We are IntechOpen,
the world's leading publisher of
Open Access books
Built by scientists, for scientists

6,900
Open access books available

185,000
International authors and editors

200M
Downloads

154
Countries delivered to

Our authors are among the

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

CLARIVATE ANALYTICS
BOOK CITATION INDEX
INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Initial Experience of Lower Limb Thermal Therapy for Patients with an Extracorporeal Left Ventricular Assist Device Awaiting Heart Transplantation

Kazuo Komamura

Department of Cardiovascular Medicine, National Cardiovascular Center
Japan

1. Introduction

Many researchers have reported that vasodilators, such as angiotensin-converting enzyme inhibitors (The CONSENSUS Trial Study Group, 1987), angiotensin receptor blockers (Cohn et al., 1999), and beta-blockers (CIBIS Investigators et al., 1994), improve prognosis in patients with chronic heart failure (CHF). Furthermore, new technologies to treat CHF, such as cardiac rehabilitation, cardiac resynchronization therapy, left ventricular assist devices, and left ventricular reconstruction surgery, have been developed over the past decade. Despite advances in therapy for heart failure, improving clinical outcomes of patients with acute decompensation of CHF remains a challenge for physicians. Re-hospitalization within $60-90$ days occurs in approximately 30% of patients with acute decompensation of CHF (Mann, 2008).

In 1989, Tei et al. developed a form of thermal therapy for heart failure that uses a variation of the traditional dry sauna with temperature maintained at 60°C (Tei et al., 1994; Tei et al., 1995). This new form of thermal treatment is defined as warming the entire body in a uniformly heated chamber for 15 min at a temperature that relaxes both the mind and body. After the core temperature has increased by 1.0–1.2°C, the patient rests outside the sauna for a further 30 min to maintain the soothing effect, and fluids corresponding to perspiration loss are supplied to protect against dehydration at the end of therapy (Tei, 2007).

Tei et al. have previously reported that the repeated use of a dry 60 °C sauna by CHF patients improves hemodynamics (Tei et al., 1995), ameliorates symptoms (Tei & Tanaka, 1996), suppresses ventricular arrhythmias (Kihara et al., 2004), and improves vascular function (Kihara et al., 2002). Recently, in a prospective multicenter case-control study, 2 weeks of dry sauna therapy was shown to improve clinical symptoms and cardiac function in CHF patients (Miyata et al., 2008). Repeated sauna therapy also improved survival in TO-2 cardiomyopathic hamsters with heart failure (Ikeda et al., 2002). A recent retrospective follow-up study (Kihara et al., 2009) has shown that sauna therapy decreased cardiac death and re-hospitalization in patients with CHF over a 60-month follow-up period.

A large number of end-stage CHF patients in Japan have been implanted with a left ventricular assist device (LVAD) because of prolonged waiting periods for heart transplants

(Osada et al., 2005). Although we wished to apply sauna thermal therapy to patients with LVAD, we do not have an appropriate sauna facility. Instead, we attempted to apply lower limb thermal therapy to the patients with LVAD awaiting a heart transplant. This paper describes for the first time the safety and effectiveness of this preliminary trial of lower limb thermal therapy for patients with end-stage heart failure.

2. Methods

2.1 Patients and study design

The study subjects included 5 consecutive end-stage CHF patients who were listed on a waiting list for heart transplants in the National Cardiovascular Center, Osaka, Japan. All patients had dilated cardiomyopathy refractory to maximal medical therapy, including angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, beta-blockers, diuretics, and digitalis. Regardless of intensive care with intravenous inotropic agents, heart failure rapidly progressed to cardiogenic shock in the patients. They were fitted with extracorporeal LVAD (VCT-50, Toyobo Ltd., Osaka, Japan) to stabilize their hemodynamics. None of the patients was implanted with a defibrillator device.

Fig. 1. Typical settings for lower limb thermal therapy for a patient with left ventricular assist device.

