Dicle Tıp Dergisi / Dicle Med J (2022) 49 (4) : 619-627

www.diclemedj.org

Original Article / Özgün Araştırma

The Effect of Low Magnitude High Frequency Vibration on Bone Healing by Clamp Method in Nonunion Tibial Fractures

Ferhat Celik[1], Hakkı Murat Bilgin[2], Hasan Akkoc[3], Emin Ozkul[4], Mehmet Gem[5], Mehmet Sirac Ozerdem[6], Mesut Karıksız[7], Mustafa Erdem[8], Serhat Elci[9]

1 Diyarbakır Atatürk Vocational School of Health Services, University of Dicle, Diyarbakır, Turkey

2 Department of Physiology, Faculty of Medicine, University of Dicle, Diyarbakır, Turkey

3 Department of Pharmacology, Faculty of Medicine, University of Dicle, Diyarbakır, Turkey

4 Department of Orthopaedics and Traumatology, Faculty of Medicine, University of Dicle, Diyarbakır, Turkey

5 Department of Orthopaedics and Traumatology, Dicle Memorial Hospital, Diyarbakır, Turkey

6 Department of Electrical and Electronics Engineering, Faculty of Engineering , University of Dicle, Diyarbakır, Turkey

7 Department of Orthopaedics and Traumatology, Private Sultan Hospital, Diyarbakır, Turkey

8 Department of Orthopaedics and Traumatology, Adıyaman University training and research hospital, Adıyaman, Turkey

9 Department of Orthopaedics and Traumatology, Private Cihanpol Hospital, Mardin, Turkey

Received: 06.10.2022; Revised: 04.12.2022; Accepted: 05.12.2022

Abstract

Introduction: This study aimed to investigate the clinical effect of Low Magnitude High Frequency Vibration (LMHFV) on nonunion tibial fractures, noninvasively.

Methods: The Experimental (n=5) and control (n=5) groups were age-matched and pooled based on the Nonunion Tibia Score System (NUSS) ($p>0.05$). LMHFV (0.35g, 50 Hz, 20 minutes x 4/day) was applied to the experimental group for three months by a mechanical stimulator that we developed using a 'clamp method'. The control group was followed during three months without any application other than routine treatment. The results were evaluated using the Radiographic Union Score for Tibial Fractures (RUST) and American Orthopedics Foot and Ankle Score (AOFAS). No statistically significant difference was observed between the groups at the beginning and in the end of the 3- month application for RUST and AOFAS scores ($p>0.05$).

Results: Pain and function assessment, at the beginning and end of the study, as a part of The AOFAS scorewere not statistically different ($p>0.05$) in the control group. However, increases in pain and function AOFAS scores were statistically significant in the experimental group at the end of the 3- month application ($p<0.034$ and $p<0.043$, respectively).

Conclusion: In this study, LMHFV contributed to the pain and function parameters of AOFAS in the experimental group; however, there was no significant difference between the groups in terms of total RUST and AOFAS scores.

Key words: tibial fracture, nonunion, AOFAS, RUST, Low Magnitude High Frequency Vibration

DOI: 10.5798/dicletip.1220904

Correspondence / Yazışma Adresi: *Ferhat Çelik, Diyarbakır Atatürk Vocational School of Health Services, University of Dicle, Diyarbakır, 21280, Turkey*

e-mail: staphylococ@gmail.com

Nonunion Tibia Kırıklarında Kelepçe Metoduyla Uygulanan Düşük Frekans Yüksek Yoğunluklu Titreşimin Kemik İyileşmesine Etkisi

Öz

Amaç: Bu çalışmanın amacı, Düşük Yoğunluklu Yüksek Frekanslı Titreşimin (DYYFT) nonuniontibia kırıkları üzerindeki klinik etkisini noninvaziv olarak araştırmaktı.

