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Original Article

Vibration therapy as an intervention for trochanteric hip fractures – A randomized double-blinded, placebo-controlled trial

Ronald Man Yeung Wong [a,*], Pui Yan Wong [a], Chaoran Liu [a], Chun Sing Chui [a], Wing Hong Liu [b], Ning Tang [b], James Griffith [c], Ning Zhang [a], Wing Hoi Cheung [a]

[a] Department of Orthopaedics & Traumatology, The Chinese University of Hong Kong, Hong Kong SAR, China
[b] Department of Orthopaedics & Traumatology, Prince of Wales Hospital, Hospital Authority, Hong Kong SAR, China
[c] Department of Imaging and Interventional Radiology, The Chinese University of Hong Kong, Hong Kong SAR, China

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ABSTRACT

Background: Hip fractures are one of the most serious forms of fragility fractures. Low-magnitude high-frequency vibration (LMHFV) is a biophysical intervention that provides non-invasive, systemic mechanical stimulation. The objectives of this study were to investigate the efficacy of LMHFV in trochanteric hip fracture elderly patients to (i) accelerate trochanteric fracture healing and (ii) improve clinical and functional outcomes.

Methods: A randomized double-blinded, placebo-controlled clinical trial was conducted. Participants were randomly assigned into LMHFV or placebo intervention for 14 days. Primary outcome assessments were fracture healing assessed with CT scan and X-rays. Dual X-ray Absorptiometry (DXA) scan was performed to assess bone mineral density change. Secondary outcome assessments were clinical and functional outcomes with quadriceps muscle strength, balancing ability, handgrip strength, Time Up and Go (TUG) test, quality of life outcomes, pain, falls, and mortality.

Results: 237 patients were screened for eligibility by the inclusion and exclusion criteria. 62 patients were recruited and randomly assigned to placebo group (n = 32, mean age: 83.6 ± 7.0 years, women: 71.9 %) or LMHFV group (n = 30, mean age: 81.5 ± 5.7 years, women: 73.3 %). For fracture healing, CT scan at 6 weeks showed improved osseous union for the LMHFV group at 71.5 ± 19.4 % compared to placebo group at 58.8 ± 30.5 %, but no statistical significance detected. X-rays showed fractures healed at 12 months. LMHFV group had significantly higher quadriceps muscle strength compared to placebo group on affected leg using maximum reading (week 26: 8.8 ± 3.6 kg vs. 6.1 ± 4.1 kg; p = 0.011) and average reading (week 26: 8.0 ± 3.7 kg vs. 5.2 ± 3.3 kg; p = 0.008) amongst 3 trials. The balancing ability test could not be performed in most of the subjects at the baseline measurement. However, from week 6 to week 26, LMHFV group had significantly improved balancing compared to placebo group for overall stability index (week 26: 1.6 ± 1.1 vs. 3.4 ± 2.6; p = 0.006), anteroposterior stability index (week 26: 1.1 ± 0.7 vs. 2.1 ± 1.9; p = 0.048) and medial-lateral stability index (week 26: 0.9 ± 0.7 vs. 2.2 ± 2.2; p = 0.008). There was a significant increase in success in performing TUG test in LMHFV group from baseline (13.3 %) to 26 weeks (57.1 %) (p = 0.004). Quality-of-life outcomes by SF-36 showed LMHFV group had a significant improvement at a score of 62.1 ± 18.9 compared to control group at a score of 48.5 ± 18.9 after adjusting for the baseline measurement (p = 0.044).

Conclusion: A short duration of LMHFV during in-patient stay can improve clinical outcomes and can potentially be incorporated as a practical measure during the recovery of fragility hip fractures.

The translational potential of this article: 14 days of LMHFV treatment is generally within the common in-patient stay period for hip fracture patients and therefore can potentially be incorporated into clinical practice with physiotherapy to facilitate recovery of hip fracture patients.

Clinical trial registration number: NCT04063891.

* Corresponding author. 5/F, Lui Che Woo Clinical Sciences Building, Department of Orthopaedics & Traumatology, the Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong SAR, China.
E-mail address: ronald.wong@cuhk.edu.hk (R.M.Y. Wong).

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1. Introduction

Hip fractures are one of the most serious forms of fragility fractures and are associated with high rates of mortality reaching up to 36 % in 1 year [1]. Fracture Liaison Services (FLS) have been established worldwide to provide improved care of fragility fracture patients and decrease secondary fractures [2–4] but the risk of subsequent disability is still substantially high despite current aggressive interventions including timely operations and rehabilitation [1,5]. Interestingly, it is now well known that the risk of a subsequent fracture is not constant with time and was reported to be the highest within 2 years after an initial fracture, and a subsequent fracture could occur shortly after an initial one, also known as an imminent risk of fracture [6–8], which often results from a low-energy fall. Numerous studies have therefore been conducted to assess and recommend effective exercise interventions that can prevent falls and fractures [2,9,10], but there still exists an issue of feasibility and compliance amongst hip fracture patients [11]. Therefore, unfortunately there is often poor functional recovery and quality of life amongst these patients, warranting novel treatment modalities in a practical setting.

Low-magnitude high-frequency vibration (LMHFV) is a biophysical intervention that provides non-invasive, systemic mechanical stimulation [12]. A previous large-scale randomized controlled trial showed that LMHFV had significant positive effects in reaction time, movement velocity, maximum excursion of balancing ability and quadriceps muscle strength after 18 months of treatment. More importantly, with LMHFV there were significantly lower fall incidence compared to control group [12]. Previous pre-clinical studies have shown that LMHFV improves muscle parameters by promoting myogenic proliferation in both soleus and gastrocnemius muscles [13]. Increased muscle contractibility and fast-fiber switching to muscle fiber type IIA were also observed in gastrocnemius muscles [13,14].