The patients' general condition stabilized thereafter and the status of heart failure at the time of study was New York Heart Association (NYHA) class II. Although this status remained stable for at least 6 months, the patients' cardiac function did not sufficiently recover to allow discontinuation of LVAD support. All patients provided written informed consent to enter into the clinical trial for lower limb thermal therapy. The Ethics Committee

at the National Cardiovascular Center approved the protocol, and the study was conducted in accordance with the Declaration of Helsinki. The study consisted of clinical examinations before and after a 2-week treatment consisting of daily thermal therapy using a steam bath at 42 $\circ$C applied to the lower legs and feet (Fig. 1). After 15 min of therapy at 42 $\circ$C, the patient remained seated in the steam bath with the lower legs and feet wrapped with a blanket for a further 30 min. The procedure was accompanied by electrocardiographic monitoring. The patient remained on the same medications with same dose throughout the study period.

A typical example of lower limb thermal therapy is illustrated in Fig.1. The study protocol for the 2-week treatment was illustrated in Fig.2.
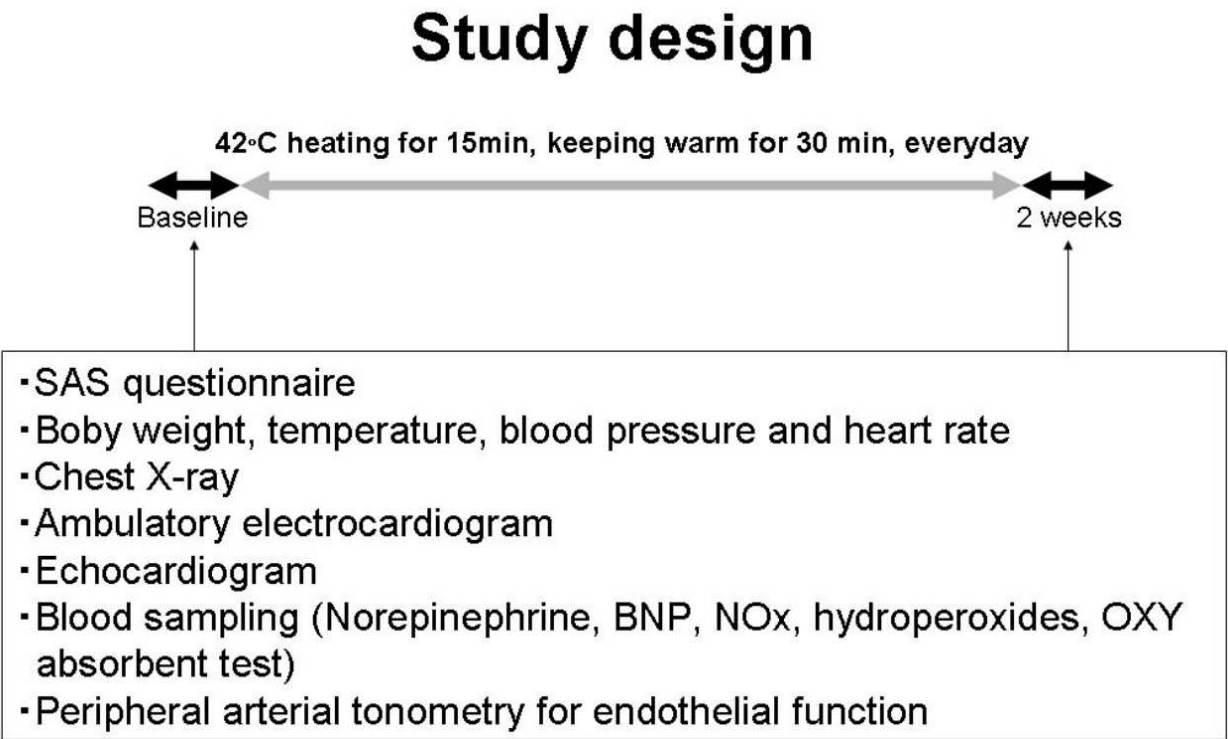
Study design

42∘C heating for 15min, keeping warm for 30 min, everyday

Baseline   2 weeks

- SAS questionnaire
- Boby weight, temperature, blood pressure and heart rate
- Chest X-ray
- Ambulatory electrocardiogram
- Echocardiogram
- Blood sampling (Norepinephrine, BNP, NOx, hydroperoxides, OXY absorbent test)
- Peripheral arterial tonometry for endothelial function

Fig. 2. Illustrative presentation of the study design for lower limb thermal therapy.

