Author/s:
Starkey, SC;Diamond, LE;Hinman, RS;Saxby, DJ;Knox, G;Hall, M

Title:
Muscle Forces during Weight-Bearing Exercises in Medial Knee Osteoarthritis and Varus Malalignment: A Cross-Sectional Study

Date:
2022-09-01

Citation:
Starkey, S. C., Diamond, L. E., Hinman, R. S., Saxby, D. J., Knox, G. & Hall, M. (2022). Muscle Forces during Weight-Bearing Exercises in Medial Knee Osteoarthritis and Varus Malalignment: A Cross-Sectional Study. Medicine and Science in Sports and Exercise, 54 (9), pp.1448-1458. https://doi.org/10.1249/MSS.0000000000002943.

Persistent Link:
https://hdl.handle.net/11343/333629

Title: Muscle forces during weightbearing exercises in medial knee osteoarthritis and varus malalignment: a cross-sectional study

Running title: forces during exercise in knee osteoarthritis

Authors: Scott C Starkey[1], Laura E Diamond[2,3], Rana S Hinman[1], David J Saxby[2,3], Gabrielle Knox[1], Michelle Hall[1]

Affiliations:

[1]Centre for Health, Exercise and Sports Medicine, University of Melbourne, Victoria, Australia

[2]Griffith Centre of Biomedical and Rehabilitation Engineering (GCORE), Menzies Health Institute Queensland, Griffith University, Gold Coast, QLD, Australia

[3]School of Health Science and Social Work, Griffith University, Gold Coast, QLD, Australia

Corresponding author:

Dr Michelle Hall
Centre for Health, Exercise and Sports Medicine
Department of Physiotherapy
The University of Melbourne
Victoria, 3010, Australia
Tel: +61 3 8344 0556
Email: halm@unimelb.edu.au

ABSTRACT

Purpose: To test the hypothesis that common weightbearing exercises generate higher lower-limb muscle forces but do not increase medial tibiofemoral contact force (MTCF) when compared to walking in people with medial knee osteoarthritis and varus malalignment.

Methods: Twenty-eight participants aged ≥50 years with medial knee osteoarthritis and varus malalignment were recruited from the community. Three-dimensional lower-body motion, ground reaction forces and surface electromyograms from 12 lower-limb muscles were acquired during five squat, lunge, single-leg heel raise and walking trials, performed at self-selected speeds. An electromyogram-informed neuromusculoskeletal model with subject-specific bone geometry was used to estimate muscle forces (N) and bodyweight (BW) normalised MTCF. The peak forces for muscle groups (knee extensors, knee flexors, ankle plantar flexors and hip abductors) and peak MTCF were compared to walking using a multivariate analysis of variance model.

Results: There was a significant main effect ($p<0.001$). Post-hoc tests (mean difference [95% confidence intervals]) showed that compared to walking, participants generated higher peak knee extensor and flexor forces during squatting (extensor: 902 N [576, 1227], flexor: 192 N [9.39, 375]) and lunging (extensor: 917 N [604, 1231], flexor: 496 N [198, 794]), and lower peak hip abductor force during squatting (-1975 N [-2841, -1108]) and heel raises (-1217 N [-2131, -303]). Compared to walking, MTCF was lower during squatting (-0.79 BW [-1.04, -0.53]) and heel raises (-0.27 BW [-0.50, -0.04]). No other significant differences were observed.

Conclusion: Participants generated higher peak knee flexor and extensor forces during squatting and lunging but did not increase peak MTCF compared to walking. Clinicians can use these findings to reassure themselves and patients that weightbearing exercises in these positions do not adversely increase forces within the osteoarthritic joint compartment.

Keywords: neuromusculoskeletal modelling; electromyography; strengthening; physical therapy; lower limb; loading; tibiofemoral contact force

INTRODUCTION

Knee osteoarthritis (OA) of the medial tibiofemoral compartment is a prevalent chronic condition that results in pain, loss of function and reduced quality of life (1). People with knee OA have lower-limb muscle weakness (2-4), and knee extensor (5) and hip abductor (6) muscle weakness has been associated with tibiofemoral structural decline in this population. Strengthening exercise is recommended in all current clinical guidelines to self-manage knee OA (1, 3, 7), with gains in knee muscle strength shown to partly mediate knee pain relief and improvement in physical function (8).

While the best type of strengthening exercise for clinical benefits in knee OA is unclear (3, 9), weightbearing exercises are often used to provide resistance and/or facilitate neuromotor control (9-12). Weightbearing exercise integrates multiple muscle groups and agonist/antagonist pairs and is more reflective of functional movements (e.g., standing up from seated position) than non-weightbearing exercises which tend to isolate a single muscle group (9, 10). Furthermore, this type of exercise has the advantage of using body weight to apply resistance, eliminating the need for exercise equipment or resistance machines. As a primary aim of strengthening exercise is to increase muscle force generating capacity (3), there is an underlying assumption that weightbearing strengthening exercises will increase the force generating capacity in muscle groups that produce functional movements. However, no research has directly evaluated the muscle forces produced during different weightbearing exercises or compared them to those developed during activities of daily living, such as walking. Knowledge of the forces produced by relevant muscle groups during different weightbearing exercises will help guide clinicians in selecting the most appropriate exercises for inclusion in exercise programs for people with knee OA.

A common misconception for patients with knee OA is that weightbearing exercise will aggravate their symptoms or hasten structural decline. Accordingly, kinesiophobia and pain catastrophising towards exercise is common in knee OA (13-15). The stigma surrounding weightbearing exercise also extends to the clinician: there is no consensus amongst physiotherapists that exercise is suitable for knee OA (15) and uncertainty about the effects of exercise in people with knee OA is known to reduce the likelihood of general practitioners to use exercise in this population (16). A subgroup of interest are people who have medial knee OA and varus malalignment, who have greater functional and structural decline (17) than those with neutrally-aligned medial knee OA. Uncertainty towards weightbearing exercise may arise because the pathogenesis of medial knee OA is likely due, at least in part, to increased medial tibiofemoral compartment loading (18). It is known that medial tibiofemoral contact forces (MTCF) during walking in people with knee OA and varus malalignment average ~2 times bodyweight (19), yet limited research has evaluated articular knee loads during different weightbearing exercises in people with knee OA (20). Understanding how knee loads during weightbearing exercise compare with those developed in daily activities (e.g., walking) will assist clinicians to make informed decisions regarding exercise prescription in knee OA.