Apart from the issue of disability, one of the major goals of fracture fixation is to achieve bone union, and delayed fracture healing can be devastating. Previous pre-clinical studies have shown that osteoporotic fractures can have impaired healing from bone formation, angiogenesis and mineralization [15]. Interestingly, LMHFV has been shown to enhance fracture healing in normal rats, which led to callus formation being significantly larger and remodeling into mature bone significantly faster. Mechanical strength of the healed fracture in treatment group were also significantly greater [16]. Even with osteoporotic rats, LMHFV demonstrated an acceleration of fracture healing [17]. Our previous animal study showed that LMHFV could enhance fibrinolytic factors to accelerate this process by decreasing fibrin content in the callus and increasing callus formation after 2 weeks, indicating its effect for accelerating fracture healing at an early time point [18].

Based on the current existing clinical problem and previous evidence in literature, the objectives of this study were to investigate the efficacy of LMHFV on trochanteric hip fracture elderly patients to (i) accelerate trochanteric fracture healing and (ii) improve clinical and functional outcomes.

2. Methodology

2.1. Ethics statement

This study was approved by the Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee (CREC Ref No.: 2018.584) and was registered in ClinicalTrials.gov (NCT04063891). The study was conducted in compliance to Declaration of Helsinki and ICH-Good Clinical Practice (GCP). The Consolidated Standards of Reporting Trials (CONSORT) guidelines were used [19]. Informed consents were obtained from all the subjects prior data collection.

2.2. Participant recruitment

A randomized double-blinded, placebo-controlled clinical trial with 1:1 allocation was conducted. Our protocol had previously been published [20]. In brief, patients were recruited from the Prince of Wales Hospital from 2021 to 2023. The inclusion criteria were (i) patients aged 65 or older, (ii) unilateral trochanteric hip fracture (AO classification A1-3), (iii) unintentional level ground fall (iv) cephalomedullary device fixation. Exclusion criteria were (i) open fracture, (ii) bilateral lower limb fracture (iii) multiple injury affecting balance/standing on platform, (iv) pathological fractures e.g., infection, tumor, (v) history of medication/disease affecting bone metabolism e.g., hypo/hyperthyroidism, malignancy, (vi) chairbound or bedbound, (vii) cognitive problems e.g., severe dementia. The original proposed sample size was 120, due to the COVID outbreak, the sample size was recalculated based on the expected difference in the muscle strength of 2.06 $\pm$ 2.75 kg [12] and vertebral cancellous BMD gains of 4 % [21] between LMHFV group and control group from the previous studies. A sample size of 28 subjects in each group will result in a power of 0.80 at a significance level of 5 %.

2.3. Study procedures

Randomization was achieved by generating a computer set of random allocations which were sealed in an opaque envelope. Participants opened the sealed opaque envelope and were randomly assigned into LMHFV group (V-Health Limited, Hong Kong; 35 Hz, 0.3 g (g = gravitational acceleration) for 20 min/day, 5 times/week for 14 days) or placebo group (sham treatment by standing on the LMHFV platform for 20 min/day, 5 times/week with only 3 s of vibration at the start for 14 days) by an independent research assistant. The intervention was conducted for patients during in-patient stay as soon as the patient could stand up for a total of 20 min for treatment after receiving hip fracture surgery. Usual clinical practice was continued for all patients including orthogeriatric co-care and physiotherapy. Patients and investigators were blinded to treatment assignment. Outcome assessors and statistician were also blinded by keeping the treatment assignment in a password-protected file, and only the independent research assistant knew the password. Patients would also undergo the usual physiotherapy intervention.

2.4. Outcome measurements

Primary outcome assessments (short-term outcomes) were fracture healing assessed by CT scan (at 6 weeks; % osseous union) and X-rays (at 12 weeks; union of 3 out of 4 cortices in anteroposterior and lateral films is defined as a healed fracture). Dual X-ray Absorptiometry (DXA) scan was performed to assess bone mineral density change (baseline and 6 weeks). Secondary outcome assessments (long-term outcomes) were clinical and functional outcomes including quadriceps muscle strength by isometric dynamometer (model EH101, Camry), handgrip strength by Smedley dynamometer (model EH101, Camry) was added as a supplementary measurement for sarcopenia when the subjects were unable to perform the quadriceps muscle strength test, balancing ability by the Biodex Balance System SD (Biodex Medical System Inc., USA) with higher values indicate poor balance control, Time Up and Go (TUG) test, quality of life outcomes by short form-36 (SF-36) [22], pain by verbal descriptor scale [23], SARC F questionnaires [24], falls, and mortality (Clinical Management System (CMS) from Hospital Authority). Secondary outcome assessments were performed at baseline, 2, 6, 12 and 26 weeks. Compliance rate of treatment was considered as high if patients received vibration or placebo treatment for $\geq$10 days, moderate if within 7–9 days and low if $<$ 7 days.

2.5. Statistical analysis

Analyses were conducted by an intention-to-treat (ITT) approach.

