Arthritis Care & Research
Vol. 75, No. 6, June 2023, pp 1351–1361
DOI 10.1002/acr.25001

American College of Rheumatology
Empowering Rheumatology Professionals

REVIEW

Relationship Between Knee Biomechanics and Pain in People With Knee Osteoarthritis: A Systematic Review and Meta-Analysis

Laura Hutchison,[1] Jane Grayson,[1] Claire Hiller,[1] Nicole D'Souza,[1] Sarah Kobayashi,[2] and Milena Simic[1]

Objective. Our primary aim was to determine the cross-sectional relationship between knee biomechanics during gait and pain in people with medial knee osteoarthritis. Our secondary aim was to evaluate differences in knee biomechanics between symptomatic and asymptomatic participants with medial knee osteoarthritis.

Methods. Four online databases were searched from inception to July 2021. Eligible studies included people with medial/nonspecific knee osteoarthritis and a reported relationship between knee biomechanics during gait and pain or biomechanics of symptomatic and asymptomatic participants. Two reviewers independently extracted data and evaluated risk of bias. Random-effects meta-analyses were performed when three or more studies reported the same biomechanical variable for pooling (knee adduction moment [KAM], KAM impulse, varus thrust, and peak knee flexion moment [KFM]).

Results. Forty studies were included. Methodological quality ranged from 4 to 9/10. Forty-seven unique biomechanical variables were reported. For the KAM, there was no correlation with pain for peak values pooled (early stance and overall) (r = 0.00, 95% confidence interval [95% CI]: −0.12, 0.11, k = 16), a small negative correlation for early stance peak alone (r = −0.09, 95% CI −0.18, −0.002, k = 12), and a medium positive correlation for the overall peak during stance (r = 0.30, 95% CI 0.17, 0.42, k = 4). Metaregression identified that body mass index moderated the peak KAM–pain relationship ($P < 0.001$). KAM impulse had a small positive correlation with pain (r = 0.23, 95% CI 0.04, 0.40, k = 5), and people with varus thrust had 3.84 greater odds of reporting pain compared with people without (95% CI 1.72, 8.53, k = 3). Meta-analyses for the peak KFM and pain correlation and secondary aim were nonsignificant.

Conclusion. Some knee gait biomechanics were associated with pain in this cohort. Longitudinal studies are required to determine causality.

INTRODUCTION

Osteoarthritis (OA) is a chronic musculoskeletal condition and a leading cause of worldwide disability (1). OA commonly affects the knee (2), resulting in chronic pain, reduced quality of life (3), limited physical function (4), mental health deterioration (5), and significant economic cost (6). No cure exists for knee OA, and knee replacement is recommended for end-stage disease (7). Because there is no OA cure, research has focused on strategies to slow or stop disease progression. Recent meta-analyses have found that 2 biomechanical variables, increased peak external knee adduction moment (KAM) and varus thrust presence at baseline, are associated with almost 2-times greater odds of medial tibiofemoral OA disease progression (8). The KAM is a valid (9) and reliable (10) surrogate for medial knee joint load during gait (11) and can be reduced with the use of load-modifying interventions such as gait retraining (12), lateral wedge insoles (13), or valgus knee bracing (14). Varus thrust presence is related to KAM and is visualized by rapid lateral movement of the knee during the stance phase of gait, with return to less varus

Ms. Hutchison's work was supported by the Arthritis Australia National Research Program Scholarship (funded by Arthritis Western Australia) and the Sports and Exercise Podiatry Australia Research Scholarship. Ms. D'Souza's work was supported by the Westmead Charitable Trust, Allied Health Career Development grant. Dr. Simic's work was supported by the University of Sydney's SOAR fellowship.

[1]Laura Hutchison, BPod (Hons), GradCertTAEd, Jane Grayson, BSc, MPhty St, M.Phty (Sports), PhD, Claire Hiller, BAppSc (Physio), MAppSc, PhD, Nicole D'Souza, BSc, MPhty, Milena Simic, BPhysio (Hons), PhD: The University of Sydney, Camperdown, New South Wales, Australia; [2]Sarah Kobayashi, BLAS, PhD: The University of Sydney, Camperdown, New South Wales, Australia, and Australian Catholic University, North Sydney, New South Wales, Australia.

Author disclosures are available at https://onlinelibrary.wiley.com/action/downloadSupplement?doi=10.1002%2Facr.25001&file=acr25001-sup-0001-Disclosureform.pdf.

Address correspondence via email to Ms. Laura Hutchison, BPod (Hons), GradCertTAEd, at laura.hutchison@sydney.edu.au.

Submitted for publication April 20, 2022; accepted in revised form August 16, 2022.

SIGNIFICANCE & INNOVATIONS

- Most knee biomechanics during gait were not strongly related to pain in people with knee osteoarthritis. In particular, when early stance and overall peak external knee adduction moment (KAM) outcomes were pooled, there was no correlation between peak KAM and pain.
- Varus thrust presence was associated with almost four times increased odds of reporting pain compared with people without varus thrust. Therefore, varus thrust presence should be identified early in clinical assessment.
- Metaregression identified that body mass index (BMI) significantly moderated the relationship between peak KAM and pain. For each 1-unit increase in BMI, the peak KAM–pain correlation coefficient decreased by almost 0.1. This indicates BMI is important for clinicians and researchers to consider regarding load-reducing interventions.

alignment during swing (15). Addressing these biomechanical variables may be important therapeutic targets for minimizing disease progression.

Although the association between knee biomechanics and OA disease progression is established, there is currently no clear consensus on the relationship between knee biomechanics and pain in people with knee OA. The impact of knee biomechanics during gait may be a crucial aspect in understanding pain associated with knee OA. The pain experience in people with knee OA is complex, multifactorial, and often considered in a biopsychosocial context (16). However, traditionally, pain due to knee OA has been regarded as nociceptive because of abnormal loading of a damaged joint (17), a theory not always supported by the available evidence. Though widely investigated, there is evidence for a positive (18), a negative (19), and no correlation (20) between pain and biomechanical variables such as the KAM in people with knee OA. There is also conflicting evidence whether knee biomechanics in people with knee OA differ between symptomatic and asymptomatic cohorts (21,22). As well as reaching consensus on the relationship between knee biomechanics and pain, meta-analyses in this area bring the opportunity to explore the interaction of potential moderating factors.

Given that pain management is likely the motivating factor for people with knee OA to seek health care (23), it is important to examine the relationship between pain and knee biomechanics in this cohort. This could ensure treatments appropriately target biomechanical variables linked to pain as well as disease progression outcomes. The primary aim of this study was to determine the cross-sectional relationship between knee biomechanics during gait and pain in people with medial knee OA. Our secondary aim was to determine whether a difference exists in knee biomechanics during gait between symptomatic and asymptomatic participants with medial knee OA.

METHODS

We conducted a systematic review and meta-analysis of the relationship between knee biomechanics during gait and pain in people with medial knee OA, following the recommendations of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. Our protocol was registered prospectively (PROSPERO CRD42020173496).

