Methods & Protocols

Effect of biomechanical correction of tibia on medial joint space loading, varus deformity and functional tasks in patients with medial tibiofemoral joint osteoarthritis: a two-group pre-test, post-test randomized clinical trial study protocol

Efeito da correção bimecânica de tíbia sobre carregamento de articulação medial, deformidade vária e tarefas funcionais em pacientes com osteoartrite de articulação tibiofemoral medial: um pré-teste de dois grupos, processo de estudo clínico randomizado pós-teste

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ABSTRACT | BACKGROUND/OBJECTIVES: Knee osteoarthritis (KOA) is the most prevalent chronic disease of joints. Various biomechanical factors affect the alignment of the knee joints resulting in the varus or valgus deformities, which leads to unequal loading on the joints structures. The study's primary aim is to determine the biomechanical corrections on tibia and varus deformity in Medial Tibiofemoral Knee Joint Osteoarthritis (MTKJOA). A secondary aim is to see the improvement in the physical functions of the patients. **METHODOLOGY/DESIGN**: A Two Group Pretest-Posttest Equivalent Randomized Clinical Trial. Total '52' patients will be included between 35 to 80 years with medial tibiofemoral joint osteoarthritis. Subjects will be divided into the biomechanical correction group (Manual varus deformity correction technique in addition to conventional physiotherapy treatment). Conventional physiotherapy group, which includes electrotherapy and exercise therapy. For measuring the pain, the Numeric Pain Rating Scale (NPRS) will be taken, for a range of motion goniometer will be taken, Western Ontario McMaster Universities Arthritis Index (WOMAC) will be taken for assessing the physical performance, and TraumaCaD Software will be used to determine the alignment of the affected limb. In both groups, conventional physiotherapy treatment will be given for nine days. A total of nine sessions will be given in three weeks, and each week, 3 sessions will be given on alternate days. The outcome will be measured at baseline. **TRIAL REGISTRATION:** Clinical Trials Registry – India. (NCT04324931). UNIVERSAL TRIAL NUMBER: U1111-1249-3661. **DISCUSSION:** To our knowledge, this study will be the first to correct the biomechanical axis of knee joints. After Biomechanical Correction, the weight-bearing distribution will be adjusted, and progression of deformity can be reduced, which will help improve the functional tasks and prevent early Total Knee Arthroplasty (TKA).

KEYWORDS: Exercise Therapy. Knee Joint. Osteoarthritis. Physical Functional Performance. Tibia.

RESUMO | ANTECEDENTES / OBJETIVOS: A osteoartrite do joelho (OAJ) é a doença crônica das articulações mais prevalente. Existem vários fatores biomecânicos que afetam o alinhamento das articulações do joelho, resultando em deformidades em varo ou valgo, o que leva a cargas desiguais nas estruturas articulares. O objetivo principal do estudo é determinar as correções biomecânicas na tíbia e deformidade em varo na osteoartrite tibiofemoral medial do joelho (MTKJOA). O objetivo secundário é ver a melhora nas funções físicas dos pacientes. **METODOLOGIA / DESENHO:** Um ensaio clínico randomizado equivalente de dois grupos pré-teste-pós-teste. O total de '52' pacientes será incluído entre a idade de 35 a 80 anos com osteoartrite da articulação tibiofemoral medial. Os sujeitos serão divididos no grupo de correção biomecânica (Técnica de correção manual de deformidade em varo além do tratamento fisioterapêutico convencional). E grupo de fisioterapia convencional, que inclui eletroterapia e terapia por exercícios. Para medir a dor, será realizada a Escala Numérica de Dor (NPRS) para o goniômetro de amplitude de movimento. O Índice de Artrite da Western Ontario McMaster Universities (WOMAC) será utilizado para avaliar o desempenho físico; e o Software TraumaCaD será utilizado para determinar o alinhamento do membro afetado. Em ambos os grupos, o tratamento fisioterapêutico convencional será realizado por 9 dias. No total, 9 sessões serão dadas em três semanas, e em cada semana, 3 sessões serão dadas em dias alternativos. O resultado será medido no início do estudo. **REGISTRO DE ENSAIOS:** Registro de Ensaios Clínicos - Índia. (NCT04324931). **NÚMERO UNIVERSAL DE ENSAIO:** U1111-1249-3661. **DISCUSSÃO:** Até onde sabemos, este estudo será o primeiro a corrigir o eixo biomecânico das articulações do joelho. Após a Correção Biomecânica, a distribuição da descarga de peso será ajustada e a progressão da deformidade poderá ser reduzida, o que ajudará a melhorar as tarefas funcionais e evitar a realização precoce da Artroplastia Total do Joelho (ATJ).