Statistical analyses were done by the original assigned groups. Patients with no baseline measurements and not receiving any treatment were excluded in the analysis. The baseline characteristics in both groups were expressed as mean (standard deviation) or frequency (percentage). For body compositions measured by DEXA scan, analysis of covariance (ANCOVA) was used to compare the body composition at week 6 between two groups and adjusted for baseline values, gender, age and BMI. Independent two-sample T test was used to compare the osseous union (%) measured by CT at week 6 between the two groups, subgroup analysis by gender on fracture healing was performed. A linear mixed model was used for analyzing the change of clinical outcomes over the 26 weeks. In the model, treatment and time were included as fixed effect, and baseline measurement as covariate. The unstructured covariance structure is used. The linear mixed model could account for missing values of response variables properly and no imputation is needed. To compare the within-group difference (baseline vs week 26), paired sample t-test was used for continuous variables that followed a normal distributions and Wilcoxon signed rank test was used for continuous variables which did not follow normal distribution. For TUG test, number of success and failure in completing the test was considered and was treated as categorical variables, McNemar Test was used for comparing within-group differences. For the adverse outcomes, Fisher's Exact test was used to compare the number of deaths and serious adverse events between two groups within the study period. All statistical analyses were conducted using SPSS 29.0.1.0 (Chicago, IL, USA). $P < 0.05$ (two-sided) was considered as statistically significant.

3. Results

3.1. Patient demographics

The study recruitment was from 2021 to 2023. 237 patients were screened for eligibility by the inclusion and exclusion criteria. Patients that did not have any baseline measurements and did not receive any treatment were excluded (n = 20). 62 patients were recruited and randomly assigned to placebo group (n = 32, mean age: 83.6 ± 7.0 years, women: 71.9 %) or LMHFV group (n = 30, mean age: 81.5 ± 5.7 years, women: 73.3 %). The body mass index of the placebo group was 21.7 ± 4.8 kg/m^2, and 22.4 ± 4.9 kg/m^2 for the LMHFV group. No patients had been diagnosed with osteoporosis or had any osteoporosis medication before joining this study. Refer to Table 1. Statistical test for baseline differences was not conducted as in line with CONSORT guidelines [25]. The number of days for the patients to be able to receive treatment by standing up ranged from 1 day to 20 days after surgery, 83.9 % of the included patients started to receive treatment within 10 days after surgery. High compliance rate (vibration or placebo treatment ≥10 days) was achieved in 86.7 % (26 of 30 subjects) of LMHFV group, and 84.4 % (27 of 32 subjects) of placebo group. Refer to Fig. 1.

3.2. Fracture healing and bone mineral density outcomes

For fracture healing in the short term, CT scan at 6 weeks showed improved osseous union for the LMHFV group at 71.5 ± 19.4 % compared to placebo group at 58.8 ± 30.5 %, but there was no statistical significance detected. Examples of CT scan images of fracture healing in LMHFV group and placebo groups were shown in Fig. 2. Analyzed by gender, for females, improved osseous union for the LMHFV group was at 71.7 ± 18.9 % compared to placebo group at 60.7 ± 30.7 %. Whilst for males, improved osseous union for the LMHFV group was at 71.0 ± 23.0 % compared to placebo group at 54.2 ± 32.5 %. There was no significant difference between both treatment groups in female ($p = 0.278$) or male ($p = 0.357$) subgroups, respectively. X-rays showed that all fractures had healed at 12 months. Bone mineral density and T-score at hip neck and spine did not show significant differences between groups at 6 weeks (Fig. 3).

Table 1
Baseline characteristics of included subjects.

Characteristics	Placebo (n = 32)	LMHFV (n = 30)
Age (years)	83.63 (7.033)	81.47 (5.746)
Women	23 (71.9 %)	22 (73.3 %)
Height (cm)	153.214 (10.336)	154.311 (7.111)
Weight (kg)	51.071 (14.228)	53.519 (13.679)
BMI (kg/m^2)	21.682 (4.771)	22.350 (4.928)
Body composition		
ASMI/height^2	5.278 (0.947)	4.941 (0.815)
Total body fat (%)	34.072 (5.488)	38.316 (6.713)
Fat mass (g)	18149.4 (7131.3)	20373.6 (6581.1)
Lean mass (g)	32559.7 (8628.9)	30303.7 (4706.6)
Hip BMD-neck (g/cm^2)	0.499 (0.138)	0.52411 (0.157)
Hip T-score-neck	−3.053 (1.397)	−2.979 (1.411)
Spine BMD (g/cm^2)	0.755 (0.155)	0.809 (0.155)
Spine T-score	−2.132 (1.376)	−1.633 (1.422)
Muscle performance		
HGS (left)- Max (kg)	11.400 (9.221)	15.756 (5.695)
HGS (right)- Max (kg)	12.144 (7.137)	15.594 (7.257)
QS (affected)-Max (kg)	4.065 (3.175)	4.623 (3.702)
QS (unaffected)- Max (kg)	7.012 (3.625)	8.914 (4.684)
Questionnaire		
VDS (Pain score)	2.48 (1.180)	2.40 (1.329)
SF-36 score (total)	280.4 (117.7)	432.0 (170.5)
-Pf	3.87 (11.307)	21.50 (33.326)
-Rph	0.0 (0.00)	30.0 (46.609)
-Rep	37.63 (49.609)	72.22 (44.7)
-E/F	49.84 (22.003)	54.83 (18.822)
-Ewb	61.03 (19.404)	67.63 (20.515)
-Sf	40.323 (24.729)	55.00 (31.928)
-P	36.210 (18.573)	44.00 (25.878)
-GH	42.74 (18.387)	48.50 (17.77)
-HC	17.74 (21.596)	38.33 (21.509)

LMHFV, low-magnitude high-frequency vibration; Pf, physical functioning; Rph, role limitations due to physical health, Rep, role limitations due to emotional problems; E/F, energy/fatigue; Ewb, emotional well being; Sf, social functioning; P, pain; Gh, General health; HC, health change. VDS, Verbal descriptor scale; ASMI, Appendicular lean body mass, BMD, bone mineral density; QS, quadricep strength. Data are expressed as mean (standard deviation), or frequency (%).