Search strategy and study selection. We conducted a systematic search of online databases (MEDLINE, AMED, Embase, and CINAHL) from inception until July 27, 2021. Searches were unrestricted by language. Search terms were related to OA, the knee joint, biomechanics, and pain (Supplementary Methods 1, available on the *Arthritis Care & Research* website at https://onlinelibrary.wiley.com/doi/10.1002/acr.25001). We performed bibliographic and citation searches of included studies. After duplicate removal, 2 reviewers independently screened records by 1) title and abstract and 2) full text against predetermined inclusion and exclusion criteria, using Covidence (Veritas Health Innovation, Melbourne, Australia). Two reviewers also independently performed data extraction and risk of bias assessment, with a third independent reviewer available to resolve conflicts.

Eligibility criteria. Eligible study designs were case-control, cross-sectional, or longitudinal. Relevant baseline or control group data from experimental studies were also eligible. Participants were adults (age ≥18 years) diagnosed with knee OA. For the secondary analysis, asymptomatic participants must have received an OA diagnosis via imaging (radiograph or magnetic resonance imaging). Studies in which the predominant knee compartment affected with OA was the patellofemoral or lateral tibiofemoral were excluded because of evidence of different joint loading patterns compared with people with medial knee OA (24,25). Studies not specifying the knee compartment affected were included because OA commonly affects the medial compartment (26). Study outcomes included the association between pain and knee biomechanics or the difference in knee biomechanics during gait between symptomatic and asymptomatic groups. Eligible biomechanical metrics included any kinetic or kinematic knee outcomes assessed during walking gait. Knee biomechanics were assessed in a three-dimensional (3-D) motion analysis laboratory or rated for presence of biomechanical variables such as varus thrust by examiners using a 2-D video recording. Knee joint moment outcomes were included regardless of normalization or normalization method.

Studies analyzing either a fixed or self-selected walking speed were eligible. If studies assessed multiple walking speeds,

the self-selected/normal speed was extracted. Experimental studies observing changes in knee biomechanics in response to interventions such as analgesia or induced pain were ineligible because we aimed to determine the relationship between knee biomechanics and pain due to knee OA. Within-participant studies (designs comparing bilateral knee biomechanics within the same participant) were excluded because it is hypothesized that biomechanical adaptations to knee OA are at least partially systemic and not exclusively based on the physiologic characteristics of the affected knee (27). Studies using composite symptom scoring systems not clearly separated into majority pain subscales, as well as reviews, meta-analyses, opinion pieces, and conference abstracts, were ineligible.

Risk of bias assessment. Risk of bias was assessed using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (28). This tool contains 14 questions regarding study objective, population, recruitment, sample size, analyses, exposures, outcome measures, blinding, follow-up, and confounding variables. The questions can be answered with "yes," "no," or "other" (cannot determine, not reported, not applicable). Because of the cross-sectional nature of extracted data, items 6, 7, 10, and 13 (measuring biomechanics prior to pain, allowing sufficient time frame to see an association, assessing biomechanics more than once over time, and participant drop-out) were not applicable; therefore, the maximum score each study could receive was 10 points.

Data extraction. The following data were extracted: country of origin, study design, recruitment information and demographic data, knee OA diagnosis and severity, pain assessment tool, pain scores, gait speed, knee biomechanics values (e.g., KAM), association between knee biomechanics and pain (e.g., Pearson's correlation coefficient [r], odds ratio [OR], beta or regression coefficients), or differences in knee biomechanics between symptomatic and asymptomatic groups (*P* values).

Authors were emailed if further information was required. Studies were excluded from meta-analyses if relevant data remained unavailable. If studies used multiple pain assessment tools, data extraction was prioritized according to a published hierarchy (29).

Meta-analyses. To evaluate associations between knee biomechanics and pain, we pooled Pearson's r values. The correlation was inverted for studies that reported pain assessment tools with higher numbers indicating lower pain levels. When appropriate, R^2 values were converted to r by obtaining the square root value, then all r-values were transformed to Fisher's Z and corresponding sample variances calculated (30). ORs and 95% confidence intervals (95% CIs) were calculated for studies that reported dichotomous biomechanical variables as the predictor and pain as the outcome variable.

To determine whether differences in knee biomechanics existed between symptomatic versus asymptomatic groups, we estimated the relative effect of each study by calculating the standardized mean difference in knee biomechanics between groups.

Studies were considered heterogeneous if they used different pain assessment tools or had an I^2 value >50% (31). In meta-analyses in which studies were deemed heterogeneous, random-effects models were used, whereas fixed effects were chosen if studies were homogenous. Meta-analyses were conducted if ≥3 studies reported the same association measure for a particular biomechanical variable regarding its relationship with pain. Sensitivity analyses were identified and performed (depending on data availability) based on any potential confounding variables. Metaregression was considered for any suitable explanatory variable with 10 or more studies.

The term "biomechanical metrics" includes umbrella knee kinetic or kinematic outcomes (e.g., KAM, knee flexion angle). "Biomechanical variables" describes these metrics at specific time points during the gait cycle (e.g., early stance peak KAM, knee flexion angle at initial contact) (8). For meta-analyses, only biomechanical variables collected at the same time point were pooled. As the early stance (first) peak KAM is typically the largest (32), overall and early stance peak KAM were pooled in the same meta-analysis, before sensitivity analyses conducted separately for early stance and overall peaks. "Peak KAM" refers to both early stance and overall peaks pooled, whereas "early stance peak KAM" refers to the peak KAM during the first 50% of stance, and "overall peak KAM" refers to the largest peak during the entire stance phase. We classified the peak KAM as early stance peak KAM when 1) "early stance" or "first peak" KAM was clearly stated in the paper, 2) we were able to clarify with the author that the peak KAM was extracted during the first half of stance, or 3) the average peak KAM occurred during the first half of stance as illustrated in a graph. If it remained unclear whether the peak KAM was extracted from the first half of stance, the study was included in the peak KAM meta-analysis and the overall peak KAM sensitivity analysis. Meta-analyses were conducted using Comprehensive Meta-Analysis Software V3 (Biostat). Correlation coefficient strength was interpreted as per Cohen (33).

RESULTS

The search identified 3,679 independent records, and 40 studies were deemed eligible for inclusion (Figure 1, PRISMA diagram). Included studies were cross-sectional (k = 30), case-control (k = 4), longitudinal (k = 4), or experimental (k = 2). Sample sizes ranged from 10 (34) to 699 (35), with an average age range between 45.5 (36) and 73.4 (37) years and body mass index (BMI) range from 22.5 kg/m^2 (35) to 37.3 kg/m^2 (38). Most studies included participants with a range of OA severities (Kellgren/Lawrence [K/L] grades 0–IV). Four studies (10%) (35,39–41) included participants with K/L grade 0, mostly