PALAVRAS-CHAVE: Terapia por Exercício. Articulação do Joelho. Osteoartrite. Desempenho Funcional Físico. Tíbia.

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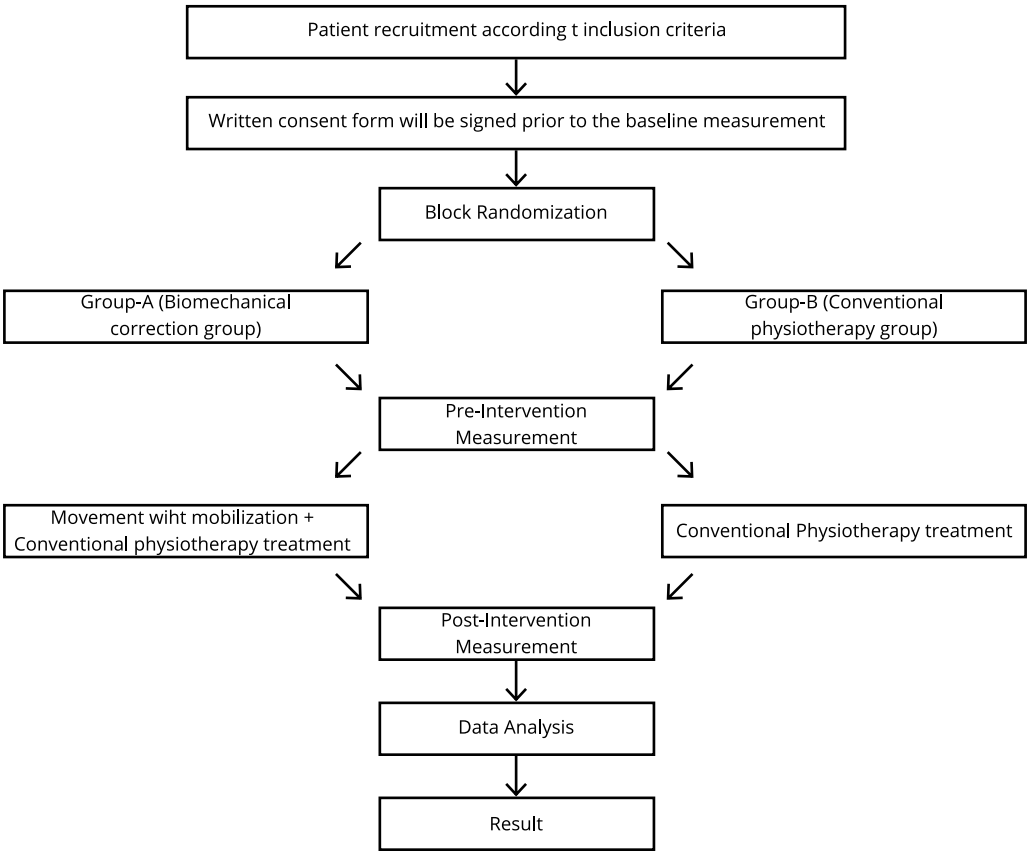
Introduction

About 8% of adults are suffering from Osteoarthritis (OA). Aging is powerful related to osteoarthritis.[1] Twenty-two percent to thirty-nine percent population is tortured from OA among the 1.252 billion people.[2] The ratio will increase about thirty-five percent until 2030. The prevalence of knee joint involvement is twenty-nine percent.[3]Some reasons such as unequal loads, unnatural positions, skeletal deformation (varus or valgus deformations), and excess pressure because of obesity altered the joint mechanics and promote the OA in knee joint.[4]

There are surgical and non-surgical treatment procedures such as partial knee arthroplasty or complete knee arthroplasty, fibular osteotomy, exercise therapy, resistant training, Hydrocollator packs, movement with mobilization (alone or in addition with tapping), and pharmacological treatment (Diclofenac and Chondroitin), which improves physical functions (6-min walk distance, stair climb time, turning, floor sit-to-stand and chair sit-to-stand), joint range of motion, the strength of the knee muscles(flexors and extensors) and reduces the knee pain and stiffness.[5-8] However, these studies have some limitations due to which we will going to perform a randomized controlled trial of biomechanical correction of the tibia in medial tibiofemoral joint osteoarthritis.

