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ORIGINAL ARTICLE

Efficacy of Combining Whole-body Vibration Training and Closed Kinetic Chain Exercises in Early Knee Osteoarthritis: A Preliminary Study

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Objectives: We aimed to conduct a preliminary evaluation of the effectiveness of integrating whole-body vibration training (WBVT) into conventional closed kinetic chain (CKC) exercises as an intervention strategy for early knee osteoarthritis (KOA). **Methods**: This non-randomized comparative study conducted at an orthopedic clinic involved 53 patients (with Kellgren–Lawrence grades 1–2); 37 patients received only physical therapy (CKC group), and 16 patients received both physical therapy and WBVT (WBVT group). The primary outcome was the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) subscale score for pain, and the secondary outcomes were the WOMAC subscale score for physical function and muscle-strength assessments [isometric knee extension strength and the 30-second chair-stand test (CS-30) score]. Propensity score matching (PSM) was used to adjust for bias between the control and intervention groups. **Results**: After PSM adjustment, 13 patients were selected from each group. The WBVT group showed a significant improvement in the WOMAC pain score (d=1.16, P=0.007) and a significant increase in the CS-30 score (d=0.81, P=0.049). However, for the WOMAC physical function score, the between-group difference remained statistically insignificant (d=0.59, P=0.146). **Conclusions**: WBVT may be effective in reducing the pain of early KOA. WBVT is a non-invasive and convenient method, underscoring its potential as a novel therapeutic option.

Key Words: healthcare; osteoarthritis; pain; propensity score matching

INTRODUCTION

Knee osteoarthritis (KOA) is characterized by pain and worsening symptoms that affect activities of daily living as the disease progresses.[1] The American College of Rheumatology (ACR) classification defines the pathological progression of KOA.[2] Patients with stage 3 or higher disease often exhibit severe structural joint damage[3] and demonstrate limited treatment efficacy.[4] As a result, there is a general consensus to prioritize early diagnosis and treatment, with a significant focus on addressing early KOA.[5–7]

Early KOA is characterized by the absence of any evidence of joint space narrowing on plain radiographs but marked by structural changes in the articular cartilage, subchondral bone, meniscus, and synovial membrane, along with a consistent level of pain and other symptoms.[7] Pain progression in patients with early KOA may indicate the potential need for knee replacement surgery.[8] Early diagnosis of KOA may

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contribute to delayed disease progression and improved patient outcomes. Interventions targeting early KOA pain may effectively prevent disease progression and improve the quality of life of patients with KOA.

Low-frequency whole-body vibration training (WBVT) is effective in reducing pain, improving physical function, and increasing knee extensor strength in patients with KOA.[9,10] Wang et al.[11] showed that low-frequency WBVT reduced the expression of inflammatory cytokines in an early KOA mouse model. These findings suggest that low-frequency WBVT may reduce early KOA pain. However, the efficacy of low-frequency WBVT for pain reduction, particularly in early KOA, remains unknown.[12]

In KOA rehabilitation, closed kinetic chain (CKC) exercises are utilized extensively, with numerous studies underscoring their advantages.[13] However, despite a lack of evidence of adverse effects of CKC exercises in early KOA, concerns remain regarding their implementation.[14] Consequently, CKC exercises may be both low risk and advantageous for early KOA.

This study aimed to assess the efficacy of CKC exercises on pain when combined with low-frequency WBVT compared with the use of CKC exercises alone. We hypothesized that treatment using CKC exercises and WBVT would yield greater pain improvement than the use of CKC exercises alone.

MATERIALS AND METHODS

Design and Setting

The study was an open-label, 12-week, non-randomized, controlled trial with two cohorts, comprising a total of 55 men and women who met the diagnostic criteria for early KOA at a single orthopedic clinic. The first cohort included 39 control participants who underwent non-WBVT (CKC group) between March 2018 and August 2019. The second cohort consisted of 16 participants in the intervention group (WBVT group) who underwent CKC combined with WBVT between August and December 2020.

