



ELSEVIER



# Extracorporeal Shock Wave Therapy Induces Therapeutic Lymphangiogenesis in a Rat Model of Secondary Lymphoedema

F. Serizawa<sup>a</sup>, K. Ito<sup>b</sup>, M. Matsubara<sup>c</sup>, A. Sato<sup>a,\*</sup>, H. Shimokawa<sup>b</sup>, S. Satomi<sup>a</sup>

<sup>a</sup> Division of Advanced Surgical Science and Technology, Tohoku University Graduate School of Medicine, 1-1 Seiryomachi, Aoba-ku, Sendai 980-8574, Japan

<sup>b</sup> Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan

<sup>c</sup> Division of Molecular Medicine, Centre for Translational and Advanced Animal Research, Tohoku University School of Medicine, Sendai, Japan

Submitted 17 September 2010; accepted 5 February 2011

## KEYWORDS

Shock wave therapy;  
Lymphangiogenesis;  
Lymphoedema

**Abstract Objective:** Lymphoedema is a common complication after cancer treatment. We have reported that low-energy extracorporeal shock wave (SW) therapy up-regulates vascular endothelial growth factor (VEGF) in ischaemic myocardium. As VEGF plays an important role in lymphangiogenesis, we investigated whether our low-energy SW therapy enhances lymphangiogenesis in rats.

**Methods:** We created a tail model of lymphoedema in rats. The tail was treated with or without low-energy SW therapy ( $0.25 \text{ mJ mm}^{-2}$ , 500 impulses) four times (days 3, 5, 7, and 9). The tail volume and the fluorescence intensity of indocyanine green (ICG) were measured. The expression of VEGF-C and basic fibroblast growth factor (bFGF) were evaluated by RT-PCR, and the lymphatic vessel density was assessed histochemically.

**Results:** The tail volume increased significantly in the control group and was significantly improved in the SW group. The lymphatic system function (evaluated with fluorescence intensity of ICG), the lymphatic vessel density, and the expression of VEGF-C and bFGF were all enhanced by the SW therapy (all  $P < 0.05$ ).

**Conclusions:** The low-energy SW therapy induces therapeutic lymphangiogenesis by up-regulating VEGF-C and bFGF, and improves lymphoedema in a rat-tail model, suggesting that low-energy SW therapy could be a non-invasive and effective strategy for lymphoedema in humans.

© 2011 European Society for Vascular Surgery. Published by Elsevier Ltd. All rights reserved.

\* Corresponding author. Tel.: +81 22 717 7214; fax: +81 22 717 7217.  
E-mail address: [attkas@med.tohoku.ac.jp](mailto:attkas@med.tohoku.ac.jp) (A. Sato).