Previous research that has investigated muscle force in knee OA has focused on metrics derived from electromyograms (EMG), such as activation ratios or co-contractions (21-24), which only infers muscle coordination rather than muscle force production. Furthermore, research evaluating knee loads during exercise in knee OA is limited to the external knee adduction moment (KAM), a surrogate measure of internal load sharing (20). However, the external KAM has a weak and variable relationship with the internal medial tibiofemoral joint contact force (MTCF) during walking (25, 26), and this relationship is not observed in other functional tasks such as side-stepping or running (26). An alternative to assessing the external KAM is to implement electromyogram (EMG)-informed neuromusculoskeletal modelling (24, 26-29). This method integrates subject- and task-specific muscle activation patterns to estimate internal load measures (i.e., MTCF) and absolute muscle forces (28).

The aim of this study was to use EMG-informed neuromusculoskeletal modelling to test the hypothesis that common weightbearing exercises will generate larger lower-limb muscles forces than walking in people with medial knee osteoarthritis and varus malalignment. A secondary aim was to test the hypothesis that peak MTCF would be no larger during these exercises compared to walking.

METHODS

A cross-sectional study design was used to compare the muscle forces and MTCF during walking to three weightbearing exercise tasks: squat, lunge, and single-leg heel raise. Ethical approval was obtained from the Institutional Human Research Ethics Committee (#1853473) and participants provided their written informed consent prior to testing. The study was conducted within The Centre for Health, Exercise and Sports Medicine at The University of Melbourne, with all biomechanical data collected and processed by the same researcher (SCS).

Participants

Twenty-eight community volunteers were recruited from a clinical trial investigating the 8-week effect of a valgus knee brace (Australian New Zealand Clinical Trials Registry number: 12619000622101) (19). Knee OA was classified according to the American College of Rheumatology clinical and radiographic criteria (30). Participants were included if they: i) were aged 50 years or older; ii) reported knee pain of ≥4 on a numerical rating scale during walking within the past week; iii) reported knee pain on most days of the past month for >3 months; iv) demonstrated radiographic tibiofemoral joint OA (Kellgren & Lawrence grade ≥2) (31); v) have a female shoe size 6-11 US or male shoe size 8-13 US and fit into standard width shoes (due to participants consenting to concurrent data collection for a cross-sectional footwear study); and vi) had varus malalignment. Varus malalignment was defined as an anatomic axis angle of <183° for males and <181° for females, measured on weightbearing anterior-posterior x-rays (32). Exclusion criteria were: i) lateral joint space narrowing greater than or equal to medial joint space narrowing; ii) lateral osteophyte grade greater than or equal to medial compartment osteophyte grade; iii) any knee surgery over the past 6 months; iv) planning to see an orthopaedic surgeon about a knee problem over the next 8 weeks; v) awaiting or planning any back or lower-limb surgery over the next 3 months; vi) systemic arthritis; vii) current or past (6 months) muscular or joint condition other than knee OA; vii) current, past (6 months), use of or intention to use (next 8 weeks) a knee brace, walking stick or other gait aid; ix) current or past (3 months) use of oral or intra-articular corticosteroid; and x) unwillingness or inability to undergo magnetic resonance imaging (MRI) or wear a knee brace. If both knees were eligible, the more painful knee was selected as the test leg for biomechanical analysis.

Testing procedures

Five barefoot trials for each of the three weightbearing exercises were collected in the following order: single leg heel raise, double leg squat and forward lunge. These were chosen to reflect a different range of weightbearing exercises and positions often used within knee OA programs (9-12). Furthermore, the exercises are easy to perform, require little or no equipment, and target key muscle groups involved in walking and other functional tasks (knee extensors, knee flexors, ankle plantar flexors and hip abductors) (27). Exercises were divided into three phases: (i) ascent/descent from starting pose to the end of self-selected range (Phase 1); (ii) a three-second isometric hold, verbally counted by the researcher (Phase 2); and (iii) ascent/decent back to the initial starting pose (Phase 3). Examples of the start/end and hold positions for each exercise are shown in Figure 1. Participants were instructed to perform each task at a self-selected, controlled pace, using their preferred strategy while still executing the task according to instruction provided. Participants were permitted to perform a practice trial of the exercise for familiarisation purposes. A trial was excluded and repeated if there was a significant loss of balance or an insufficient hold phase.

Squat

Participants stood with feet shoulder width apart on a foam wedge (Slant by OPTP, Minneapolis, USA), such that their feet were positioned in approximately 15 degrees of plantar flexion (33). The wedges were used to encourage an increase in hip flexion and to prevent restriction in squat depth by limited ankle dorsiflexion range of motion. This was done on the basis that people with knee OA have been shown to have restricted hip and ankle range of motion (34). Participants were instructed to maintain an even weight distribution between their feet and position their arms to the front (parallel to floor) for balance, then squat as deep as possible, hold for three seconds, then return to the starting position.

Lunge

Participants stood with feet shoulder width apart with a cross marked on the floor in front of them, the distance of which was normalised to 70% of their measured test leg length, measured from the greater trochanter to the lateral malleolus (35). Participants were then instructed to step forwards with their test leg onto the cross, bend their front leg by dropping their pelvis down vertically as much as comfortably possible while keeping the torso erect, hold for three seconds, then push through the front leg to return to the starting position. Participants were instructed to position their arms to the side (parallel to the floor) for balance and to keep weight on their front foot only.