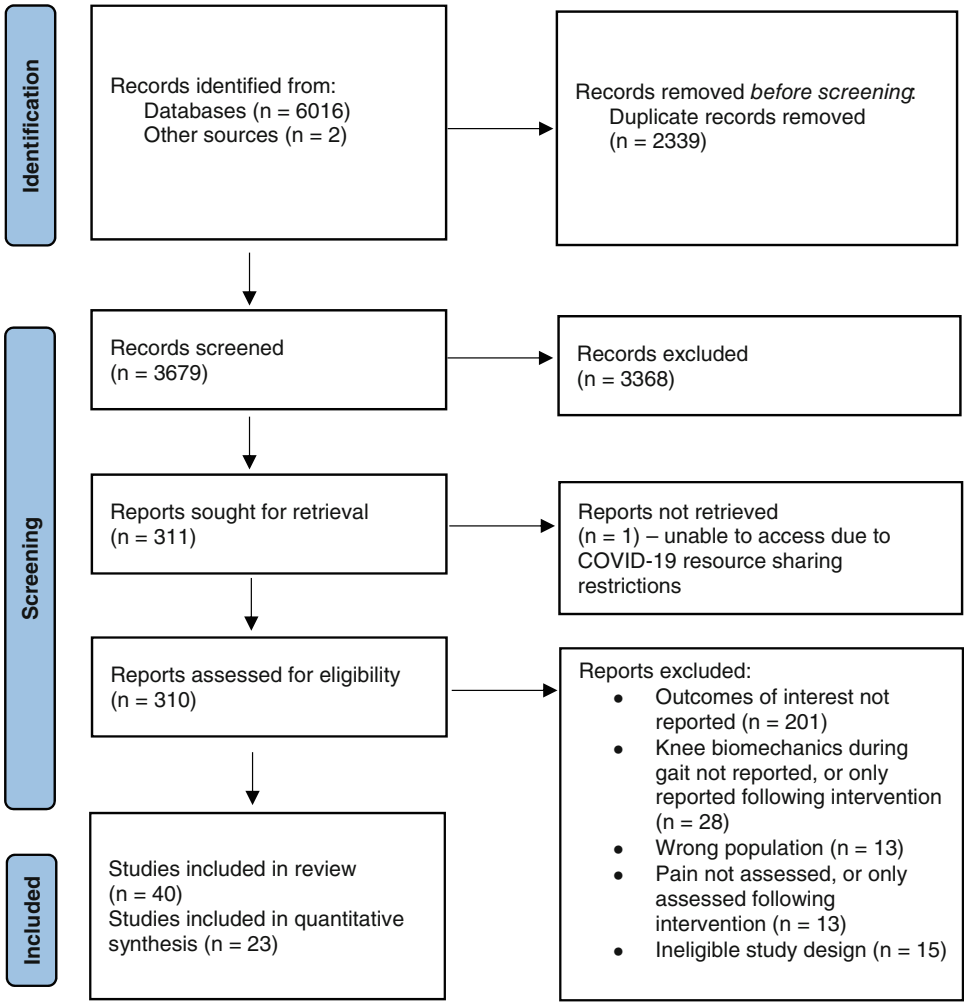

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram.

because of clinical OA diagnosis. Twenty-eight studies (70%) explicitly recruited participants with medial knee OA, and 12 (30%) studies did not specify the main compartment affected.

Overall, 23 unique knee biomechanical metrics (47 variables) were reported. The most frequently reported were early stance peak KAM (k = 16) (19–22,36,39,41–50), overall peak KAM (k = 9) (18,34,38,51–56), KAM impulse (k = 7) (21,38,43,44,54,57,58), peak knee flexion moment (KFM) (k = 5) (19,41,46,49,59), and varus thrust presence (k = 5) (35,37,60–62). Common pain assessment tools were the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (k = 15) (20–22,35,36,39,44–46,49–51,59,62,63), the Knee Injury and Osteoarthritis Outcome Score (k = 8) (19,40–43,47,58,64), and visual analogue scale (k = 6) (34,38,53,54,65,66) (Supplementary Table S1, available on the *Arthritis Care & Research* website at https://onlinelibrary.wiley.com/doi/10.1002/acr.25001).

Risk of bias. Methodological quality ranged from a score of 4 (48) to 9 (38,46) out of a possible 10 points (Supplementary Table S2, available on the *Arthritis Care & Research* website at https://onlinelibrary.wiley.com/doi/10.1002/acr.25001). Well-performed items included stating study objective, consistent population recruitment period, quantifying knee biomechanics, using valid and reliable outcome measures, blinding, and adjustment for sex and age. Poorly performed items included defining recruitment location and population, specifying the number of eligible participants, and sample size justification.

Study results and meta-analyses. Study results are reported in Supplementary Tables S3 and S4 (available on the *Arthritis Care & Research* website at https://onlinelibrary.wiley.com/doi/10.1002/acr.25001) and meta-analyses in Table 1. Meta-analyses were conducted on 5 outcomes (4 biomechanical metrics for the relationship with pain and 1 biomechanical metric for the difference in biomechanics between symptomatic and asymptomatic groups). Because of heterogeneity (I^2 >50% and/or different pain assessment tools used), we used random-effects models for all analyses.

Table 1. Meta-analysis results*

Meta-analysis group	Sensitivity analysis (sample)	Studies, no.	Participants, no.	Statistics	Overall effect (95% CI)	I^2 (%)
Peak KAM and pain correlation	–	16 (18–20,34,36,39,42–45, 47–50,53,54)	898	r	0.00 (−0.12, 0.11)	61
Early stance and overall peak KAM pooled (Supplementary Figure S1)†						
	Medial knee OA (Supplementary Figure S2)†	13 (18,20,34,36,39,42,44, 47–50,53,54)	729	r	0.05 (−0.07, 0.18)	57
	Medial knee OA and varus alignment (Supplementary Figure S3)†	3 (18,36,54)	296	r	0.19 (−0.08, 0.42)	81
Early stance peak KAM only (Supplementary Figure S4)†	–	12 (19,20,36,39,42–45,47–50)	689	r	−0.09 (−0.18, −0.002)‡	17
	Medial knee OA (Supplementary Figure S5)†	9 (20,36,39,42,44,47–50)	520	r	−0.05 (−0.15, 0.05)	10
Overall peak KAM only	Medial knee OA (Supplementary Figure S6)†	4 (18,34,53,54)	209	r	0.30 (0.17, 0.42)‡	0
KAM impulse and pain correlation (Supplementary Figure S7)†	–	5 (43,44,54,57,58)	370	r	0.23 (0.04, 0.40)‡	66
	Medial knee OA (Supplementary Figure S8)95%†	4 (44,54,57,58)	317	r	0.26 (0.03, 0.47)‡	73
Peak KFM and pain correlation (Supplementary Figure S9)†	–	4 (19,41,49,59)	136	r	−0.18 (−0.38, 0.04)	25
Varus thrust presence and pain association (Supplementary Figure S10)	–	3 (35,61,62)	671	OR	3.84 (1.72, 8.53)‡	68
Difference in peak KAM between symptomatic/asymptomatic OA groups	–	4 (21,22,46,56)	264	SMD	0.24 (−0.08, 0.56)	32
Early stance and overall peak KAM pooled (Supplementary Figure S11)†						
Early stance peak KAM only	Medial knee OA (Supplementary Figure S12)†	3 (21,22,46)	223	SMD	0.27 (−0.16, 0.69)	53

* 95% CI = confidence interval; KAM = knee adduction moment; KFM = knee flexion moment; OA = osteoarthritis; OR = odds ratio; r = correlation coefficient; SMD = standardized mean difference.
† available on the *Arthritis Care & Research* website at https://onlinelibrary.wiley.com/doi/10.1002/acr.25001.
‡ Significant.