Yöntemler: Deney (n=5) ve kontrol (n=5) grupları yaş-uyumlu NonunionTibia Skor Sistemine (NUSS) göre oluşturuldu (p>0.05). Deney grubu için geliştirdiğimiz mekanik stimülatör 'Kelepçe Yöntemi' ile DYYFT (0.35g, 50 Hz, 20 dakika x 4/gün) üç ay süreyle uygulandı. Kontrol grubu rutin tedavi dışında herhangi bir uygulama yapılmadan üç ay boyunca takip edildi. Sonuçlar, Radyolojik Kaynama Skorlama Sistemi (RUST) ve Amerikan Ortopedi Ayak ve Ayak Bileği Skoru (AOFAS) kullanılarak değerlendirildi. 3 aylık uygulamanın başında ve sonunda RUST ve AOFAS skorları açısından gruplar arasında istatistiksel olarak anlamlı fark gözlenmedi (p>0.05).

Bulgular: Çalışmanın başında ve sonunda AOFAS kapsamındaki ağrı ve fonksiyon skorları kontrol grubunda istatistiksel olarak anlamlı değildi (p>0.05). Ancak 3 aylık uygulama sonunda deney grubunda ağrı ve fonksiyon AOFAS skorlarındaki artış istatistiksel olarak anlamlıydı (sırasıyla p<0.034 ve p<0.043).

Sonuç: Bu çalışmada DYYFT, deney grubunda AOFAS'ın ağrı ve fonksiyon parametrelerine katkıda bulunmuştur; ancak toplam RUST ve AOFAS puanları açısından gruplar arasında anlamlı fark yoktu.

Anahtar kelimeler:tibial kırıklar, nonunion, AOFAS, RUST, Düşük Yoğunluk Yüksek Frekanslı Titreşim.

INTRODUCTION

Bone fractures threaten human health and the most commonly fractured long bone is the tibia[1]. Incidence rates of adult tibial fractures was shown to be 13.5 per 1000,000 in all population and only 10%–12% of that patients are nonunion[2]. Delayed union or non-union are occasionally observed in tibial shaft fractures and it may take more time for patients to recover completely; thus, needing further surgical procedures[3]. Determination of fracture healing involves both radiographic and clinical assessment. Various sources have given different periods for non-healing fractures as Gomez-Barrena et al. reported fractures that do not heal within 4 months following the bone fracture should be termed 'delayed healing'. They noted that if bone healing is not observed with radiological evidence within 6 months, then it should be called nonunion[4].

The AOFAS (American Orthopedic Foot & Ankle Society) Ankle-Hindfoot Scale total score, pain andfunctionsubscores has been used as an evaluation method on patients who have undergone foot and ankle surgery[5,6]. This score contains subjective and objective components.The validity, reliability, and responsiveness of this system have been reported in other studies[6,7].

Non-union can only be diagnosed on the basis of the absence of specific changes such as callus formation, radiologically. RUST scoring contains the assessment of cortical bridging and score the callus formation quantitatively that is important in the progression of nonunion cases in a standardized manner on conventional radiographs[8,9].

Osteoblastic lineage bone cells are known to sense and respond to mechanical stimuli. So, non-invasive techniques are being investigated for the healing process of bone fractures as different vibration applications can be applied to bone tissue. Therefore, mechanical stimuli such as Low Magnitude High Frequency Vibration (LMHFV) may affect bone metabolism. Previous reports have shown that bone demonstrates mechano-sensitivity to LMHFV[10,11,12]. LMHFV has a frequency greater than 20 Hz and less than 90 Hz as well as an amplitude (g) less than 0.52 g, taking into account the safety parameters12 for human health specified by the World Health Organization[13].

There have been numerous animal and human studies focusing on LHMFV and its impact on bone tissue[10,14,15]. In different studies, a positive effect on bone mineral density was observed in women who underwent LMHFV[10,16].

As it can be seen above, few clinical studies in the literature focusing on the impact of LMHFV on fracture healing. The aim of this study was to investigate the clinical effect of locally applied LMHFV on nonunion tibial fractures.