3.3. Functional outcomes

For clinical and functional outcomes in the longer term, LMHFV group had significantly higher quadriceps muscle strength compared to placebo group on the affected leg (fracture side) using maximum reading across 26 weeks (At week 26: 8.8 ± 3.6 kg vs. 6.1 ± 4.1 kg; $p = 0.011$) and average reading (At week 26: 8.0 ± 3.7 kg vs. 5.2 ± 3.3 kg; $p = 0.008$) amongst 3 trials. Compared with baseline, both LMHFV group ($p < 0.001$ and $p < 0.001$, respectively) and placebo group ($p = 0.005$ and $p = 0.004$, respectively) had significant improvement for quadriceps muscle strength using maximum and average readings too.

LMHFV group also had higher quadriceps muscle strength in the unaffected leg compared to placebo group using the maximum reading (11.0 ± 6.8 kg vs. 7.4 ± 4.0 kg; $p = 0.242$) and average reading (10.0 ± 5.9 kg vs. 6.6 ± 3.7 kg; $p = 0.175$) amongst 3 trials. However, the results were not significant. Compared with baseline, LMHFV group ($p = 0.046$) had significant improvement for the quadriceps muscle strength using average reading (Fig. 4).

As most of the subjects were unable to perform the baseline balancing ability test soon after receiving the hip surgery, the analysis could only be performed from week 6 to week 26 for balancing ability test. LMHFV group had significantly improved balancing compared to placebo group for overall stability index (At week 26: 1.6 ± 1.1 vs. 3.4 ± 2.6; $p = 0.006$), anterior/posterior stability index (1.1 ± 0.7 vs. 2.1 ± 1.9; $p = 0.048$) and medial/lateral stability index (0.9 ± 0.7 vs. 2.2 ± 2.2; $p = 0.008$).

There was an improved TUG test for LMHFV at 31 ± 30.9s compared to placebo group at 45.1 ± 36.7 s at week 26, but this was statistically insignificant. However, there was a significant increase in success in