No relationship was detected between peak KAM (early stance and overall peaks pooled) and pain in participants with knee OA (Table 1 and Supplementary Figure S1, available on the *Arthritis Care & Research* website at https://onlinelibrary.wiley.com/doi/10.1002/acr.25001). No relationship was detected between peak KAM and pain in participants with medial knee OA, and those with varus alignment (Table 1 and Supplementary Figures S2 and S3, available at https://onlinelibrary.wiley.com/doi/10.1002/acr.25001). Metaregression revealed that for a 1-unit increase in BMI, the peak KAM–pain correlation coefficient in those with knee OA decreased by 0.08 (k = 10, $P < 0.001$) (18,20,36,39,43,44,47,49,50,54) (Figure 2). There was a small negative correlation between early stance peak KAM and pain (Table 1 and Supplementary Figure S4, available at https://onlinelibrary.wiley.com/doi/10.1002/acr.25001), but this became nonsignificant when only participants with medial knee OA were analyzed (Table 1 and Supplementary Figure S5). Correlation between overall peak KAM and pain revealed a medium positive relationship in those with medial knee OA (Table 1 and Supplementary Figure S6). There was a small positive correlation between KAM impulse and pain (Table 1 and Supplementary Figure S7, available on the *Arthritis Care & Research* website at https://onlinelibrary.wiley.com/doi/10.1002/acr.25001), which remained when considering only participants with medial knee OA (Table 1 and Supplementary Figure S8). Peak KFM was not correlated with pain in people with knee OA (Table 1 and Supplementary Figure S9). People with knee OA and varus thrust presence had 3.84 greater odds of reporting pain compared with people without varus thrust (Table 1 and Supplementary Figure S10, available at https://onlinelibrary.wiley.com/doi/10.1002/acr.25001).

There was no difference in peak KAM between symptomatic and asymptomatic groups with knee OA (Table 1 and Supplementary Figure S11), which remained when sensitivity analysis was conducted based on early stance peak KAM in people with medial knee OA (Table 1 and Supplementary Figure S12, at https://onlinelibrary.wiley.com/doi/10.1002/acr.25001).

Of the biomechanical variables from studies unable to be included in meta-analyses, there were 24 with no pain relationship (19,20,36,38–42,44,45,48,50–52,55,65–67), 12 with a positive (34,37,38,50,57,60,64,68), and 10 with a negative relationship (20,38,44,45,63,64,68). For those studies reporting knee biomechanics of symptomatic and asymptomatic groups not included in meta-analyses, there were 11 reported variables with no between-group differences (21,46,56), whereas 5 biomechanical variables were significantly larger in the symptomatic compared with the asymptomatic group (21,22,46) (Supplementary Tables S3 and S4, available on the *Arthritis Care & Research* website at https://onlinelibrary.wiley.com/doi/10.1002/acr.25001).

DISCUSSION

We identified evidence of some knee biomechanics during gait being associated with pain in people with knee OA; however, relationships were not strong. The biomechanical variables evaluated via meta-analyses are considered proxy measures of load imbalance in the knee during gait. Our meta-analysis demonstrated that people with varus thrust presence had 3.84 greater

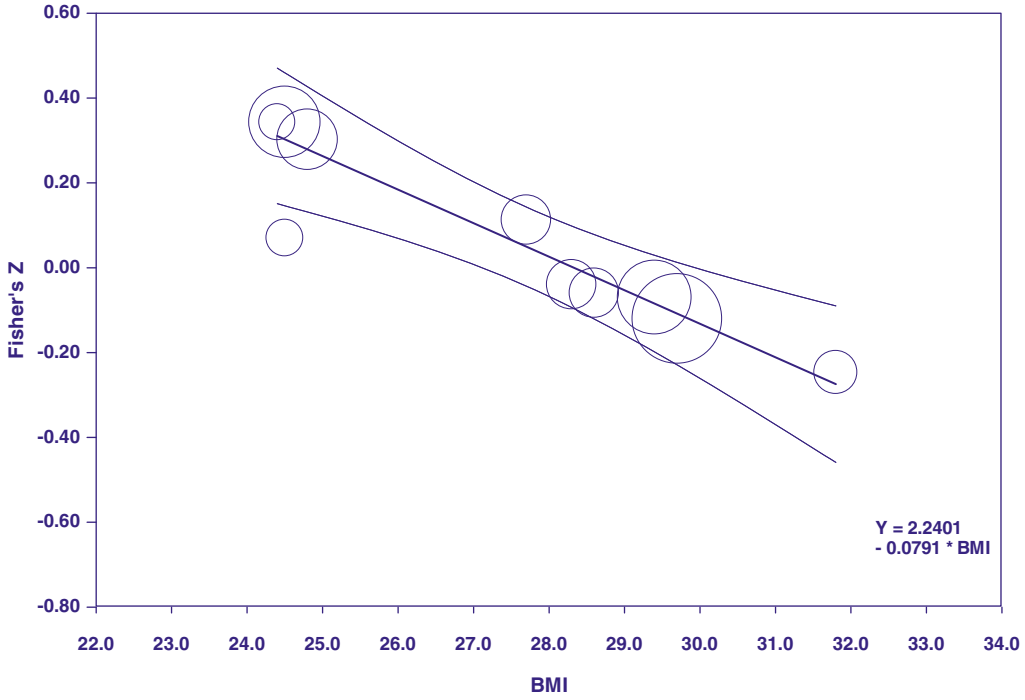

Figure 2. Regression of Fisher's Z (pain and peak knee adduction moment [KAM] [early stance and overall peak KAM pooled]) on body mass index (BMI). Color figure can be viewed in the online issue, which is available at http://onlinelibrary.wiley.com/doi/10.1002/acr.25001/abstract.

odds of reporting pain compared with people without varus thrust. There was a medium positive relationship between overall peak KAM and pain in those with medial knee OA, and BMI moderated the peak KAM–pain relationship. All other displayed relationships between biomechanics and pain were small (positive or negative), or there was no relationship. However, because of the complexity of pain and previously reported small r- and OR values for factors known to be associated with pain in people with knee OA, these results were not unexpected. We found no difference in knee biomechanics during gait between symptomatic and asymptomatic groups.

The varus thrust association with pain is clinically meaningful, as varus thrust can be identified upon visual gait analysis without expensive equipment and technical expertise. Varus thrust presence has also been associated with increased odds of medial tibiofemoral OA disease progression (OR 1.97) (8). As varus thrust occurs throughout the course of OA disease (60,69), early identification and intervention could be impactful regarding both pain and disease progression. The significant associations with both pain and OA disease progression in those with varus thrust presence may point to the connection between pain and joint load, as varus thrust may be a clinical marker of excessive medial joint load (70). Three short-term studies have reported that lateral wedge insoles (n = 38) (71), soft knee braces (n = 6) (conference abstract) (72), and gait retraining (n = 1) (73) may reduce varus thrust magnitude and pain in those with medial knee OA. However, there are no large randomized controlled trials investigating long term effects of interventions on varus thrust presence and pain in people with knee OA.