Biomechanical correction is an important technique used to treat the medial tibiofemoral joint's misalignment in OA. The null hypothesis is that there may not be any significant effect of the biomechanical corrections on tibia and varus deformity in improving functional tasks. The alternative hypothesis is that there may be a significant effect of the biomechanical differences on tibia and varus deformity in improving functional tasks. There is a real need to conduct the study to determine the biomechanical correction on tibia or varus deformity. There is scanty literature available that targets the pathomechanics dysfunction of tibiofemoral joints. The study's objective is to determine the efficacy of the biomechanical correction of the tibia on medial joint space loading or varus deformity, and the secondary objective is to determine the improvement in the patients' functional activities with KOA.

Figure 1. Flow diagram of study protocol



Trial registration

Ethical clearance was attained on December 10, 2019, from the Institutional Ethical Committee (IEC) of Maharishi Markandeshwar (Deemed to be University) (IEC/MMU/2019/1527) with U1111-1249-3661 [Universal Trial Number (UTN)] by WHO ICTRP. This study will be executed in consonance with the Helsinki Declaration's instruction (Revised 2013) and the National ethical guidelines for biomedical & health research involving human participants, 2017.

The trial was certified on March 26, 2020, by ClinicalTrials.gov with a unique ID: NCT04324931 before the assessment consent form was taken from the Hindi and English language subjects.

Study design

A single-centered, single-blinded equivalent two-group pretest-posttest Randomized Clinical Trial. This study design has two groups, and assessment will be taken before and after the intervention.

Participation Recruitment

In table number 1, the inclusion and exclusion criteria are given. The subjects will be included from the recognized tertiary care hospital. The data collection will be conducted from December 2020 to March 2021. The flow diagram of the study is explained in Figure 1.

Table 1. Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
35-80 years of age patients will be included in this study	6 months previous history of Knee meniscal injuries or ligament injuries
BMI 26-30 kg/m^2	6 months previous history of lower limb trauma and surgery
Subjects with morning stiffness for more than 10 minutes and knee pain for more than 4 in NPRS.	Fracture within 6 months in lower extremity
Subjects complaining of pain in knee joints that aggravates by performing 2 or more of the following functional activities: prolonged cross sitting, stair ascent and descent, squatting and kneeling.	In lower extremity metal plantation before 6 months
Subjects who are willing to take participation	Cardiovascular conditions
Individuals who obey the commands properly	Patella Dislocation/subluxation
Q angle >12 degree for male and >15 degrees for female and external tibial torsion >15 degrees	

Randomization

Subjects will be separated by block randomization technique in both groups. The researcher will establish four blocks and thirteen rows for Group-A (Biomechanical correction group) and Group-B (Conventional physiotherapy group) by matrix design which is 4×13=52. Block randomization design is shown in figure 2. The primary investigator will perform the allocation concealment. The allocation concealment will be established by sequentially numbered, opaque, sealed envelope (SNOSE) technique. The randomization groups will be written on paper and will be kept in an opaque sealed envelope. On the envelope, a serial number will be labeled. Then the researcher will open the sealed envelope once the patient signs the informed consent form. Then researcher will assign the treatment group respectively. This study will be single-blinded in which the data analysts will be blinded to patients and intervention. Then the whole procedure of the study will be explained to the participants before taking the baseline assessment. Assessment will be taken before and after the three weeks of intervention. The primary investigator collects and will keep all the information of participants safely in written form.