All participants provided written informed consent prior to participation. This study was approved by the Ethics Committee of the Fukuoka Reha Orthopedic Clinic in Japan (number FRH2020-R-008), and it was registered in the University Hospital Medical Information Network Clinical Trials Registry (study ID: UMIN000043253).

Participants

This study included men and women aged 40 years and older diagnosed with early KOA. The diagnosis of early KOA, as described by Mahmoudian et al.,[5] was determined based on the Kellgren–Lawrence (KL) grading system (grade 0, 1, or 2) according to the ACR criteria on radiograph analysis. To confirm the diagnosis, patients were required to report experiences of at least two episodes of knee pain, each lasting more than 10 days, within the previous year.

The following data were provided for all participants: (1) articular cartilage morphology score, (2) meniscal tear grade, and (3) bone marrow lesion size on magnetic resonance imaging. Patients were excluded based on the following criteria: (1) inability to provide consent to participate in the study; (2) traumatic pain and history of lower limb surgery; (3) a diagnosis of rheumatoid arthritis; (4) history of fracture or malignancy in the lower limb; (5) inability to attend the clinic alone; (6) psychiatric illness such as schizophrenia; (7) presence of neurological findings such as Parkinson's disease or stroke; (8) inability to provide information on articular cartilage morphology score, meniscal tear grade, and bone marrow lesion size on magnetic resonance imaging; (9) doctor's order to drop out during the study; or (10) an intervention frequency of less than once a week.

Interventions

The duration of intervention in both groups was 40 min (two or three times per week). Physical therapists conducted an initial assessment according to a physical therapy (PT) intervention protocol,[15] which included history-taking and physical examination. The therapists identified issues related to symptoms and musculoskeletal function impairments, and imaging findings were assessed. Although the protocol was based on interventions that focused on the knee joint, the physical therapist also implemented joint mobilization exercises, manual therapy, and exercise therapy interventions for the hip, lumbar spine, and ankle joints when evaluation indicated that KOA symptoms contributed to symptoms and movement limitations in other joints. The following PT interventions were common to all participants: patient education and joint mobilization training, manual therapy, and exercise therapy focusing on the knee joint. Patient education was provided on KOA symptoms, exercise benefits, and the importance of self-management. Exercise therapy focused on the knee joint, encompassing both open kinetic chain (OKC) and closed kinetic chain (CKC) exercises for muscle strengthening. OKC exercises included (1) patella setting, (2) active straight leg raises, and (3) leg extensions, whereas CKC exercises comprised (1) squats, (2) split squats, and (3) lunges. Initially, patellar setting and squat exercises were ini-

Table 1. Whole-body vibration training protocol

Week	Frequency (Hz)	Duration (s)	Number of sets	Rest interval (s)
1	25	30	6	30
2	25	30	6	30
3	25	30	7	30
4	25	30	8	30
5	25	30	8	30
6	25	30	8	30
7	30	45	8	45
8	30	45	8	45
9	30	45	8	30
10	30	45	8	30
11	30	45	8	30

tiated at 10 repetitions for three sets. Subsequently, based on knee pain, muscle strength, and current condition, exercises progressed from type (1) to types (2) and (3), with repetitions and frequency gradually increasing within the range of 10–20 repetitions and three to five sets. Aerobic exercise was performed on a stationary bike ergometer for 10–15 min at moderate intensity (Borg scale 11–13), considering appropriate load and pain-free range.

