

## Lampiran. 1 Database Artikel

The image displays three screenshots of search results for the query: ("Vibration") AND ("Wound Healing") ("Foot Ulcer" OR "Plantar Ulcer") AND ("Diabetic").

**Top Screenshot: Google Scholar**  
The search results show approximately 1,470 articles. The top results include:

- HTML | mdpi.com**: "The Effect of Vibration on the Acceleration of Wound Healing of Diabetic Neuropathic Foot Ulcer: A Prospective Experimental Study on Human Patients" by S. Syabariyah, E. Nuradimala, B. Widjaja, S. Prasetyo, et al. (2023). Abstract: "We propose complementary diabetic neuropathic foot ulcer wound care for diabetic patients using vibration therapy to enhance the wound recovery rate and accelerate the wound..."
- PDF | academia.edu**: "Effect of mechanical vibration therapy on healing of foot ulcer in diabetic polyneuropathy patients" by HG Mahran, GE Helal, AAR El-Eiky, et al. (2013). Abstract: "... for wound healing. In the present study, the effectiveness and safety of mechanical vibration that has ... To minimize situational bias, the same foot ulcer treatment and care regimen was..."
- PDF | researchsquare.com**: "Protocol for a Randomised Controlled Trial to Investigate the Enhancement of Diabetic Foot Ulcer Healing Using Low-Magnitude High-Frequency Vibration ..." by SKK Ling, NCL Hung, WH Cheung, PSH Yung, et al. (2021). Abstract: "... 107 Animal studies on low-magnitude high-frequency vibration showed improved ... of 96 diabetic rats with foot wounds showed that LMHFV significantly accelerated 111 wound healing..."

**Middle Screenshot: ScienceDirect**  
The search results show 305 results. The top results include:

- Research article**: "Improved wound healing of diabetic foot ulcers using human placenta-derived mesenchymal stem cells in gelatin electrospun nanofibrous scaffolds plus a platelet-rich plasma gel: a randomized clinical trial" by Rabkhaah Maamar, Lela Ghassemi-Mobarkeh, et al. (2023).
- Research article**: "Cellulose nanofibrils reinforced chitosan-gelatin based hydrogel loaded with nanoemulsion of oregano essential oil for diabetic wound healing assisted by low level laser therapy" by Sinjunnisa Abdul Razak, Yeachen Lee, et al. (2023).
- Research article**: "Platelet-rich plasma-loaded bioactive chitosan@sodium alginate@gelatin shell-core fibrous hydrogels with enhanced sustained release of growth factors for diabetic foot ulcer healing" by Qiwei Huang, Tinglin Wu, et al. (2023).

**Bottom Screenshot: SpringerLink**  
The search results show 14 results for the query. The top result is:

- Article**: "Phenytoin-loaded bioactive nanoparticles for the treatment of diabetic pressure ulcers: formulation and in vitro/in vivo evaluation" by Marwa M. Sheir, Maha M. A. Nasra, et al. (2022). Abstract: "Drug repurposing offers the chance to explore the full potential of existing drugs while reducing drug development time and costs. For instance, the anticonvulsant drug phenytoin (PHT) has been investigated for..."
- Article**: "EPMA-World Congress 2015" by A1 Predictive and prognostic biomarker panel for targeted application of radioembolisation improving individual outcomes in hepatocellular carcinoma.

Search all BMC articles

("Vibration") AND ("Wound Healing") ("Foot Ulcer" OR "Plantar Ulcer") AND ("Diabetic")


**34 result(s) for {"Vibration"} AND {"Wound Healing"} {"Foot Ulcer" OR "Plantar Ulcer"} AND {"Diabetic"} within BMC**

Page 1 of 2 Sort by: Relevance | [Date](#)

**Translational development of ABCB5<sup>+</sup> dermal mesenchymal stem cells for therapeutic induction of angiogenesis in non-healing diabetic foot ulcers**

While rapid healing of diabetic foot ulcers (DFUs) is highly desirable to avoid infections, amputations and life-threatening complications, DFUs often respond poorly to standard treatment. GMP-manufactured skin...