2.2 Measurements

Systolic and diastolic blood pressure (BP), heart rate, body weight, and surface and deep body temperature (axillary and sublingual) were measured daily throughout the study. Chest X-ray, ambulatory electrocardiogram, echocardiogram, and peripheral arterial tonometry were recorded and blood was sampled prior to and 2 weeks after the treatment. Blood samples were used for measurement of plasma BNP, serum NT-proBNP, plasma nitrates and nitrites, plasma hydroperoxides and HClO expense test.

Medical interviews were done every morning to evaluate the clinical status of CHF by NYHA functional class, and to estimate the patients' daily life activities using a Specific Activity Scale (SAS). We used the Specific Activity Scale as a measure of QOL, in which self perceived exercise tolerance is expressed by an energy cost spent in the maximal physical activity that the patient can perform (Sasayama et al., 1992). The Specific Activity Scale allows expression of the extent of submaximal physical activity. Sasayama et al. actually measured the metabolic

costs of various types of physical activity by hooking subjects up to a mask to measure oxygen consumption and the volume of carbon dioxide exhaled. They then prepared questionnaires about specific physical activities that a patient would perform either customarily or sporadically in daily life and each patient was asked to specify whether he/she could perform each type of activity without symptomatic limitations. Summarizing the questionnaire data, a given number of metabolic costs (Specific Activity Scale) were derived for each patient with regard to their self-perceived exercise tolerance. As a clear linear correlation was observed between Specific Activity Scale and peak oxygen consumption, the Specific Activity Scale was considered to provide a reliable prediction of exercise capacity (Sasayama et al., 1992)

Prior to and 2 weeks after the treatment, the cardiothoracic ratio (CTR) was measured by chest radiography and the count of premature ventricular beats was evaluated daily with an ambulatory electrocardiogram. Prior to and 2 weeks after the treatment, two-dimensional echocardiography were performed to determine left ventricular systolic (LVDs) and diastolic dimension (LVDd), left atrial dimension (LAD), LVEF and degree of mitral regurgitation. The left ventricular (LV) end-diastolic and end-systolic volumes were determined according to a modification of Simpson's method. LVEF was calculated as end-diastolic minus end-systolic volume divided by end-diastolic volume.

Each patient was instructed to lie quietly and undisturbed for at least 30 min, and then a venous blood sample was withdrawn through an indwelling catheter in the forearm. Plasma was immediately separated and stored at 70°C until analysis.

Norepinephrine (NE) concentrations were determined by high performance liquid chromatography and electrochemical detection. Plasma brain natriuretic peptide (BNP) was determined by the chemiluminescent enzyme immunoassay.

For nitric oxide (NO) measurement, the blood specimen was placed immediately in an ice bath and centrifuged within 30 seconds for 5 minutes at $2000g$. The serum fraction was diluted 1:1 with nitrite- and nitrate-free distilled water, and 400 mL of the diluted sample was centrifuged at $2000g$ in an ultra-free MC microcentrifuge device (Millipore) to remove substances larger than 10 kD. The filtrate was passed through a copper-plated cadmium column to reduce nitrate to nitrite and then reacted with Griess reagents consisting of 0.1% naphthylethylenediamine dihydrochloride in distilled water and 1% sulfanilamide in 5% H_3PO_4, after which absorbance was measured at 540 nm to provide the total amount of plasma NO end products (nitrate plus nitrite). The efficiency of the cadmium column in the conversion of nitrate to nitrite was confirmed to be 100% by measuring both nitrate and nitrite standards before and after sample measurement (Node et al., 1997).

Plasma hydroperoxides, which were determined by the Diacron reactive oxygen metabolites test, were used as a marker of oxidative stress (Cesarone et al., 1999) while the OXY absorbent test was used to measure buffering potential against the oxidant action of hypochlorous acid (HClO), which was quantified by HClO neutralization, and represented a marker of anti-oxidative potency (Trotti et al., 2001).