METHODS

Approval was obtained from İnönü University Malatya Clinical Research Ethics Committee (2018/182) and Ministry of Health Medical Devices Institution (2018/182). Due to the low incidence of nonunion tibia fractures in the community, the study was conducted in 5 different centers: Dicle University Faculty of Medicine Orthopedics and Traumatology Department; TR Ministry of Health Mardin State Hospital; Adıyaman Training and Research Hospital/Orthopedics Clinic; SBU Diyarbakır Regional Training and Research Hospital/Orthopedics and Traumatology Clinic; and Harran University Faculty of Medicine/Department of Orthopedics and Traumatology.

A total of 10 volunteers participated in the study. Volunteers included in the study were male (9) and female (1) subjects between the ages of 18-45 years old with nonunion tibial shaft fractures. The volunteers were divided into two groups: an experimental group (n = 5) and a control group (n = 5). The study gained the patients' informed consent.

Inclusion criteria were previous history of an intramedullary nail or plate applied to the tibia and a score of 10 or less on the RUST (Radiographic Union Scale in Tibial Fractures) scale. Volunteers were patients with radiological follow-up up to 6-9 months for the shaft (diaphyseal) fractures and with radiological findings accompanied by clinical symptoms. During this period, radiologically poor callus tissue formed patients were diagnosed as nonunion.

Exclusion criteria included those with systemic diseases, renal failure, rheumatoid arthritis, connective tissue diseases, post-traumatic arthritis, a history of knee replacement surgery, and plegic and non-ambulatory patients were not included in the study.

Experimental and control groups were pooled based on the Nonunion Tibia Score System (NUSS). LMHFV was given to the volunteers in the experimental group at dosages stated below, and the control group members were selected from the volunteers who did not want to use the device or who had images such as CT and X-Ray in the system for three months without any treatment.

Vibrations were conducted by a mechanical stimulator (0.35 g–50 Hz) in the LMHFV group using a “clamp method” that we developed. A mechanical stimulator circuit suitable for LMHFV was arranged for the vibration application. In the circuit, a battery with 1.55V width (Sony,Tokyo, Japan) and a motor (10mm Vibration Motor-3mm Type Model:310–003, Precision Microdrives, London, UK) generating 50 Hz vibration were used for the stimulation.

The device was placed at a distance of 3-5 cm from the nonunion site following patient training (Figure 1). Volunteers were asked to practice four sessions a day, 20 minutes in each session. The volunteers were contacted at each stage of the device application, and the volunteers were called for regular controls to confirm the information about the usage of the device.

Figure 1. Application of the LMHFV device using the 'Clamp Method' on the patients

In order to have the statistical data of the volunteers, The Non-Union Scoring System (NUSS)[17] scale, which has recently received positive results in international validity and reliability studies, was used[18].

We assessed the objective results using the AOFAS Ankle-Hindfoot score developed by the American Orthopedic Foot & Ankle Society (AOFAS). This test is among the most frequently used tests by clinicians for the below-knee body region[19]. The AOFAS Ankle-Hindfoot Scale aims to measure pain, function and smoothness scores with various observations and questions as individually or combined.

Radiographic Union Scale for Tibial (RUST) Fractures is based on the assessment of each cortex individually in accordance with the definition of nonunion. The RUST score is determined by the presence of callus without visible fracture line (3 points), presence of callus with visible fracture line (2 points) or absence of any callus (1 point) on each of cortices on anteroposterior (A-P) and lateral radiographs. Images were presented in random order and surgeons were blinded as to outcome and time of radiograph[9].

This score, which ranges from 3 to 12, was used for the interpretation of CT and Radiological images. A common consensus was sought in the radiographs interpreted by four senior orthopaedic trauma surgeons and the scoring was given accordingly.

The numerical data obtained in the study were expressed as arithmetic mean±standard deviation. The SPSS program was used to compare the data. A Mann-Whitney U test was used to compare independent groups, while the Wilcoxon test was used to compare before and after data. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The data of the control and experimental groups are shown in Table 1. When the mean ages of the volunteers in the control and experimental groups participating in the study were compared, no significant difference was found between the data ($p>0.05$, Table 1). There was no significant difference between the groups in terms of AOFAS and RUST score ($p>0.05$, Table 1, Figure 2 and Figure 3). When pain and function scores from AOFAS were compared, no statistically significant difference between the control and experimental groups for previous pain, previous function, or later function values ($p>0.05$, Table 1). In terms of pain score obtained 3 months following the device use, the score in the experimental group was found to be significantly higher than the score in the control group ($p=0.041$, Table 1). In terms of NUSS, no statistically significant difference was found between the experimental and control groups ($p>0.05$, Table 1).