Andreas Kerstan, Kathrin Dieter, Elke Niebergall-Roth, Sabrina Klingele, Michael Jünger, Christoph Hasslacher, Georg Daeschlein, Lutz Stemler, Ulrich Meyer-Pannwitt, Kristin Schubert, Gerhard Klausmann, Titus Raab, Matthias Goebeler, Korinna Kraft, Jasmina Esterlechner,



pubmed.ncbi.nlm.nih.gov/?term=%28Vibration%29+AND+%28Wound+Healing%29+%28Foot+Ulcer%29+OR+%28Plantar+Ulcer%29+AND+%28Diabetic%29

An official website of the United States government. [Here's how you know.](#)

**NIH** National Library of Medicine  
National Center for Biotechnology Information

**PubMed**

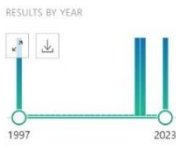
("Vibration") AND ("Wound Healing") ("Foot Ulcer" OR "Plantar Ulcer") AND ("Diabetic")

Advanced Create alert Create RSS User Guide

Save Email Send to Sorted by: Best match Display options

MY NCBI FILTERS 4 results

RESULTS BY YEAR



TEXT AVAILABILITY

The Effect of **Vibration** on the Acceleration of **Wound Healing** of Diabetic Neuropathic **Foot Ulcer**: A Prospective Experimental Study on Human Patients.

Cite Syabariyah S, Nurachmah E, Widjono BD, Prasetyo S, Sanada H, Irianto, Nakagami G, Suriadi, Kardiatus T, Hisan UK.

Share Healthcare (Basel). 2023 Jan 9;11(2):191. doi: 10.3390/healthcare11020191. PMID: 36673559 [Free PMC article](#).

This result suggests that there is evidence that vibrations may accelerate **diabetic neuropathic ulcer healing** in human patients. However, to the best of our knowledge, the effect of **vibration** on the enhancements of **diabetic foot ulcer**...

tandfonline.com/action/doSearch?AllField=%28Vibration%29+AND+%28Wound+Healing%29+%28Foot+Ulcer%29+OR+%28Plantar+Ulcer%29+AND+%28Diabetic%29

Taylor & Francis Online

Home Search

("Vibration") AND ("Wound Healing") ("Foot Ulcer" OR "Plantar Ulcer") AND ("Diabetic")

Advanced search

**Modify your search**

Anywhr ("Vibration") AND ("Wound Healing") ("Foot Ulcer" OR "Plantar Ulcer") AND ("Diabetic")

**Search**

**Search results**

Showing 0 of 0 results for search: [All: "vibration"] AND [All: "wound healing"] AND ([All: "foot ulcer"] OR [All: "plantar ulcer"]) AND [All: (" AND [All: "diabetic"].)]

**Your search did not match any articles.**

Suggestions:

- The search string needs to contain some keywords that are not stopwords.
- Make sure all terms are spelled correctly.
- Try different terms.
- Try more general terms.
- Try fewer terms.
- Placing "NOT" at the beginning of a search query is not supported unless you are searching within previous results.

garuda.kemdikbud.go.id/documents?g=%28Vibration%29+AND+%28Wound+Healing%29+%28Foot+Ulcer+OR+Plantar+Ulcer%29+AND+%28Diabetic%29

**GARUDA**  
SARANA RIJOUKUN DIGITAL

Home Publisher Journal / Conference Subject Suggest Guidebook

Search By: Title  
Keywords: ["Vibration"] AND ["Wound Healing"] ("Foot Ulcer" OR "Plantar Ulcer") AND ("Diabetic")  
Publisher: Publisher Name

Downloadable PDF Only

Filter By Year: 0000

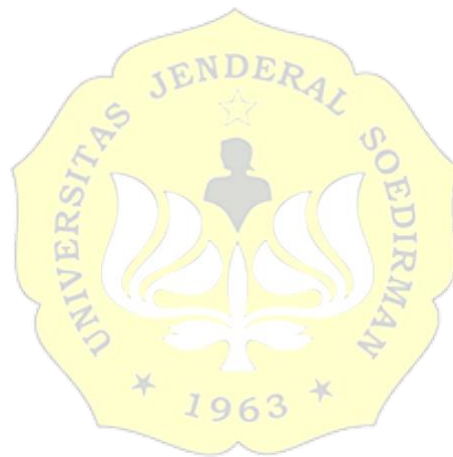
From: To: Filter Reset

**Found 0 documents**  
Search ("Vibration") AND ("Wound Healing") (&quot;Foot Ulcer&quot; OR &quot;Plantar Ulcer&quot;) AND ("Diabetic").