Meta-analyses between overall peak KAM and KAM impulse with pain revealed positive relationships. These findings align with the traditional hypothesis that in people with knee OA, pain occurs because of abnormal loading of a damaged joint (17). However, meta-analysis between early stance peak KAM and pain revealed a small negative correlation, which may render this relationship clinically insignificant. This negative correlation may appear counterintuitive, as it would seem logical that larger loads applied to joints with OA would increase pain. However, the negative correlation could indicate evidence for a protective mechanism, meaning participants experiencing greater pain alter their gait to offload the medial knee. A protective mechanism has previously been postulated (19,39,57) and is supported by studies demonstrating reduced pain and higher KAM after intra-articular hyaluronic acid injections (74,75) or oral piroxicam (76). There is also evidence that knee pain seems to alter motor strategies to facilitate joint unloading (77). Therefore, it may be pain that influences biomechanics. Compensatory gait adaptations to alter knee loading, e.g., altering foot progression angle, trunk lean, or walking speed, may account in part for the different individual study correlation coefficients between KAM and pain. Furthermore, compensation mechanisms used to reduce one biomechanical metric [e.g., walking with toe-in gait (78) or slower walking speed (79) to reduce peak KAM] may concurrently increase another (e.g., KAM impulse).

Based on our varying meta-analyses results and conflicting findings of individual studies, it is important to note the nociceptive theory linking knee loading to pain in OA may be inadequate. This may also depend on the OA disease stage. The general symptom nature in early OA is activity-related symptoms that appear nociceptive, progressing over the disease course to a more constant pain that likely reflects other processes, e.g., neurobiologic mechanisms (16). However, because of reported data, we were unable to perform analyses based on OA disease severity. We acknowledge that pain is multifactorial, and a biopsychosocial model is needed to better understand pain due to OA.

Our metaregression showed that studies with cohorts who had larger BMI on average (>28 kg/m^2) displayed negative KAM–pain correlations, whereas studies with smaller BMI (<28 kg/m^2) had positive correlations. This analysis, although subject to aggregation bias, could indicate that participants may use protective gait alterations when they are overweight/obese and may explain conflicting findings from previous studies regarding the relationship between peak KAM and pain. The opposing correlation coefficients with pain from overall and early stance peak KAM meta-analyses may be due to a difference in biomechanical variable timing or participant characteristics between studies. A smaller percentage of studies in the early stance peak KAM analysis reported healthy BMI compared with the overall peak KAM analysis. This may indicate participants in the overall peak KAM analysis were more likely to display positive KAM–pain relationships based on our metaregression findings.

Potential mechanisms regarding our metaregression result could include mechanical loading (e.g., increased joint load and altered walking kinematics in individuals with obesity compared with normal-weight individuals) (80) and/or systemic factors such as metabolically driven inflammation in obesity (81) or pain sensitivity. Recent work has found that in those with knee pain, low pressure pain thresholds are associated with both higher visceral fat area and body fat percentage (82). This may in part explain why those studies with higher BMI (>28 kg/m^2) displayed a negative knee loading–pain relationship. Unfortunately, because of lack of data, investigation into potential mechanisms such as inflammation was unable to be performed because this was not assessed in included studies. There is also evidence that BMI interacts with peak KAM and impulse to predict loss of medial tibial cartilage volume over 2.5 years in people with knee OA. Greater peak KAM and impulse were both associated with reductions in medial tibial cartilage volume in obese individuals; however, in normal/overweight individuals, the KAM was of little importance in predicting medial tibial cartilage volume change (83).

Regarding secondary outcomes, we found no difference in peak KAM between symptomatic and asymptomatic groups. The meta-analysis based on peak KAM difference between

groups included 4 studies (total n = 264) (21,22,46,56), and only 1 study (22) (n 71) identified a significantly larger KAM in the symptomatic group.

Because of previously reported weak relationships of known factors relating to pain in people with knee OA, our results displaying small relationships between biomechanics and pain were not unexpected. Previously reported factors associated with pain in those with knee OA include BMI (84), sleep duration (85), and depression (86). Apart from the odds of pain in an obese group with knee OA (adjusted OR 7.5), adjusted OR for sleep duration and depression have been reported as 1.32 (85) and 3.01 (86), respectively, which are lower than our ORs for pain with varus thrust presence. It is possible the relationship between pain and joint loading is more difficult to examine in continuous variables because of small changes in precise data. Relationships may also be complicated by variation in biomechanics between studies due to research design, e.g., differences in motion capture systems, researcher expertise, coordinate systems, anatomical landmarks, modeling, and filtering decisions. However, small correlation coefficients for factors stated to be correlated with pain in knee OA have been reported for age (87) and serum hyaluronan level (K/L grade III–IV) (88).

Pain is a challenging outcome to assess because it is multifactorial, subjective (89), and influenced by psychological, biological, and social factors, and the intensity of daily pain due to OA varies significantly (16). This means it is impossible for any one factor alone to explain pain variability. Additionally, many factors contributing to pain variation between participants cannot be feasibly assessed and controlled for in most studies because of the number of factors influencing pain (16). Responses to pain, e.g., central sensitization (reduction of the threshold for mechanically induced pain) (16), may further complicate observed relationships. We performed relevant sensitivity analyses and metaregression when possible, per our protocol. However, when between-participant confounding is reduced by a within-patient study design, strong associations have been observed between medial knee load and increased knee pain during walking (90).

Most included studies (82%) utilized a reliable and valid knee pain questionnaire. However, multiple pain assessment tools were used and standardized to different scales/directions. Some studies asked a single pain question, which is unlikely to capture the full pain experience (16). Two studies analyzed the pain relationship with biomechanics from a single WOMAC item instead of the total pain score (49,62). In studies not utilizing standardized knee pain questionnaires, pain was assessed across different time periods, or a period was unspecified. In these studies, discrepancies also arose with pain being assessed during everyday life (38), walking (34,52,54,55), or movement (53). Some studies provided limited detail regarding pain assessment. Because all studies assessed pain due to knee OA, we deemed it appropriate to pool results; however, we acknowledge the associated limitations. Many outcomes extracted were secondary/post hoc analyses from studies not designed to answer our primary aim. Included studies had a broad range of participants (e.g., sex distribution, age, BMI, geographic location, and OA severity grade) and some were limited by small sample size (≤20) (34,41,42,48,53,59,63). When correlations between knee biomechanics and pain were small or nonexistent, they may have been impacted by research design or affected by multiple confounders, or it may be that the relationship with pain is discordant for some biomechanical variables.

It is recommended that future studies are well-designed to specifically determine the relationship between knee biomechanics during gait and pain, and longitudinal studies are necessary to infer causation of relationships already established. Within-participant studies also present a practical design to account for confounders that cannot be feasibly assessed and controlled/adjusted for in between-participant designs, although it may be that the biomechanical adaptations to knee OA are at least partially systemic and not exclusively based on the physiological characteristics of the involved knee (27). Future studies may consider a targeted approach to investigate the complex pain–biomechanics relationship, e.g., stratifying participants based on BMI and adjustment as practicable for confounding factors. They should also report factors such as knee compartment affected, calculation method of biomechanical variables, and the phase of gait biomechanical metrics were extracted from. We suggest a standardized use of pain assessment tools (such as WOMAC) including consistent scale, direction, and clear interpretation of results.