Table I: Comparison of the data of the control and experimental groups.

	Control (n=5) Mean±SD	Experiment (n=5) Mean±SD	P-value
Age	27.8±4.3	33.8±6.7	0.142
RUST (Before)	5.4±1.9	5.0±1.73	0.906
RUST (After)	6.0±2.0	6.4±1.5	0.663
AOFAS Total (Before)	38.8±21.5	49.4±22.0	0.347
AOFAS Total (After)	49.8±29.7	67.4±18.5	0.251
AOFAS Pain (Before)	4.0±3.9	1.0±0.0	0.317
AOFAS Pain (After)	10.0±9.1	28.0±4.47	0.041*
AOFAS Function (Before)	28.4±13.2	27.0±18.0	0.917
AOFAS Function (After)	33.4±14.8	40.0±10.2	0.295
NUSS	16.8±7.1	16.0±6.8	0.600

Abbreviation; RUST: Radiographic Union Score for Tibial Fractures, AOFAS: Ankle-Hindfoot Scale, NUSS: Non-Union Scoring System

** p < 0.05*

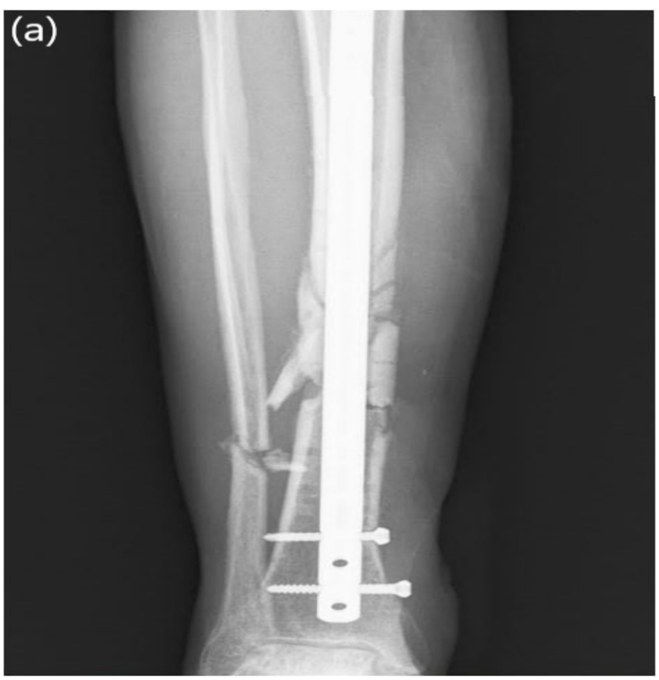

Figure 2a. Immediate post-operative radiography of the control patient

Figure 2b. 12th week radiography of the control patient

Figure 3a. Immediate post-operative radiography of the experimental patient

Figure 3b. 12th week radiography of the experimental patient

The RUST, AOFAS, pain, and function before and after score values of the subjects in the control and experimental groups at the time of enrollment and three months after enrollment are presented in Table 2. In terms of RUST and AOFAS values, the results revealed no statistically significant difference between the before scores and after scores of both control and experimental groups (p>0.05, Table 2). When the pain and function scores from AOFAS were evaluated separately, there was no statistically significant difference between the before scores and after scores in the control group (p>0.05, Table 2). It was observed that the pain and function scores from AOFAS in the experimental group at three months after enrollment increased significantly compared to the before scores which were taken at the time of enrollment (p<0.034 and p<0.043, respectively, Table 2).

Table II: Evaluation of the scores obtained at the beginning and end of the period determined for the study by the Wilcoxon test of the Control and Experimental groups.