Sinta Bima Arjuna PDDIKTI Risbang Scopus Rama

Kementerian Pendidikan, Kebudayaan, Riset, dan Teknologi  
(The Ministry of Education, Culture, Research, and Technology)  
© 2018

30°C Cerah 16:46 23/05/2023



## Artikel 1

### Effect of Mechanical Vibration Therapy on Healing of Foot Ulcer in Diabetic Polyneuropathy Patients.

Hesham G. Mahran<sup>1</sup>, Omar Farouk Helal<sup>2</sup>, Amir Abdel-Raouf El Fiky<sup>3</sup>

<sup>1</sup>. Department of Physical Therapy for Surgery, Faculty of Physical Therapy, Cairo University, Egypt.

<sup>2</sup>. Physical Therapy Department, Faculty of Applied Medical Sciences, Umm Al Qura University. KSA.

<sup>3</sup>. Department of Physical Therapy for Neurological Disorders and its Surgery, Cairo University. Egypt.

[dr.mon5@hotmail.com](mailto:dr.mon5@hotmail.com).

**Abstract:** Diabetic foot complications are the most common cause of non-traumatic lower extremity amputations in the industrialized world. The risk of lower extremity amputation is higher in diabetics than in persons who do not have diabetes mellitus. Furthermore, foot complications are the most frequent reason for hospitalization in patients with diabetes. Diabetic neuropathy is the impact of diabetes on the nervous system, most commonly causing numbness, tingling and pain in the feet and also increasing the risk of skin damage due to altered sensation. Together with vascular disease in the legs, neuropathy contributes to the risk of diabetes-related foot problems (such as diabetic foot ulcers) that can be difficult to treat and occasionally require amputation. Early detection and appropriate treatment of these ulcers may prevent up to 85 percent of amputations. **Purpose:** To detect the effect of low mechanical vibration on healing of diabetic foot ulcer. **Methods:** Twenty nine diabetic patients with type 2 diabetes (21 males and 8 females) suffer from diabetic ischemic foot ulcer (grade A1) will be divided into 2 groups; 1st study group received low mechanical vibration for 15 minutes for session, 3session/day, 5day/week for 4 weeks and control group received no treatment. Assessment of wound size (length, width and area) by Visitrak device for both groups was done 3 times as follow; 1st assessment done before assessment, the 2nd assessment was done 2 weeks after the beginning of treatment and the 3rd assessment was done 4 weeks after beginning of treatment. **Results:** In study group; there was significant difference between pre- treatment mean value of ulcer area and two weeks post- treatment mean value of ulcer area as *p* value .019, there was significant difference between two weeks mean value of ulcer area and four weeks post- treatment mean value of ulcer area as *p* value 0.014, and there was significant differences between pre- treatment mean value of ulcer area and four weeks post- treatment mean value of ulcer area as *p* value .032. Between groups; there was significant difference between the study and control groups in mean value of ulcer areas after two weeks of treatment as *p* value 0.014, and there was highly significant difference between the study and control groups in mean value of ulcer area after four weeks of treatment *p* value 0.008. **Conclusion:** It can be concluded that low mechanical vibration may improve healing of diabetic foot ulcer. [Mahran HG, Helal OF, El-Fiky AA. **Effect of Mechanical Vibration Therapy on Healing of Foot Ulcer in Diabetic Polyneuropathy Patients.** *J Am Sci* 2013;9(7):76-87]. (ISSN: 1545-1003). <http://www.iofamericanscience.org>. 8

**Key words:** (diabetic polyneuropathy, foot ulcer, mechanical vibration).

#### 1-Introduction:

Diabetes mellitus, or simply diabetes, is a group of metabolic diseases in which a person has high blood sugar, either because the body does not produce enough insulin, or because cells do not respond to the insulin that is produced. This high blood sugar produces the classical symptoms of polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger). All forms of diabetes increase the risk of long-term complications (David G. and Gardner, 2011).

The major long-term complications relate to damage to blood vessels. Diabetes doubles the risk of cardiovascular disease. The main "macrovascular" diseases (related to atherosclerosis of larger arteries) are ischemic heart disease (angina and myocardial infarction), stroke and peripheral vascular disease. Diabetes also damages the capillaries (causes micro angiopathy). Diabetic neuropathy is the impact of

diabetes on the nervous system, most commonly causing numbness, tingling and pain in the feet and also increasing the risk of skin damage due to altered sensation. Together with vascular disease in the legs, neuropathy contributes to the risk of diabetes-related foot problems (such as diabetic foot ulcers) that can be difficult to treat and occasionally require amputation (Boussageon, 2011).