There are many strengths of our review. We developed and piloted a rigorous protocol that was registered prospectively. We conducted a comprehensive search of four databases and extracted all relevant biomechanical variables. Random-effects meta-analyses with large sample sizes were performed on multiple biomechanical variables with sensitivity analyses and metaregression.

There are some limitations of our review. We only considered cross-sectional relationships and associations between knee biomechanics and pain and did not include longitudinal data because of the small number of studies available during piloting. Radiographic diagnosis of knee OA was not required for inclusion (except for studies relating to the secondary aim). However, of the 36 studies relating to the primary aim, only 2 studies did not report using imaging (34,43), and they both required participants to meet the American College of Rheumatology clinical criteria for knee OA (91). We accepted studies regardless of walking speed, which is a potential confounder. However, 85% of studies reported self-selected walking speed, indicating that most studies asked participants to walk with a natural gait. We pooled studies regardless of KAM normalization or normalization method. In our meta-analyses, all studies reported KAM normalized to either body mass (Nm/kg) or body weight times height (%BW*Ht), except one (n = 20) (42) that reported unnormalized data. We deemed this

appropriate because of research indicating that weight explains 45% of the variance in the unnormalized KAM, whereas height only explains a further 3%, and significant correlations have been reported between the unnormalized KAM and both height and weight (92).

In conclusion, varus thrust was associated with almost 4-times greater odds of reporting pain in people with knee OA compared with those without varus thrust. Although we cannot currently establish causation, this finding is significant because varus thrust can be assessed and potentially modified clinically and early during the OA disease course. All other biomechanical variables assessed had a medium, a small, or no correlation with pain, which may render them clinically irrelevant. However, because of previously reported small r- and OR values for known factors associated with pain in those with knee OA and the complexity of assessing pain, small correlations between biomechanics and pain were not unexpected. We found that BMI significantly moderated the peak KAM–pain relationship, which reinforces the importance of considering BMI when implementing load-reducing interventions. High quality, longitudinal studies are required to comprehensively evaluate the relationship between knee biomechanics and pain. In the short term, clinical trials may focus on strategies to address varus thrust presence, KAM variables, and evaluate pain and disease progression outcomes.

ACKNOWLEDGMENTS

We acknowledge the technical assistance of Jim Matthews of the Sydney Informatics Hub, a core research facility of the University of Sydney, and Kanchana Ekanayake of the University of Sydney Library. We also acknowledge the authors of included studies who kindly responded to requests for further information and the study reviewers for providing thoughtful insights regarding our manuscript. Open access publishing facilitated by The University of Sydney, as part of the Wiley - The University of Sydney agreement via the Council of Australian University Librarians.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Ms. Hutchison had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Hutchison, Grayson, Hiller, Simic.
Acquisition of data. Hutchison, D'Souza, Kobayashi.
Analysis and interpretation of data. Hutchison, Grayson, Hiller, Simic.

REFERENCES

1. Cross M, Smith E, Hoy D, et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. Ann Rheum Dis 2014;73:1323–30.
2. Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: part II. Arthritis Rheum 2008;58:26–35.
3. Jüni P, Hari R, Rutjes AW, et al. Intra-articular corticosteroid for knee osteoarthritis. Cochrane Database Syst Rev 2015;2015:CD005328.
4. Sharma L, Cahue S, Song J, et al. Physical functioning over three years in knee osteoarthritis: role of psychosocial, local mechanical, and neuromuscular factors. Arthritis Rheum 2003;48:3359–70.
5. Park HM, Kim HS, Lee YJ. Knee osteoarthritis and its association with mental health and health-related quality of life: a nationwide cross-sectional study. Geriatr Gerontol Int 2020;20:379–83.
6. Losina E, Paltiel AD, Weinstein AM, et al. Lifetime medical costs of knee osteoarthritis management in the United States: impact of extending indications for total knee arthroplasty. Arthritis Care Res (Hoboken) 2015;67:203–15.
7. Van Manen MD, Nace J, Mont MA. Management of primary knee osteoarthritis and indications for total knee arthroplasty for general practitioners. J Am Osteopath Assoc 2012;112:709–15.
8. D'Souza N, Charlton J, Grayson J, et al. Are biomechanics during gait associated with the structural disease onset and progression of lower limb osteoarthritis? A systematic review and meta-analysis. Osteoarthritis Cartilage 2022;30:381–94.
9. Kutzner I, Trepczynski A, Heller MO, et al. Knee adduction moment and medial contact force: facts about their correlation during gait. PLoS One 2013;8:e81036.
10. Birmingham TB, Hunt MA, Jones IC, et al. Test–retest reliability of the peak knee adduction moment during walking in patients with medial compartment knee osteoarthritis. Arthritis Rheum 2007;57:1012–7.
11. Hinman RS, Wrigley TV, Metcalf BR, et al. Unloading shoes for osteoarthritis of the knee: protocol for the SHARK randomised controlled trial. BMC Musculoskelet Disord 2014;15:48.
12. Simic M, Hinman RS, Wrigley TV, et al. Gait modification strategies for altering medial knee joint load: a systematic review. Arthritis Care Res (Hoboken) 2011;63:405–26.
13. Arnold JB, Wong DX, Jones RK, et al. Lateral wedge insoles for reducing biomechanical risk factors for medial knee osteoarthritis progression: a systematic review and meta-analysis. Arthritis Care Res (Hoboken) 2016;68:936–51.
14. Moyer RF, Birmingham TB, Bryant DM, et al. Biomechanical effects of valgus knee bracing: a systematic review and meta-analysis. Osteoarthritis Cartilage 2015;23:178–88.
15. Chang A, Hayes K, Dunlop D, et al. Thrust during ambulation and the progression of knee osteoarthritis. Arthritis Rheum 2004;50:3897–903.
16. Neogi T. The epidemiology and impact of pain in osteoarthritis. Osteoarthritis Cartilage 2013;21:1145–53.
17. Fu K, Robbins SR, McDougall JJ, et al. Osteoarthritis: the genesis of pain. Rheumatology (Oxford) 2018;57 Suppl 4:iv43–50.
18. Miyazaki T, Wada M, Kawahara H, et al. Dynamic load at baseline can predict radiographic disease progression in medial compartment knee osteoarthritis. Ann Rheum Dis 2002;61:617–22.
19. Heiden TL, Lloyd DG, Ackland TR. Knee joint kinematics, kinetics and muscle co-contraction in knee osteoarthritis patient gait. Clin Biomech (Bristol, Avon) 2009;24:833–41.
20. Maly MR, Costigan PA, Olney SJ. Mechanical factors relate to pain in knee osteoarthritis. Clin Biomech (Bristol, Avon) 2008;23:796–805.
21. Astephen Wilson JL, Stanish WD, Hubley-Kozey CL, et al. Asymptomatic and symptomatic individuals with the same radiographic evidence of knee osteoarthritis walk with different knee moments and muscle activity. J Orthop Res 2017;35:1661–70.
22. Thorp LE, Sumner DR, Wimmer MA, et al. Relationship between pain and medial knee joint loading in mild radiographic knee osteoarthritis. Arthritis Rheum 2007;57:1254–60.
23. Papandony MC, Chou L, Seneviwickrama M, et al. Patients' perceived health service needs for osteoarthritis (OA) care: a scoping systematic review. Osteoarthritis Cartilage 2017;25:1010–25.