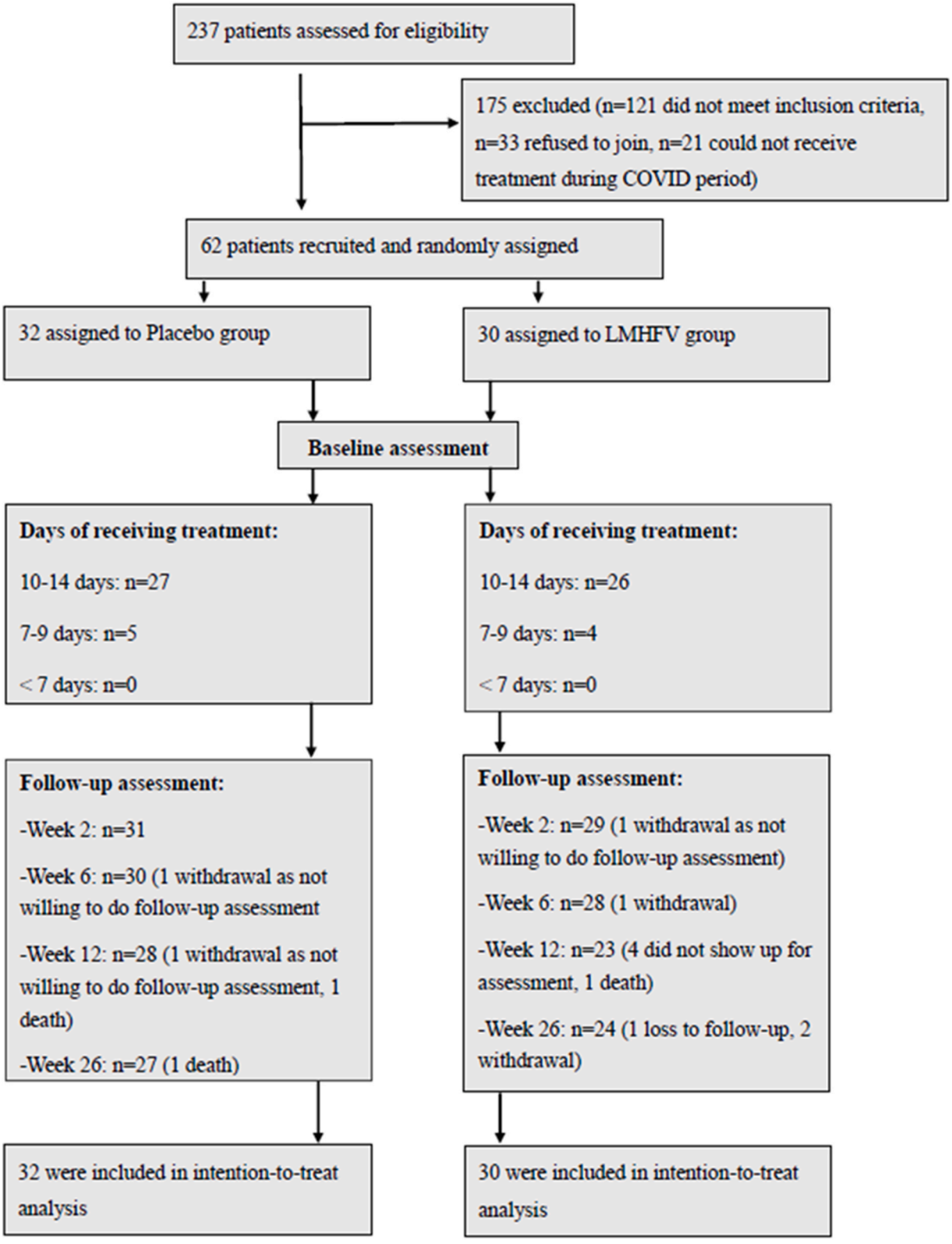

Fig. 1. Flow diagram of this randomized controlled trial.

performing TUG test in the LMHFV group from baseline (13.3 %) to 26 weeks (57.1 %) ($p = 0.004$). There were no significant differences for handgrip strength between LMHFV and placebo groups. Refer to Supplementary Table 1.

3.4. Quality of life and pain outcomes

Quality-of-life outcomes by the SF-36 showed that LMHFV had a significant improvement at a score of 62.1 ± 18.9 compared to control group at a score of 48.5 ± 18.9 ($p = 0.044$). Subgroup analysis showed that LMHFV significantly improved outcomes in physical functioning (p

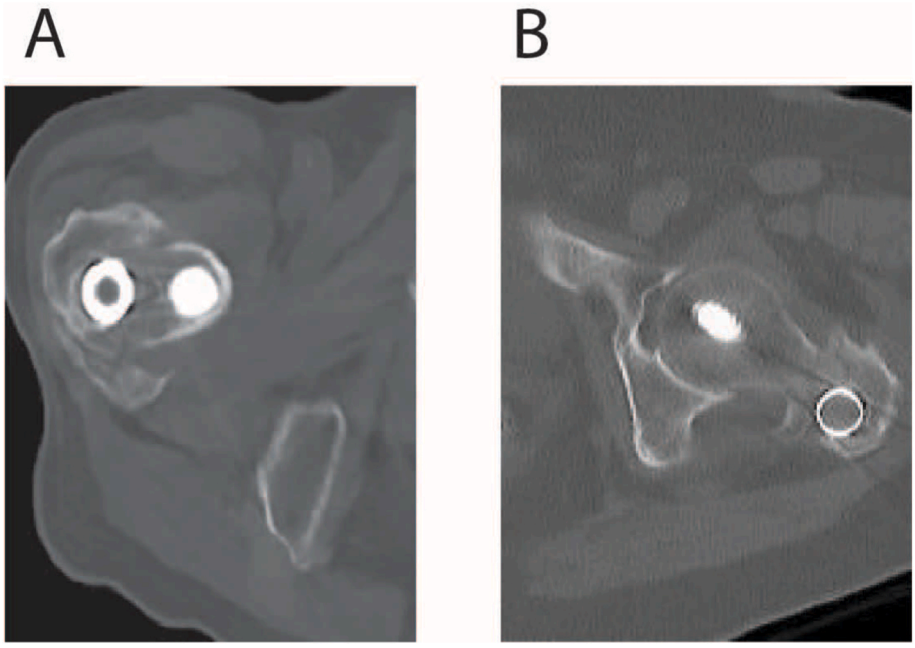

Fig. 2. CT scan images showing fracture healing at week 6 after treatment in a subject from (A) LMHFV group showing 80 % of osseous union and (B) placebo group showing 35 % of osseous union.