WBVT in the WBVT group was performed after PT sessions. The WBVT program was introduced as an alternative to the CKC exercises that had been conducted in the CKC group. The WBVT group underwent WBVT during exercise therapy sessions, specifically during squat exercises as mentioned earlier. The WBVT device used in this study was the Power Plate® Pro5TM (Performance Health Systems, Northbrook, IL, USA). The research protocol used WBVT conditions that were within the conditions reported to be potentially hazardous to the human body (30 Hz, 4.0 mm, 10 min/day).[16] Therefore, the program was based on a low-frequency protocol of 10–30 Hz in accordance with previous studies.[10,17,18]

During the first session, interventions were performed at a frequency of 25 Hz for 30 s, followed by a 30-s rest period. This process was repeated for five additional sets. The number of sets increased to seven and eight starting on weeks 3 and 4, respectively. From week 7, the sessions were performed at a frequency of 30 Hz over 45 s, with rest intervals of 45 s. However, from week 9, the resting interval was reversed to 30 s, and this regimen was maintained until week 12 (**Table 1**). A low amplitude (2–4 mm) was used for all interventions. Based on previous research,[17] the participants performed squatting movements during the sessions to provide 10°–60° of knee flexion, alternating every 3 s between extension and flexion.

Outcomes

The assessment measurements were conducted at baseline and 12 weeks post-baseline before the intervention. The primary outcome was pain, whereas physical function, muscle strength, and performance were assessed as secondary outcomes. Baseline demographic data, including age, height, weight, body mass index (BMI), sex, and KL grade, were either measured directly or extracted from medical records.

Primary Outcome

The Japanese version of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used for the assessment.[19] The WOMAC is a self-administered scale designed to measure the severity of pain and difficulty in daily activities associated with KOA. It has three main sections: right knee pain (5 items), left knee pain (5 items), and physical function (17 items). Each item is rated on a five-point Likert scale (1–5 points), with higher scores indicating more severe pain and functional impairment. The pain subscale of the WOMAC was used as the primary outcome.

Secondary Outcomes

The physical function subscale of the WOMAC and muscle strength were used as the secondary outcomes. The WOMAC pain scale was used to assess the side diagnosed with early KOA. Muscle strength was assessed by evaluating isometric knee extension, and functional performance was assessed with the 30-s chair-stand test (CS-30).

Muscle strength was assessed by using a handheld dynamometer (μTas F-1; ANIMA, Tokyo, Japan) to measure isometric knee extension muscle strength (knee extension) in accordance with previous studies.[20] The strap length was adjusted to ensure that the knee joint was flexed at 90°. During measurement, the trunk was maintained in an upright position with both arms supported by the bed. The participants performed isometric knee extension twice on the affected side for approximately 3 s with maximum effort at intervals exceeding 30 s, and the average of the two measurements was used for analysis. The obtained values were normalized to body weight and reported as weight-related isometric knee extensor strength.

The CS-30 serves as a validated method for assessing lower limb muscle strength in adults, demonstrating both reliability and validity in a previous study.[21] Initially, participants were positioned to sit with their legs shoulder-width apart, arms crossed over their chest, and knees flexed at an angle of 100°–110°. At a given signal, the participants were instructed to stand up to a fully erect position, extend both the hip and knee joints, and then return to the seated position. This sequence was continued for 30 s. The measurement was performed once after a break following five to ten practice exercises.

Analysis

Propensity score matching (PSM) is recognized as an effective method for correcting potential bias between the control and intervention groups.[22] This method allows accurate comparisons of treatment effects across cohorts.[23] In this study, confounding variables, including age, sex, BMI, analgesic use, and baseline values for each outcome, were included in a logistic regression model to calculate the propensity scores. These scores were used to plot a receiver operating characteristic curve, which showed an area under the curve (AUC) value of 0.748. This value demonstrated the appropriateness of the PSM application, which was subsequently adopted.

Pre-intervention characteristics and outcomes were described as follows: quantitative variables were expressed as mean and standard deviation, whereas categorical variables were expressed as number and percentage. An independent *t*-test, chi-squared test, or Wilcoxon rank-sum test was used for comparison between groups, as appropriate. The effect sizes were calculated using Cohen's d (assessment criteria: $0.3 \leq$ small < 0.5, $0.5 \leq$ medium < 0.8, and $0.8 \leq$ large).

