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Waon Therapy is Effective as the Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome

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Abstract

Background: Myalgic Encephalomyelitis/Chronic fatigue syndrome (ME/CFS) is an illness characterized by disabling fatigue. We examined the applicability of Waon therapy as a new method of fatigue treatment in patients with ME/CFS.

Methods: Nine female ME/CFS patients (mean age, 38.4 ± 11.2 years old; range, 21–60) who fulfilled the criteria of the Canadian clinical case definition of ME/CFS participated in this study. Patients received 30 sessions of modified Waon therapy, infrared-ray dry sauna maintained at an even temperature of 40°C or 45°C for 15 minutes twice a day for 3 weeks in a hospital, or once a day for five weeks at an outpatient clinic. Their functional health and well-being scores were determined using SF-36 and compared with those of six ME/CFS patients who did not undergo Waon therapy.

Results: Seven of nine Waon therapy patients experienced a significant improvement in physical and mental condition, and the effect continued throughout the observation period. Waon therapy brought improvements in the scores of: Role physical ($p < 0.05$); Bodily pain ($p < 0.05$); General health perceptions ($p < 0.05$); and Role emotional ($p < 0.05$) of SF-36 in those who responded well (good responders) to the therapy. In two patients who responded poorly (poor responders) to Waon therapy, and in the non-Waon therapy patients, no significant improvement in the scores was observed.

Conclusions: Waon therapy is effective for the treatment of ME/CFS.

Keywords: myalgic encephalomyelitis, chronic fatigue syndrome, Waon therapy, thermal therapy, SF-36

I INTRODUCTION

Myalgic encephalomyelitis/Chronic fatigue syndrome (ME/CFS) is a serious disorder characterized by persistent post-exertional fatigue, unrefreshing sleep, pain and substantial symptoms related to cognitive, immune and autonomous dysfunction. Disease mechanisms are complex, with no single causal factor identified^{1)–3)}. Yet there are indications that infections and immunological dysfunction contribute to the development and maintenance of symptoms,

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probably interacting with genetic and psychosocial factors⁴⁾. There are many reports concerning treatment⁵⁾⁻¹³⁾. Because of the unclear etiology, diagnostic uncertainty, and the resultant heterogeneity of the ME/CFS population, there are no firmly-established recommended treatments at present for ME/CFS. In 1989, Dr. Chuwa Tei developed a form of thermal therapy for heart failure that utilizes a far-infrared ray dry sauna with temperature maintained at 60°C, which differs from the traditional sauna. In 2007, he changed the therapy's name to "Waon therapy". "Wa" means 'soothing', while "On" means 'warmth', hence "Waon" or "soothing warmth", implying a warmth that comfortably refreshes the mind and body¹⁴⁾. In 2005, Masuda & Tei reported on two CFS cases in which thermal therapy using a far-infrared ray sauna improved the patients' subjective symptoms¹⁵⁾. In Canada, far-infrared ray saunas are approved by the Canadian Standards Association and are sold to the public. The sauna manufacturers claim numerous health benefits; however, the published evidence to substantiate these claims is limited. In a review paper of the literature concerning the health benefits of far-infrared sauna use, R. Beever quoted Masuda's paper stating that there was weak preliminary support for far-infrared sauna therapy in treating chronic fatigue syndrome¹⁶⁾.

Waon therapy using far-infrared ray saunas may be a promising method for the treatment of ME/CFS. We examined the applicability of Waon therapy as a new treatment for patients with ME/CFS.

II PATIENTS AND METHODS

1. Patients' characteristics (Table 1)

Potential participants comprised 48 consecutive female patients who were referred to the women's health clinic of Seifuso Hospital in Saitama Prefecture for assessment and treatment of possible ME/CFS through the outpatient clinic or primary care. Eighteen females fulfilled both the criteria of the Ministry of Health, Labor and Welfare of Japan and the Canadian clinical case definition of ME/CFS, based on their medical histories, the results of physical and mental examinations, and laboratory tests. None of the women had any history of psychiatric illness.

In Japan, the case definition proposed by the Ministry of Health, Labor and Welfare has been used. The Canadian Clinical case definition had been developed by 2003, utilizing the term "ME/CFS", as opposed to "CFS", to refer to the illness. In 2011, a new case definition, the International Consensus Criteria for myalgic encephalomyelitis (ME-ICC), was published.

Both the Canadian clinical case definition and the International consensus criteria are utilized to select cases with less psychiatric comorbidity, more physical/functional impairment, greater fatigue or weakness, and more neuropsychiatric/neurological symptoms such as confusion, disorientation, and difficulty retaining information. As evidenced by prior studies, patients who met different case definitions displayed differences in symptomatology and impairment. We used the Canadian case definition. This case definition requires that the following symptoms be present: unexplained, chronic physical or mental fatigue; post-exertional malaise from which at least 24 hours are required to recover; significant pain (e.g., myalgias, arthralgias); sleep

Table 1 Clinical features of patients

		No.	Age/Sex	Duration of ME/CFS(Years)	PS score at the first medical examination	PS score at the follow-up examination	Follow-up duration (months)
Waon therapy (Inpatient)	good responder	1	21F	3	8	7	30
		2	33F	1	8	5	35
		3	33F	3	5	4	33
		4	48F	4	8	5	7
		5	43F	1	7	6	35
		6	39F	1	7	6	17
		7	38F	6	7	7	40
	poor responder	8	60F	5	7	7	28
		9	31F	4	7	7	40
Non Waon therapy (Outpatient)	good responder	10	36F	10	7	8	33
		11	41F	7	8	8	25
		12	33F	3	8	8	36
	poor responder	13	32F	15	6	6	29
		14	42F	18	6	6	38
		15	37F	7	5	5	31

F : female, PS : performance status

dysfunction (e.g., unrefreshing sleep, sleep rhythm disturbance); and two neurological or cognitive symptoms (e.g., confusion, memory impairment, and/or loss of concentration). Additionally, individuals must report symptoms from two of the following categories: autonomic manifestations (e.g., orthostatic intolerance, nausea, irritable bowel problems); neuroendocrine manifestations (e.g., intolerance of temperature extremes, loss of appetite); and/or immune manifestations (e.g., fever, recurrent sore throats).