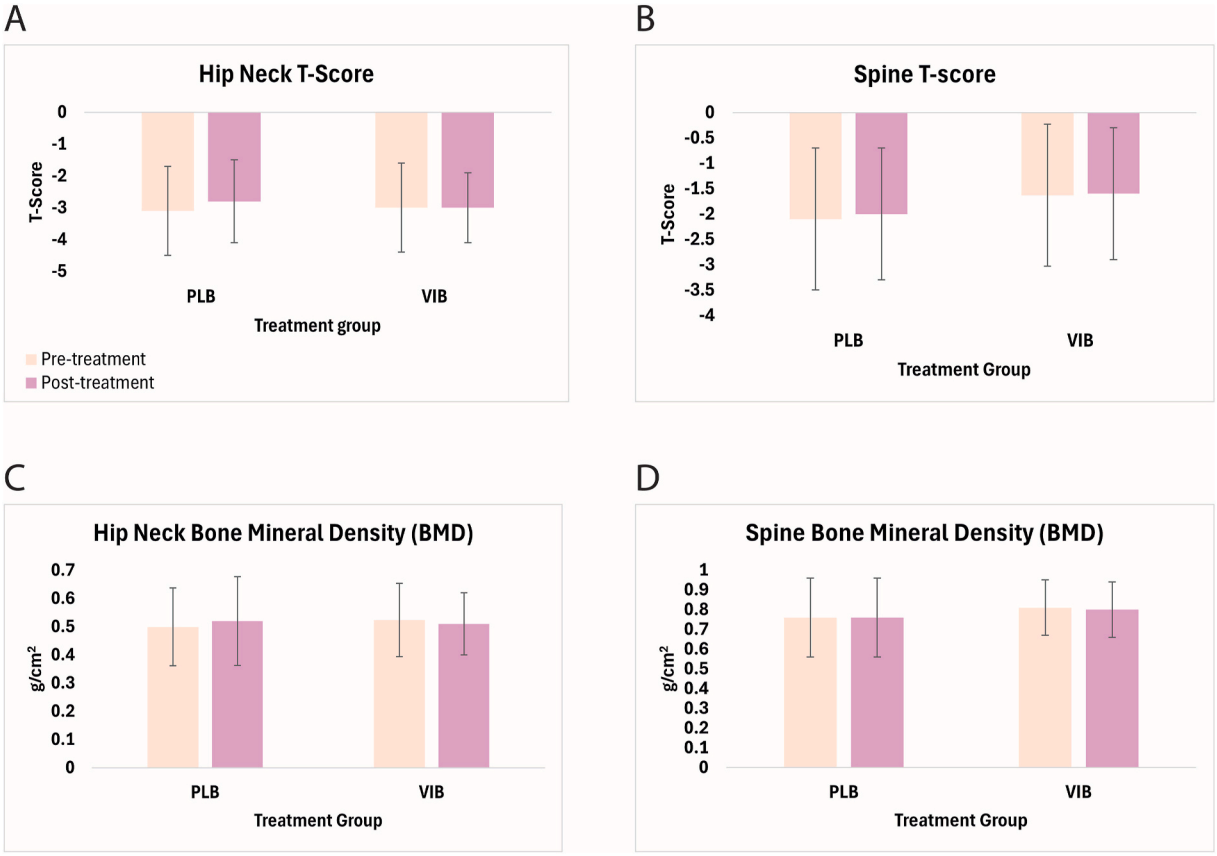

Fig. 3. Changes in bone mineral density (BMD) and T score measured by dual-energy X-ray absorptiometry at week 6 (post-treatment) between placebo group and LMHFV group (A) Hip Neck T-score ($p = 0.120$) (B) Spine T-score ($p = 0.635$) (C) Hip neck bone mineral density ($p = 0.124$) (D) Spine bone mineral density ($p = 0.699$).

$= 0.002$), role limitations due to physical health ($p = 0.001$), role limitations due to emotional problems ($p = 0.013$), and health change ($p = 0.038$). Compared with baseline, both LMHFV group ($p = 0.009$) and placebo group ($p < 0.001$) had significant improvement for the SF-36. Subgroup analysis showed for LMHFV group, significant improvement occurred for physical functioning ($p < 0.001$), role limitations due to