Figure 2. Matrix Design 4×13 (Block Randomization)

Blocks / Rows	1	2	3	4
1	1E	2C	1C	2E
2	•	•	•	•
3	•	•	•	•
4	•	•	•	•
5	•	•	•	•
6	•	•	•	•
7	•	•	•	•
8	•	•	•	•
9	•	•	•	•
10	•	•	•	•
11	•	•	•	•
12	•	•	•	•
13	•	•	•	•

Intervention

A thorough summary of the treatment is given in table 2. 52 subjects with medial side tibiofemoral joint OA will be included in the study. The data analysts will be blinded to the participant group and the intervention. Then the whole procedure will be explained to the subjects. After that, anthropometric measurements will be taken. This study will be of nine sessions in three weeks, and in each week, an intervention will be given for three alternative days. After that, again assessment will be taken after three weeks. Only one therapist will conduct the complete intervention. The summary of the complete intervention is given in Table 2.

Table 2. Summary of the interventions for both the groups

Interventions	Position	Procedure	Frequency	Duration
Biomechanical correction technique				
Mobilization with Movement (MWM)	**Patient position:** Prone **Therapist position:** Standing at the foot end of the couch	Therapist will place their hand on posterior superior tibia. Then he/she will apply traction and rotate the tibia laterally.	10 repetitions × 1set	Nine treatment sessions (3 weeks for alternate days)
Electro Therapy	**Patient position/ Placement**	**Frequency/Time**		
Hydrocollatoral pack	**Patient position:** Supine/ Moist heat pack will be placed on medial side of knee joint.	20 Minutes		
Interferential Therapy	**Patient Position:** Supine/ Pair of electrodes will be placed on medial side of knee joint.	At the frequency of 4000Hz, Sweep frequency 40 Hz, Base frequency 90 Hz, Beat frequency 90-130 Hz for 20 minutes		
Manual Therapy	**Patient Position and Procedure**	**Repetitions/Sets**	**Hold/time**	
Strengthening Exercises Quadriceps Muscle	The patient will be in the supine position, a small towel roll placed underneath the knee joint. Then patient have to tighten the quadriceps muscle on top of the thigh and press the towel roll in a downward direction	10 Repetitions ×3 Sets	5 seconds hold each time along with 5 second interval in between each repetition	
Hamstring Muscle	The patient has to lie in the supine position, a small towel roll placed underneath the ankle joint. Then patient have to tighten the hamstring muscle on top of the thigh and press the towel roll in a downward direction	10 Repetitions ×3 Sets	5 seconds hold each time along with 5 second interval in between each repetition	
Patellar Glides (superior, inferior, medial and lateral)	Supine Lying	**Repetitions/Sets**		
		10 Repetition ×3 Sets		

Group-A (Biomechanical Correction Group)

A total of 26 subjects will be included in this group. Before taking all the anthropometric measurements, the whole procedure will be explained to the subjects. Then the CAD software assessment, NPRS, and WOMAC will be taken. When the subject was in the supine position, the glides were examined in all the potential directions using the subsequent path: sagittal plane (posterior/anterior), frontal plane (lateral/medial), and in rotation. The glide was preferred in which the patient's pain was relieved and upgraded the knee range. Overpressure was added in the end range if the patient does not make a pain complaint. If pain was not occurring in the supine position, then the direction of glides was tested in a weight-bearing position. If all the glides showed the same results in the supine position, then these glides were executed in a weight-bearing position to find out the highly effective glide direction. When the knee joint was in mid-range, the glide pressure was enforced on the tibia bone. Then the pressure was sustained while the patient was extending and flexing the knee joint in a full range of motion. In the end range of the movement, the overpressure was applied. The same glide was performed ten times. The complete procedure will be given for the three weeks, and each week, the intervention will be given for the three alternative days. Baseline measurements will be taken, and after the three weeks of period again, all the assessments will be taken to see the effect of treatment.

Group-B (Conventional physical Group)

A total of 26 subjects will be included in this group. Before taking all the anthropometric measurements, the whole procedure will be explained to the subjects. Then the Trauma Cad software assessment, NPRS, and WOMAC will be taken. Then the conventional physical treatment will be given to the subjects. Conventional therapy includes a Moist Heat pack (MHP) for 20 minutes with the dimensions of 22.86 ×22.86-cm (9 ×9-in) of standard size (because in such time the heat reaches the joint and relaxes the joint muscles, increase the circulation and increase the joint range of motion)[9]; Interferential therapy for 20 minutes (because it generates the lower resistance to the skin and it grants the immersed penetration into the soft tissues of the knee joint)[10] frequency 4000 Hz, Sweep frequency 40 Hz, base frequency 90 Hz, beat frequency 90-130 Hz, quadripolar/ two-channel; and exercise program of 3 sessions for 20 minutes on alternate days for three weeks for knee osteoarthritis management. Before giving the treatment, all the measurements will be taken, and after the three weeks of period again, all the assessments will be taken to see the treatment's effect.

