

## 16.7 FIR for Healthy Heart & Healthy Blood Vessels -Vascular Endothelial Function

### **Summary of Endothelial Dysfunction**

#### **Definition:**

The Vascular Endothelial cells are the thin layer of **cells** that line the interior surface of **blood vessels**.

#### **Endothelial Dysfunction**

*J Am Soc Nephrol.* 2004 Aug;15(8):1983-92.

Endemann DH, Schiffrin EL.

#### **Abstract**

Endothelial dysfunction is characterized by a shift of the actions of the endothelium toward reduced vasodilation, a proinflammatory state, and prothrombic properties. It is associated with most forms of cardiovascular disease, such as hypertension, coronary artery disease, chronic heart failure, peripheral artery disease, diabetes, and chronic renal failure. Mechanisms that participate in the reduced vasodilatory responses in endothelial dysfunction include reduced nitric oxide generation, oxidative excess, and reduced production of hyperpolarizing factor. Upregulation of adhesion molecules, generation of chemokines such as macrophage chemoattractant peptide-1, and production of plasminogen activator inhibitor-1 participate in the inflammatory response and contribute to a prothrombic state. Vasoactive peptides such as angiotensin II and endothelin-1; the accumulation of asymmetric dimethylarginine, an endogenous nitric oxide inhibitor; hypercholesterolemia; hyperhomocysteinemia; altered insulin signaling; and hyperglycemia can contribute to these different mechanisms. Detachment and apoptosis of endothelial cells (anoikis) are associated phenomena.

Endothelial dysfunction is an important early event in the pathogenesis of atherosclerosis, contributing to plaque initiation and progression. Reductions in circulating endothelial progenitor cells that participate in regeneration of the endothelium participate in endothelial pathophysiology.

The severity of endothelial dysfunction has been shown to have prognostic value for cardiovascular events. Correction of endothelial dysfunction may be associated with reduced cardiovascular risk.

### **1. Effect of repeated (Far Infrared) sauna treatment on exercise tolerance and endothelial function in patients with chronic heart failure.**

*Am J Cardiol.* 2012 Jan 1;109(1):100-4. doi: 10.1016/j.amjcard.2011.08.014. Epub 2011 Sep 23.

Ohuri T, Nozawa T, Ihori H, Shida T, Sobajima M, Matsuki A, Yasumura S, Inoue H.

**Source:** Second Department of Internal Medicine, Graduate School of Medicine, University of Toyama, Japan.

#### **Abstract**

Repeated sauna treatment, known as Waon (Far Infrared) therapy, has been shown to improve cardiac function as well as exercise tolerance in patients with chronic heart failure. However, the underlying mechanisms of this therapy regarding these improvements remain to be elucidated. Forty-one patients with chronic heart failure (mean age  $68.3 \pm 13.5$  years old) underwent Waon (Far Infrared) therapy 5 times a week for 3 weeks. Before and after treatment, a number of assessments were performed in all subjects: 6-minute walk test, echocardiography, determination of neurohumoral factors and number of circulating CD34(+) cells, and a flow-mediated dilation (FMD) test of endothelial function. Cardiopulmonary exercise testing was also performed in 20 patients. Waon (Far Infrared) therapy increased the left ventricular ejection fraction (from  $30.4 \pm 12.6\%$  to  $32.5 \pm 12.8\%$ ,  $p = 0.023$ ) and reduced plasma levels of norepinephrine (from  $400 \pm 258$  to  $300 \pm 187$  pg/ml,  $p = 0.015$ ) and brain natriuretic peptide (from  $550 \pm 510$  to  $416 \pm 431$  pg/ml,  $p = 0.035$ ). Waon (Far Infrared) therapy increased the 6-minute walk distance (from  $337 \pm 120$  to  $379 \pm 126$  m,  $p < 0.001$ ) in association with an improvement in FMD (from  $3.5 \pm 2.3\%$  to  $5.5 \pm 2.7\%$ ,  $p < 0.001$ ) and an increase in the number of circulating CD34(+) cells ( $p = 0.025$ ). Changes in

6-minute walk distance were correlated positively with those in the left ventricular ejection fraction and FMD and negatively with those in plasma levels of norepinephrine and brain natriuretic peptide levels. A multivariate analysis revealed that an increase in FMD was the only independent determinant of 6-minute walk distance improvement. Finally, Waon (Far Infrared) therapy significantly increased peak Vo(2), and this increase was also correlated with changes in FMD.

*In conclusion, repeated (Far Infrared) sauna therapy in patients with chronic heart failure improves exercise tolerance in association with improvement in endothelial function.*

## **2. FIR therapy inhibits vascular endothelial inflammation via the induction of heme oxygenase-1.** *Arterioscler Thromb Vasc Biol. 2008 Apr;28(4):739-45. doi: 10.1161/ATVBAHA.107.160085. Epub 2008 Jan 17.*

Lin CC1, Liu XM, Peyton K, Wang H, Yang WC, Lin SJ, Durante W.

### **Abstract**

**OBJECTIVE:** Survival of arteriovenous fistulas (AVFs) in haemodialysis patients is associated with both far infrared (FIR) therapy and length polymorphisms of the heme oxygenase-1 (HO-1) promoter. In this study, we evaluated whether there is an interaction between (Far Infrared) FIR radiation and HO-1 in regulating vascular inflammation.