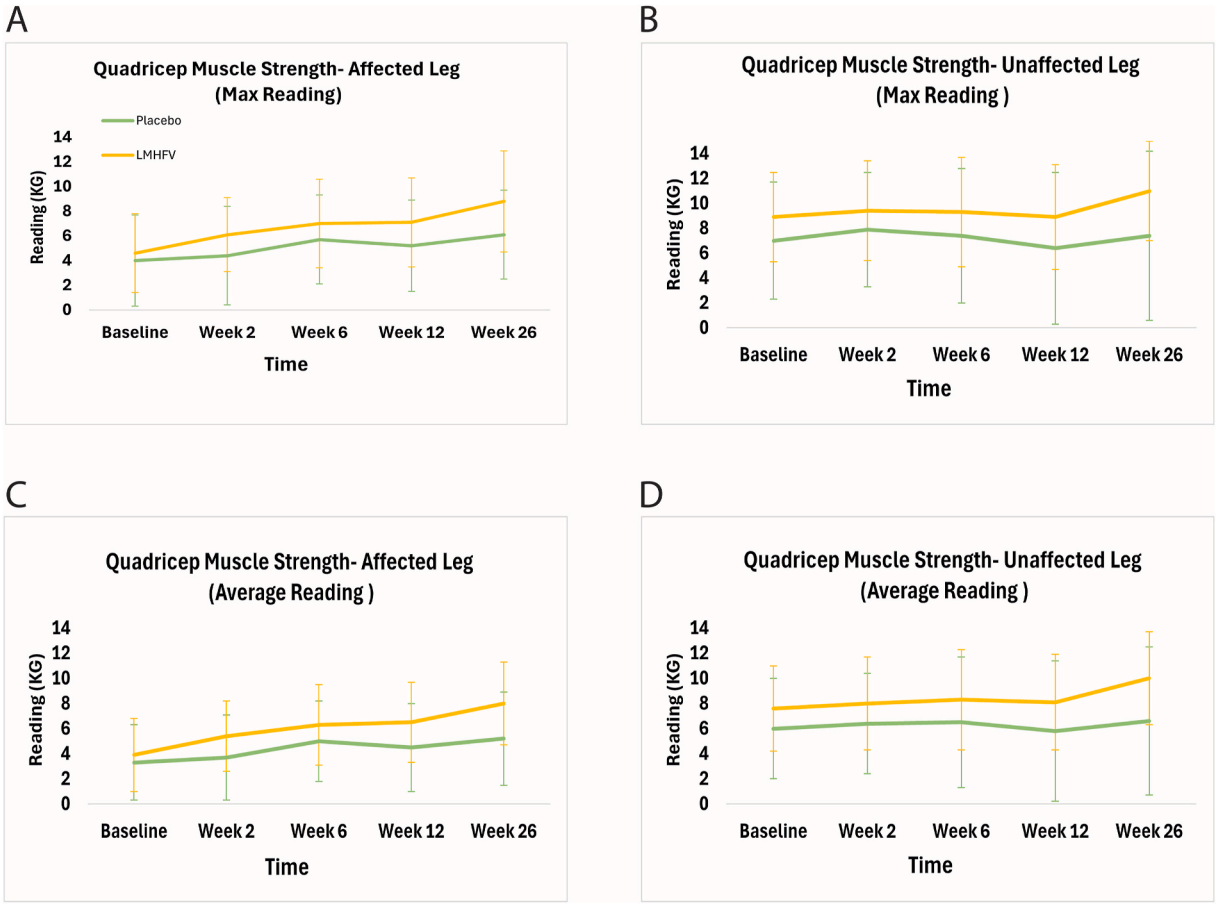

Fig. 4. Trend of quadricep muscle strength changes from baseline to week 26 in placebo group and LMHFV group. Quadricep muscle strength was measured (A) in affected leg using maximum reading ($p = 0.011$) (B) in unaffected leg using maximum reading ($p = 0.242$) (C) in affected leg using average reading ($p = 0.008$) and (D) in unaffected leg using average reading ($p = 0.175$).

physical health ($p = 0.049$), energy/fatigue ($p = 0.009$), emotional well-being ($p = 0.036$), pain ($p < 0.001$), and general health ($p < 0.001$). Subgroup analysis showed for placebo group, significant improvement occurred for physical functioning ($p < 0.001$), role limitations due to emotional problems ($p = 0.041$), energy/fatigue ($p < 0.001$), emotional well-being ($p = 0.004$), social functioning ($p = 0.019$), pain ($p < 0.001$), general health ($p = 0.006$) and health change ($p < 0.001$). There were no significant differences for pain outcomes with VDS between the two groups. However, compared with baseline, both LMHFV group ($p < 0.001$) and placebo group ($p < 0.001$) had significant improvement for VDS. Refer to Supplementary Table 1.

3.5. Serious adverse events and mortality

During the 20-min treatment period, the status of patients was monitored by the research staff standing aside. The patient would be asked if they felt fatigued and needed a rest, and or if pain/discomfort was experienced during and after receiving treatment. To summarize, 3 patients reported feelings of dizziness during the treatment in the LMHFV group, 1 reported edema in their feet after treatment in placebo group, 2 felt increased feet pain and 1 felt stomachache after treatment in the LMHFV group. The vital signs including systolic and diastolic blood pressure and heart rate were within clinically acceptable ranges after treatment at the day of discharge in both groups. There was no report of cardiovascular-related discomfort during or after the treatment. There was no record of fall event in all subjects within the study period through asking the subjects or searched via CMS. Serious adverse events occurred in 6 of placebo group and 3 of LMHFV group, which were due to hospitalizations of other causes. Mortality occurred in 2 of placebo group and 1 in LMHFV group, which occurred during acute hospitalization from other medical cause. For both serious adverse events and mortality, there were no significant difference between the two groups.

4. Discussion

Our results showed LMHFV treatment significantly improved muscle parameters and functional recovery including quadriceps muscle strength and balancing abilities in patients with trochanteric hip fracture after surgical fixation. The intra-group comparison showed there was also a significant increase in patients that could perform the TUG test from baseline to 26 weeks in the LMHFV group, while the increase in success was not significant in control group. This study showed LMHFV could be a potential treatment for enhancing long-term outcomes of functional recovery in patients with trochanteric hip fracture. Sarcopenia has become a pressing problem amongst fragility fracture patients and can reach up to 64 % in females and 95 % in males [26]. Sarcopenia is characterized by a progressive loss of muscle mass and function that is associated with adverse clinical outcomes including disability, fall, and mortality. Unfortunately, as of now, there is still no Food and Drug Administration (FDA) approved drug to treat this disease. The mainstay of treatment for sarcopenia is therefore resistance exercises and nutrition [27]. However, feasibility and compliance can be an issue amongst hip fracture patients, therefore warranting novel treatments. Previous preclinical studies showed that 2 weeks LMHFV could significantly improve fracture healing, but the effect of this short-term treatment on

muscle has not been studies yet [18]. In this study, LMHFV intervention was only used for 14 days showing positive results for muscle parameters on quadriceps muscle strength on the affected leg with hip fracture, balancing and ability to perform TUG test. Interestingly, the muscle strength of patients in the unaffected leg after 14 days of LMHFV treatment also had an increase trend according to the average values across 26 weeks of the study. This may attributable to the improved lower limb physical functions, despite results being insignificant in this study. For balancing ability, LMHFV group showed significant improvements after vibration treatment compared with control group. Besides, subjects tend to spend less time in completing 6-m gait speed and 5-time chair tests in the LMHFV group compared with the control group at week 6 post-surgery. However, there were very few baseline measurements in the balancing ability, 6-m gait speed and 5-time chair test as most of the patients were reluctant to or had difficulty moving their injured leg due to pain or functional limitations. The missing baseline measurements of these tests could affect the analysis for the treatment outcomes. Also, due to the limited data, the baseline sarcopenia status, which may affect the treatment response, could not be taken into account in this study as the sarcopenia status is determined by a combination of appendicular skeletal muscle mass, muscle strength and physical performance as diagnostic criteria according to the Asian Working Group for Sarcopenia (AWGS) 2019 guidelines [28]. The effect of LMHFV treatment on mobility in hip fracture patients receiving fixation operation and the effect of baseline sarcopenia status on treatment response needs to be further explored in future studies. Previous studies have shown that LMHFV can reduce falls and can improve muscle strength and balancing abilities amongst elderlies after 18 months. It has now been recommended by the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) that there should be co-primary endpoint for clinical trials aiming at treatment for sarcopenia with functional performance and patient reported outcome measure. For our study, SF-36 score was improved and also ability to perform TUG test, as well as quadriceps muscle strength test. Although hand grip strength was not improved, and quadriceps muscle strength is not a parameter in the diagnosis of sarcopenia, our study did show promising effects, and further research can be carried out.