Endothelial function was quantified by the reactive hyperemic (RH) change in digital blood flow after arm occlusion using a peripheral fingertip arterial tonometry (PAT) device (Endo-PAT 2000 system; Itamar-Medical, Caesarea, Israel)(Bonetti et al., 2004; Hamburg & Benjamin, 2009). After 5 min of baseline recording, a BP cuff was inflated to supra-systolic pressure in the test arm. After 5 min of occlusion, the cuff was rapidly deflated, with PAT tracings recorded. The reactive hyperemic PAT (RH-PAT) response was determined as the ratio of PAT amplitude in the test arm to that in the control arm, averaged over 30-s intervals after cuff deflation, divided by the average PAT ratio measured for the 140-s interval before cuff inflation. RH-PAT ratio was assessed between 60 s and 120 s after

Initial Experience of Lower Limb Thermal Therapy for Patients
with an Extracorporeal Left Ventricular Assist Device Awaiting Heart Transplantation

129

occlusion and was the log-transformed value of the post-deflation to baseline pulse amplitude in the hyperemic finger normalized to the contralateral finger.

2.3 Statistical analysis

All data are expressed as means ±S.D. Value of BNP was log-transformed to remove skewness of data distribution. The data prior to and 2 weeks after treatment were compared using a paired *t*-test. A *p*-value of <0.05 was considered statistically significant.

3. Results

3.1 Clinical findings and physical examinations

Table 1 summarizes the results of clinical findings and physical examinations. During the study, none of the patients treated with lower limb thermal therapy showed worsened clinical symptoms. The changes in the clinical findings and variables after 2 weeks are indicated in Table 1. Although the NYHA functional class remained similar, activity of daily life estimated by SAS system tended to decrease (p=0.058). Systolic and diastolic blood pressure and heart rate did not differ between the baseline and 2 weeks after therapy. No significant change was noted in body weight.

	Before	After	p value
Sample size	5	5	
Age (years)	35.4±8.8		
NYHA functional class	2.8±0.4	2.6±0.5	0.374
Activity of Daily Life (METs)	2.66±0.85	3.12±1.11	0.058
Ventricular Premature Beats (per day)	121.8±70.2	71.6±62.2	0.143
Body Weight (kg)	53.0±10.1	52.9±10.1	0.355
Systolic blood pressure (mmHg)	97.4±13.0	99.2±17.0	0.505
Diastolic blood pressure (mmHg)	55.0±10.4	58.2±9.4	0.216
Heart Rate (bpm)	80.0±34.8	79.6±29.7	0.914
Morning Body Temperature (C)	35.9±0.45	36.0±0.39	0.296
Deep Body Temperature (C)	36.0±0.29	36.8±0.23	0.004
Cardiothoracic Ratio (%)	53.7±14.8	52.2±14.7	0.082
Norepinephrine (pg/mL)	974.2±584.8	801.6±482.7	0.041
log BNP (pg/mL)	2.128±0.516	2.080±0.505	0.035
Nitrogen oxide (μmol/L)	25.1±6.7	47.6±19.8	0.028
Hydroperoxides (carr U)	501.4±77.5	430.4±84.2	0.0003
OXY absorbent test (μmol HClO/mL)	397.6±41.9	461.6±56.4	0.096
LAD (mm)	42.8±11.2	42.4±10.0	0.731
LVDd (mm)	54.4±12.0	53.0±13.3	0.184
LVDs (mm)	43.1±15.4	39.7±15.9	0.014
LV Ejection Fraction (%)	43.0±19.3	51.1±18.5	0.0007
Mitral Regurgitation (grade)	2.2±1.1	1.4±0.9	0.016
RH-PAT ratio	1.39±0.24	2.05±0.30	0.02

BNP brain natriuretic peptide, LAD left atrial dimension, LVDd left ventricular diastolic dimension, LVDs left ventricular systolic dimension, NYHA New York Heart Association, RH-PAT reactive hyperemic peripheral arterial tonometry