Ten of the above-mentioned eighteen women who fulfilled the criteria approved of their undergoing Waon therapy (hereafter, "Waon therapy patients") for the treatment of their ME/CFS, while eight patients chose not to undergo the therapy (hereafter, "non-Waon therapy patients"). A major reason for the latter group's declining it was that Waon therapy is not covered by health insurance and is therefore expensive. As one of the Waon therapy patients and two of the non-Waon therapy patients dropped out of follow-up examinations, ultimately, 15 (nine Waon therapy and six non-Waon therapy) patients participated in this study until the end. All of them were post infectious and were suffering from acute onset of the illness.

2. Waon therapy and other therapies utilized

Waon therapy, a form of thermal therapy, uses a far-infrared dry sauna room maintained at a uniform temperature of 60°C for 15 minutes, with patients in a supine position or a sitting position. For this study, we utilized portable sauna equipment, with the Waon therapy patients in a sitting position, with the original uniform temperature of 60°C. However, most of the patients could not tolerate temperatures over 45°C for 15 minutes. Thus, we had the patients sit in a far-infrared ray dry sauna maintained at a steady temperature of 45°C for 15 minutes;

this was intended to sooth the minds and bodies of the patients. After leaving the sauna, each patient was transferred to a room maintained at 26–27°C, where they were covered with a warm blanket from the neck down to keep them warm for 30 minutes. This method is somewhat different from the original definition of Waon therapy, so it was, in the strict sense of the word, a form of modified Waon therapy. All patients were weighed before and after therapy, and oral hydration with water was used to compensate for any weight loss due to perspiration. They received 30 sessions of modified Waon therapy, twice a day for three weeks in the hospital, or else once a day for five weeks at an outpatient clinic from Mondays to Saturdays.

All patients participating in this study received several different treatments according to the best clinical practice of the time. Treatments, prescribed as single-agent or combinations thereof, included different classes of drugs: nutritional supplements (such as vitamins B2, B12 and C, minerals, amino acids, and, fatty acids); pain-killer analgesics; sleeping pills; antidepressants; and sedatives. Drugs were changed according to patients' response to therapy, or when there was an intolerance to the drugs prescribed.

3. Outcome measures

For the Waon therapy patients, functional health and well-being scores were determined using SF-36 before Waon therapy, after 30 treatments and during follow-up; for non-Waon therapy patients, the scores were determined before the other therapies were carried out and during subsequent follow-up. The SF-36 is a multi-purpose, short-form health survey consisting of 36 questions¹⁷⁾. It yields an 8-scale profile of functional health and well-being scores as well as psychometrically-based physical and mental health summary measures in surveys of general and specific populations, comparing the relative burden of diseases, and differentiating the health benefits produced by a wide range of different treatments.

The interpretation of results has been made much easier with the standardization of mean scores and standard deviation for all SF-36 scales. Specifically, norm-based scoring has proven to be very useful when interpreting differences across scales in the SF-36 profile, and for monitoring disease groups over time. In norm-based scoring, each scale was calibrated to have the same average (50) and the same standard deviation (10 points). Without referring to norms, it is clear that anytime a scale score is below 50, health status is below average, and each point is one-tenth of a standard deviation.

Regarding the SF-36 scales: a low Physical functioning (PF) score means a patient is limited in performing all physical activities, including bathing or dressing. A low Role physical (RP) score means a patient has problems with work or other daily activities as a result of their physical health. A low Bodily pain (BP) score means a patient has very severe and extremely limiting pain. A low General health (GH) score means a patient's personal health is poor, and is likely to get worse. A low Vitality (VT) score means a patient feels tired and worn out much of the time. A low Social functioning (SF) score means a patient has extreme and frequent interference with normal social activities due to physical and emotional problems. A low Role emotional (RE) score means a patient has problems with work or other daily activities as a

result of emotional problems. A low Mental health (MH) score means a patient has feelings of nervousness and depression all of the time.

Additionally, fatigue severity was evaluated before and after Waon therapy and during follow up for the Waon therapy patients, as well as before therapy and during follow-up for non-Waon therapy patients, using a scale of performance status for patients with ME/CFS¹⁸⁾. This descriptive scale, ranging from 0 (best performance status) to 9 (worst performance status) indicates that ME/CFS patients are: 0) able to carry on a normal life style without fatigue and to act without limitations; 1) able to carry on a normal social life and work, but are often aware of fatigue; 2) able to carry on a normal social life and work, but require frequent rest due to general fatigue; 3) unable to carry on a normal social life or work several days a month due to general fatigue, and require rest at home; 4) unable to carry on a normal social life or work several days a week due to general fatigue, and require rest at home; 5) able to perform light tasks, but find it difficult to carry on a normal social life and work, and require rest at home several days a week; 6) able to perform light tasks on good days, but require rest at home for at least half a week; 7) unable to carry on a normal social life or light tasks, but are able to care for themselves without assistance; 8) able to care for themselves to some extent, but require frequent assistance and spend at least half the day in bed; and 9) unable to care for themselves, and require continuous assistance, while spending all day in bed.

A brief self-rating questionnaire for depression (SRQ-D) was also used to evaluate the degree of depressive state. SRQ-D consists of 12 relevant and 6 control questions. Answers to each question were scored 0 to 3, so that the total scores of the 12 relevant questions ranged from 0 to 36. Any individual with a score of 12 or higher should be considered to have some degree of depression¹⁹⁾.

A state-trait anxiety inventory (STAI) was also used to measure anxiety. STAI has forty questions with a range of four possible responses to each²⁰⁾. STAI clearly differentiates between the temporary condition of "state anxiety (scene uneasiness)" and the more general and long-standing quality of "trait anxiety (characteristic uneasiness)"²⁰⁾. Trait anxiety (T-anxiety) implies differences between people in their disposition to respond to stressful situations with varying amounts of state anxiety (S-anxiety). But whether or not people who differ in T-anxiety will show corresponding differences in S-anxiety depends on the extent to which each person perceives a specific situation as psychologically dangerous or threatening, and this is greatly influenced by each individual's past experiences. Scores on the STAI S-anxiety scale increase in response to physical danger and psychological stress, and decrease as a result of relaxation training. An individual with a score higher than 46.79 should be considered to have some degree of scene uneasiness. On the STAI T-anxiety scale, consistent with the trait anxiety construct, psychoneurotic and depressed patients generally have high scores. An Individual with a score higher than 48.29 should be considered to have some degree of characteristic uneasiness.

