

# BASHAR et al, 2014 META-ANALYSIS ABSTRACTS and REFERENCE AVF Maturation and Survival in Hemodialysis and Post-angioplasty Results with Far Infrared Therapy

## **1. Dr. Kahlil Bashar et al, 2014 Meta-analysis**

### **Role of Far Infra-Red Therapy in Dialysis Arterio-Venous Fistula Maturation and Survival: Systematic Review and Meta-Analysis.**

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**Bashar K, (2014),** Healy D, Brown LD, Kheirelseid EAH, Walsh MT, et al.( 2014) *PLoS ONE* 9(8): e104931. doi:10.1371/journal.pone.0104931

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#### **Abstract**

**Introduction:** A well-functioning arteriovenous fistula (AVF) is the best modality for vascular access in patients with end- stage renal disease (ESRD) requiring haemodialysis (HD). However, AVFs' main disadvantage is the high rate of maturation failure, with approximately one third (20%–50%) not maturing into useful access. This review examines the use of Far-Infra Red therapy in an attempt to enhance both primary (unassisted) and secondary (assisted) patency rates for AVF in dialysis and pre-dialysis patients.

**Method:** We performed an online search for observational studies and randomised controlled trials (RCTs) that evaluated FIR in patients with AVF. Eligible studies compared FIR with control treatment and reported at least one outcome measure relating to access survival. Primary patency and secondary patency rates were the main outcomes of interest.

**Results:** Four RCTs (666 patients) were included. **Unassisted patency assessed in 610 patients, and was significantly better among those who received FIR (228/311) compared to (185/299) controls (pooled risk ratio of 1.23 [1.12–1.35], p = 0.00001).** In addition, **the two studies which reported secondary patency rates showed significant difference in favour of FIR therapy- 160/168 patients - compared to 140/163 controls (pooled risk ratio of 1.11 [1.04–1.19], p = 0.003).**

**Conclusion:** FIR therapy may positively influence the complex process of AVF maturation improving both primary and secondary patency rates. However blinded RCTs performed by investigators with no commercial ties to FIR therapy technologies are needed.

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AVF Maturation and Survival in Hemodialysis and Post-angioplasty  
Results with Far Infrared Therapy

**2. Randomized Controlled Trials Included:**

**(1) Post-angioplasty far infrared radiation therapy improves 1-year angioplasty-free hemodialysis access patency of recurrent obstructive lesions.**

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Lai CC (2013), Fang HC, Mar GY, Liou JC, Tseng CJ, Liu CP. *Eur J Vasc Endovasc Surg.* 2013 Dec;46(6):726-32.

**(2) Far-infrared therapy: a novel treatment to improve access blood flow and unassisted patency of arteriovenous fistula in hemodialysis patients. \*Lin CC**

(2007), Chang CF, Lai MY, Chen TW, Lee PC, Yang WC. *J Am Soc Nephrol.* 2007 Mar18(3):985-92.

**(3) Effect of far infrared therapy on arteriovenous fistula maturation: An open-label randomized controlled trial.**

Lin CC (2013 AKJD), Yang WC, Chen MC, Liu WS, Yang CY, Lee PC *Am J Kidney Dis.* 2013.62(2):304-311.

**(4) Length polymorphisms of heme oxygenase-1 determine the effect of far-infrared therapy on the function of arteriovenous fistula in hemodialysis patients: A novel physiogenomic study.**

Lin CC (2013 NDT), Chung MY, Yang WC, Lin SJ, Lee PC. *Nephrol Dial Transplant.* 2013 May; 28(5):1284-93

**3. Reference:**

**Far Infrared Therapy Inhibits Vascular Endothelial**

**Inflammation via the Induction of Heme Oxygenase-1**

Chih-Ching Lin, Xiao-Ming Liu, Kelly Peyton, Hong Wang, Wu-Chang Yang, Shing-Jong Lin, William Durante. *Arterioscler Thromb Vasc Biol.* 2008;28:739-745

## ABSTRACTS

### (1) Far-Infrared Therapy: A Novel Treatment to Improve Access Blood Flow and Unassisted Patency of Arteriovenous Fistula in Hemodialysis Patients