Outcome Measures

The researcher takes the anthropometric measurements (age, gender, height, and weight). The primary outcome will be varus deformity and medial joint space loading using Standard Protocol Items: Recommendation for Intervention Trials schedule for participation (SPIRIT) 2013 statement, the specific time frame.

Primary Outcome measure

The primary outcome will be varus deformity and medial joint space loading. For that, the Trauma Cad Software will be used. From this software, we will be able to calculate the Medial Proximal Tibial Angle (MPTA) and normal value for MPTA is 87° (85-90°), Lateral Distal Femoral Angle (LDFA), and normal value for LDFA is 88° (85-90°), Joint Line Convergence Angle (JLCA) and normal value for JLCA is 0-2°, Lateral Distal Tibial Angle (LDTA) and normal value for LDTA is 89° (86-92°), Medial Joint Space (MJS) and normal value for MJS is 4.8mm (female) and 5.7mm (male) and Mechanical Axis Distance (MAD) and normal value for MAD is 8±7mm (medial).[11]

Secondary outcome measures

Secondary outcomes will be functional tasks and range of motion. For functional tasks, we will take the WOMAC. WOMAC includes three subscales (Pain, stiffness, and physical function) under which the patient has to tell the score. The total score of WOMAC is 100, out of which 0-20 is for pain, 0-8 is for stiffness, and 0-68 is for physical function. The test question is scored on 0-4, which relates to None (0), Mild (1), Moderate (2), Severe (3), and Extreme (4). Worst pain, functional limitations, and stiffness indicate the higher score on the WOMAC.[12]

Numeric Pain Rating Scale: NPRS is used to measure pain management. It has a total of eleven points from 0 to 10. Zero is no pain at all, and ten is the worst pain/ unbearable pain. Cut off score in mild pain situated between three to four, and in moderate pain, it situated between six to eight. The Minimal Clinically Important Difference (MCID) value of NPRS is 1.7, and MDC value is three, and the SEM value is 0.9 points. The concurrent validity is adequate (0.63), and test-retest reliability is excellent (0.95).[13]

Goniometer: It is a measuring tool that is used to measure the joints' range of motion. The goniometer's MCID range is 6.1 to 6.4, the MDC value is nine, and the SEM range is 1.0 to 6.9. The inter-rater and intra-rater reliability is excellent, which is 0.96. The values will be shown in degree (°).[14]

Trauma Computer Added Software: Trauma Computer-Aided Software (TraumaCaD) is used to measure the joints' biomechanical alignment. A full-length x-ray is needed to see the biomechanical alignment. The reliability and validity of TraumaCaD software are excellent, which are 0.984 and 0.962, respectively. Intra-rater reliability is 0.99, and the SEM value is 2.1. The angles will be measured in degree (°), and medial joint space will be measured "in" "mm".[11]

Western Ontario and McMaster Universities Arthritis Index: WOMAC is used to measure functional mobility, quality of life, gait, general health, and ADLs. It consists of 24 items divided into three categories: pain, which further consists of 5 items; the second is stiffness, which further consists of 2 items; and last is a physical function consisting of 17 items. The score range for pain is 0-20, for stiffness is 0-8, and 0-68 is for physical function. The MCID value is 11.[15]

Figure 3. Standard Protocol Items: Recommendations for Intervention Trials schedule for participation

	Study duration				
	Enrollment	Allocation	Post-allocation Treatment		Follow-up
Time Point	0 week	0 week	0 week	3rd week	3rd week
Enrollment					
Eligibility screen	×				
Informed consent	×				
Selection criteria	×				
Allocation		×			
Intervention					
Biomechanical correction			×	×	
Conventional physiotherapy treatment			×	×	
Assessment					
Demographic data		×			×
WOMAC		×			×
NPRS		×			×
Goniometer		×			×
Trauma Cad		×			×