Fracture healing is an essential part of the recovery process for trochanteric hip fractures. Previous pre-clinical studies have shown that osteoporotic fracture healing is delayed in all phases of fracture healing [15]. In the early phase, delays occur during mesenchymal stem cell recruitment, angiogenesis and estrogen receptor expression. During the mid-phase, there is delayed callus formation and at the late phase, the callus remodeling and mechanical properties are affected [15]. Although this evidence has not been shown clinically, the consequences of delayed fracture healing can be devastating including pain, disability, and implant complications. To provide optimal recovery, accelerating osteoporotic fracture healing can be a major factor as there is expected improved rehabilitation. There were no significant difference in the BMD of hip neck and spine measured by DXA at week 6 in this study, the results aligned with a study which investigated the long-term treatment effect of LMHFV on BMD changes, in which no significant difference was found in the overall BMD changes after treatment compared with the control group at 18 months [12] in postmenopausal women. Besides, our results did not show a significant improvement in using LMHFV in accelerating time to fracture healing, but there was a trend of increased osseous union in LMHFV group. Previous preclinical studies demonstrated that the effect of fracture healing after LMHFV was influenced by the estrogen status, in which LMHFV significantly improved callus properties and increased bone formation in ovariectomized (OVX), estrogen-deficient mice, and these effects were eliminated by subcutaneous estrogen application [29]. Previous animal studies also demonstrated that in Sprague–Dawley (SD) rats, there was significantly improved fracture healing at week 8 with vibration treatment in osteoporotic bone [30]. In this study, there was also no significant difference in fracture healing between LMHFV group and placebo group in the female subgroup and the male subgroup respectively. One of the reasons could be due to the duration of the LMHFV treatment, as the protocol was previously changed from 6 months of LMHFV to 2 weeks of treatment due to COVID-19 [20], and this may affect the results of this outcome. Future studies can be conducted to assess a longer duration of LMHFV and follow-up period with larger sample size in accelerating fracture healing.

It was shown that quality of life was improved with LMHFV. The SF-36 consists of several domains and it was found that LMHFV significantly improved outcomes in physical functioning, role limitations due to physical health, role limitations due to emotional problems, and health change. As LMHFV had positive effects on muscle parameters based on our results, the improvement in functional and physical scores for the SF-36 are expected. A previous meta-analysis had also shown that vibration therapy can improve quality of life amongst older adults [31]. There was no difference in pain between the LMHFV group and placebo group, which is expected as the fracture would have healed. There are already several rehabilitation strategies for hip fracture patients, including structured exercise, balance training, progressive resistance training, and treadmill training [32]. Compared to these, short-term LMHFV also has multiple benefits for hip fracture patients, but can also be started at an early stage and is easy to adhere to. LMHFV treatment is considered as a relatively safe treatment with only minor and transient adverse effects reported in this study. Vibration training may be attractive for those are not willing or unable to do convention exercise such as physiotherapy due to pain or physical limitations [33]. Therefore, LMHFV could be potentially incorporated as one of the post-acute rehabilitation approaches to facilitate the recovery of fragility fracture patients.

The strengths of this study were that it was a randomized double-blinded placebo-controlled trial, with good compliance to interventions, and follow-up. The main limitations of this study include the change of protocol from 6 months LMHFV to 2 weeks due to COVID-19, which may affect the results especially for fracture healing outcomes. As there were strict infection control measures, the recruitment was affected and the sample size was recalculated. We could only have analysis of 62 patients, which was decreased from the original proposed sample size of 120. Also, most of the subjects could not do the MRI scans due to the suspension of equipment service within the COVID-19 period. However, as the use of LMHFV is only 2 weeks in-patient use, this also allows the intervention to be practical in Fracture Liaison Services (FLS) [3]. FLS are services that actively recruit fragility fracture patients to have holistic care including rehabilitation and the prevention of secondary fractures. Further clinical trials should be conducted based on a larger sample size and long interventional durations to further demonstrate the results especially in terms of fracture healing. Future studies can also assess the effects of LMHFV compared to exercises or in combination with exercises for fragility fracture patients.

In conclusion, this study showed that a short duration of LMHFV during in-patient stay can improve clinical outcomes including the functional recovery and quality of life outcomes. Also, there was an increase trend in osseous union after LMHFV, though with no significance. 14 days of LMHFV treatment can potentially be incorporated as a practical measure during the recovery of fragility hip fractures within the in-patient stay for post-acute rehabilitation after surgery.

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Declaration of competing interest

A conflict of interest occurs when an individual's objectivity is potentially compromised by a desire for financial gain, prominence, professional advancement or a successful outcome. The Editors of the

Journal of Orthopaedic Translation strive to ensure that what is published in the Journal is as balanced, objective and evidence-based as possible. Since it can be difficult to distinguish between an actual conflict of interest and a perceived conflict of interest, the Journal requires authors to disclose all and any potential conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jot.2025.01.002.

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