		Before	**After**	**P-value**
RUST	Control	5.4±1.9	6.0±2.0	0.180
	Experiment	5.0±1.73	6.4±1.5	0.066
AOFAS Total	Control	38.8±21.5	49.8±29.7	0.317
	Experiment	49.4±22.0	67.4±18.5	0.279
AOFAS Pain	Control	4.0±3.9	10.0±9.1	0.317
	Experiment	1.0±0.0	28.0±4.47	0.034*
AOFAS Function	Control	28.4±13.2	33.4±14.8	0.317
	Experiment	27.0±18.0	40.0±10.2	0.043*

Abbreviation; RUST: Radiographic Union Score for Tibial Fractures, AOFAS: Ankle-HindfootScale. p < 0.05*

DISCUSSION

Non-invasive methods have been made to develop for the healing process along with the surgical treatment that is based on mechanical vibrations and allows early treatment in the repair process.

In our study, we have observed the positive impact of LMHFV application on pain and function parameters in tibia nonunion fractures of patients. There have been studies examining the effects of LMHFV at the cellular and molecular level. Lau et al. investigated the effects of LMHFV in MLO-Y4 cell lines with osteoblast-like morphology. They determined that osteocytes were sensitive to LMHFV through their responses to COX2 and RANKL, which had inhibitory effects on bone resorption as a result of stimulation[20]. Wu et al. also found changes in the nitric oxide, PGE2, and intracellular calcium concentrations of the cells against different frequency values of LMHFV (10, 30, 60, 90 Hz) in their study[21]. Chen et al. reported that LMHFV caused osteogenic differentiation in mesenchymal stem cells, and this was due to the Wnt/β-catenin pathway[22].Özcivici et al. also suggested that LMHFV might cause osteoblastogenesis in bone marrow stem cells[23].

There are also studies performed in animal models. In the study of Judex et al., they applied LMHFV (90 Hz, 45 Hz; 0.2 g) to the whole body by giving vibration from the bottom in rats whose ovaries were removed, and as a result, larger cortical and trabecular bone presence was detected compared to the control group[14].Shi et al. created fractures on osteoporotic rats whose ovaries were removed and found a significant difference in callus tissue bridging time and callus tissue formation rates in rats treated with Whole Body-LMHFV[24]. Matsumoto et al. suggested that Whole Body- LMHFV increases fracture healing by increasing vascularization but also stated that there was a need for further studies on the parameters and mechanism of action of LMHFV[15].

Apart from the whole body application of LMHFV, a method specified in the literature as radial application or local application has also been tested in animals. Wang et al. anesthetized the rabbits, placed implants in their tibia, and performed LMHFV at different frequencies only in that area. As a result, there was an increase in new bone formation and bone density in the LMHFV group compared to the control group[25].Sun et al. found a significant increase in bone density in rats in which they applied 35 Hz, 45 Hz and 55 Hz LMHFV by pinching their tails in the mechanism where they eliminated microgravity[26].

LMHFV studies in humans first started with whole body applications. In the study of Rubin et al. on postmenopausal women, they found a significant difference between the volunteers who were given LMHFV for 20 minutes a day for one year and a control group about the bone loss parameter[10].Marín-Cascales et al. in their meta-analysis study reported a positive effect of whole-body LMHFV applications on bone mineral density in the femoral neck and vertebrae in 462 postmenopausal women[16].

Bilgin et al. defined a new application method using the pulsed electromagnetic field in the literature. In this method, which is called the "Clamp Method", they attached the small LMHFV device -which they invented- on the operated tibia bones and made applications to 30 Sprague-Dawley type rats without anesthetizing or any physical restrictions. Rats were left in their cages in this way and exposed to LMHFV for 15 minutes/day. As a result, a higher callus tissue formation and an increase in serum osteocalcin levels were observed in rats treated with LMHFV compared to the control group. According to the results of stereological analysis, there was an osteogenic increase detected in the LMHFV group[27].

In the literature review conducted regarding our study, neither clinical nor animal experiments examining the relationship between LMHFV and nonunion were found. Therefore, no study exists to compare out study clinically. In addition, we could not find any publication examining the clinical relationship between local LMHFV application and fractures (in-vivo) except for osteoporotic fractures.