Single leg heel raise

Participants stood with feet shoulder width apart with both hands lightly placed on a four-point walking frame for balance. With minimal weight through the frame and keeping their knee straight, participants were instructed to lift their non-test leg off the ground, then keeping weight through the inner (first and second) toes, raise their heels as high as possible, hold at end of range for three seconds, then descend to the start position. People with knee OA have a higher risk of falling (36), subsequently aids such as a frame, chair or wall are commonplace in clinical practice when performing this exercise. Ground reaction forces (GRF) imparted via the frame were monitored in real time, with the trial excluded if this compensatory strategy was observed.

Walking trials

Following all exercise trials, five barefoot walking trials were obtained where participants ambulated across a 10m level walkway. Walking trials were matched to ±5% of the participants self-selected walking speed, measured using two photoelectric beams.

Data collection

One trial for each exercise and one walking trial (four in total) were used for model calibration purposes and the remaining four trials for each condition (16 in total) were for model execution and subsequent analyses. Body motion and GRF data were recorded using a 12-camera motion analysis system (Vicon MX, Oxford Metrics, UK) sampled at 120 Hz and three ground-embedded force plates (AMTI, MASS, USA) sampled at 1200 Hz, respectively. A full body marker set, consisting of 67 reflective markers were placed atop the participant's skin according to the University of Western Australia marker set (37). Surface EMG were sampled at 1200Hz during the exercise and walking trials using a wireless telemetered 16-channel Telemyo direct transmission system (Noraxon, AZ, USA) for 12 lower-limb muscles: gluteus medius (GM), tensor fascia latae (TFL), vastus lateralis (VL), rectus femoris (RF), vastus medialis (VM), biceps femoris (BF), semimembranosus (SM), lateral gastrocnemius (LG), medial gastrocnemius (MG), soleus (SOL), tibialis anterior (TA) and peroneus longus (PL). The skin surface above the muscle belly was prepared and electrodes placed consistent with the Surface EMG for Non-invasive Assessment of Muscles (SENIAM) guidelines (38). Participants performed maximum isometric voluntary contraction (MVC) trials to elicit maximal EMG for the instrumented muscles in the following positions: (i) seated knee extension, (ii) seated knee flexion, (iii) seated ankle eversion, (iv), seated ankle dorsiflexion, (v) standing hip abduction. Participants performed three maximal efforts (5 second duration) for each contraction against resistance with 30 seconds rest in between efforts. Participants received standardised verbal encouragement to contract maximally during these tasks.

Magnetic resonance imaging

A three-dimensional (3D) T_1-weighted sagittal volumetric interpolated breath-hold examination (VIBE) of the study knee and a 3D T_1-coronal lower-limb scan were undertaken using a 3 T MRI machine (Siemens Medical Systems, Erlangen, Germany). The 3D images of the lower-limb bones and tibiofemoral joint cartilage were then semi-manually segmented using Mimics software (Materialise, Leuven, Belgium). These segmentations were used to inform subject-specific anatomical geometry during the musculoskeletal modelling process.

Medial tibiofemoral joint contact force analysis

Laboratory marker, force plate and EMG data were pre-processed within Matlab 2019b (MathWorks, Natick, MASS, USA) using the MOtoNMS toolbox (39). The EMG data were band-pass filtered (30–400 Hz) and full-wave rectified, then low-pass filtered using a zero-lag 2nd order Butterworth filter with a nominal 6 Hz cut-off frequency. The linear envelopes of the ankle plantar flexors were normalised to the maximum EMG value recorded during the single leg heel raise exercise, as we considered this a maximal task for this muscle group in this population. The remaining linear envelopes were amplitude-normalized to the maximum EMG value recorded during the MVC trials. These normalisation methods are acceptable given this is a within-subject study design conducted within a single session (40).

A generic, full-body musculoskeletal model (41) was used within OpenSim (42). The model had three rotational degrees of freedom at the hip, one at the knee (with abduction/adduction, internal/external rotations prescribed as a function of knee angle), and one at the ankle. Contact bodies were added to the medial and lateral compartments of the knee to enable the calculation of net joint moments and muscle tendon unit moment arms about each compartment (27). The locations of these points were determined in 3-matic (Materialise, Leuven, Belgium) by an extrema analysis of the most distal point of the respective femoral condyles. The hip joint centre was obtained in 3-matic as the centre of a sphere fitted on the respective MRI segmented femoral head. Subject-specific scaling of the pelvic, femoral and tibial dimensions, as well as their mass inertia properties was undertaken by measuring the respective segmented bone lengths and widths using standardised anatomical landmark coordinates. Foot and torso model segment dimensions and mass inertia properties were linearly scaled to match the individual's anthropometry using markers acquired during a static pose in the gait laboratory.

After model scaling, inverse kinematics, inverse dynamics, and muscle analysis tools were used in OpenSim (Version 3.3) (42) to determine lower-limb joint angles, joint moments, and muscle-tendon unit kinematics, respectively (42). The modelled joint moments, muscle-tendon unit kinematics, and processed EMG (excitations) from four trials were then used to calibrate a neuromusculoskeletal model for each participant using the Calibrated EMG-Informed Neuromusculoskeletal Modelling toolbox (CEINMS) (28). The twelve experimental EMG signals were mapped to twenty muscle-tendon units in the model (28, 43). Of note, GM excitations were mapped to corresponding anterior, middle and posterior fibres (GMED1, GMED2, GMED3); Vastus intermedius (VI) excitations were obtained as average of VL and VM excitations; Semitendinosis (ST) excitations were obtained from SM excitations; biceps femoris long head (BFLH) and short head (BFSH) excitations were obtained from the BF excitations. For each participant, optimal fibre and tendon slack lengths of these lower-limb muscles were adjusted using morphometric scaling to preserve their operating ranges (44). Muscle activation dynamics and internal muscle parameters were then functionally calibrated in CEINMS as per our previously reported methods using one of the experimentally acquired trials for each condition (four in total) (26). Following calibration, CEINMS was used in assisted-mode (43) to estimate muscle forces and tibiofemoral contact forces for the remaining four exercise or walking trials not used during CEINMS calibration. The assisted–mode neural solution synthesized excitation patterns using optimization criteria for knee spanning muscles without experimental EMG (sartorius and gracilis) and minimally adjusted excitations for muscles with experimental EMG (43). The knee spanning muscle forces were used as inputs into a planar knee mechanism to estimate bodyweight (BW)-normalised MTCF (27) (Figure 2). The muscle and external contribution to compartmental tibiofemoral contact force were determined by summing the frontal plane muscle moments, external torques, and contact reaction moments about the medial and lateral tibiofemoral contact points (26, 27). Absolute muscle force (N) was extracted for all muscle tendon units.