Table 1. Summary of changes in parameters before and after the thermal therapy

3.2 Chest radiography and echocardiography

Table 1 also   presents the results of chest radiography and echocardiography. Chest radiography showed a non-significant decrease of the CTR after 2 weeks of treatment when compared with the baseline.
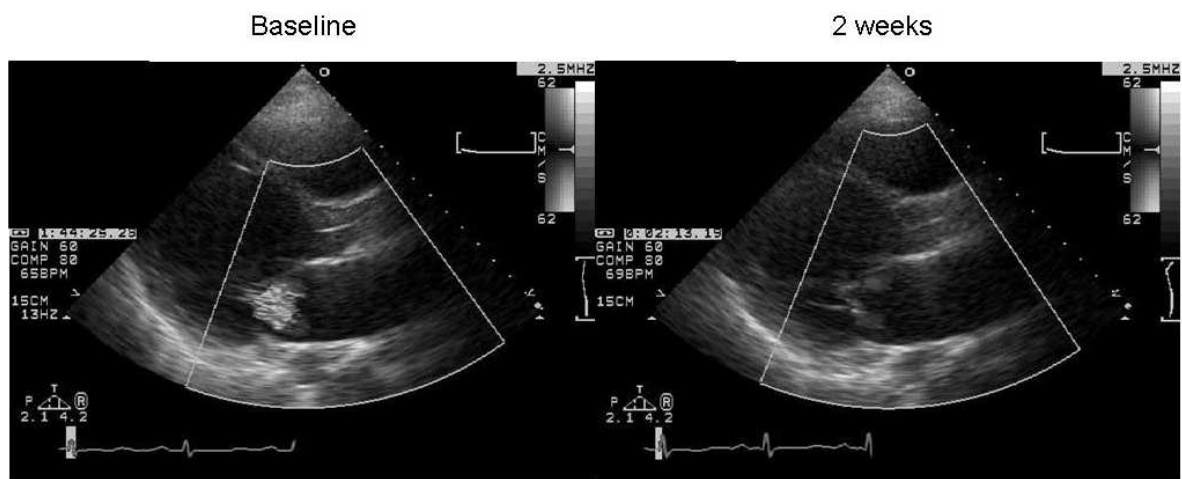
Doppler echocardiography

Fig. 3. Representative illustration of the extent of mitral regurgitation prior to and after the therapy
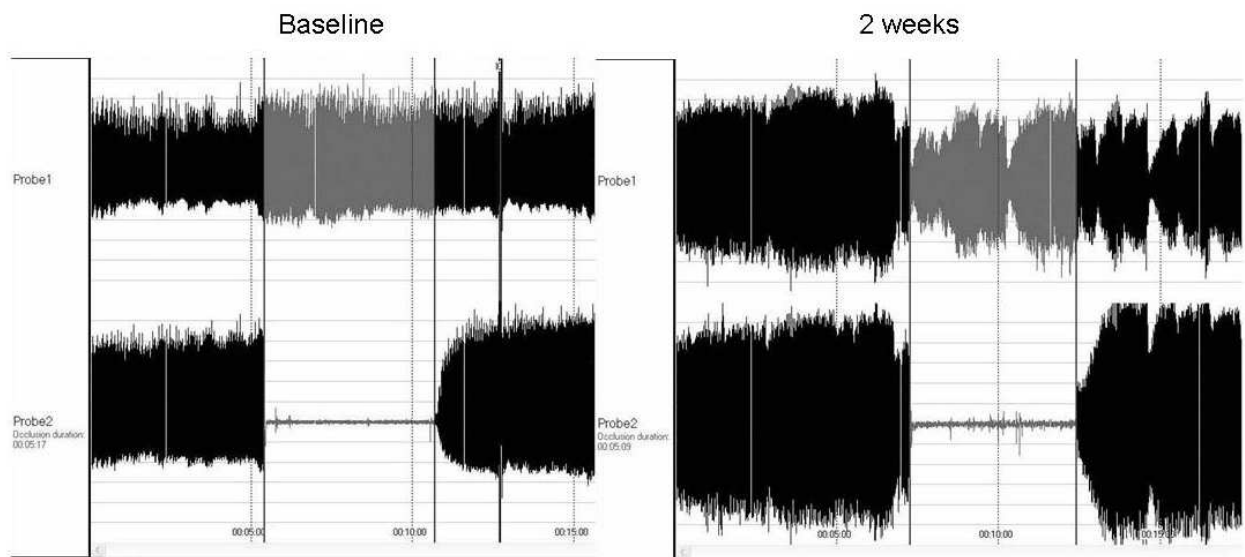
Reactive Hyperemic Peripeheral Arterial Tonometry