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**Vascular access malfunction**, usually presenting with an inadequate access flow (Qa), is the leading cause of morbidity and hospitalization in hemodialysis (HD) patients. Many methods of thermal therapy have been tried for improving Qa but with limited effects. This randomized trial was designed to evaluate the effect of far-infrared (FIR) therapy on access flow and patency of the native arteriovenous fistula (AVF). A total of 145 HD patients were enrolled with 73 in the control group and 72 in the FIR group. A WS TY101 FIR emitter was used for 40 min, and hemodynamic parameters were measured by the Transonic HD02 monitor during HD. The Qa1/Qa2 and Qa3/Qa4 were defined as the Qa measured at the beginning/at 40 min later in the HD session before the initiation and at the end of the study, respectively. The incremental change of Qa in the single HD session with FIR therapy was significantly higher than that without FIR therapy (13.2  $\pm$  114.7 versus  $\pm$  33.4  $\pm$  132.3 ml/min;  $P = 0.021$ ). In comparison with control subjects, patients who received FIR therapy for 1 yr had (1) a lower incidence (12.5 versus 30.1%;  $P < 0.01$ ) and relative incidence (one episode per 67.7 versus one episode per 26.7 patient-months;  $P = 0.03$ ) of AVF malfunction; (2) higher values of the following parameters, including  $\pm$ (Qa4  $\pm$  Qa3) (36.2  $\pm$  82.4 versus  $\pm$  12.7  $\pm$  153.6 ml/min;  $P = 0.027$ ),  $\pm$ (Qa3  $\pm$  Qa1) (36.3  $\pm$  166.2 versus  $\pm$  51.7  $\pm$  283.1 ml/min;  $P = 0.035$ ),  $\pm$ (Qa4  $\pm$  Qa2) (99.2  $\pm$  144.4 versus  $\pm$  47.5  $\pm$  244.5 ml/min;  $P < 0.001$ ), and  $\pm$ (Qa4  $\pm$  Qa2)  $\pm$ (Qa3  $\pm$  Qa1) (62.9  $\pm$  111.6 versus  $\pm$  4.1  $\pm$  184.5 ml/min;  $P = 0.032$ ); and (3) a better unassisted patency of AVF (85.9 versus 67.6%;  $P < 0.01$ ).

**IN CONCLUSION**, FIR therapy, a noninvasive and convenient therapeutic modality, can improve Qa and survival of the AVF in HD patients through both its thermal and its nonthermal effects.

*J Am Soc Nephrol* 18: 985–992, 2007. doi: 10.1681/ASN.2006050534

# BASHAR et al, 2014 META-ANALYSIS ABSTRACTS and REFERENCE AVF Maturation and Survival in Hemodialysis and Post-angioplasty Results with Far Infrared Therapy

## (2) Effect of Far Infrared Therapy on Arteriovenous Fistula

### Maturation: An Open-Label Randomized Controlled Trial

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**Background:** Malfunction of the arteriovenous fistula (AVF) is an important cause of morbidity and hospitalization in hemodialysis (HD) patients. The aim of this study is to evaluate the effect of far infrared therapy on the maturation and patency of newly created AVFs in patients with chronic kidney disease stage 4 or 5.

**Study Design:** Randomized controlled study.

**Setting & Participants:** Patients with estimated glomerular filtration rate of 5-20 mL/min/1.73 m<sup>2</sup>.

**Intervention:** 40 minutes of far infrared therapy 3 times weekly for a year.

**Outcomes:** The primary outcome is the rate of AVF malfunction within 12 months, with malfunction defined as either: (1) thrombosis without thrill for AVFs not undergoing HD or (2) receiving any type of interventional procedure due to a lower Kt/V (<1.2) for patients undergoing HD. Secondary outcomes include: (1) cumulative primary unassisted AVF patency, defined as time from creation of the AVF to the first episode of AVF malfunction; (2) physiologic maturation of the AVF by the definition of AVF access blood flow (Qa) >500 mL/min and AVF diameter >4 mm at 3 months; and (3) clinical maturation of the AVF suitable for HD at 1 year.

**Measurements:** AVF Qa was measured by Doppler ultrasonography at 2 days and 1, 2, 3, and 12 months. **Results:** We enrolled 122 patients who were randomly allocated to the intervention (n = 60) and control (n = 62) groups. In comparison to controls, patients in the intervention group had higher Qa values at 1, 2, 3, and 12 months; a higher rate of physiologic maturation (90% vs 76%; *P* = 0.04) at 3 months; and a lower rate of AVF malfunction (12% vs 29%; *P* = 0.02) but higher rates of AVF cumulative unassisted patency (87% vs 70%; *P* = 0.01) and clinical maturation (82% vs 60%; *P* = 0.008) within 12 months.

**Limitations:** This is a single-center nonblinded study.

**Conclusions:** Far infrared therapy improves the access flow, maturation, and patency of newly created AVFs in patients with chronic kidney disease stages 4 and 5.

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**Index Words:** Arteriovenous fistula (AVF); chronic kidney disease (CKD); far infrared therapy; hemodialysis (HD); maturation.