Kinematic, kinetic, MTCF and individual muscle forces were spline interpolated to 101 time points across stance phase for the walking trials, and to 300 time points for each exercise cycle (100 time points for each phase). Where events could be detected from forceplate data (i.e., walking and lunging), a force threshold of 10 N was used to define heel-strike and toe-off. Otherwise, exercise phases were determined using a customised Matlab script, with events defined when key marker positions exceeded or returned to within two standard deviations of the relevant resting value. All automated events were then checked manually by the researcher for accuracy (SCS). The individual muscle forces were combined into their respective muscle groups: knee extensors (VL, RF, VI, VM), knee flexors (BFLH, BFSH, SM, ST), ankle plantar flexors (LG, MG, SOL) and hip abductors (GMED1, GMED2, GLMED3, TFL). The peak force for each muscle group and peak normalised MTCF were then extracted. The mean muscle and external load contributions were obtained and expressed as a relative percentage of the total contact loading experienced by the medial tibiofemoral compartment.

Statistical methods

Statistical analysis was conducted using Statistical Package for Social Sciences (SPSS), version 26 (IBM, New York, USA) with significance at $p<0.05$. Dependent variables were peak 1) knee extensor force; 2) knee flexor force; 3) ankle plantar flexor force; 4) hip abductor force; and 5) MTCF. Differences in the dependent variables were compared using a multivariate analysis of variance model (MANOVA), with condition (four levels: squat, lunge, heel raise and walking) as the independent variable. The MANOVA was chosen as it evaluates the main effects and interaction of the independent variable on the dependent variables collectively, thus controlling for experiment-wise error rate. Assumptions of homogeneity of variance of the residuals, independent observations and normal distribution of the residuals were evaluated. We were primarily interested in the main effect of each exercise condition (squat, lunge, heel raise) compared to walking. In the event of a significant main or interaction effect, post-hoc pairwise comparison (mean difference [95% confidence interval (95%CI)]) with Bonferroni correction was performed to explore significant effects.

RESULTS

The cohort (n=28) had slightly more males than females and was overweight on average (Table 1). Descriptive spatiotemporal, kinematic, and kinetic data for walking and exercise conditions are provided in Supplementary Table 1. The results of the MANOVA showed a significant main effect between conditions (p<0.001). Subsequent pairwise comparisons are provided in Table 2, Figures 3 and 4, and detailed below.

Squat

Compared to walking, participants generated higher peak knee extensor force (mean difference 902 N 95%CI [576, 1227]), higher peak knee flexor force (192 N 95%CI [9.39, 375]), and a lower peak hip abductor force (-1975 N 95%CI [-2841, -1108]) during the squat task. No difference was observed between squatting and walking for peak plantar flexor force (-399 N 95%CI [-913, 114]).

Lunge

Compared to walking, participants generated higher peak knee extensor force (917 N 95%CI [604, 1231]) and higher peak knee flexor force (496 N 95%CI [198, 794]) during the lunge task. No difference was observed between lunging and walking for peak plantar flexor force (-156 N 95%CI [-648, 336]) or peak hip abductor force (-281 N 95%CI [-1178, 616]).

Heel raise

Compared to walking, participants generated lower peak hip abductor force (1217 N 95%CI [-2131, -303]) during the heel raise task. No difference was observed between heel raises and walking for peak knee extensor force (-46.1 N 95%CI [-274, 182]), peak knee flexor force (90.0 N 95%CI [-119, 298]) or peak plantar flexor force (-85.8 N 95%CI [-533, 362]).

Medial tibiofemoral joint contact force

Compared to walking, participants generated lower peak MTCF during the squat (-0.79 BW 95%CI [-1.04, -0.53]) and heel raise tasks (-0.27 BW 95%CI [-0.50, -0.04]). There was no difference in peak MTCF between lunging and walking (-0.01 BW 95%CI [-0.25, 0.24]).

DISCUSSION

Strengthening exercises are strongly recommended for people with knee OA (1, 3, 7). Weightbearing exercises are often prescribed with the intention to increase the force generating capacity of muscles in the context of functional movements (10, 11). However, little is known about the muscle forces experienced during common weightbearing exercises and how these compare to everyday movements such as walking. Indeed, if weightbearing exercises generate larger lower-limb muscle forces than walking without increasing knee contact forces, patients and clinicians can be reassured that weightbearing exercises are suitable for knee OA, which may increase prescription of and adherence to exercise programs. We implemented an EMG-informed musculoskeletal modelling approach to estimate peak muscle forces and MTCF developed during a range of therapeutic tasks and walking. Compared to walking, participants generated higher peak knee extensor force and higher peak knee flexor force during lunging and squatting, and a lower peak hip abductor force during lunging and heel raises. The MTCF was lower during the heel raises and squatting, but similar between lunging and walking. Collectively, these results support the inclusion of these types of weightbearing exercise for people with knee OA, however the effectiveness of individual exercises in generating force is both task and muscle dependent.