The strength of our study is that LMHFV has not been clinically studied in any type of fracture, except postmenopausal fractures, and it has never been studied in nonunion tibia fractures. In our study, LMHFV was applied to nonunion tibia fractures. On the other hand, with the "clamp method", which we described in Bilgin et al., a localized application was applied for the first time in the clinic in our present study, apart from whole-body applications that have been applied to date.

The fact that nonunion tibia fractures are observed in only fractions of millions in the whole society has created the biggest limitation. As the small number of patients is our most significant limitation, we used non parametric test as statistical analysis; further studies involving a higher number of patients are needed. Whenever the number of the patients and the treatment period can be increased, an improvement at the functional scores as well as the pain scores will be obtained. Although this limitation, it is important that this method is being used in humans firstly.

The RUST score is a radiographic assessment of fracture healing that has improved observer reliability compared to other radiographic assessments[8,9,28].Litrenta et al., as determined by 12 orthopaedic surgeons on radiographs of 27 distal femur fractures at various stage of healing and reviewers stated a fracture was healed when radiographic union corresponded with a RUST score of [10]. RUST score less than 8 were considered not healed by all reviewers[8]. No significant difference was found in the comparison of RUST scores in which callus tissue was evaluated between the experimental groups and the control groups (p>0.05). However, based on the above studies, better results can be obtained in a more comprehensive and long-term study.

Besides presenting the variation of function and smoothness, AOFAS Ankle-Hindfoot Scale provides a consistent observation related with changes of pain symptom. In the published data, although reported for other orthopedic and traumatic foot and ankle disorders[6,7], we could not find a study that compared the AOFAS ankle-hindfoot score for Nonunion Tibial Fractures.

CONCLUSION

Low Magnitude High Frequency Vibration contributed significantly to the pain and function parameters of AOFAS in the patient group with nonunion tibia fracture. To the best of our knowledge, this is the first study focusing on the impact of localized LMHFV application on nonunion tibia fractures in the clinic.

Ethics Committee Approval: Approval was obtained from İnönü University Malatya Clinical Research Ethics Committee (2018/182) and Ministry of Health Medical Devices Institution (2018/182).

Conflict of Interest: The authors declared no conflicts of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Sprague S, Bhandari M. An economic evaluation of early versus delayed operative treatment in patients with closed tibial shaft fractures. Archives of orthopaedic and trauma surgery 2002; 122:315-23.

2. Dailey HL, Wu KA, Wu PS, McQueen MM, Court-Brown CM. Tibial fracture non union and time to healing following reamed intramedullary nailing: Risk factorsbased on a single-centrereview of 1003 patients. Journal of OrthopaedicTrauma 2018;32(7): 263-69.

3. Heckman JD, Sarasohn-Kahn J. The economics of treating tibia fractures. The cost of delayed unions. Bulletin 1997; 56:63-72.

4. Gomez-Barrena E, Rosset P, Lozano D, et al. Bone fracture healing: cell therapy in delayed unions and nonunions. Bone 2015;70:93-101.

5. Button G, Pinney S. A meta-analysis of outcome rating scales in foot and ankle surgery: is there a valid, reliable, and responsive system? Foot Ankle Int 2004; 25:521–25.

6. Ibrahim T, Beiri A, Azzabi M, et al. Reliability and validity of the subjective component of the American Orthopaedic Foot and Ankle Society clinical rating scales. J Foot Ankle Surg2007;46:65–74.

7. SooHoo NF, Vyas R, Samimi D. Responsiveness of the foot function index, AOFAS clinical rating system, and SF-36 after foot and ankle surgery. Foot Ankle Int 2006; 27:930–34.

8. Litrenta J, Tornetta P, Mehta S, et al. Determination of radiographic healing: an assessment of consistency using RUST and modified RUST in metadiaphyseal

fractures. Journal of orthopaedic trauma. J. Orthop. Trauma 2015; 29: 516–20.

9. Cooke ME, Hussein AI, Lybrand KE, et al. Correlation between RUST assessments of fracture healing to structural and biomechanical properties. J. Orthop. Res 2017; 36, 945–53.