Fig. 4. Representative illustration of the changes in the tracing of peripheral arterial tonometry before and after the therapy

While, echocardiography demonstrated similar dimensions in LAD and LVDd after treatment, LVDs and LVEF significantly decreased after the therapy (Table 1). Doppler echocardiography demonstrated that the extent of mitral regurgitation decreased after treatment (Table 1, Fig. 3).

3.3 Plasma levels of norepinephrine, BNP, nitrogen oxide and hydroperoxides, and result of OXY adsorbent test

Table 1 shows the changes in plasma concentration of norepinephrine, BNP, nitrogen oxide (nitrate plus nitrite) and hydroperoxides. Plasma concentration of norepinephrine significantly decreased after 2 weeks of the therapy. The plasma concentration of BNP significantly decreased after 2 weeks of the therapy. Plasma concentration of nitrogen oxide (nitrate plus nitrite), the stable metabolite of nitric oxide, significantly increased after 2 weeks of the therapy. Plasma concentration of hydroperoxides, a biomarker that reflects oxidative stress, significantly decreased after 2 weeks of the therapy. The OXY absorbent test, a marker of anti-oxidative potency, showed a non-significant increase after 2 weeks of the therapy.

3.4 Endothelial function

The RH-PAT ratio was augmented 2 weeks after the therapy (Table 1, Fig.4).

4. Discussion

This is the first report of lower limb thermal therapy being applied to patients implanted with LVAD and awaiting heart transplantation. Whole body sauna therapy for CHF is widely recognized to result in improved clinical symptoms, cardiac function, quality of life, and ventricular arrhythmia, and in decreased levels of abnormally activated neurohumoral factors (Tei et al., 1995; Tei & Tanaka, 1996; Tei 2007; Kihara et al., 2002; Kihara et al., 2004). However, whole body sauna therapy is impractical for patients with CHF in general hospitals that lack specialized sauna facilities, whereas lower limb thermal therapy using a steam bath can be applied routinely right in the patients' rooms.

Increases in deep body temperature of 1.0−1.2 ◦C during sauna therapy dilate systemic arteries and veins, thereby reducing systemic preload and afterload and resulting in increased cardiac output (Tei et al., 1995; Tei & Tanaka, 1996; Tei 2007; Kihara et al., 2002; Kihara et al., 2004). The sublingual temperature of the patients in the present study was increased by about 0.8 ◦C after the therapy. Nevertheless, the benefits seemed to be similar to those of sauna therapy. Ikeda et al. found that repeated sauna therapy increases endothelial nitric oxide synthase expression and nitric oxide production, and improves cardiac function in animal models of heart failure (Ikeda et al., 2001; Ikeda et al., 2005). Serum nitrate plus nitrite levels doubled in our patients, when compared with the baseline values, as did the index of endothelial function determined by RH-PAT.

Patients implanted with an LVAD for long periods often develop serious hemorrhage in the cerebrum or elsewhere, as well as drive-line infection. We were concerned that the therapy would aggravate hemorrhage or infection in patients through its vasodilatory effects. However, we found that oozing of blood at the insertion site of the LVAD drive-line tended to resolve during therapy. Sauna thermal therapy attenuates psychological stress (Kihara et al., 2004). Because of a donor shortage in Japan, patients must remain attached to an LVAD

and stay in hospital for over 2 years while waiting for a heart transplant (Takatani et al., 2005). The decrease in plasma norepinephrine indicated that appendicular thermal therapy also might attenuate psychological, as well as physical stress.

Compared to pharmacological vasodilator therapy and other non-pharmacological therapy, such as cardiac resynchronization therapy and physical therapy, lower limb thermal therapy for CHF has several advantages. 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 who have severe congestive heart failure, uncontrolled ventricular arrhythmias, and orthopedic limitations are not excluded from undergoing lower limb thermal therapy. Fourth, this treatment promotes mental and physical relaxation. Lower limb thermal therapy may thus be a valuable adjunct to pharmacological or non-pharmacological intervention in the management of CHF.