Compared to walking, the MTCF was similar during lunging and lower during squatting and heel raises. For lunging and squatting, this occurred despite higher knee flexor and extensor muscle force. This can be explained through examination of the planar mechanism (27) used to estimate MTCF in this study (Figure 2). First, there was a concomitant decrease in external loads that prevented an increase in MTCF when compared to walking. The mean relative external contribution to MTCF was highest during walking (53% ± 12%), then progressively decreased with heel raises (47% ± 17%), lunging (25% ± 16%) and squatting (-9% ± 18%) (Supplementary Figure 1). The decrease in external load contribution to MTCF was predominantly caused by a lower external KAM, particularly during squatting (Supplementary Table 1). Similar findings have been demonstrated using EMG-informed modelling in a healthy cohort where the mean relative external contribution to MTCF during walking (52% ± 10%) was higher compared to more vigorous functional tasks of running (17% ± 20%) and sidestepping (9% ± 12%) (26). Second, there is a non-linear relationship between absolute muscle force and muscle contribution to the MTCF. The transfer of muscle force to MTCF is mediated by muscle kinematics (e.g., moment arm and line of action) (Figure 2). Subsequently, the non-dependent relationship between muscle force and MTCF should be considered when interpreting our results.

We selected absolute muscle force as the primary outcome in this study as it is relevant to clinicians wanting to understand the force output of key lower-limb muscle groups during common weightbearing exercises. Compared to walking, peak knee extensor force was ~3 times higher during squatting and lunging and peak knee flexor forces were 1.6 and 2.5 times higher, respectively (Table 2, Figure 4). These are important observations given these muscles stabilise the knee during the loading response of walking, which is where the peak MTCF occurs (19, 26, 27). These findings also explain the larger knee external knee flexion moment during squatting and lunging compared to walking (Supplementary Table 1), given this moment is primarily generated by the knee extensors (26). In contrast, none of the exercises evaluated in this study generated hip abductor force significantly larger than the peak observed during walking. This finding for hip abductor force is understandable given the hip abductors are not a prime mover for any of the selected exercises. During walking, the hip abductors are active throughout single-leg stance to provide frontal plane stability to the pelvis in response to substantial inertial forces. Only the heel raise exercise involved a period of single-leg stance, however participants used a frame support to assist with balance, which likely reduced the requirement of the hip abductors to stabilise the pelvis. It is likely that targeted hip abductor exercises (e.g., non-weightbearing with resistance) (45), neuromuscular exercises that specifically challenge pelvic stability (9-12) or more demanding weightbearing strengthening exercises (e.g., single leg squat) are required in addition to the exercises investigated in this study to enhance the force generating capacity of the hip abductors. Indeed, future research is warranted to determine whether these exercises can generate a peak hip abductor force larger than walking.

Surprisingly, the peak plantar flexor force did not differ to walking during any of the evaluated exercises. These observations contradict clinical expectations, given the heel raise task selectively targets this muscle group. Upon closer inspection, the heel raise was performed with the knee approaching terminal extension (Supplementary Table 1). In this posture, soleus, the primary force generator of the plantar flexors (41), was less likely to be recruited compared to walking. Inspection of individual muscle forces confirmed this hypothesis, where peak soleus force was ~2 times larger during walking compared to the heel raise where the gastrocnemii were dominant (data not shown). Based on these findings, single leg heel raises, as evaluated in this study, do not appear to generate sufficient lower-limb muscle force to warrant inclusion in a strengthening program for knee OA, unless the clinical goals are to selectively strengthen the gastrocnemii. Alternatively, clinicians could consider adding resistance (e.g., holding weights) as a baseline exercise rather than a progression and/or prescribing heel raises in a flexed knee position. However, further research is warranted to evaluate ankle plantar flexor force for these alternative exercises. It is also plausible that this exercise may target muscles groups that were not evaluated in this study (e.g., ankle evertors), or alternatively may be prescribed to target different outcomes such as balance re-training.

Unfortunately, clinicians and their patients often refer to knee OA as “wear and tear” or “bone on bone” (13), which leads to negative attitudes towards exercise as a self-management strategy in this clinical population (13-15). Patients often fear that weightbearing exercise will further damage their knee (13, 14), and some clinicians are hesitant to prescribe weightbearing exercises for fear of aggravating patient symptoms (15, 16). However, our findings suggest that, on average, peak MTCF during squatting, lunging and heel raises did not exceed peak MTCF during walking. Squatting elicited the lowest average peak MTCF, followed by heel raises, then lunging (1.32, 1.83 and 2.12 BW, respectively) (Table 2, Figure 3). The MTCF during squatting was significantly lower than walking, which is understandable given it is a dual-limb task, while the lunges and heel raises were predominantly single-limb tasks. A previous study of young, healthy adults using static optimisation modelling methods found the MTCF was higher than walking during the majority of evaluated weightbearing exercises (sit to stands, step-ups/downs, lunging and hopping), and equivalent during squatting (46). However, it has been shown that static optimisation approaches overestimate muscle forces and tibiofemoral joint contact forces and cannot account for variations in muscle activation patterns between tasks and individuals (28, 47, 48). It is also possible that this observation stems from biomechanical differences between a population with symptomatic knee OA and a young, healthy population. For example, our knee OA sample may have shifted their body weight to the contralateral leg during squatting. Supplementary analyses of vertical GRF data found a 6.1% lower peak and a 7.6% lower impulse in the study leg compared to the contralateral leg during squatting (Supplementary Table 2). Considering the free-body diagram in Figure 2, this weight shift would likely reduce the KAM and may explain reduce both the KAM moment arm, (r_{KAM}) and GRF (F_{KAM}) may explain the small peak KAM observed during squatting in our cohort (Supplementary Table 1) It is also likely that people with symptomatic knee OA walk and perform weightbearing exercises with lower movement speed than healthy populations. Our cohort performed a squat more slowly than a younger, healthy cohort (cohort: descent 12 cm·s^{-1}, ascent 15 cm·s^{-1} (Supplementary Table 1); control: descent 58 cm·s^{-1}, ascent 69 cm·s^{-1} (33)). Indeed, it is likely that movement speed will influence peak MTCF, as it does during analysis of walking (29). Importantly, the self-selected walking speed of the cohort was 1.24 m·s^{-1} (±0.13), which is consistent with self-selected walking speeds in other knee OA studies (mean range 1.08-1.26 m·s^{-1}) (9, 18, 21, 22). Therefore, our findings with respect to walking speed can be generalised to other people with knee OA.