Safety and Adverse outcomes

Outcome measures will be used, such as Trauma Cad software, WOMAC, NPRS, and goniometer. Before and after the intervention, the outcome measures will be used. Adverse effects of the intervention will be recorded by the therapist, who will give the intervention. The therapist (who will provide intervention) will follow all the safety measures like gloves, PPE kit, and masks, according to the WHO guidelines. Temperature monitoring will be check before and after every intervention session. For the intervention, a separate cabin will be provided. After and before every session, sanitization will be performed, and the bed sheet will be changed. Patients will be strictly asked to wear face masks and personal protective equipment.

Data Monitoring

An independent researcher will perform all the statistical analyses. The treating physiotherapist will monitor treatment sessions.

Follow up

For the follow-up, the researcher will call the included patients on preset dates. The physiotherapist will motivate the included patients to come to hospitals for further sessions.

Sample Size Calculation

The sample size estimation was performed using the formula of comparison of two means. The value of Zα is 1.96 where α is taken 0.05 to minimize type-1 error largely, the value of Zβ is 0.80, S is 14, and d will be 11. With this formula, the total sample size came 52, i.e., 26 in each group with 20% dropouts.[15]

Data analysis

The data will be analyzed using the statistical software, statistical package for social sciences, SPSS 16 (SPSS, version-16.0 Inc., Chicago IL). Level of significance will be set at 0.05 (p-value=0.05). Normality will be checked by the Kolmogorov Smirnov Test. If the data follows the normal distribution, then the parametric Paired-t-test will be used and will show the result with descriptive mean and Standard Deviation (SD), and if the data does not follow the normal distribution, then the non-parametric test will be used, which will be Wilcoxon signed-rank test and will show the data with median and Interquartile Range (IQR). After analysis, if the result will be significant, then be used Cohen's d (sample size >20) or Hedge's g (sample size <20) effect to determine the effect of intervention with the levels of Cohen's d, which is 0.1 (small), 0.25 (medium) and 0.4 (large). The formula for Cohen's d will be "Cohen's d= m1-m2/sd pooled" where 'm1' and 'm2' will be a difference of means and 'sd' pooled will be pooled standard deviation and "Hedge's g= m1-m2/ sd*pooled" where 'm1' and 'm2' will be a difference of means and sd* pooled will be pooled and weighted standard deviation. Results will be represented in a Box and Whisker plot or error plot and line graph. Box and Whisker graph will be shown the first quartile, median, minimum values, third quartile, and maximum value of a data set. Error graph will show the SD, standard error of means (SE), the range of data, percentiles, and a confidence interval. The line graph will represent the changes constantly with time. The primary investigator will have the final data and will analyze the data.

Discussion

The purpose of the present study is to determine whether the biomechanical correction can correct the misalignment of the tibia bone and varus deformity can improve osteoarthritis patients' functional activities. Various treatment procedures were used to perform to reduce the pressure on medial joint space narrowing[16]. Such as partial and complete knee arthroplasty[17], fibular osteotomy[18], footwear modification[19], lateral wedge insole treatment[20], and manual therapy are very effective therapeutic procedures.[21]

To our best knowledge, there is not a single study that was done on the correction of biomechanical misalignment of medial tibiofemoral joints without any surgical intervention. So, in the present study, we will perform the mobilization with movement to correct the biomechanical misalignment of the tibia bone, reduce the medial joint space loading, and improve patients' physical activities osteoarthritis problems in the knees.

Total Knee Reconstruction (TKR) (partial or complete)[22], fibular osteotomy, medical management treatment procedures are very costly[23], time-consuming, and hospital stay is more. Most of the studies were performed on females, and in some studies, more specifically older females, males were excluded[24]. In some studies, lack of follow-up was also the limitation. In the present study, we will correct the knee joint's biomechanical misalignment manually, in which surgery is not required that. This technique is not time-consuming, and patients do not have to stay in the hospital. In the present study, males are also included with grade 2˚ or 3˚ as per the present study inclusion criteria.