The vast majority of diabetic foot complications resulting in amputation begin with the formation of skin ulcers. Early detection and appropriate treatment of these ulcers may prevent up to 85 percent of amputations. Careful inspection of the diabetic foot on a regular basis is one of the easiest, least expensive and most effective measures for preventing foot complications (Bethesda, 1987).

Diabetic foot ulcers result from the simultaneous action of multiple contributing causes. The major underlying causes are noted to be



## Whole body vibration training improves leg blood flow and adiposity in patients with type 2 diabetes mellitus

Borja Sañudo · Rosa Alfonso-Rosa ·  
Borja del Pozo-Cruz · Jesus del Pozo-Cruz ·  
Delfin Galiano · Arturo Figueroa

Received: 19 February 2013 / Accepted: 24 April 2013  
© Springer-Verlag Berlin Heidelberg 2013

**Abstract** This study aimed at examined the effect of a 12-week whole body vibration (WBV) training program on leg blood flow and body composition in people with type 2 diabetes mellitus (T2DM). Forty participants were randomly assigned to either a WBV training group (WBV;  $n = 20$ ) or usual-care control group (CON;  $n = 20$ ). Body composition [waist circumference, waist to hip ratio (WHR), weight, height, percentage of body fat and fat-free mass], heart rate, and blood flow [femoral artery diameter, maximum systolic velocity, maximum diastolic velocity (DV), time averaged mean, pulsatility index and resistance index (RI), mean velocity ( $V_{med}$ ), and peak blood velocities (PBV)] were assessed at baseline and after 12 weeks. There were significant increases in the blood flow ( $p = 0.046$ ),  $V_{med}$  ( $p = 0.050$ ), and DV ( $p = 0.037$ ) after WBV compared with CON. Within-group analysis showed significant differences in  $V_{med}$ , PBV, and DV in the WBV

group. Significant decreases after the intervention in weight ( $p < 0.001$ ), waist circumference ( $p < 0.001$ ), WHR ( $p < 0.05$ ), and body fat ( $p < 0.05$ ) were also found, with significant between-groups decreases in all these outcomes in the WBV group. Significant correlations existed between changes in percent body fat and blood flow [blood flow ( $-0.761$ ),  $V_{med}$  ( $-0.607$ ), PBV ( $-0.677$ ), and RI (0.0510)]. WBV training can be considered an effective means to increase leg blood flow and to reduce adiposity in patients with T2DM.

**Keywords** Doppler ultrasound · Femoral artery · Body fat · Fat-free mass · Vibration training

### Introduction

The prevalence of type 2 diabetes mellitus (T2DM) is increasing and is reaching epidemic proportions worldwide. Obesity, hypertension, insulin resistance, and hyperglycemia may contribute to the impaired arterial function in T2DM (Chudyk and Petrella 2011; Gerich 2007). Reduction in peripheral blood flow in T2DM is endothelial dependent (Lalande et al. 2008; Lohman et al. 2007). Arteries in lower extremities develop more severe dysfunction than those in upper extremities in middle-aged adults with T2DM (Silber et al. 2007).

Exercise therapy has been reported to reduce hyperglycemia, insulin resistance, dyslipidemia, and hypertension which lead to improved vascular function in T2DM (Sato et al. 2007) and, therefore, is recognized as a cornerstone of diabetes management (Chudyk and Petrella 2011). Evidence of vasodilation following aerobic and resistance exercise training in individuals with T2DM (Okada et al. 2010) suggests that exercise increases arterial

Communicated by Guido Ferretti.

Trial Number: ACTRN1261300021774.


**Electronic supplementary material** The online version of this article (doi:10.1007/s00421-013-2654-3) contains supplementary material, which is available to authorized users.