Collectively, these findings can give clinicians and their patients confidence that the weightbearing exercises evaluated in this study will generate peak knee extensor and knee flexor forces larger than normal walking while exposing the medial compartment to similar, or lower loads. Despite clinical practice guidelines advocating exercise as a core treatment for all people with knee OA based on robust research evidence (1,3,7), there is still uncertainty amongst physiotherapists about whether exercise is effective and/or safe for all people with knee OA (15). Furthermore, exercise use is significantly greater among general practitioners who agree that knee extensor strengthening and general exercises are suitable for people with knee OA (16). Our novel findings can be used to reinforce positive attitudes of clinicians towards weightbearing exercise and increase its prevalence within conservative management plans. Understanding the generation of tibiofemoral contact forces during exercise will also enable clinicians to progressively load the tibiofemoral compartments. For example, squatting and lunging generated similar peak knee extensor forces, however the peak MTCF was much lower during squatting. Given the minimal detectable change scores for MTCF using a scaled-generic EMG-driven model during walking is ~12% (49), this difference may be meaningful. Squats may then be preferred as an exercise of choice over lunges in the early phases of strengthening given the lower MTCF with squats may be less likely to aggravate knee pain. A patient could then progress to lunges as part of a graduated program.

To our knowledge, this is the first study to use an EMG-informed neuromusculoskeletal modelling approach to estimate the muscle and tibiofemoral contact forces during common weightbearing exercise tasks, in any population. We used MRI imaging to implement subject-specific lower-limb joint geometry, which has been shown to improve predictions of MTCF (48). However, some limitations do warrant consideration. First, these findings are only generalisable to participants with knee OA who also have varus knee malalignment. Second, participants performed all tasks in barefoot to avoid footwear confounding the study results. While there is no consensus whether shoes should be worn during strengthening exercise in knee OA, caution should be made if translating findings to patients who prefer to perform weightbearing exercise in shoes. Third, our study sample included slightly more males than females, however knee OA is more prevalent in women than men (50). Fourth, participants were permitted to self-select their movement speed and range of movement during the tasks. This was done to be consistent with clinical practice and with the acknowledgement that range of movement and movement speed is highly variable as it is often limited by pain in knee OA. However, it is possible that others with knee OA may perform these exercises differently to our cohort and thus encounter different outcomes. Fifth, we tested the exercises from least to most complex to allow a stepwise progression, as per clinical practice in a symptomatic population. However, by not randomising the testing order of tasks, we may have confounded study results. Last, comprehensive validation of our EMG-informed neuromusculoskeletal modelling is currently restricted by limited datasets to provide a direct validation of MTCF predictions (48).

Our exploratory findings suggest that squatting and lunging generate higher peak knee extensor and knee flexor force yet do not increase peak MTCF when compared to walking in people with medial knee OA and varus malalignment. Clinicians can use these novel findings to reassure themselves and patients that weightbearing exercise in these positions do not adversely increase forces within the osteoarthritic joint compartment.

ACKNOWLEDGEMENTS

CEINMS was developed by the Rehabilitation Engineering Group at University of Padua, Italy, and the Menzies Health Institute Queensland, Griffith University, Queensland, Australia.

CONTRIBUTIONS

MH and LD conceived the idea for the paper. SCS, GK and MH acquired the data. SCS performed data analysis. SCS, MH, LD, DJS and RSH interpreted the data. SCS wrote the first draft of the manuscript. All authors revised the manuscript for intellectual content and approved the final version for submission.

ROLE OF FUNDING SOURCES

This project was supported by funding from the Australian National Health and Medical Research Council (NHMRC) (Project Grant #1124418). SCS is supported by an Australian Government Research Training Program Scholarship. MH is supported by an NHMRC Investigator Grant (#1172928). RSH is supported by a NHMRC Senior Research Fellowship (#1154217). The study sponsors did not play any role in the study design, data collection, analysis and interpretation of the data, writing of the manuscript or the decision to submit the manuscript for publication.

COMPETING INTERESTS

None of the authors have any competing interests to declare. the results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The results of the present study do not constitute endorsement by ACSM.

REFERENCES

1. Kolasinski SL, Neogi T, Hochberg MC et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. *Arthritis Care Res. (Hoboken)*. 2020;72(2):149-62.
2. Hinman RS, Hunt MA, Creaby MW, Wrigley TV, McManus FJ, Bennell KL. Hip muscle weakness in individuals with medial knee osteoarthritis. *Arthritis Care Res. (Hoboken)*. 2010;62(8):1190-3.
3. Fransen M, McConnell S, Harmer AR, Van der Esch M, Simic M, Bennell KL. Exercise for osteoarthritis of the knee: a Cochrane systematic review. *Br J Sports Med*. 2015;49(24):1554-7.
4. Alnahdi AH, Zeni JA, Snyder-Mackler L. Muscle impairments in patients with knee osteoarthritis. *Sports Health*. 2012;4(4):284-92.
5. Segal NA, Glass NA, Torner J et al. Quadriceps weakness predicts risk for knee joint space narrowing in women in the MOST cohort. *Osteoarthr Cartil*. 2010;18(6):769-75.
6. Chang AH, Chmiel JS, Almagor O et al. Hip muscle strength and protection against structural worsening and poor function and disability outcomes in knee osteoarthritis. *Osteoarthr Cartil*. 2019;27(6):885-94.
7. Bannuru RR, Osani MC, Vaysbrot EE et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthr Cartil*. 2019;27(11):1578-89.
8. Hall M, Hinman RS, Wrigley TV, Kasza J, Lim BW, Bennell KL. Knee extensor strength gains mediate symptom improvement in knee osteoarthritis: secondary analysis of a randomised controlled trial. *Osteoarthr Cartil*. 2018;26(4):495-500.
9. Bennell KL, Kyriakides M, Metcalf B et al. Neuromuscular versus quadriceps strengthening exercise in patients with medial knee osteoarthritis and varus malalignment: a randomized controlled trial. *Arthritis Rheumatol*. 2014;66(4):950-9.
10. Ageberg E, Link A, Roos EM. Feasibility of neuromuscular training in patients with severe hip or knee OA: The individualized goal-based NEMEX-TJR training program. *BMC Musculoskelet Disord*. 2010;11(1):126.
11. Skou ST, Roos EM. Good Life with osteoArthritis in Denmark (GLA:D™): evidence-based education and supervised neuromuscular exercise delivered by certified physiotherapists nationwide. *BMC Musculoskelet Disord*. 2017;18(1):72.
12. Bennell KL, Keating C, Lawford BJ et al. Better Knee, Better Me™: effectiveness of two scalable health care interventions supporting self-management for knee