Each test was done before Waon therapy, after 30 treatments, and during follow-up for Waon

therapy patients, as well as before therapy and during follow-up for non-Waon therapy patients.

4. Response definitions and statistical analyses

The patients who showed improvements relative to baseline after Waon or other therapy on more than four of the eight SF-36 scales were designated as 'good responder' and those without improvements were designated as 'poor responder'.

To compare the baseline characteristics of Waon therapy patients and non-Waon therapy patients, good responders and poor responders, Mann-Whitney's U test or Fisher's exact test were used. To determine the effects of health-related QOL measured by SF-36, norm-based scores for each scale before and after treatment, as well as before treatment and during follow up observation of Waon or other therapies, the Wilcoxon signed-rank test was used to test mean values. A *p* value <0.05 was considered statistically significant. All data analyses were conducted using SPSS Statistics 19 (IBM).

5. Ethics

Informed consent to participate in this study was obtained from all 15 patients who participated until the study conclusion. The study protocol was approved by the ethics committee of Seifuso hospital.

III RESULTS

Table 1 shows clinical details about the nine Waon and the six non-Waon therapy patients who participated in this study. Participants ranged in age from 21–60 years old (mean age, 37.8 ± 8.8 years old).

All patients were post-infectious and had suffered acute onset of illness, reporting prolonged fatigue lasting ≥ 1 year with impairments in memory and concentration, headaches, muscle and/or multi-joint pain and un-refreshing sleep. Additionally, they complained of multiple neurological/cognitive, autonomic, neuroendocrine and/or immune symptoms such as nausea, irritable bowel syndrome, intolerance of extremes of heat and cold, loss of appetite, lymph nodes tender to palpitation, etc.

The mean illness duration from onset to first medical examination was 3.1 ± 1.8 years (range, 1–6) for Waon-therapy patients and 10.0 ± 5.6 years (range, 3–18) for non-Waon therapy patients. The mean illness duration from onset to first medical examination was significantly longer in the non-Waon therapy patients.

All patients but one (Patient #3) had quit their jobs because of ME/CFS; the one who had not left her job had taken a leave of absence from work. The mean performance state on first medical examination was 7.1 ± 0.9 (range, 5–8) for Waon therapy patients and 6.7 ± 1.2 (range, 5–8) for non-Waon therapy patients. The mean follow-up period was 27.9 ± 10.5 months (range, 9–40) for Waon therapy patients and 32.0 ± 4.7 months (range, 25–38) for non-Waon therapy patients.

A single far-infrared ray dry sauna at 45°C for 15 minutes elevated patients' average core body temperature by 0.5°C.

Figure 1&2 show individual results of SF-36 before Waon therapy, after 30 treatments and during follow-up for Waon therapy patients, as well as before therapy and during follow-up for non-Waon therapy patients.

Before therapy there were significant differences between Waon-therapy patients and non-Waon therapy patients on two of eight SF-36 scales, Role physical (12.27 ± 8.76 vs. 36.47 ± 6.67 , $P < 0.001$) and Social functioning (18.33 ± 12.63 vs. 38.10 ± 13.07 , $P < 0.018$). Non-Waon therapy patients originally showed better SF-36 scores compared to Waon therapy patients.

Seven of the nine Waon therapy patients showed improvements relative to baseline after 30 treatments of Waon therapy on more than four of the eight SF-36 scales, and the effect continued throughout the follow-up period for four of them (Figure 1). In two patients, no improvement was observed after Waon therapy (Figure 1).

Three of the six non-Waon therapy patients showed improvements relative to baseline during follow-up on more than four of the eight SF-36 scales (Figure 2). In the other three patients, no improvement was observed (Figure 2).

The Waon therapy ME/CFS patients showed especially low scores in Physical functioning (17.1 ± 9.8 for good responders and 5.8 ± 0.2 for poor responders), Role physical (12.8 ± 9.5 for good responders and 10.3 ± 7.2 for poor responders), General health (27.8 ± 5.3 for good responders and 26.3 ± 3.8 for poor responders), Social functioning (21.4 ± 12.6 for good responders and 7.8 ± 4.7 for poor responders), and Role emotional (28.0 ± 16.0 for good responders and 29.0 ± 21.0 for poor responders) before Waon therapy (Figure 3).

Good responders among Waon therapy patients showed statistically significant improvements relative to baseline after Waon therapy on two of the eight SF-36 scales - the scores for Role physical (22.1 ± 10.0 , $p < 0.05$) and General health (38.7 ± 8.7 , $p < 0.05$) (Figure 3). In Figure 4, the individual changes of norm-based scoring of SF-36 of the nine Waon-therapy patients before and after Waon therapy and during follow-up are shown. Good responders are illustrated by circles and poor responders are illustrated by triangles. During the follow-up period, three of the seven good responders regressed in terms of Role physical and General health.

Before therapy, the non-Waon therapy patients showed low scores in Physical functioning (15.37 ± 20.43 for good responders and 30.47 ± 16.26 for poor responders), Bodily pain (24.4 ± 20.04 for good responders and 16.4 ± 8.6 for poor responders), and General health (19.67 ± 15.36 for good responders and 30.77 ± 13.1 for poor responders).

No significant improvement relative to baseline was seen in non-Waon therapy patients on the eight SF-36 scales during follow-up.

After Waon therapy six of nine Waon therapy patients (6 good responders) showed improved performance status (PS) compared to before therapy (Table 1). The performance status of the three patients who did not show improvement (PS scores remaining unchanged) was an average of 7.