Group differences were represented by the changes in scores and 95% confidence intervals (CIs) for the pre- and post-comparisons for each group. The Bonferroni method within a general linear model framework was employed for the analysis. Cohen's d was calculated as the effect size at this stage. The analyses were conducted using an intention-to-treat approach. The significance threshold was set at 5% for all statistical analyses. Analyses were performed using IBM SPSS Statistics for Windows version 25 (IBM, Armonk, NY, USA).

RESULTS

After PSM, the PT and WBVT groups included 13 patients each. No dropouts were reported throughout the intervention phase (**Fig. 1**). **Table 2** compares patient characteristics and outcomes between the intervention and control cohorts before the intervention. Most participants were women, and grade 2 was the most common KL grade. No significant difference was observed between the two groups for the number of interventions, analgesic medication status, or pre-intervention group.

As the primary outcome, the total WOMAC pain scores of the WBVT group and the CKC group had declined after treatment. However, the decrement in the WOMAC pain score for the WBVT group was significantly larger than the decline in the pain score for the CKC group (difference between groups: −2.9, 95% CI: −5.0 to −0.9, d=1.16; **Table 3**). For the secondary outcome, represented by the WOMAC physical function score, although the decline in the function score was larger in the WBVT group, the between-group difference was statistically insignificant (d=0.59, P=0.146; **Table 3**). Improvement in knee extension strength showed no intergroup difference in relation to body weight (d=0.25, P=0.533). However, the improvement in the CS-30 score was significantly higher in the WBVT group than in the CKC group (d=0.81, P=0.049; **Table 3**).

DISCUSSION

In this study, we evaluated the efficacy of a 12-week program of low-frequency WBVT in middle-aged and older adults who met the diagnostic criteria for early KOA. The WBVT group demonstrated significant improvements in pain reduction and performance compared with the CKC group, with no dropouts. In particular, the benefits related to pain reduction and improved performance test scores were remarkable.

The innovation of this study lies in demonstrating the application of low-frequency WBVT for pain management in early KOA. WBVT, administered for approximately 6–10 min at a low frequency of 25–30 Hz, was introduced in addition to CKC exercises. Given that a clinically significant

