental QOL in association with improved LV function and exercise tolerance in CHF patients.

WT improved not only PC of SF-36, but also MC. However, the improvement of MC was not directly related to changes in PC, and was independent of changes in LV function and exercise capacity. The mechanism of WT-induced improvement of mental QOL in patients with CHF remains unclear, but a previous study reported that 4-week WT diminished appetite loss and subjective complaints in mildly depressed patients.[31] Mild warming of the whole body exhibits sedative effects through sensory nerve endings,[19] and increased plasma levels of β-endorphin.[20,21]

There was a negative correlation between the changes in MC and systolic blood pressure before starting WT (Table III), ie, patients with lower systolic blood pressure at baseline received greater improvement of MC by WT. WT-induced improvement of MC was not different between patients treated with and without β-blocker. There was a positive correlation between the changes in MC and BNP at baseline in univariate analysis, ie, patients with higher BNP at baseline were associated with greater improvement of MC, although it did not reach statistical significance in multivariate analysis (Table III). WT may achieve greater benefit of mental QOL in patients with advanced heart failure, such as patients with higher BNP or lower systolic blood pressure before WT.

CHF is characterized by generalized sympathetic activation and parasympathetic withdrawal. Footbathing with mechanical stimulation produced changes in autonomic responses, indicating a shift to increased parasympathetic and decreased sympathetic activity in association with an increase in NK cell activity.[32] Patients with chronic insomnia were associated with nocturnal sympathetic arousal that was coupled with decrease in NK cell activity.[33] In the present study, NK cell activity significantly increased after WT, although plasma levels of norepinephrine did not decrease significantly by WT. Taken together, WT-induced improvement of mental QOL may result, at least in part, from the modulation of autonomic nervous activity, ie, a shift to parasympathetic predominance,[18] in addition to the soothing and relaxing effects of WT.[34]

Limitations: There were several limitations in the present re-

sults. First, the study consisted of a relatively small number of patients and lacked a control group that did not receive WT. The present patients who underwent WT once a day for 3 weeks were in hospital, and, therefore, a control study should also have been performed in hospital. CHF patients who were in a compensated, stable condition at the time of enrollment did not want to stay in hospital for more than 3 weeks without WT. The study period was relatively short and the long-term effect of WT remained undetermined. A further, large scale and randomized study will be required to draw a definitive conclusion. Second, QOL in patients with CHF was assessed using SF-36 in the present study, but not using other modules such as the Minnesota Living with Heart Failure Questionnaire and Kansas City Cardiomyopathy Questionnaire. Although the SF-36 is not specific to heart failure, it covers a wide range of QOL domains and is a well-validated instrument that has been used in a number of studies with cardiac patients.[6,25,29]

Although limited for these reasons, the present study indicated WT could improve mental and physical QOL in addition to improvement of cardiac and vascular endothelial function and exercise tolerance. Thus, WT could be a novel promising therapy for CHF.

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