As for the non-Waon therapy patients, none of the six patients showed any improvement, while one patient actually deteriorated slightly, in terms of performance status compared to

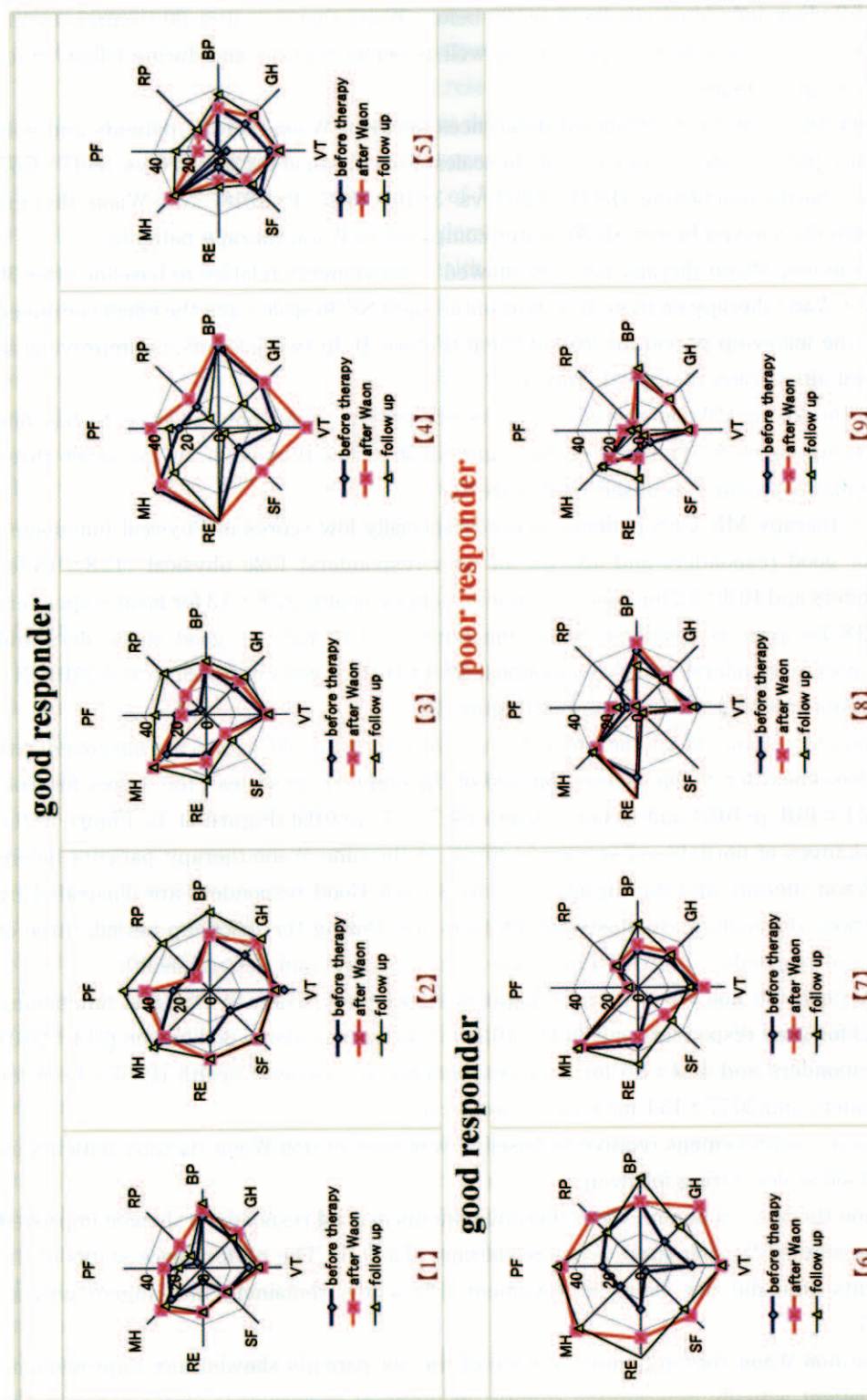


Fig. 1 Eight SF-36 scales of good responders and poor responders before therapy, after therapy and during follow-up period in nine Waon therapy patients.
PF: Physical functioning, RP: Role physical, BP: Bodily pain, GH: General health
VT: Vitality, SF: Social functioning, RE: Role emotional, MH: Mental health

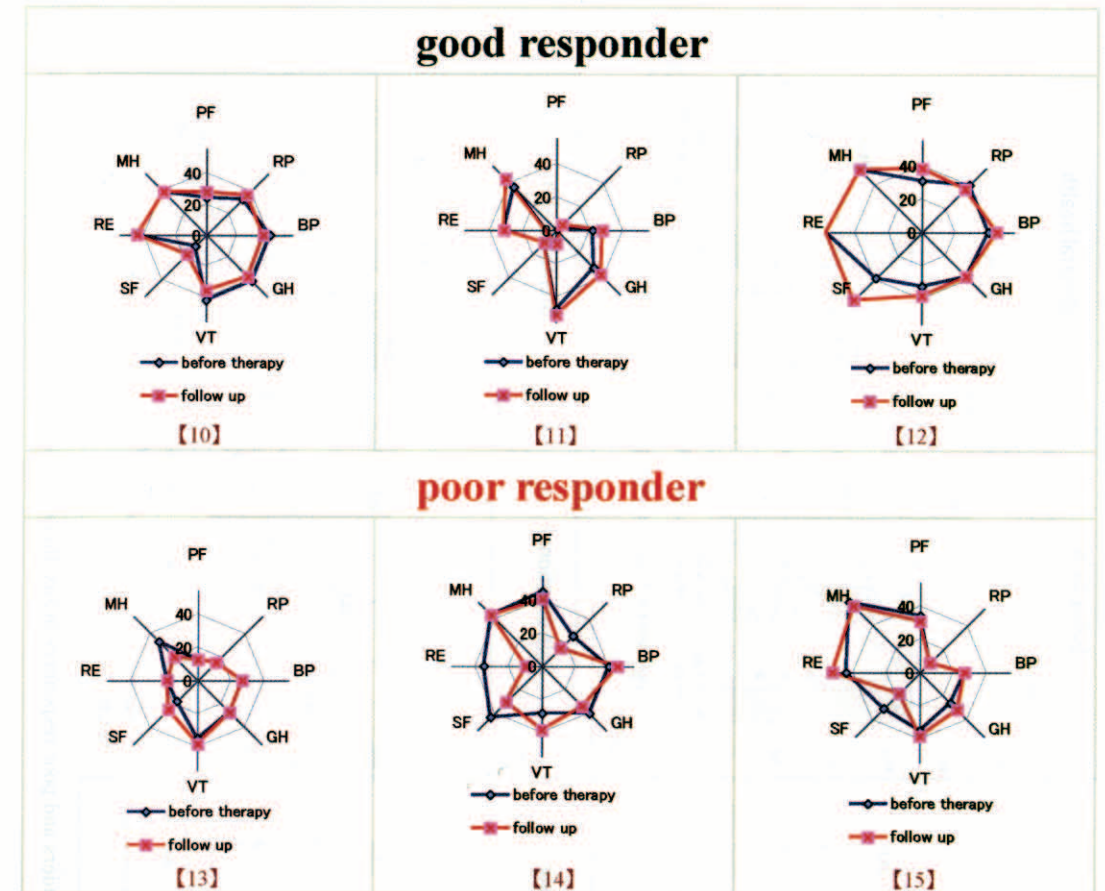


Fig. 2 Eight SF-36 scales of good responders and poor responders before therapy and during follow-up period in six non-Waon therapy patients.