5. Study limitation

Although the present study is preliminary one, sample size was only five patients. Recruitment of study subjects is still ongoing. In the present protocol, the study subjects were implanted with LVAD for end-stage heart failure, and were therefore unlike typical patients with CHF.

6. Conclusion

Although the study used a very small cohort, I confirmed that lower limb thermal therapy was quite safe and that it improved clinical symptoms and cardiac function in patients with extracorporeal LVAD who were awaiting heart transplantation. The procedure of lower limb thermal therapy might benefit other patients, including those with end-stage heart failure.

7. References

Bonetti PO, Pumper GM, Higano ST, Holmes Jr DR, Kuvin JT, Lerman A. (2004) Noninvasive identification of patients with early coronary atherosclerosis by assessment of digital reactive hyperemia. J Am Coll Cardiol 44:2137—41.

Cesarone MR, Belcaro G, Carratelli M, Cornelli U, De Sanctis MT, Incandela L, Barsotti A, Terranova R, Nicolaides A. (1999) A simple test to monitor oxidative stress. *Int Angiol* 18:127—30.

CIBIS Investigators and Committees. (1994) A randomized trial of beta-blockade in heart failure. *Circulation* 90:1765—73.

Cohn JN, Tognoni G, Glazer RD, Spormann D, Hester A. (1999) Rationale and design of the Valsartan Heart Failure Trial: a large multinational trial to assess the effects of valsartan, an angiotensin-receptor blocker, on morbidity and mortality in chronic congestive heart failure. *J Card Fail* 5:155—60.

Hamburg NM, Benjamin EJ. (2009) Assessment of endothelial function using digital pulse amplitude tonometry. Trends Cardiovasc Med 2009;19:6 –11.

Ikeda Y, Biro S, Kamogawa Y, Yoshifuku S, Eto H, Orihara K, Kihara T, Tei C. (2001) Repeated thermal therapy upregulates arterial endothelial nitric oxide synthase expression in Syrian golden hamsters. *Jpn Circ J* 65:434—8.

Ikeda Y, Biro S, Kamogawa Y, Yoshifuku S, Kihara T, Minagoe S, Tei C. (2002) Effect of repeated sauna therapy on survival in TO-2 cardiomyopathic hamsters with heart failure. *Am J Cardiol* 90:343−5.

Ikeda Y, Biro S, Kamogawa Y, Yoshifuku S, Eto H, Orihara K, Yu B, Kihara T, Miyata M, Hamasaki S, Otsuji Y, Minagoe S, Tei C. (2005) Repeated sauna therapy increases arterial endothelial nitric oxide synthase expression and nitric oxide production in cardiomyopathic hamsters. *Circ J* 69: 722−9.

Kihara T, Biro S, Imamura M, Yoshifuku S, Takasaki K, Ikeda Y, Otuji Y, Minagoe S, Toyama Y, Tei C. (2002) Repeated sauna treatment improves vascular endothelial and cardiac function in patients with chronic heart failure. *J Am Coll Cardiol* 39:754−9.

Kihara T, Biro S, Ikeda Y, Fukudome T, Shinsato T, Masuda A, Miyata M, Hamasaki S, Otsuji Y, Minagoe S, Akiba S, Tei C. (2004) Effects of repeated sauna treatment on ventricular arrhythmias in patients with chronic heart failure. *Circ J* 68:1146−51.

Kihara T, Miyata M, Fukudome T, Ikeda Y, Shinsato T, Kubozono T, Fujita S, Kuwahata S, Hamasaki S, Torii H, Lee S, Toda H, Tei C. (2009) Waon therapy improves the prognosis of patients with chronic heart failure. *J Cardiol*. 53(2):214-8.

Mann DL. (2008) Management of heart failure patients with reduced ejection fraction. In: Libby P, Bonow RO, Mann DL, Zipes DP, editors. *Braunwald's heart disease: a textbook of cardiovascular medicine. 8th ed.* Philadelphia: WB Saunders; 2008. p. 611−40.