For many years, orthopedics or physiotherapists have suggested partial knee arthroplasty, total knee arthroplasty[17], fibular osteotomy, exercise programs[25], strength training, and shoe modifications to correct the misalignment of the tibia in medial tibiofemoral joints OA. However, the present study is the first randomized clinical trial in which a non-surgical procedure, a movement with mobilization technique, will be used to treat the malalignment of knee joints and improve physical functions and quality of life in a patient with knee osteoarthritis. In the future, this study can be performed on different communities' populations to make the result generalizable.

Author contributions

Saini S contributed to designing the methodology of the study and scripting the original draft. Goyal M contributed to conceiving and planning the methodology and revising the manuscript. Samuel A contributed to planning the methodology, writing, reviewing, and correcting the manuscript.

Competing interests

No financial, legal, or political competing interests with third parties (government, commercial, private foundation, etc.) were disclosed for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.).

References

1. Haq SA, Davatchi F. Osteoarthritis of the knees in the COPCORD world. Int J Rheum Dis. 2011;14(2):122–9. https://doi.org/10.1111/j.1756-185x.2011.01615.x

2. Pal CP, Singh P, Chaturvedi S, Pruthi KK, Vij A. Epidemiology of knee osteoarthritis in India and related factors. Indian J Orthop. 2016;50(5):518–22. https://dx.doi.org/10.4103%2F0019-5413.189608

3. Wan H, Goodkind D, Kowal P. An aging world: 2015 [Internet]. Washington: U.S Government Publishing Office; 2015. Available from: https://www.census.gov/library/publications/2016/demo/P95-16-1.html

4. Farshid G. Biomechanical Factors in Osteoarthritis. Best Pract Res Clin Rheumatol. 2011;25(6):815–23. https://doi.org/10.1016/j.berh.2011.11.013

5. Alkhawajah HA, Alshami AM. The effect of mobilization with movement on pain and function in patients with knee osteoarthritis: a randomized double-blind controlled trial. BMC Musculoskelet Disord. 2019;20(1):2841-44. https://doi.org/10.1186/s12891-019-2841-4

6. Taglietti M, Dela Bela LF, Dias JM, Pelegrinelli ARM, Nogueira JF, Batista Junior JP, et al. Postural Sway, Balance Confidence, and Fear of Falling in Women With Knee Osteoarthritis in Comparison to Matched Controls. PM R. 2017;9(8):774–80. https://doi.org/10.1016/j.pmrj.2016.11.003

7. Liu B, Chen W, Zhang Q, Yan X, Zhang F, Dong T, et al. Proximal fibular osteotomy to treat medial compartment knee osteoarthritis: Preoperational factors for short-term prognosis. PLoS One. 2018;13(5):e0197980. https://doi.org/10.1371/journal.pone.0197980

8. Rannou F, Pelletier J-P, Martel-Pelletier J. Efficacy and safety of topical NSAIDs in the management of osteoarthritis: Evidence from real-life setting trials and surveys. Semin Arthritis Rheum. 2016;45(Supl 4):S18-21. https://doi.org/10.1016/j.semarthrit.2015.11.007

9. Petrofsky JS, Laymon M. Heat transfer to deep tissue: the effect of body fat and heating modality. J Med Eng Technol. 2009;33(5):337–48. https://doi.org/10.1080/03091900802069547

10. Gundog M, Atamaz F, Kanyilmaz S, Kirazli Y, Celepoglu G. Interferential current therapy in patients with knee osteoarthritis: comparison of the effectiveness of different amplitudemodulated frequencies. Am J Phys Med Rehabil. 2012;91(2):107–13. https://doi.org/10.1097/phm.0b013e3182328687

11. Anas I, Musa TA, Kabiru I, Yisau AA, Kazaure IS, Abba SM, et al. Digital radiographic measurement of normal knee joint space in adults at Kano, Nigeria. Egypt J Radiol Nucl Med. 2013;44(2):253–8. https://doi.org/10.1016/j.ejrnm.2013.03.005

12. Salaffi F, Leardini G, Canesi B, Mannoni A, Fioravanti A, Caporali R, et al. Reliability and validity of the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index in Italian patients with osteoarthritis of the knee. Osteoarthr Cartil. 2003;11(8):551–60. https://doi.org/10.1016/s1063-4584(03)00089-x