PF: Physical functioning, RP: Role physical, BP: Bodily pain, GH: General health
VT: Vitality, SF: Social functioning, RE: Role emotional, MH: Mental health

before therapy (Table 1).

In all of the ME/CFS patients, SRQ-D showed a score of slightly higher than normal before and after Waon therapy and during the follow-up period (Figure 5, 6). On state-trait anxiety inventory tests, all patients but one non-Waon therapy patient showed normal scores both for state-anxiety and trait-anxiety (Figure 5, 6).

None of the patients showed any deterioration in their condition during, or after the conclusion of, the Waon therapy sessions. Furthermore, Waon therapy was applicable for patients who were unable to have baths.

IV DISCUSSION

The worldwide prevalence of ME/CFS is about 400 cases per 100,000 (300 cases per 100,000 in Japan). It is estimated that more than 377,000 people in Japan have ME/CFS; and it is more

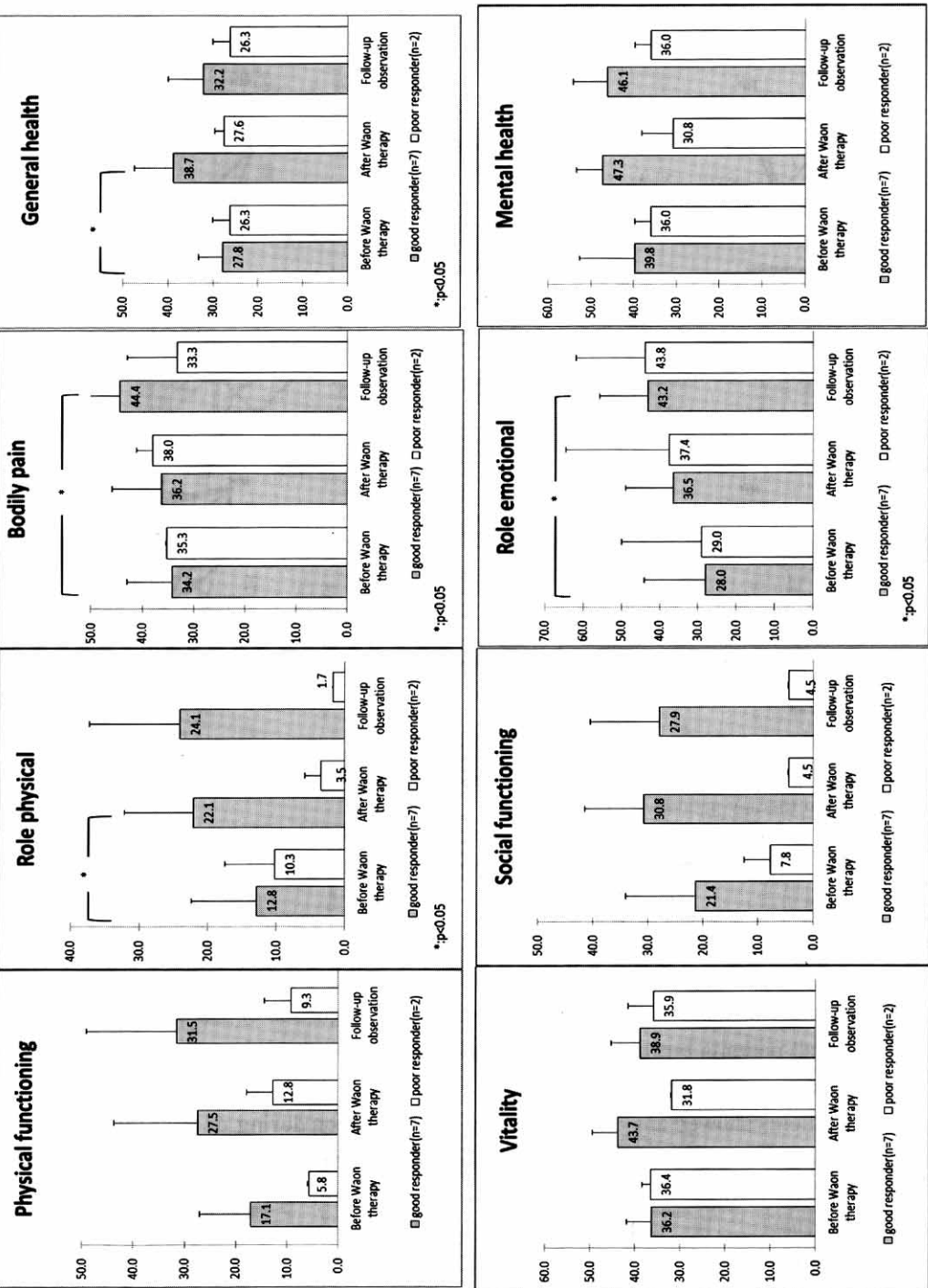


Fig. 3 Average of norm-based scoring of SF-36 good responders and poor responders before therapy, after therapy and during follow-up period in nine Waoon therapy patients.