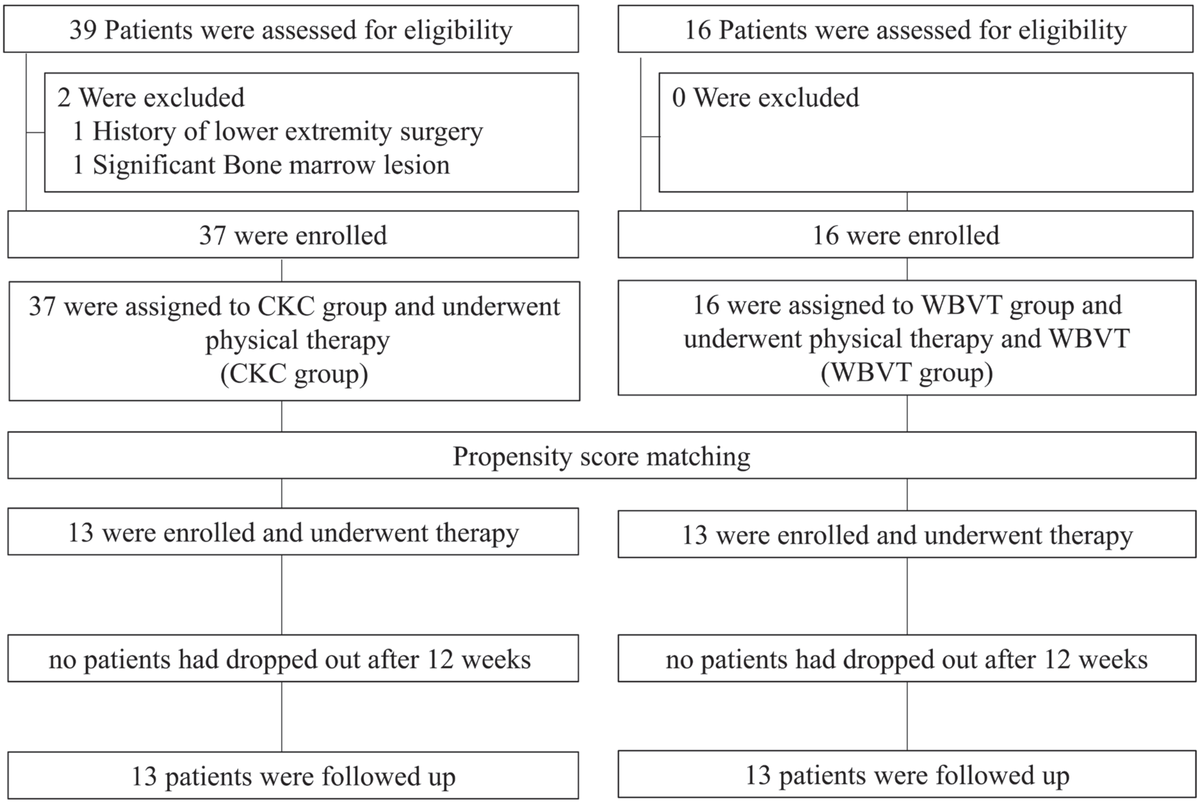

Fig. 1. Flowchart of patient recruitment and participation.

Table 2. Baseline descriptive characteristics before and after propensity score matching

Characteristic	Unadjusted			Adjusted		
	WBVT group (n=16)	CKC group (n=37)	P	WBVT group (n=13)	CKC group (n=13)	P
Age, years	62.9 ± 8.1	66.1 ± 8.0	0.06	62.9 ± 9.2	64.8 ± 8.8	0.60
Sex, female	12 (75)	28 (76)	0.96	10 (52.6)	9 (47.4)	0.66
BMI, kg/m^2	24.3 ± 3.8	23.4 ± 2.7	0.36	23.6 ± 3.6	24.0 ± 3.0	0.76
KL grade			0.96			0.66
Grade 0	0 (0)	0 (0)		0 (0)	0 (0)	
Grade 1	4 (25)	9 (24)		4 (30.8)	3 (23.0)	
Grade 2	12 (75)	28 (76)		9 (69.2)	10 (77.0)	
Interventions	17.5 ± 6.3	18.8 ± 4.4	0.40	18.5 ± 5.8	18.3 ± 4.2	0.91
Analgesics use	5 (31)	12 (32)	0.93	5 (38.5)	4 (30.8)	0.68
WOMAC pain	11.7 ± 3.9	11.8 ± 3.4	0.89	12.2 ± 4.3	12.2 ± 2.7	0.96
WOMAC function	29.6 ± 10.5	31.5 ± 11.8	0.65	30.6 ± 11.9	30.6 ± 13.0	1.00
Knee extension, kgf/kg	0.28 ± 0.08	0.30 ± 0.13	0.47	0.38 ± 0.09	0.40 ± 0.16	0.62
CS-30, repetitions	12.7 ± 2.1	14.7 ± 3.9	0.08	13.0 ± 1.9	13.2 ± 3.7	0.83

Data are given as mean ± standard deviation or number (percentage).

Table 3. Comparison of baseline and follow-up outcomes between groups

Outcome	WBVT group (n=13)	CKC group (n=13)	Difference in change between groups	P	Cohen's d
Primary					
WOMAC pain	−5.46 (−6.90, −4.02)	−2.54 (−3.99, −1.01)	−2.92 (−4.96, −0.88)	0.007	1.16
Secondary					
WOMAC function	−12.1 (−18.1, −6.1)	−5.9 (−11.9, 0.1)	−6.2 (−14.6, 2.3)	0.146	0.59
Knee extension	0.09 (0.04, 0.15)	0.07 (0.02, 0.12)	0.02 (−0.05, 0.10)	0.533	0.25
CS-30	5.6 (4.2, 7.0)	3.6 (2.2, 5.0)	2.0 (0.01, 3.9)	0.049	0.81

Data shown as difference (95% confidence interval).

change in pain on the WOMAC pain scale is 2 points,[24] the mean difference between the groups (2.92 points) in this study confirms the efficacy of WBVT. WBVT is a non-invasive and convenient method, highlighting its potential as a novel therapeutic option. WBVT may alleviate pain in early KOA, potentially delaying symptom progression and contributing to reduced healthcare costs over the long term.