Miyata M, Kihara T, Kubozono T, Ikeda Y, Shinsato T, Izumi T, Matsuzaki M, Yamaguchi T, Kasanuki H, Daida H, Nagayama M, Nishigami K, Hirata K, Kihara K, Tei C. (2008) Beneficial effects of Waon therapy on patients with chronic heart failure: results of a prospective multicenter study. *J Cardiol* 52:79−85.

Node K, Kitakaze M, Yoshikawa H, Kosaka H, Hori M. (1997) Reduced plasma concentrations of nitrogen oxide in individuals with essential hypertension. *Hypertension*. 30:405-8.

Osada K, Imaizumi T. (2005) Heart Transplant Candidate Registry Committee of the Japanese Circulation Society. Special report from the heart transplant candidate registry committee in Japan. *J Heart Lung Transplant* 24: 810−4.

Sasayama S, Asanoi H, Ishizaka S, Miyagi K. (1992) Evaluation of functional capacity of patients with congestive heart failure. In: Yasuda H, Kawaguchi H, editors. *New aspects in the treatment of failing heart.* Tokyo: Springer-Verlag; 113 – 117.

Takatani S, Matsuda H, Hanatani A, Nojiri C, Yamazaki K, Motomura T, Ohuchi K, akamoto T, Yamane T. (2005) Mechanical circulatory support devices (MCSD) in Japan: current status and future directions. *JArtif Organs* 8:13−27.

Tei C, Horikiri Y, Park JC, Jeong JW, Chang KS, Tanaka N, Toyama Y. (1994) Effects of hot water bath or sauna on patients with congestive heart failure: acute hemodynamic improvement by thermal vasodilation. *J Cardiol*. 24 (3): 175-183. Japanese.

Tei C, Horikiri Y, Park JC, Jeong JW, Chang KS, Toyama Y, Tanaka N. (1995) Acute hemodynamic improvement by thermal vasodilation in congestive heart failure. *Circulation*. 91(10):2582-2590.

Tei C, Tanaka N. (1996) Thermal vasodilation as a treatment of congestive heart failure: a novel approach. *J Cardiol* 27:29−30.

Tei C. (2007) Waon therapy: soothing warmth therapy. *J Cardiol* 49:301−4.

The CONSENSUS Trial Study Group. Effects of enalapril on mortality in severe heart failure. *N Engl J Med* 1987;316:1429—35.

Trotti R, Carratelli M, Barbieri M, Micieli G, Bosone D, Rondanelli M, Bo P. (2001) Oxidative stress and a thrombophilic condition in alcoholics without severe liver disease. *Haematologica* 86:85—91. 186
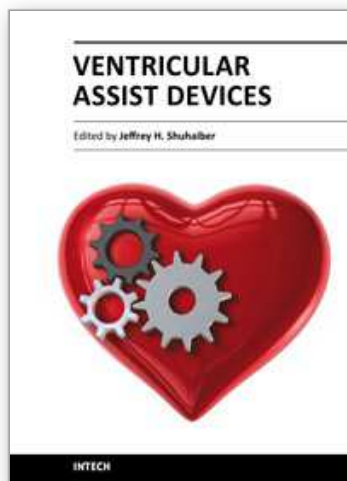
Ventricular Assist Devices

Edited by Dr. jeffrey Shuhaiber

The assist devices will continue adding a large number of years of life to humans globally and empower the medical society to optimize heart failure therapy. While expensive and cumbersome task, the foundation provided in this book reflects a contemporary product of original research from a multitude of different experts in the field. We hope this cumulative international effort provides the necessary tools for both the novice as well as the active practitioner aiming to change the outcome of these complex patients.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Kazuo Komamura (2011). Initial Experience of Lower Limb Thermal Therapy for Patients with an Extracorporeal Left Ventricular Assist Device Awaiting Heart Transplantation, Ventricular Assist Devices, Dr. jeffrey Shuhaiber (Ed.), ISBN: 978-953-307-164-0, InTech, Available from:

http://www.intechopen.com/books/ventricular-assist-devices/initial-experience-of-lower-limb-thermal-therapy-for-patients-with-an-extracorporeal-left-ventricula

INTECH
open science | open minds