10. Rubin C, Recker R, Cullen D, et al. Prevention of postmenopausal bone loss by a low-magnitude, high-frequency mechanical stimuli: a clinical trial assessing compliance, efficacy, and safety. Journal of bone and mineral research: the official journal of the American Society for Bone and Mineral Research 2004;19:343-51.

11. Wolf S, Augat P, Eckert-Hubner K, et al. Effects of high-frequency, low-magnitude mechanical stimulus on bone healing. Clinical orthopaedics and related research 2001;385:192-8.

12. Xie L, Jacobson JM, Choi ES, et al. Low-level mechanical vibrations can influence bone resorption and bone formation in the growing skeleton. Bone 2006;39:1059-66.

13. International Organization for Standardization. Guide for the evaluation of human exposure to whole body vibration. Part 1: General requirements. ISO 2631-1, 2nd edition. 1997,ISO, Geneva

14. Judex S, Lei X, Han D, et al. Low-magnitude mechanical signals that stimulate bone formation in the ovariectomized rat are dependent on the applied frequency but not on the strain magnitude. Journal of biomechanics 2007;40:1333-39.

15. Matsumoto T, Goto D. Effect of low-intensity whole-body vibration on bone defect repair and associated vascularization in mice. Medical & biological engineering & computing 2017;55:2257-66.

16. Marin-Cascales E, Alcaraz PE, Ramos-Campo DJ, et al. Whole-body vibration training and bone health in postmenopausal women: A systematic review and meta-analysis. Medicine 2018.97:e11918.

17. van BastenBatenburg M, Houben IB, Blokhuis TJ. The Non-Union Scoring System: an interobserver reliability study. European journal of trauma and emergency surgery: official publication of the European Trauma Society 2019;45:13-19.

18. Calori GM, Phillips M, Jeetle S, Tagliabue L, Giannoudis P V. Classification of non-union: need for a new scoring system? Injury 2008; 39(2):59-63.

19. Kitaoka HB, Alexander IJ, Adelaar RS, et al. Clinical rating systems for the ankle-hindfoot, midfoot, hallux, and lesser toes. Foot & ankle internationa. 1994;15:349-53.

20. Lau E, Al-Dujaili S, Guenther A, et al. Effect of low-magnitude, high-frequency vibration on osteocytes in the regulation of osteoclasts. Bone 2010; 46:1508-15.

21. Wu XT, Sun LW, Qi HY, Shi H, Fan YB. The bio-response of osteocytes and its regulation on osteoblasts under vibration. Cell biology international 2016; 40:397-406.

22. Chen B, Lin T, Yang X, et al. Low-magnitude, high-frequency vibration promotes the adhesion and the osteogenic differentiation of bone marrow-derived mesenchymal stem cells cultured on a hydroxyapatite-coated surface: The direct role of Wnt/beta-catenin signaling pathway activation. International journal of molecular medicine 2016;38:1531-40.

23. Ozcivici E, Luu YK, Adler B, et al. Mechanical signals as anabolic agents in bone. Nature reviews Rheumatology 2010;6:50-59.

24. Shi HF, Cheung WH, Qin L, Leung AHC, Leung KS. Low-magnitude high-frequency vibration treatment augments fracture healing in ovariectomy-induced osteoporotic bone. Bone 2010; 46:1299-1305.

25. Wang S, Liu Y, Tang Y, et al. Direct Radial LMHF Microvibration Induced Bone Formation and Promoted Implant Osseointegration. Clinical implant dentistry and related research 2016;18:401-09.

26. Sun LW, Luan HQ, Huang YF, Wang Y, Fan YB. Effects of local vibration on bone loss in -tail-suspended rats. International journal of sports medicine 2014;35:615-24.

27. Bilgin HM, Celik F, Gem M, et al. Effects of local vibration and pulsed electromagnetic field on bone fracture: A comparative study. Bioelectromagnetics2017;38:339-48.

28. Timm K, Walter N, Heinrich M, et al. Influence of Thoracic Trauma on Fracture Healing in Long Bones-A Retrospective Analysis. J. Clin. Med 2022; 11(3): 717.