# BASHAR et al, 2014 META-ANALYSIS ABSTRACTS and REFERENCE AVF Maturation and Survival in Hemodialysis and Post-angioplasty Results with Far Infrared Therapy

## **(3) Post-angioplasty Far Infrared Radiation Therapy Improves 1-Year Angioplasty-Free Hemodialysis Access Patency of Recurrent Obstructive Lesions**

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**Objective:** To explore the role of far infrared (FIR) radiation therapy for hemodialysis (HD) access maintenance after percutaneous transluminal angioplasties (PTA).

**Methods:** This was a prospective observational study. Eligible patients were those who received repeated PTA with the last PTA successfully performed within 1 week before the study enrollments. Consecutively enrolled patients undergoing successful HD treatments after PTA were randomly assigned to the FIR-radiated group or control group without radiation. FIR-radiated therapy meaning 40-minute radiation at the major lesion site or anastomosed site three times a week was continued until an end-point defined as dysfunction-driven re-PTA or the study end was reached.

**Results:** Of 216 participants analyzed, including 97 with arteriovenous grafts (AVG) (49 FIR-radiated participants and 48 control participants) and 119 with arteriovenous fistulas (AVF) (69 FIR-radiated participants and 50 control participants), the FIR-radiated therapy compared with free-radiated usual therapy significantly enhanced PTA-unassisted patency at 1 year in the AVG subgroup (16.3% vs. 2.1%;  $p < .01$ ), but not the AVF subgroup (25.0% vs. 18.4%;  $p = .50$ ), and this accounted for the overall improved patency rates (21.4% vs. 10.3%;  $p = .02$ ).

**Conclusions:** This study suggests FIR-radiated therapy improves PTA-unassisted patency in patients with AVG who have undergone previous PTA.

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**Keywords:** Arteriovenous fistula, Arteriovenous graft, Far infrared radiation, Hemodialysis, Intimal hyperplasia, Patency, Percutaneous transluminal angioplasty

# BASHAR et al, 2014 META-ANALYSIS ABSTRACTS and REFERENCE AVF Maturation and Survival in Hemodialysis and Post-angioplasty Results with Far Infrared Therapy

## **(4) Length polymorphisms of heme oxygenase-1 determine the effect of far infrared therapy on the function of arteriovenous fistula in hemodialysis patients: a novel physcogenomic study.**

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### **Abstract**

**BACKGROUND:** The objective of this study was to evaluate the interaction between the length polymorphism of the guanosine thymidine repeat [(GT)n] in the heme oxygenase-1 (HO-1) gene and far-infrared (FIR) therapy on access flow (Qa) and arteriovenous fistula (AVF) patency in hemodialysis (HD) patients.

**METHODS:** A total of 280 HD patients were randomized into a control group (n = 141) and the FIR group (n = 139) who received 40 min of FIR therapy three times weekly for a year during the study period from May 2005 to December 2007. Access flow was measured during HD. The [(GT)n] was determined with the definition of long (L) allele as [(GT)n] ≥ 30 and short (S) allele as [(GT)n] < 30.

**RESULTS:** The Qa decreased from S/S to S/L and further to the L/L group but increased by FIR therapy with the highest Qa increase in the S/S group. The incidence of AVF malfunction decreased both from the L/L, S/L to S/S group (32.4 versus 17.2 versus 10.9%, P = 0.007) and from the control group to FIR group (27.5 versus 12.6%, P = 0.004). Significant associations were found between AVF malfunction and the following factors (hazard ratio, P-value): a past history of AVF malfunction (2.45, P = 0.044), FIR therapy (0.369, P = 0.03) and L/L genotypes of HO-1 (2.531 versus S/S + S/L genotypes). The 1-year unassisted patency decreased from 91.9 and 77.6% in S/S and S/L subgroups with and without FIR therapy to 75.8 and 60% for L/L subgroup with and without FIR therapy, respectively (P < 0.001).

**CONCLUSIONS:** FIR therapy improves Qa and patency of AVF in HD patients, with the best protective effect in those with S/S genotype of HO-1.

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# BASHAR et al, 2014 META-ANALYSIS ABSTRACTS and REFERENCE AVF Maturation and Survival in Hemodialysis and Post-angioplasty Results with Far Infrared Therapy

## **(5) Far Infrared Therapy Inhibits Vascular Endothelial Inflammation via the Induction of Heme Oxygenase-1**

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**Objective**—Survival of arteriovenous fistulas (AVFs) in hemodialysis 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 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 FIR therapy exerts a potent anti-inflammatory effect via the induction of HO-1. The ability of FIR therapy to inhibit inflammation may play a critical role in preserving blood flow and patency of AVFs in hemodialysis patients.

**Arterioscler Thromb Vasc Biol. 2008;28:739-745**

**Key Words:** endothelium \_ far infrared therapy \_ inflammation \_ leukocyte adhesion