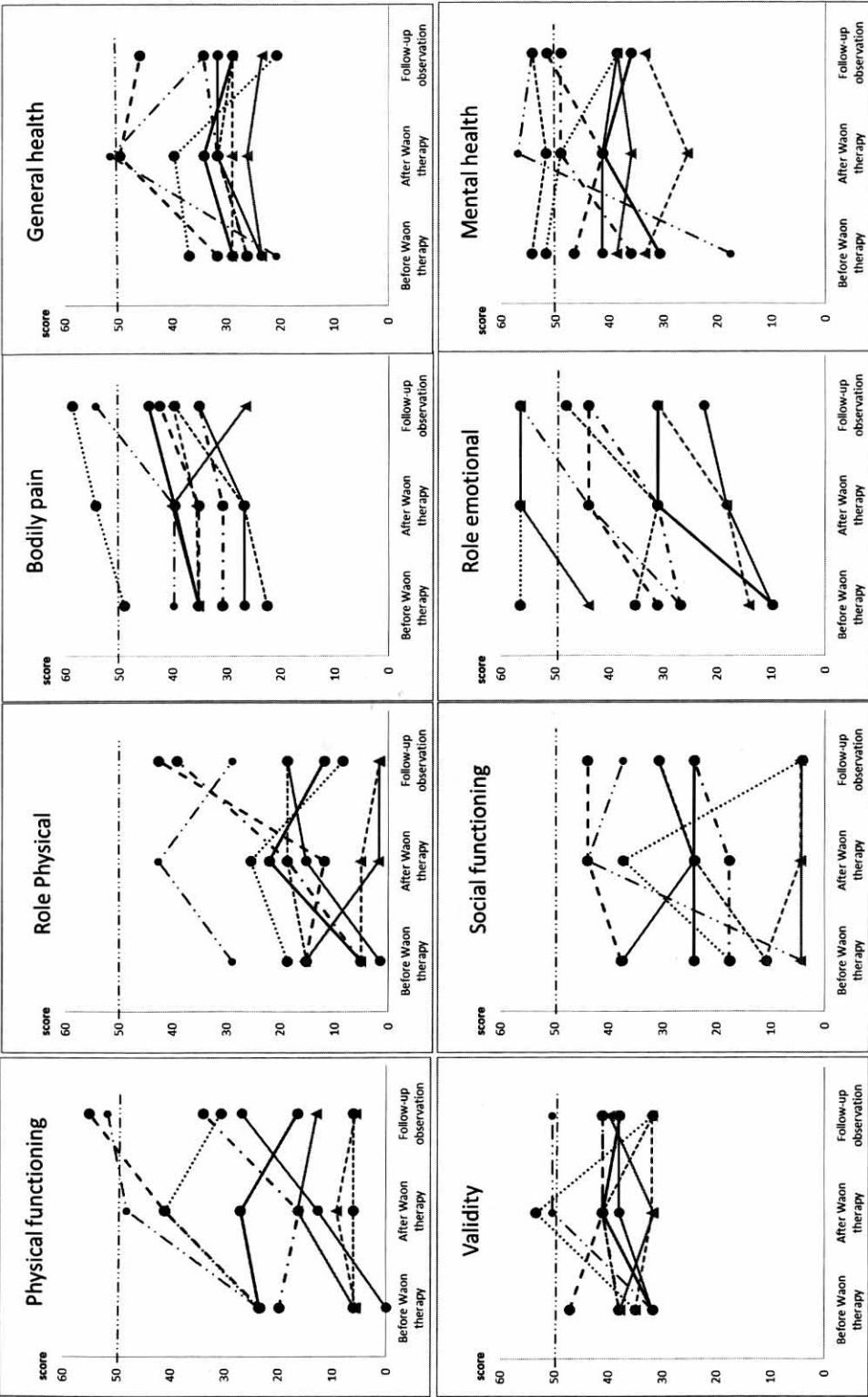


Fig. 4 Individual change of norm-based scoring of SF-36 in nine Waoon therapy patients before therapy, after therapy and during follow-up period.

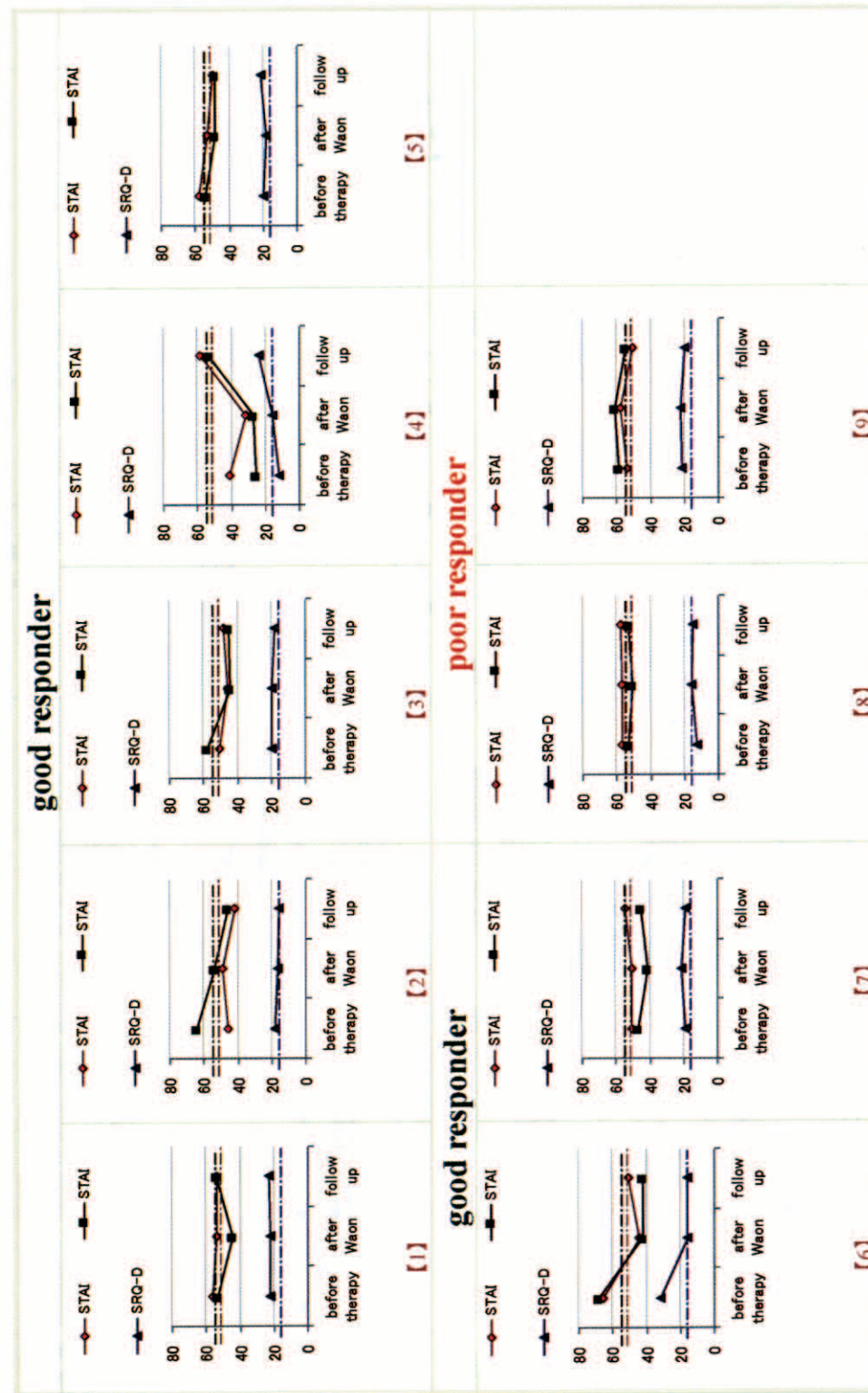


Fig. 5 SRQ-D and STAI before therapy, after therapy and during follow-up period in nine Waon therapy patients.