B. Sañudo (✉) · R. Alfonso-Rosa · B. del Pozo-Cruz ·  
J. del Pozo-Cruz  
Physical Education and Sports Department, University of  
Seville, Pirotécnia s/n, 41012 Seville, Spain  
e-mail: bsancor@us.es

D. Galiano  
University Pablo de Olavide, Seville, Spain

A. Figueroa  
Department of Nutrition, Food and Exercise Sciences,  
The Florida State University, Tallahassee, FL, USA

Published online: 09 May 2013

 Springer



Contents lists available at ScienceDirect

Maturitas

journal homepage: [www.elsevier.com/locate/maturitas](http://www.elsevier.com/locate/maturitas)



## Effects of a 12-wk whole-body vibration based intervention to improve type 2 diabetes



Borja del Pozo-Cruz<sup>a,\*</sup>, Rosa M. Alfonso-Rosa<sup>b</sup>, Jesus del Pozo-Cruz<sup>b</sup>, Borja Sañudo<sup>b</sup>, Michael E. Rogers<sup>c</sup>

<sup>a</sup> Department of Sport and Exercise Science, University of Auckland, Auckland, New Zealand

<sup>b</sup> Department of Physical Education and Sports, University of Seville, Seville, 5, Spain

<sup>c</sup> Department of Human Performance Studies, Wichita State University, Wichita, KS, 6, USA

### ARTICLE INFO

#### Article history:

Received 27 July 2013

Received in revised form 18 August 2013

Accepted 4 September 2013

#### Keywords:

Glycemic control  
Diabetic patients  
Vibration therapy  
Exercise therapy  
Prevention therapy

### ABSTRACT

**Objective:** To test the feasibility, safety and effectiveness of a 12-wk whole body vibration (WBV) intervention on glycemic control, lipid-related cardiovascular risk factors and functional capacity among type 2 diabetes mellitus (T2DM) patients in a primary care context.

**Methods:** Fifty non-insulin dependent T2DM patients were randomized 1:1 to an intervention group that, in addition to standard care, received a 12-wk WBV intervention, and a control group receiving only standard care (from February 2012 through May 2012). Outcomes, including glycated hemoglobin (HbA1c), fasting blood glucose, lipid-related cardiovascular risk factors (i.e., cholesterol, triglycerides, lipoproteins, LDL/HDL and atherogenic index) and functional capacity were measured at baseline and after the 12-wk intervention.

**Results:** After intervention, there was a reduction in HbA1c and fasting blood glucose when compared to the control group, with a mean difference in change scores between groups of  $-0.55\%$  (95% CI  $-0.15$  to  $-0.76$ ) and  $-33.95$  mm/dl (95% CI  $-51.38$  to  $-3.47$ ), respectively. Similarly, most lipid-related cardiovascular risk factors (i.e., cholesterol, triglycerides and atherogenic index) were also reduced ( $p < 0.05$ ).

**Conclusion:** A 12-wk WBV intervention in a primary care context is feasible, safe and effective in improving glycemic profile, lipid-related cardiovascular risk factors and functional capacity among T2DM patients.

**Trial number:** ACTRN1261300021774.

© 2013 Elsevier Ireland Ltd. All rights reserved.

### 1. Introduction

Type 2 diabetes mellitus (T2DM) is a prevalent and costly chronic metabolic disorder characterized by hyperglycemia and insufficiency of secretion or action of endogenous insulin [1]. Likewise, T2DM is an independent risk factor for vascular diseases and also is frequently associated with other cardiovascular diseases [2]. Therefore, the major causes of morbidity and mortality among T2DM patients are cardiovascular diseases [3]. Consequently, it is necessary to address both T2DM outcomes (i.e., glycated hemoglobin (HbA1c) and fasting blood glucose) and modifiable cardiovascular disease risk factors (e.g., dyslipidemia or blood pressure) for a complete therapeutic approach among this population.

Along with nutrition, exercise has long been recognized as a cornerstone for T2DM management in both primary and secondary prevention. Although there are no definitive conclusions, results from different meta-analyses [4–6] show that aerobic exercise or resistance training reduce HbA1c, fasting blood glucose, dyslipidemia or blood pressure when compared with standard care. Nonetheless, greater achievements seem to be reached by combining both modes of exercise. Moreover, better functional capacity is associated with better outcomes among diabetic patients [7].

Whole-body vibration (WBV) training is a relatively new form of exercise that has been shown to be effective in healthy subjects [8] and individuals with a range of medical disorders [8]. Moreover, WBV training has been shown to be useful among frail individuals who were previously physically untrained [9,10], as most diabetics patients are, and because WBV training takes less time than other kinds of exercise such aerobic or resistance training, this method could be a very good alternative to exercising in clinical contexts. Unfortunately, the effects of WBV training have seldom been investigated among T2DM patients. Existing studies [11–13] have yielded inconsistent results and no studies have been conducted to test the effects of WBV training on cardiovascular risk factors

\* Corresponding author at: Department of Sport and Exercise Science, University of Auckland, Private Bag 92019, Auckland 1142, New Zealand.  
Tel.: +64 9 373 7599x86990.