**METHODS AND RESULTS:** Treatment of cultured human umbilical vein endothelial cells (ECs) with FIR radiation stimulated HO-1 protein, mRNA, and promoter activity. HO-1 induction was dependent on the activation of the antioxidant responsive element/NF-E2-related factor-2 complex, and was likely a consequence of heat stress. FIR radiation also inhibited tumor necrosis factor (TNF)-alpha-mediated expression of E-selectin, vascular cell adhesion molecule-1, intercellular cell adhesion molecule-1, monocyte chemoattractant protein-1, interleukin-8, and the cytokine-mediated adhesion of monocytes to ECs. The anti-inflammatory action of FIR was mimicked by bilirubin, and was reversed by the HO inhibitor, tin protoporphyrin-IX, or by the selective knockdown of HO-1. Finally, the anti-inflammatory effect of FIR was also observed in patients undergoing hemodialysis.

**CONCLUSIONS:** These results demonstrate that (Far Infrared) FIR therapy exerts a potent anti-inflammatory effect via the induction of HO-1. The ability of (Far Infrared) FIR therapy to inhibit inflammation may play a critical role in preserving blood flow and patency of AVFs in haemodialysis patients.

## **3. Repeated sauna treatment improves vascular endothelial and cardiac function in patients with chronic heart failure.**

*J Am Coll Cardiol. 2002 Mar 6;39(5):754-9.*

Kihara T, Biro S, Imamura M, Yoshifuku S, Takasaki K, Ikeda Y, Otuji Y, Minagoe S, Toyama Y, Tei C .**Abstract**

**OBJECTIVES:** The purpose of this study was to determine the mechanism by which 60 degrees C sauna treatment improves cardiac function in patients with chronic heart failure (CHF).

**BACKGROUND:** We have previously reported that repeated 60 degrees C (FIR) sauna treatment improves hemodynamic data and clinical symptoms in patients with CHF. We hypothesized that the sauna restores endothelial function and then improves cardiac function.

**METHODS:** Twenty patients (62 plus minus 15 years) in New York Heart Association (NYHA) functional class II or III CHF were treated in a dry sauna at 60 degrees C for 15 min and then kept on bed rest with a blanket for 30 min, daily for two weeks. Ten patients with CHF, matched for age, gender and NYHA functional class, were placed on a bed in a temperature-controlled (24 degrees C) room for 45 min as the nontreated group. Using high-resolution ultrasound, we measured the diameter of the brachial artery at rest and during reactive hyperemia (percent flow-mediated dilation, %FMD: endothelium-dependent dilation), as well as after sublingual administration of nitroglycerin (%NTG: endothelium-independent dilation). Cardiac function was evaluated by measuring the concentrations of plasma brain natriuretic peptide (BNP).

**RESULTS:** Clinical symptoms were improved in 17 of 20 patients after two weeks of sauna therapy. The %FMD after two-week sauna treatment significantly increased from the baseline value, whereas the %NTG-induced dilation did not. Concentrations of BNP after the two-week sauna treatment decreased significantly. In addition, there was a significant correlation between the change in %FMD and the percent improvement in BNP concentrations in the sauna-treated group. In contrast, none of the variables changed at the two-week interval in the nontreated group.

**CONCLUSIONS:** Repeated sauna treatment improves vascular endothelial function, resulting in an improvement in cardiac function and clinical symptoms.

#### 4. Repeated thermal therapy improves impaired vascular endothelial function in patients with coronary risk factors.

J Am Coll Cardiol. 2001 Oct;38(4):1083-8.

Imamura M1, Biro S, Kihara T, Yoshifuku S, Takasaki K, Otsuji Y, Minagoe S, Toyama Y, Tei C.

##### Abstract

**OBJECTIVES:** We sought to determine whether sauna therapy, a thermal vasodilation therapy, improves endothelial function in patients with coronary risk factors such as hypercholesterolemia, hypertension, diabetes mellitus and smoking.

**BACKGROUND:** Exposure to heat is widely used as a traditional therapy in many different cultures. We have recently found that repeated sauna therapy improves endothelial and cardiac function in patients with chronic heart failure.

**METHODS:** Twenty-five men with at least one coronary risk factor (risk group: 38 +/- 7 years) and 10 healthy men without coronary risk factors (control group: 35 +/- 8 years) were enrolled. Patients in the risk group were treated with a 60 degrees C far infrared-ray dry sauna bath for 15 min and then kept in a bed covered with blankets for 30 min once a day for two weeks. To assess endothelial function, brachial artery diameter was measured at rest, during reactive hyperemia (flow-mediated endothelium-dependent dilation [%FMD]), again at rest and after sublingual nitroglycerin administration (endothelium-independent vasodilation [%NTG]) using high-resolution ultrasound.

**RESULTS:** The %FMD was significantly impaired in the risk group compared with the control group (4.0 +/- 1.7% vs. 8.2 +/- 2.7%,  $p < 0.0001$ ), while %NTG was similar (18.7 +/- 4.2% vs. 20.4 +/- 5.1%). Two weeks of sauna therapy significantly improved %FMD in the risk group (4.0 +/- 1.7% to 5.8 +/- 1.3%,  $p < 0.001$ ). In contrast, %NTG did not change after two weeks of sauna therapy (18.7 +/- 4.2% to 18.1 +/- 4.1%).

**CONCLUSIONS:** Repeated sauna treatment improves impaired vascular endothelial function in the setting of coronary risk factors, suggesting a therapeutic role for sauna treatment in patients with risk factors for atherosclerosis.