24. Butler RJ, Barrios JA, Royer T, et al. Frontal-plane gait mechanics in people with medial knee osteoarthritis are different from those in people with lateral knee osteoarthritis. Phys Ther 2011;91:1235–43.
25. Thoma LM, McNally MP, Chaudhari AM, et al. Differential knee joint loading patterns during gait for individuals with tibiofemoral and patellofemoral articular cartilage defects in the knee. Osteoarthritis Cartilage 2017;25:1046–54.
26. McAlindon TE, Snow S, Cooper C, et al. Radiographic patterns of osteoarthritis of the knee joint in the community: the importance of the patellofemoral joint. Ann Rheum Dis 1992;51:844–9.
27. Messier SP, Beavers DP, Herman C, et al. Are unilateral and bilateral knee osteoarthritis patients unique subsets of knee osteoarthritis? A biomechanical perspective. Osteoarthritis Cartilage 2016;24:807–13.
28. National Heart Lung and Blood Institute. Quality assessment tool for observational cohort and cross-sectional studies. URL: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools.
29. Juhl C, Lund H, Roos EM, et al. A hierarchy of patient-reported outcomes for meta-analysis of knee osteoarthritis trials: empirical evidence from a survey of high impact journals. Arthritis 2012;2012:136245.
30. Quintana DS. From pre-registration to publication: a non-technical primer for conducting a meta-analysis to synthesize correlational data. Front Psychol 2015;6:1549.
31. Higgins JP, Green, S, editors. Cochrane handbook for systematic reviews of interventions. Version 5.1.0. Hoboken (NJ): Wiley; 2011.
32. Walter JP, D'Lima DD, Colwell CW Jr, et al. Decreased knee adduction moment does not guarantee decreased medial contact force during gait. J Orthop Res 2010;28:1348–54.
33. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. New York (NY): Routledge; 1988.
34. Yang F, Liu W. Knee joint biomechanics of simplified 24 Tai Chi forms and association with pain in individuals with knee osteoarthritis: a pilot study. Osteoarthr Cartil Open 2021;3:100149.
35. Omori G, Narumi K, Nishino K, et al. Association of mechanical factors with medial knee osteoarthritis: a cross-sectional study from Matsudai Knee Osteoarthritis Survey. J Orthop Sci 2016;21:463–8.
36. Hunt MA, Birmingham TB, Bryant D, et al. Lateral trunk lean explains variation in dynamic knee joint load in patients with medial compartment knee osteoarthritis. Osteoarthritis Cartilage 2008;16:591–9.
37. Iijima H, Aoyama T, Eguchi R, et al. Effects of interaction between varus thrust and ambulatory physical activity on knee pain in individuals with knee osteoarthritis: an exploratory study with 12-month follow-up. Clin Rheumatol 2019;38:1721–9.
38. Henriksen M, Aaboe J, Bliddal H. The relationship between pain and dynamic knee joint loading in knee osteoarthritis varies with radiographic disease severity. A cross sectional study. Knee 2012;19:392–8.
39. Kudo K, Nagura T, Harato K, et al. Correlation between static limb alignment and peak knee adduction angle during gait is affected by subject pain in medial knee osteoarthritis. Knee 2020;27:348–55.
40. Mahmoudian A, van Dieën JH, Bruijn SM, et al. Dynamic and static knee alignment at baseline predict structural abnormalities on MRI associated with medial compartment knee osteoarthritis after 2 years. Gait Posture 2017;57:46–51.
41. Asay JL, Erhart-Hledik JC, Andriacchi TP. Changes in the total knee joint moment in patients with medial compartment knee osteoarthritis over 5 years. J Orthop Res 2018;36:2373–9.
42. Lewinson RT, Maag CP, Lun VM, et al. A three dimensional approach for quantifying resultant loading at the knee. Knee 2017;24:31–9.
43. Calder KM, Acker SM, Arora N, et al. Knee power is an important parameter in understanding medial knee joint load in knee osteoarthritis. Arthritis Care Res (Hoboken) 2014;66:687–94.
44. Hall M, Bennell KL, Wrigley TV, et al. The knee adduction moment and knee osteoarthritis symptoms: relationships according to radiographic disease severity. Osteoarthritis Cartilage 2017;25:34–41.
45. Hurwitz DE, Ryals AB, Case JP, et al. The knee adduction moment during gait in subjects with knee osteoarthritis is more closely correlated with static alignment than radiographic disease severity, toe out angle and pain. J Orthop Res 2002;20:101–7.
46. O'Connell M, Farrokhi S, Fitzgerald GK. The role of knee joint moments and knee impairments on self-reported knee pain during gait in patients with knee osteoarthritis. Clin Biomech (Bristol, Avon) 2016;31:40–6.
47. Sorensen TJ, Langberg H, Aaboe J, et al. The association between submaximal quadriceps force steadiness and the knee adduction moment during walking in patients with knee osteoarthritis. J Orthop Sports Phys Ther 2011;41:592–9.
48. Zifchock RA, Kirane Y, Hillstrom H, et al. Are joint structure and function related to medial knee OA pain? A pilot study. Clin Orthop Relat Res 2011;469:2866–73.
49. Erhart-Hledik J, Favre J, Andriacchi TP. New insight in the relationship between regional patterns of knee cartilage thickness, osteoarthritis disease severity, and gait mechanics. J Biomech 2015;48:3868–75.
50. Kito N, Shinkoda K, Kanemura N, et al. External knee adduction moment during stepping in subjects with medial knee osteoarthrits is correlated with pain and disability. Rigakuryoho Kagaku 2008;23:633–40.
51. Maly MR, Costigan PA, Olney SJ. Role of knee kinematics and kinetics on performance and disability in people with medial compartment knee osteoarthritis. Clin Biomech (Bristol, Avon) 2006;21:1051–9.
52. Moyer RF, Birmingham TB, Chesworth BM, et al. Alignment, body mass and their interaction on dynamic knee joint load in patients with knee osteoarthritis. Osteoarthritis Cartilage 2010;18:888–93.
53. Nie Y, Ma J, Huang Z, et al. Upper partial fibulectomy improves knee biomechanics and function and decreases knee pain of osteoarthritis: a pilot and biomechanical study. J Biomech 2018;71:22–9.
54. Nie Y, Wang H, Xu B, et al. The relationship between knee adduction moment and knee osteoarthritis symptoms according to static alignment and pelvic drop. Biomed Res Int. 2019;2019:7603249.
55. Weidenhielm L, Svensson OK, Brostrom LA, et al. Adduction moment of the knee compared to radiological and clinical parameters in moderate medical osteoarthrosis of the knee. Ann Chir Gynaecol 1994;83:236–42.
56. Ko SU, Ling SM, Schreiber C, et al. Gait patterns during different walking conditions in older adults with and without knee osteoarthritis: results from the Baltimore Longitudinal Study of Aging. Gait Posture 2011;33:205–10.
57. Kito N, Shinkoda K, Yamasaki T, et al. Contribution of knee adduction moment impulse to pain and disability in Japanese women with medial knee osteoarthritis. Clin Biomech (Bristol, Avon) 2010;25:914–9.
58. Robbins SM, Birmingham TB, Callaghan JP, et al. Association of pain with frequency and magnitude of knee loading in knee osteoarthritis. Arthritis Care Res (Hoboken) 2011;63:991–7.
59. Manetta J, Franz LH, Moon C, et al. Comparison of hip and knee muscle moments in subjects with and without knee pain. Gait Posture 2002;16:249–54.
60. Fukutani N, Iijima T, Fukumoto T, et al. Association of varus thrust with pain and stiffness and activities of daily, living in patients with medial knee osteoarthritis. Phys Ther 2016;96:167–75.
61. Iijima H, Fukutani N, Aoyama T, et al. Clinical phenotype classifications based on static varus alignment and varus thrust in Japanese patients with medial knee osteoarthritis. Arthritis Rheumatol 2015;67:2354–62.