E-mail addresses: [b.delpozocruz@auckland.ac.nz](mailto:b.delpozocruz@auckland.ac.nz), [delpozob@gmail.com](mailto:delpozob@gmail.com) (B. del Pozo-Cruz).

SCIENTIFIC REPORTS **OPEN** **Low-Magnitude High-Frequency Vibration Accelerated the Foot Wound Healing of n5-streptozotocin-induced Diabetic Rats by Enhancing Glucose Transporter 4 and Blood Microcirculation**

Received: 22 May 2017  
Accepted: 30 August 2017  
Published online: 14 September 2017

Caroline Oi-Ling Yu<sup>1</sup>, Kwok-Sui Leung<sup>1</sup>, Jonney Lei Jiang<sup>2</sup>, Tina Bai-Yan Wang<sup>2</sup>, Simon Kwoon-Ho Chow<sup>1,3</sup> & Wing-Hoi Cheung<sup>1,3</sup>

Delayed wound healing is a Type 2 diabetes mellitus (DM) complication caused by hyperglycemia, systemic inflammation, and decreased blood microcirculation. Skeletal muscles are also affected by hyperglycemia, resulting in reduced blood flow and glucose uptake. Low Magnitude High Frequency Vibration (LMHFV) has been proven to be beneficial to muscle contractility and blood microcirculation. We hypothesized that LMHFV could accelerate the wound healing of n5-streptozotocin (n5-STZ)-induced DM rats by enhancing muscle activity and blood microcirculation. This study investigated the effects of LMHFV in an open foot wound created on the footpad of n5-STZ-induced DM rats (DM\_V), compared with no-treatment DM (DM), non-DM vibration (Ctrl\_V) and non-DM control rats (Ctrl) on Days 1, 4, 8 and 13. Results showed that the foot wounds of DM\_V and Ctrl\_V rats were significantly reduced in size compared to DM and Ctrl rats, respectively, at Day 13. The blood glucose level of DM\_V rats was significantly reduced, while the glucose transporter 4 (GLUT4) expression and blood microcirculation of DM\_V rats were significantly enhanced in comparison to those of DM rats. In conclusion, LMHFV can accelerate the foot wound healing process of n5-STZ rats.

Type 2 diabetes mellitus (DM) is a metabolic disease where skeletal muscles have insulin resistance<sup>1</sup>. Delayed wound healing is a type 2 DM complication with diminished peripheral blood flow<sup>2</sup> and impaired growth factor production<sup>3</sup>. DM foot ulcer is a presentation of delayed wound healing that affects more than 25% out of 150 million DM patients worldwide<sup>4</sup>, and can lead to lower limb amputations<sup>5</sup>.

DM wound is characterized by a disorder in the inflammatory and proliferative phases of the wound healing process<sup>6</sup>. Hyperglycemia contributes to delayed wound healing by exhibiting elevated levels of pro-inflammatory cytokines and proteases, which reduce levels of various growth factors<sup>7</sup> and blood flow, diminish cell migration and impairs angiogenesis response, cell proliferation and reepithelialization in wounds<sup>8</sup>. It is important to accelerate the DM wound healing process by enhancing blood flow, cell proliferation and migration, and angiogenesis in wound, and enhancing glucose uptake in muscles to reduce the blood glucose level.

<sup>1</sup>Department of Orthopaedics and Traumatology, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong SAR, China. <sup>2</sup>School of Biomedical Sciences, The Chinese University of Hong Kong, Hong Kong SAR, China. <sup>3</sup>The CUHK-ACC Space Medicine Centre on Health Maintenance of Musculoskeletal System, The Chinese University of Hong Kong Shenzhen Research Institute, Shenzhen, PR China. Correspondence and requests for materials should be addressed to W.-H.C. (email: [louis@ort.cuhk.edu.hk](mailto:louis@ort.cuhk.edu.hk))



Research article

The effects of whole-body vibration on wound healing in a mouse pressure ulcer model



Nattaya Wano<sup>a</sup>, Sompol Sanguanrungrsirikul<sup>b</sup>, Somboon Keelawat<sup>c</sup>, Juraiporn Somboonwong<sup>b,\*</sup>

<sup>a</sup> Medical Science Program, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand  
<sup>b</sup> Department of Physiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand  
<sup>c</sup> Department of Pathology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