SRQD: <10 normal, 10~15 Boundary, >15 Mild depression
STAI (Characteristic Uneasiness: green) >48.3 anxiety
STAI (Scene Uneasiness: red) >46.8 anxiety

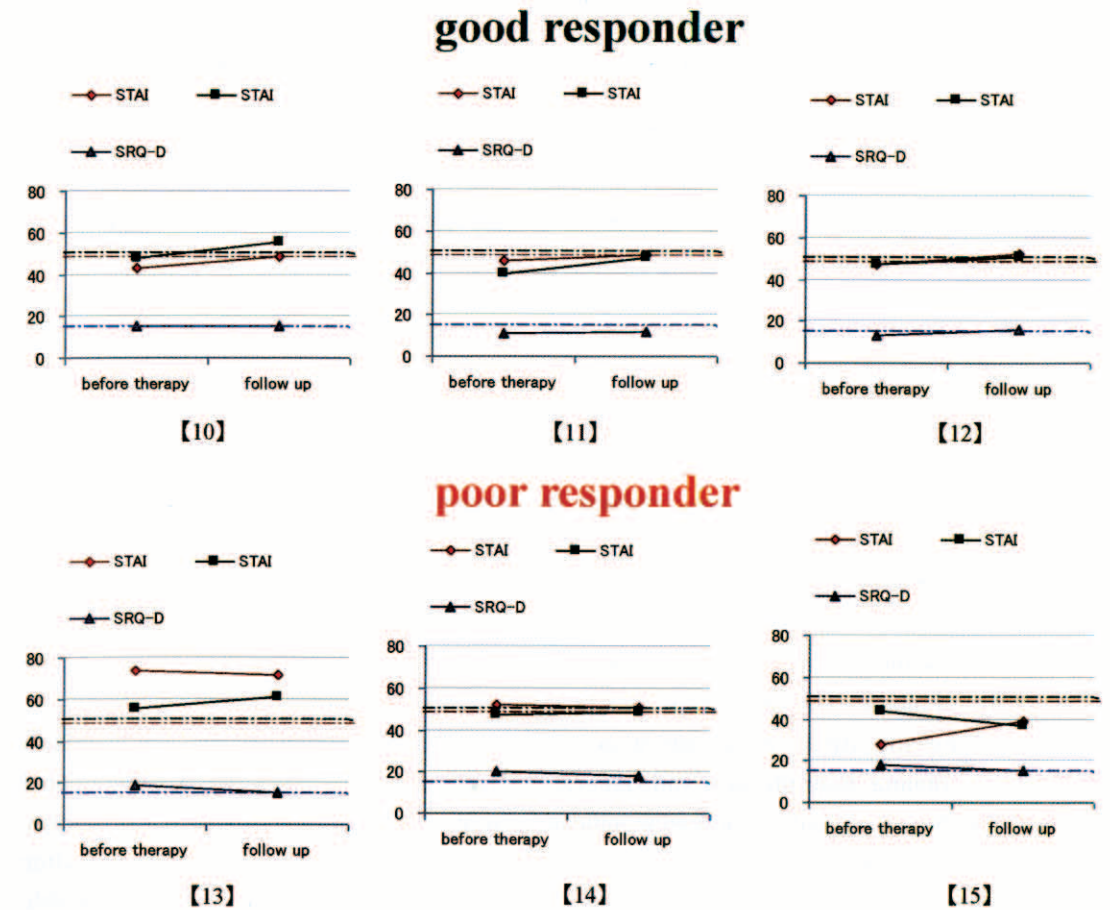


Fig. 6 SRQ-D and STAI before therapy and during follow-up period in six non-Waon therapy patients.

SRQD: <10 normal, 10~15 Boundary, >15 Mild depression
STAI (Characteristic Uneasiness: green) >48.3 anxiety
STAI (Scene Uneasiness: red) >46.8 anxiety

common in persons over 40 years old.

Many Japanese patients are severely affected. They are mostly house-bound, sometimes even chair- or bed-bound. They may experience considerable difficulty with all aspects of personal care and may need help even with meal planning/ preparation. Many are incapable of living independently. In addition, they are more likely to suffer food and chemical sensitivities, and may be extremely sensitive to light, sound, and temperature extremes. Some have severe neurological symptoms such as atypical seizures, difficulties with swallowing or speech, muscle spasms, or profound weakness. It is not known why some patients are more severely affected than others.

Four core symptoms of ME/CFS are unexplained, chronic physical or mental fatigue, post-exertional malaise from which at least 24 hours are required to recover, significant pain, sleep dysfunction, and neurological or cognitive symptoms.

Although pain and sleep are eminently treatable, there are few treatments for fatigue.

Current treatment options for fatigue include cognitive behavior therapy (CBT) and graded exercise therapy. Both of these have been shown to moderately improve energy levels, work and social adjustment, anxiety, and post-exertional malaise¹³⁾.

A large randomized, controlled study of adults with ME/CFS by White, Goldsmith, et al, confirmed that CBT had positive effects on fatigue levels, work and social adjustment, depression, anxiety, and post-exertional malaise. Most patients in that study rated themselves as "much" or "very much" better after completion¹⁰⁾. Graded exercise therapy was as effective as CBT for fatigue and the other aspects of functional impairment mentioned previously, except for depression¹⁰⁾. Disadvantage of CBT include the need for expert consultation, time considerations, and cost.