62. Lo GH, Harvey WF, McAlindon TE. Associations of varus thrust and alignment with pain in knee osteoarthritis. Arthritis Rheum 2012;64:2252–9.
63. Robon MJ, Perell KL, Fang M, et al. The relationship between ankle plantar flexor muscle moments and knee compressive forces in subjects with and without pain. Clin Biomech (Bristol, Avon) 2000;15:522–7.
64. Bensalma F, Mezghani N, Ouakrim Y, et al. A multivariate relationship between the kinematic and clinical parameters of knee osteoarthritis population. Biomed Eng Online 2019;18:58.
65. Skou ST, Wrigley TV, Metcalf BR, et al. Association of knee confidence with pain, knee instability, muscle strength, and dynamic varus-valgus joint motion in knee osteoarthritis. Arthritis Care Res (Hoboken) 2014;66:695–701.
66. Toda H, Maruyama T, Fujita K, et al. Self-perception of the knee is associated with joint motion during the loading response in individuals with knee osteoarthritis: a pilot cross-sectional study. Sensors 2021;21:4009.
67. Nebel MB, Sims EL, Keefe FJ, et al. The relationship of self-reported pain and functional impairment to gait mechanics in overweight and obese persons with knee osteoarthritis. Arch Phys Med Rehabil 2009;90:1874–9.
68. Yamagata M, Taniguchi M, Tateuchi H, et al The effects of knee pain on knee contact force and external knee adduction moment in patients with knee osteoarthritis. J Biomech 2021;123:110538.
69. Chang A, Hochberg M, Song J, et al. Frequency of varus and valgus thrust and factors associated with thrust presence in persons with or at higher risk of developing knee osteoarthritis. Arthritis Rheum 2010;62:1403–11.
70. Kuroyanagi Y, Nagura T, Kiriyama Y, et al. A quantitative assessment of varus thrust in patients with medial knee osteoarthritis. Knee 2012;19:130–4.
71. Ogata K, Yasunaga M, Nomiyama H. The effect of wedged insoles on the thrust of osteoarthritic knees. Int Orthop 1997;21:308–12.
72. Okamoto T, Asaeda M, Kono Y, et al. Soft knee brace for medial osteoarthritis knee reduces the amount of lateral thrust using gait analysis. Prosthet Orthot Int 2015;1:247. http://dx.doi.org/10.1177/0309364615591101.
73. Hunt MA, Schache AG, Hinman RS, et al. Varus thrust in medial knee osteoarthritis: quantification and effects of different gait-related interventions using a single case study. Arthritis Care Res (Hoboken) 2011;63:293–7.
74. Tang AC, Tang SF, Hong WH, et al. Kinetics features changes before and after intra-articular hyaluronic acid injections in patients with knee osteoarthritis. Clin Neurol Neurosurg 2015;129 Suppl 1:S21–6.
75. Briem K, Axe MJ, Snyder-Mackler L. Medial knee joint loading increases in those who respond to hyaluronan injection for medial knee osteoarthritis. J Orthop Res 2009;27:1420–5.
76. Schnitzer TJ, Popovich JM, Andersson GB, et al. Effect of piroxicam on gait in patients with osteoarthritis of the knee. Arthritis Rheum 1993;36:1207–13.
77. Seeley MK, Park J, King D, et al. A novel experimental knee-pain model affects perceived pain and movement biomechanics. J Athl Train 2013;48:337–45.
78. Simic M, Wrigley TV, Hinman RS, et al. Altering foot progression angle in people with medial knee osteoarthritis: the effects of varying toe-in and toe-out angles are mediated by pain and malalignment. Osteoarthritis Cartilage 2013;21:1272–80.
79. Robbins SM, Maly MR. The effect of gait speed on the knee adduction moment depends on waveform summary measures. Gait Posture 2009;30:543–6.
80. Browning RC, Kram R. Effects of obesity on the biomechanics of walking at different speeds. Med Sci Sports Exerc 2007;39:1632–41.
81. Cicuttini FM, Wluka AE. Not just loading and age: the dynamics of osteoarthritis, obesity and inflammation. Med J Aust 2016;204:47.
82. Sylwander C, Larsson I, Haglund E, et al. Pressure pain thresholds in individuals with knee pain: a cross-sectional study. BMC Musculoskelet Disord 2021;22:516.
83. Brisson NM, Wiebenga EG, Stratford PW, et al. Baseline knee adduction moment interacts with body mass index to predict loss of medial tibial cartilage volume over 2.5 years in knee osteoarthritis. J Orthop Res 2017;35:2476–83.
84. Rogers MW, Wilder FV. The association of BMI and knee pain among persons with radiographic knee osteoarthritis: a cross-sectional study. BMC Musculoskelet Disord 2008;9:163.
85. Cho Y, Jung B, Lee YJ, et al. Association between sleep duration and osteoarthritis and their prevalence in Koreans: a cross-sectional study. PLoS One 2020;15:e0230481.
86. Iijima H, Aoyama T, Fukutani N, et al. Psychological health is associated with knee pain and physical function in patients with knee osteoarthritis: an exploratory cross-sectional study. BMC Psychol 2018;6:19.
87. Nikolic G, Nedeljkovic B, Trajkovic G, et al. Pain, physical function, radiographic features, and quality of life in knee osteoarthritis agricultural workers living in rural population. Pain Res Manag 2019;2019:7684762.
88. Inoue R, Ishibashi Y, Tsuda E, et al. Knee osteoarthritis, knee joint pain and aging in relation to increasing serum hyaluronan level in the Japanese population. Osteoarthritis Cartilage 2011;19:51–7.
89. Younger J, McCue R, Mackey S. Pain outcomes: a brief review of instruments and techniques. Curr Pain Headache Rep 2009;13:39–43.
90. Birmingham TB, Marriott KA, Leitch KM, et al. Association between knee load and pain: within-patient, between-knees, case-control study in patients with knee osteoarthritis. Arthritis Care Res (Hoboken) 2019;71:647–50.
91. Altman R, Asch E, Bloch D, et al. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Arthritis Rheum 1986;29:1039–49.
92. Moisio KC, Sumner DR, Shott S, et al. Normalization of joint moments during gait: a comparison of two techniques. J Biomech 2003;36:599–603.