ARTICLE INFO

**Keywords:**  
 Whole-body vibration  
 Pressure ulcer  
 Ischemia-reperfusion injury  
 Vascular endothelial growth factor (VEGF)  
 Tumor necrosis factor alpha (TNF- $\alpha$ )  
 Wound healing

ABSTRACT

**Background:** Pressure ulcers are one of the most common complications of immobility resulting from pressure and shear. Whole-body vibration (WBV) has been shown to increase skin blood flow but little information is known about its effect on pressure ulcers. This study investigated the effects of WBV on wound healing in a mouse pressure ulcer model.  
**Methods:** Two cycles of ischemia-reperfusion were performed by external application of two magnetic plates to dorsal skin to induce stage II pressure ulcers characterized by partial-thickness skin loss with exposed dermis. A total of 32 male ICR mice were randomly and equally divided into untreated control and the WBV groups. Immediately after the completion of 2-cycle ischemia-reperfusion injury, mice in the WBV group participated in a WBV program using a vibrator (frequency 45 Hz, peak acceleration 0.4 g, vertical motion) for 30 min/day and 5 consecutive days/week. At days 7 and 14 post-ulceration, wound closure rate was assessed. Wound tissues were harvested for determination of collagen deposition in Masson's trichrome stained sections, neutrophil infiltration and capillary density in hematoxylin and eosin-stained sections, as well as TNF- $\alpha$  and VEGF levels using ELISA.  
**Results:** TNF- $\alpha$  levels and neutrophil infiltration were significantly decreased in wounds on days 7 and 14 of WBV treatment. Moreover, wound closure rate and collagen deposition were remarkably accelerated on day 14. Tissue VEGF and capillary density were unaffected by WBV at either time point.  
**Conclusions:** These findings suggest that WBV has the potential to promote the healing process of stage II pressure ulcers, as evidenced by attenuation of wound inflammation and enhancement collagen deposition.

1. Introduction

Pressure ulcers, commonly known as bed sores, are one of the most common complications that occur in immobilized patients as a result of pressure and shear force [1]. The pathophysiology of pressure ulcers involves repeated ischemia-reperfusion injury, impaired vascularization and lymphatics, and cellular distortion, all of which induce the generation of free radicals and inflammatory mediators such as tumor necrosis factor alpha (TNF- $\alpha$ ) that cause dysregulated immune response and tissue damage [2, 3, 4, 5, 6, 7]. Based on the extent of tissue loss, pressure ulcers can be divided into 4 stages: stage I non-blanchable erythema of intact skin, stage II partial-thickness skin loss with exposed dermis, stage III full-thickness skin loss, and stage IV full-thickness skin and tissue loss [1]. If improperly treated, pressure ulcers may progress to more severe stages that can result in chronic skin damage, increased risk of wound infection,

high medical care costs and a high mortality rate [8, 9]. Management of pressure ulcers includes dressings, microclimate control, nutrition, repositioning and early mobilization, and support surfaces [1]. Nonetheless, development of novel interventions is still needed in an attempt to improve the healing and care of the patients suffering from pressure ulcers. Examples of the advanced treatment modalities currently described in the literature are negative pressure therapy, low-level laser therapy, electrical stimulation, ultrasound and vibration therapy [10, 11, 12, 13].

This study focuses on the utilization of whole-body vibration (WBV), an oscillatory mechanical stimulation using a vibrator. A single bout of vibration with frequency ranging from 30-50 Hz has been proven to increase skin blood flow [14, 15, 16]. Furthermore, WBV has been reported to improve wound healing in only a few clinical and preclinical studies [17, 18, 19]. In elderly patients with stage I pressure ulcers, vibration

\* Corresponding author.  
 E-mail address: juraisom@yahoo.com (J. Somboonwong).