Impediments to graded exercise therapy include time considerations and concerns of patients that exercise will exacerbate their condition. It is true that the positive effects are usually moderate, and rarely lead to complete resolution of ME/CFS, despite the positive results with both CBT and graded exercise therapy.

In 2005, Masuda & Tei reported on two ME/CFS cases in which thermal therapy using far-infrared ray saunas improved the patients' subjective symptoms¹⁵⁾. We examined the applicability of modified Waon therapy as a new treatment for patients with ME/CFS.

In our study, the ME/CFS patients who underwent Waon therapy showed low scores in Physical functioning, Role physical and General health, Social functioning, and Role emotional at admission. Seven patients improved significantly in physical condition due to Waon therapy (good responders). They showed statistically significant improvements relative to baseline after Waon therapy on two of the eight SF-36 scales - specifically, Role physical and General health, those most closely associated with PF. The effect continued throughout the observation period (range 9–40 months) on four of patients. In two other patients, no improvement in symptoms was observed after Waon therapy (poor responders).

During the follow-up period, three of seven good responders regressed again in Physical functioning, Role physical and General health. The cause for regression was thought to be related to family circumstances - especially lack of understanding and sympathy for the women and their illness. Those who regressed were confronted with difficulties at home, while participants who did not regress were supported strongly by their families.

In all patients, SRQ-D showed a score of slightly higher than normal before and after Waon therapy and during the follow-up period. On state-trait anxiety inventory tests, all patients but one non-Waon therapy patient showed normal scores both for S-anxiety and T-anxiety. The results of SRQ-D and state-trait anxiety inventory tests showed that ME/CFS is not simply the expression of somatic symptoms by people with a primary psychological disorder.

Far-infrared rays are absorbed by the skin, with almost no absorption by air. The heat thereby produced in the skin causes thermal vasodilation, increasing skin blood flow. Blood warmed at the skin circulates throughout the body, warming up the body^{15), 16)}. A far-infrared

ray dry sauna at 60°C elevates core body temperature by 1.0°C and induces 1.5-fold increase in cardiac output²¹⁾. This dilates systemic arteries and veins to reduce the preload and afterload on the heart and significantly increases cardiac output. The higher metabolism rate and perspiration due to increased body temperature and increased blood flow, in addition to the relaxation effects of Waon therapy, corrects abnormal autonomic nervous response and neurohumoral factors, as well as decreasing subjective symptoms²²⁾. Also, far-infrared rays have a sleep-enhancing effect²³⁾. Increased brain temperature is associated with a type of neuronal activation typical of sleep in the hypothalamus and basal forebrain. Central nervous system arousal was reduced by increased blood temperature in the hypothalamus; consequently, we may be able to say that Waon therapy has a soporific effect. The efficacy of Waon therapy in relieving pain in patients with chronic psychosomatic pain or fibromyalgia has been reported on previously^{24), 25)}. The involvement of oxidative stress in the pathogenesis of ME/CFS has also been indicated²⁶⁾, and Waon therapy has been reported to reduce levels of oxidative stress²⁷⁾. All these effects of far-infrared ray dry sauna may be expected in the patients with ME/CFS.

For this study, we utilized a portable sitting Waon therapy box evenly heated to a lower temperature than the 60°C which the original Waon therapy calls for. This study's method, using a temperature setting of 45°C, elevated core body temperature by 0.5°C. Little dermal irritation due to heat occurred, so ME/CFS patients were able to warm their bodies more comfortably, thus allowing them to relax. Patients perspired to reduce about 200 g of body weight and enjoyed the relaxation effects. The systolic blood pressure decreased about 10 mmHg compared to baseline after Waon therapy. Complaints of pain and fatigue clearly decreased in number.

In an experiment using heart failure model hamsters, Waon therapy considerably increased the expression of mRNA of vascular endothelial nitric oxide synthase (eNOS) in vascular endothelial, and intensified the expression of eNOS protein^{28), 29)}. A remarkable expression of mRNA and protein of eNOS was also observed in an experiment with peripheral arterial disease models³⁰⁾. Specifically, after a femoral artery of an apolipoprotein E-knock-out mouse was removed, if Waon therapy was repeated once a day for 35 days, the expression of mRNA and the protein level of eNOS also considerably increased, while the number of blood capillaries increased, and blood flow improved remarkably in the ischemic limbs. Angiogenesis can be achieved. In other words, Waon therapy was deeply involved in the production of effects at genetic, molecular, and cellular levels, and this treatment modality therefore played an important role in the recovery of the living organisms²²⁾.

We have applied Waon therapy, a thermal therapy, to ME/CFS and found that Waon therapy improved various symptoms, QOL and prognoses. We believe that Waon therapy is a promising therapy for patients with ME/CFS. Although thermal therapy, such as onsen (hot spring) or spa treatment, may be effective, Waon therapy is more convenient; patients who wish to continue treatment can easily receive Waon therapy, because the therapy takes only about one hour and does not require expensive equipment. In addition, the safety of Waon therapy will

allow most patients with compromised physical condition to undergo treatment without adverse effects. In contrast, in the case of deep warm water baths, hydrostatic pressure increases venous return flow, which may cause adverse effects in such patients.

Although the present study included only nine Waon-therapy patients and six non-Waon therapy patients, and may be too small a sample size to sufficiently support the conclusion of this report, the effects observed herein were dramatic. Nevertheless, we need prospective evaluation of different therapies, because ME/CFS is a group of different diseases with probably different etiopathogenetic features, ME/CFS occurs after infectious agents - like what brought it about in the patients in our study, and it is a disease of unknown etiology. The efficacy of Waon therapy needs to be examined through controlled studies with a sufficient number of subjects, carried out in outpatient settings over a long period.

V CONCLUSION

ME/CFS is not simply the expression of somatic symptoms by people with a primary psychological disorder, so it should be treated. The effects of Waon therapy observed herein for the patients of ME/CFS were dramatic. As the present study included only nine Waon therapy and six non-Waon therapy patients, further clinical studies in larger ME/CFS patient populations are required to confirm the effects of this treatment method.

Competing interests

The authors declare that they have no competing interests.

Authors' Contributions

KA designed study, collected the data, analyzed the data, interpreted the results, and drafted the manuscript. AY helped to analyze the data. Both authors read and approved the final manuscript. CT helped to survey the literature and edit the manuscript.

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