13. Van Ginckel A, Bennell KL, Campbell PK, Wrigley T V, Hunter DJ, Hinman RS. Location of knee pain in medial knee osteoarthritis: patterns and associations with self-reported clinical symptoms. Osteoarthr Cartil. 2016;24(7):1135–42. https://doi.org/10.1016/j.joca.2016.01.986

14. Lomond KV, Henry SM, Hitt JR, DeDesarno MJ, Bunn JY. Altered postural responses persist following physical therapy of general versus specific trunk exercises in people with low back pain. Man Ther. 2014;19(5):425-32. https://doi.org/10.1016/j.math.2014.04.007

15. Clement ND, Bardgett M, Weir D, Holland J, Gerrand C, Deehan DJ. What is the Minimum Clinically Important Difference for the WOMAC Index After TKA? Clin Orthop Relat Res. 2018;476(10):2005-14. https://doi.org/10.1097/corr.0000000000000444

16. Hall M, Bennell KL, Wrigley TV, Metcalf BR, Campbell PK, Kasza J, et al. The knee adduction moment and knee osteoarthritis symptoms: relationships according to radiographic disease severity. Osteoarthr Cartil. 2017;25(1):34–41. https://doi.org/10.1016/j.joca.2016.08.014

17. Beard DJ, Davies LJ, Cook JA, MacLennan G, Price A, Kent S, et al. The clinical and cost-effectiveness of total versus partial knee replacement in patients with medial compartment osteoarthritis (TOPKAT): 5-year outcomes of a randomised controlled trial. Lancet. 2019;394(10200):746–56. https://doi.org/10.1016/s0140-6736(19)31281-4

18. Guo J, Zhang L, Qin D, Chen W, Dong W, Hou Z, et al. Changes in ankle joint alignment after proximal fibular osteotomy. PLoS One. 2019;14(3):e0214002. https://dx.doi.org/10.1371%2Fjournal.pone.0214002

19. Paterson KL, Bennell KL, Wrigley TV, Metcalf BR, Kasza J, Hinman RS. Effects of footwear on the knee adduction moment in medial knee osteoarthritis: classification criteria for flat flexible vs stable supportive shoes. Osteoarthr Cartil. 2017;25(2):234–41. https://doi.org/10.1016/j.joca.2016.10.001

20. Zhang J, Wang Q, Zhang C. Ineffectiveness of lateral-wedge insoles on the improvement of pain and function for medial knee osteoarthritis: a meta-analysis of controlled randomized trials. Arch Orthop Trauma Surg. 2018;138(10):1453–62. https://dx.doi.org/10.1007%2Fs00402-018-3004-z

21. Paterson KL, Bennell KL, Wrigley TV, Metcalf BR, Campbell PK, Kazsa J, et al. Footwear for self-managing knee osteoarthritis symptoms: protocol for the Footstep randomised controlled trial. BMC Musculoskelet Disord. 2018;19(1):219. https://doi.org/10.1186/s12891-018-2144-1

22. Skou ST, Roos EM, Laursen MB, Rathleff MS, Arendt-Nielsen L, Rasmussen S, et al. Total knee replacement and non-surgical treatment of knee osteoarthritis: 2-year outcome from two parallel randomized controlled trials. Osteoarthr Cartil. 2018;26(9):1170–80. https://doi.org/10.1016/j.joca.2018.04.014

23. Xing F, Lu B, Kuang MJ, Wang Y, Zhao YL, Zhao J, et al. A systematic review and meta-analysis into the effect of lateral wedge arch support insoles for reducing knee joint load in patients with medial knee osteoarthritis. Medicine (Baltimore). 2017;96(24):e7168. https://doi.org/10.1097/md.0000000000007168

24. Pal CP, Singh P, Chaturvedi S, Pruthi KK, Vij A. Epidemiology of knee osteoarthritis in India and related factors. Indian J Orthop. 2016;50(5):518-522. https://dx.doi.org/10.4103%2F0019-5413.189608

25. Xu Q, Chen B, Wang Y, Wang X, Han D, Ding D, et al. The Effectiveness of Manual Therapy for Relieving Pain, Stiffness, and Dysfunction in Knee Osteoarthritis: A Systematic Review and Meta-Analysis. Pain Physician. 2017;20(4):229–43. Cited: PMID: 28535547