osteoarthritis - protocol for a randomized controlled trial. *BMC Musculoskelet Disord*. 2020;21(1):160.

13. Hurley M, Dickson K, Hallett R et al. Exercise interventions and patient beliefs for people with hip, knee or hip and knee osteoarthritis: a mixed methods review. *Cochrane Database Syst Rev*. 2018;4(4):Cd010842.

14. Dobson F, Bennell KL, French SD et al. Barriers and Facilitators to Exercise Participation in People with Hip and/or Knee Osteoarthritis: Synthesis of the Literature Using Behavior Change Theory. *Am J Phys Med Rehabil*. 2016;95(5):372-89.

15. Holden MA, Nicholls EE, Young J, Hay EM, Foster NE. UK-based physical therapists' attitudes and beliefs regarding exercise and knee osteoarthritis: findings from a mixed-methods study. *Arthritis Rheum*. 2009;61(11):1511-21.

16. Cottrell E, Roddy E, Rathod T, Porcheret M, Foster NE. What influences general practitioners' use of exercise for patients with chronic knee pain? Results from a national survey. *BMC Fam Pract*. 2016;17(1):172.

17. Sharma L, Song J, Felson DT, Cahue S, Shamiyeh E, Dunlop DD. The Role of Knee Alignment in Disease Progression and Functional Decline in Knee Osteoarthritis. *JAMA*. 2001;286(2):188-95.

18. Brisson NM, Gatti AA, Damm P, Duda GN, Maly MR. Association of Machine Learning–Based Predictions of Medial Knee Contact Force With Cartilage Loss Over 2.5 Years in Knee Osteoarthritis. *Arthritis Rheumatol*. 2021;73(9):1638-45.

19. Hall M, Starkey SC, Hinman R et al. Effect of valgus brace on medial tibiofemoral joint contact force in medial knee osteoarthritis and varus malalignment. *Plos One (in press)*. 2021.

20. Thorstensson CA, Henriksson M, von Porat A, Sjödahl C, Roos EM. The effect of eight weeks of exercise on knee adduction moment in early knee osteoarthritis--a pilot study. *Osteoarthr Cartil*. 2007;15(10):1163-70.

21. Al-Khlaifat L, Herrington LC, Hammond A, Tyson SF, Jones RK. The effectiveness of an exercise programme on knee loading, muscle co-contraction, and pain in patients with medial knee osteoarthritis: A pilot study. *Knee*. 2016;23(1):63-9.

22. Heiden TL, Lloyd DG, Ackland TR. Knee joint kinematics, kinetics and muscle co-contraction in knee osteoarthritis patient gait. *Clin Biomech. (Bristol, Avon)*. 2009;24(10):833-41.

23. Preece SJ, Jones RK, Brown CA, Cacciatore TW, Jones AKP. Reductions in co-contraction following neuromuscular re-education in people with knee osteoarthritis. *BMC Musculoskelet Disord*. 2016;17(1):372.

24. Kumar D, Rudolph KS, Manal KT. EMG-driven modeling approach to muscle force and joint load estimations: Case study in knee osteoarthritis. *J Orthop Res*. 2012;30(3):377-83.

25. Walter JP, D'Lima DD, Colwell CW, Jr., Fregly BJ. Decreased knee adduction moment does not guarantee decreased medial contact force during gait. *J Orthop Res*. 2010;28(10):1348-54.

26. Saxby DJ, Modenese L, Bryant AL et al. Tibiofemoral contact forces during walking, running and sidestepping. *Gait Posture*. 2016;49:78-85.

27. Winby CR, Lloyd DG, Besier TF, Kirk TB. Muscle and external load contribution to knee joint contact loads during normal gait. *J Biomech*. 2009;42(14):2294-300.

28. Pizzolato C, Lloyd DG, Sartori M et al. CEINMS: A toolbox to investigate the influence of different neural control solutions on the prediction of muscle excitation and joint moments during dynamic motor tasks. *J Biomech*. 2015;48(14):3929-36.

29. Starkey SC, Lenton GK, Saxby DJ et al. Effect of exercise on knee joint contact forces in people following medial partial meniscectomy: A secondary analysis of a randomised controlled trial. *Gait Posture*. 2020;79:203-9.

30. Altman R, Asch E, Bloch D et al. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum*. 1986;29(8):1039-49.

31. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis*. 1957;16(4):494-502.

32. Kraus VB, Vail TP, Worrell T, McDaniel G. A comparative assessment of alignment angle of the knee by radiographic and physical examination methods. *Arthritis Rheum*. 2005;52(6):1730-5.

33. Diamond LE, van den Hoorn W, Bennell KL et al. Deep hip muscle activation during squatting in femoroacetabular impingement syndrome. *Clin Biomech. (Bristol, Avon)*. 2019;69:141-7.

34. Ro DH, Lee J, Lee J, Park JY, Han HS, Lee MC. Effects of Knee Osteoarthritis on Hip and Ankle Gait Mechanics. *Adv Orthop*. 2019;2019:9757369.