Low-frequency WBVT was particularly effective in reducing pain, and the effect size in our study exceeded that in other meta-analyses.[10,11] Preliminary studies have shown that patients with early KOA (KL grades 1 and 2) have elevated levels of the inflammatory markers associated with synovitis when compared with those in patients with advanced-stage osteoarthritis.[3,25] Inflammatory cytokines have been suggested to be the predominant etiological factors for pain in the early stages of KOA. WBVT has been empirically shown to have pronounced efficacy against these inflammatory cytokines.[26] Therefore, WBVT appears to align with the pathological framework of early KOA, suggesting its potential therapeutic impact.

In this study, the between-group difference in WOMAC physical function score was not significant. Participants had an average WOMAC physical function score of 30, indicating relatively mild impairment. In addition, CKC exercises have been shown to significantly improve physical function. Therefore, improvements in physical function were expected regardless of the use of WBVT. Consequently, the characteristics of the participants with early KOA and the effectiveness of the CKC exercises likely minimized the difference in the WOMAC physical function scores between the treatment groups, rendering the between-group differences statistically insignificant.

Our results also demonstrated that WBVT influenced the CS-30 scores but not knee extension. WBVT has demonstrated efficacy as an intervention to improve sit-to-stand performance and knee extension in older adults.[27] However, the effectiveness of WBVT on knee extension in patients with early KOA was not demonstrated in our study, highlighting the specific effects of WBVT in early KOA.

According to previous meta-analyses, the effects of WBVT on muscle strength appear to be limited to high-frequency applications.[10] Evidence has suggested that WBVT at 30 Hz does not elicit a distinct modulation in the electromyographic signatures of the medial and lateral vastus muscles in patients with KOA when compared with conventional resistive training modalities.[28] Therefore, the frequency used in our protocol may have been unsuitable for eliciting improvements in knee extension.

Although this study provides insights into the potential benefits of combining PT and WBVT for early KOA, the study has some limitations. First, previous studies have not demonstrated the efficacy of WBVT as a stand-alone intervention as compared with exercise alone in reducing pain over an 8-week period of managing early KOA.[29] Therefore, to elucidate the adjunctive benefits of WBVT in conjunction with CKC versus CKC alone, an evaluation at the 8-week post-intervention point is imperative. Furthermore, within the PT cohort, WBVT was replaced with a 10-min CKC exercise program. Given these considerations, researchers should exercise caution in interpreting the results favoring the combined use of PT and WBVT over PT alone. Second, being a non-randomized comparative study, this study is susceptible to the effects of unobserved or unmeasured confounding factors. Third, the nature of the intervention precluded blinding of the participants or the intervention, and non-blinded designs can potentially overestimate effect sizes.[30] Therefore, it is possible that the effect size observed in this study was overestimated. Fourth, the sample size was small, and majority of the respondents were women, introducing a potential gender bias in the results. Furthermore, the use of PSM may not have accounted for all confounding factors, potentially introducing bias. Fifth, the Japanese version of the WOMAC is currently used in a variety of diseases but has only been validated in total knee arthroplasty; direct validation in patients with KOA is expected but not yet confirmed.

CONCLUSION

The findings of this study suggest that WBVT may serve as an effective therapeutic strategy to reduce pain and improve function in patients with early KOA. Randomized controlled trials are required to elucidate the efficacy of therapeutic interventions for early KOA.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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