<https://doi.org/10.1016/j.heliyon.2021.e06893>  
 Received 21 November 2020; Received in revised form 11 April 2021; Accepted 21 April 2021  
 2405-8440/© 2021 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



Article

# The Effect of Vibration on the Acceleration of Wound Healing of Diabetic Neuropathic Foot Ulcer: A Prospective Experimental Study on Human Patients

Sitti Syabariyah <sup>1,\*</sup>, Elly Nurachmah <sup>2</sup>, Budiman Darmo Widjojo <sup>3</sup>, Sabarinah Prasetyo <sup>4</sup>, Hiromi Sanada <sup>5</sup>, Irianto <sup>6</sup>, Gojiro Nakagami <sup>5</sup>, Suriadi <sup>7</sup>, Tuter Kardiatur <sup>7</sup> and Urfa Khairatun Hisan <sup>8</sup>

- <sup>1</sup> Department of Medical Surgical Nursing, University of Aisyiyah Bandung, Bandung 40264, Indonesia
- <sup>2</sup> Department of Medical Surgical Nursing, University of Indonesia, Depok 16424, Indonesia
- <sup>3</sup> Faculty of Medicine, Universitas of Indonesia, Jakarta 10430, Indonesia
- <sup>4</sup> Faculty of Community Health, Universitas of Indonesia, Depok 16424, Indonesia
- <sup>5</sup> Department of Wound Care Management/Gerontological Nursing, Graduate School of Medicine, The University of Tokyo, Tokyo 113-8654, Japan
- <sup>6</sup> Department of General Education, Faculty of Resilience, Rabdan Academy, Abu Dhabi 22401, United Arab Emirates
- <sup>7</sup> Department of Nursing, Institut Teknologi dan Kesehatan Muhammadiyah Kalimantan Barat, Kabupaten Kubu Raya 78117, Indonesia
- <sup>8</sup> Faculty of Medicine, Universitas Ahmad Dahlan, Yogyakarta 55166, Indonesia
- \* Correspondence: sittisyabariyah@gmail.com; Tel.: +62-812-5297-1927



**Citation:** Syabariyah, S.; Nurachmah, E.; Widjojo, B.D.; Prasetyo, S.; Sanada, H.; Irianto; Nakagami, G.; Suriadi; Kardiatur, T.; Hisan, U.K. The Effect of Vibration on the Acceleration of Wound Healing of Diabetic Neuropathic Foot Ulcer: A Prospective Experimental Study on Human Patients. *Healthcare* **2023**, *11*, 191. <https://doi.org/10.3390/healthcare11020191>

Academic Editor: Ioannis Ilias

Received: 30 November 2022

Revised: 26 December 2022

Accepted: 5 January 2023

Published: 9 January 2023



**Copyright:** © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

**Abstract:** Diabetic foot ulcers are a common complication that occurs in approximately 15 percent of patients with diabetes mellitus. Over 60% of diabetic foot ulcers are caused by underlying neuropathy. Former studies on diabetic animals with foot wounds found that vibration platforms significantly accelerate wound healing by catalyzing epithelization, promoting angiogenesis, and enhancing muscle bulk. This result suggests that there is evidence that vibrations may accelerate diabetic neuropathic ulcer healing in human patients. However, to the best of our knowledge, the effect of vibration on the enhancements of diabetic foot ulcer healing in human patients is rarely investigated. Hence, in this work, we conducted an experimental study with human subjects to investigate whether vibration therapy, as a complement to the standard wound treatment, can accelerate the wound healing rate of diabetic neuropathic foot ulcers. In this prospective experimental study, 80 participants diagnosed with Wagner grades I–III diabetic neuropathic foot ulcers were randomly distributed to experimental ( $n = 40$ ) and control groups ( $n = 40$ ). Patients in the intervention group received standard wound treatment and vibration wound therapy (VWT), whereas patients in the control group retrieved only standard wound treatment. The results ( $p = 0.024$ ,  $\alpha = 0.05$ ) show notable differences in the median healing rate between the intervention group (25 days, 95% CI: 20.3–29.7) and control group (33 days, 95% CI: 25.6–40.4), with the effect-size  $r$ , Cohen’s  $d$ , Glass’s  $\Delta$ , and Hedges’  $g$ , respectively, being 0.810, 2.764, 2.311, and 2.772. Moreover, the nitric oxide (NO) level, wound closure area, and wound healing score after intervention significantly differed between the two groups ( $p < 0.05$ ), putting the intervention group on a higher level than the control group. Furthermore, positive associations were found between the NO level and wound healing closure rates. These findings suggested that VWT enhances diabetic neuropathic foot ulcer healing in terms of healing rate, wound closure area, healing score, and elevated NO level. Considering that no clinically adverse effects were found in the patients induced with vibration intervention, VWT can be regarded as a complementary therapy to the existing ones to accelerate the healing of DFUs.

**Keywords:** vibration therapy; diabetic foot ulcer (DFU); diabetic wound; wound care; nitric oxide (NO)