35. Straaten RV, Timmermans A, Bruijnes A, Vanwanseele B, Jonkers I, Baets L. Reliability of 3D Lower Extremity Movement Analysis by Means of Inertial Sensor Technology during Transitional Tasks. *Sensors (Basel)*. 2018;18(8).

36. Smith TO, Higson E, Pearson M, Mansfield M. Is there an increased risk of falls and fractures in people with early diagnosed hip and knee osteoarthritis? Data from the Osteoarthritis Initiative. *Int J Rheum. Dis*. 2018;21(6):1193-201.

37. Besier TF, Sturnieks DL, Alderson JA, Lloyd DG. Repeatability of gait data using a functional hip joint centre and a mean helical knee axis. *J. Biomech*. 2003;36(8):1159-68.

38. Hermens HJ, Freriks B, Disselhorst-Klug C, Rau G. Development of recommendations for SEMG sensors and sensor placement procedures. *J Electromyogr Kinesiol*. 2000;10(5):361-74.

39. Mantoan A, Pizzolato C, Sartori M, Sawacha Z, Cobelli C, Reggiani M. MOtoNMS: A MATLAB toolbox to process motion data for neuromusculoskeletal modeling and simulation. *Source Code Biol. Med*. 2015;10(1):12.

40. Besomi M, Hodges PW, Clancy EA et al. Consensus for experimental design in electromyography (CEDE) project: Amplitude normalization matrix. *J Electromyogr Kinesiol*. 2020:102438.

41. Rajagopal A, Dembia CL, DeMers MS, Delp DD, Hicks JL, Delp SL. Full-Body Musculoskeletal Model for Muscle-Driven Simulation of Human Gait. *IEEE Trans Biomed Eng*. 2016;63(10):2068-79.

42. Delp SL, Anderson FC, Arnold AS et al. OpenSim: open-source software to create and analyze dynamic simulations of movement. *IEEE Trans Biomed Eng*. 2007;54(11):1940-50.

43. Sartori M, Farina D, Lloyd DG. Hybrid neuromusculoskeletal modeling to best track joint moments using a balance between muscle excitations derived from electromyograms and optimization. *J. Biomech*. 2014;47(15):3613-21.

44. Modenese L, Ceseracciu E, Reggiani M, Lloyd DG. Estimation of musculotendon parameters for scaled and subject specific musculoskeletal models using an optimization technique. *J. Biomech*. 2016;49(2):141-8.

45. Bennell KL, Hunt MA, Wrigley TV et al. Hip strengthening reduces symptoms but not knee load in people with medial knee osteoarthritis and varus malalignment: a randomised controlled trial. *Osteoarthr Cartil*. 2010;18(5):621-8.

46. Rossom Sv, Smith CR, Thelen DG, Vanwanseele B, Assche DV, Jonkers I. Knee Joint Loading in Healthy Adults During Functional Exercises: Implications for Rehabilitation Guidelines. *J Orthop Sports Phys. Ther*. 2018;48(3):162-73.

47. Bennett KJ, Pizzolato C, Martelli S et al. EMG-informed neuromusculoskeletal models accurately predict knee loading measured using instrumented implants. *IEEE Trans Biomed Eng*. 2022:1-.

48. Gerus P, Sartori M, Besier TF et al. Subject-specific knee joint geometry improves predictions of medial tibiofemoral contact forces. *J. Biomech*. 2013;46(16):2778-86.

49. Gardinier ES, Manal K, Buchanan TS, Snyder-Mackler L. Minimum detectable change for knee joint contact force estimates using an EMG-driven model. *Gait Posture*. 2013;38(4):1051-3.

50. Felson DT, Naimark A, Anderson J, Kazis L, Castelli W, Meenan RF. The prevalence of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. *Arthritis Rheum*. 1987;30(8):914-8.

Figure 1: Start/end and hold positions for the squat, lunge and single leg heel raise exercise.

Figure 2: Two-point contact model used to estimate tibiofemoral contact loading (27). Where M is the medial compartment contact point, L is the lateral compartment contact point, d_{IC} is the intercondylar distance between M and L, F_{musc} is the muscle force, M_{ext}^{MC} is the summed external moment about the medial compartment, r_{musc}^{MC} is the MTU moment arm relative to the medial compartment, and F_{LC} is the lateral compartment contact load. Within the figure, the knee adduction moment force (F_{KAM}) and moment arm (r_{KAM}) is also demonstrated.

Figure 3: Left: ensemble average muscle force (± standard deviation) of squatting (grey line), lunging (yellow short dot), heel raises (blue dash-dot) and peak walking (black dashed line) for A: knee extensor, B: knee flexor, C: ankle plantar flexor and D: hip abductor muscle groups. Right: box plots of peak muscle force of squatting (grey), lunging (yellow), heel raises (blue) and walking (dashed line) for A: knee extensor, B: knee flexor, C: ankle plantar flexor and D: hip abductor muscle groups. Box: interquartile range with median (line) and mean (square). Whiskers: 5-95% of data. Scatter: individual participant data (n=28). Asterix (*) denotes significant difference compared to walking.

Figure 4: Left: ensemble average bodyweight-normalised medial tibiofemoral contact force (± standard deviation), of squatting (grey line), lunging (yellow short dot), heel raises (blue dash-dot) and peak walking (black dashed line). Right: box plots of peak bodyweight-normalised medial tibiofemoral contact force of squatting (grey), lunging (yellow), heel raises (blue) and walking (dashed line). Box: interquartile range with median (line) and mean (square). Whiskers: 5-95% of data. Scatter: individual participant data (n=28). Asterix (*) denotes significant difference compared to walking.

Supplemental Digital Content 1.docx

Supplemental Digital Content 2.tif

The mean muscle (hollow dot (o)) and external load (cross (x)) relative contributions (%) to the medial tibiofemoral compartment contact force during the walking, heel raise, lunge, and squat tasks. Box: interquartile range with medial value marked by the notch. Whiskers: 5-95% of data.

Supplemental Digital Content 3.docx