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Relation of Temporal Asymmetry During Walking to Two-Year Knee Pain Outcomes in Those With Mild-to-Moderate Unilateral Knee Pain: An Exploratory Analysis From the Multicenter Osteoarthritis Study.

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Authors
Corrigan, Patrick
Felson, David
Lewis, Cara
et al.

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Relation of temporal asymmetry during walking to 2-year knee pain outcomes in those with mild-to-moderate unilateral knee pain: an exploratory analysis from the Multicenter Osteoarthritis (MOST) Study

Patrick Corrigan, DPT, PhD[1,2], **David T. Felson, MD, MPH**[3], **Cara L. Lewis, PT, PhD**[4], **Tuhina Neogi, MD, PhD**[3], **Michael P. LaValley, PhD**[5], **K. Doug Gross, DPT, ScD**[6], **Michael C. Nevitt, PhD, MPH**[7], **Cora E. Lewis, MD, MSPH**[8], **James C. Torner, PhD**[9], **Joshua J. Stefanik, MSPT, PhD**[1]

[1]Department of Physical Therapy, Movement and Rehabilitation Sciences, Northeastern University, Boston, Massachusetts;

[2]Department of Physical Therapy and Athletic Training, Saint Louis University, St. Louis, Missouri;

[3]Section of Rheumatology, Boston University School of Medicine, Boston, Massachusetts;

[4]Department of Physical Therapy & Athletic Training, Boston University, Boston, Massachusetts;

[5]Boston University School of Public Health, Boston, Massachusetts;

[6]Department of Physical Therapy, MGH Institute of Health Professions, Boston, Massachusetts;

[7]Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, California;

[8]Department of Epidemiology, University of Alabama at Birmingham, Birmingham, Alabama;

[9]Department of Epidemiology, University of Iowa, Iowa City, Iowa

Abstract

Objective —– We aimed to 1) explore the cross-sectional relation of unilateral knee pain severity and temporal asymmetry during walking and 2) determine relations of temporal asymmetry during walking to 2-year changes in ipsilateral and contralateral knee pain in those with mild-to-moderate unilateral knee pain.

Methods —– The Multicenter Osteoarthritis Study is a prospective cohort study of adults with or at risk for knee osteoarthritis. The current study included participants with unilateral knee

Corresponding Author: Joshua J. Stefanik, 360 Huntington Ave, 457 Richards Hall, Boston, MA, USA, 02115, j.stefanik@northeastern.edu, Phone: 617-373-8934.

Author Contributions:

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CONFLICTS OF INTEREST

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pain. Gait was assessed during self-selected and fast walking at baseline. Knee pain was assessed at baseline and 2-years. We calculated limb symmetry indices (LSIs; non-painful limb/painful limb×100) for stance, single limb support, and double limb support times then examined their relations to 1) unilateral knee pain severity, 2) incident contralateral knee pain, and 3) persistent ipsilateral knee pain.

Results ––Unilateral knee pain severity was not associated with temporal asymmetry during self-selected or fast walking. At 2-years, 17.1% had incident contralateral knee pain and 51.4% had persistent ipsilateral knee pain. For self-selected walking, greater LSIs (i.e., longer time on the non-painful limb) for stance and single limb support were associated with decreased odds of incident contralateral knee pain. Measures of temporal asymmetry were not associated with persistent ipsilateral knee pain, except for single limb support during fast walking.

Conclusion ––For those with unilateral knee pain, temporal asymmetry during walking is not associated with pain severity. However, select measures of stance and single limb support during self-selected and fast walking relate to longitudinal knee pain outcomes.

1. INTRODUCTION

Knee osteoarthritis (OA) is a leading cause of pain and disability that accounts for an estimated 83% of the total burden of OA (1–3). In many cases, knee OA begins as a unilateral disease (4). Yet, nearly 90% of those with unilateral knee OA progress to bilateral knee OA within 10 years (5). The progression to bilateral knee OA is concerning because it is associated with worse function, pain, and quality of life (6–8). Furthermore, bilateral knee OA may be associated with higher healthcare costs if both knees require treatment. To this end, a critical need exists for understanding the pathway from unilateral to bilateral knee OA.

If pain affects the way persons with unilateral knee OA walk, it may play a role in the progression from unilateral to bilateral OA (i.e., unilateral knee OA → unilateral knee pain → altered walking pattern that increases loading of the contralateral knee → bilateral knee OA). Research has shown that individuals with unilateral knee OA load their painful/affected knee less than their non-painful/unaffected knee while walking (9–11). However, there have been inconsistent findings when comparing biomechanical asymmetries between those with unilateral knee OA, bilateral knee OA, and healthy controls (12–14). These inconsistencies may be attributed to defining knee OA in different ways (i.e., based on structure and/or symptoms). Currently, it remains unclear if knee pain severity explains asymmetric walking patterns in those with unilateral knee OA. This is important because increased loading is associated with OA progression (15–19) and walking is commonly recommended for managing symptoms of knee OA (20–22).

Regardless of the cause, increased time on the non-painful limb relative to the painful limb may hasten the progression from unilateral to bilateral knee OA. Ideally, measures of knee joint loading would be used to quantify asymmetric walking. However, it is not feasible to directly measure or estimate knee joint loads in most clinical settings. One of the simplest ways to quantify asymmetry during walking is with temporal measures. Even though temporal measures have not been established as surrogates of knee joint loading, they are readily available to clinicians with access to wearable and portable technologies (e.g., spatiotemporal gait mats, inertial measurement units, accelerometers, pressure-sensing shoe inserts). Therefore, exploring the relation of temporal asymmetry to longitudinal knee pain outcomes may improve our understanding of the pathway from unilateral to bilateral knee OA and provide clinicians with temporal measures that can be targeted throughout rehabilitation to optimize patient outcomes.

The first objective of the current study was to explore the cross-sectional relation of unilateral knee pain severity and temporal asymmetry during walking. We hypothesized that more severe unilateral knee pain would be associated with 1) relatively longer stance and single limb support times on the non-painful limb compared to the painful limb and 2) relatively shorter double limb support time on the non-painful limb compared to the painful limb. The second objective was to determine relations of temporal asymmetry during walking to 2-year changes in ipsilateral and contralateral knee pain in those with mild-to-moderate unilateral knee pain. We hypothesized that relatively longer stance and single limb support times on the non-painful limb compared to the painful limb as well as relatively shorter double limb support times on the non-painful limb compared to the painful limb would be associated with 1) increased odds of incident knee pain in the non-painful limb (i.e., incident contralateral knee pain) and 2) decreased odds of persistent knee pain in the painful limb (i.e., persistent ipsilateral knee pain).

2. METHODS

2.1. Study Design and Sample

The Multicenter Osteoarthritis (MOST) Study is a NIH-funded prospective cohort study of 3,026 individuals, aged 50–79 years, with or at risk for knee OA. Participants were recruited for their initial clinic visit from 2003 to 2005 in two communities in the United States: Birmingham, Alabama and Iowa City, Iowa. Full details about the MOST cohort can be found elsewhere (23). Ethics approval was obtained from the institutional review boards at each of the study sites and all participants provided written consent after study procedures and risks were disclosed. The current study used data from clinic visits that occurred 60- and 84-months after the initial clinic visit. The 60-month clinic visit was the baseline visit for the current study because this was the first time point where gait data were collected in the MOST cohort.

For the current study, individuals with unilateral knee pain at the 60-month clinic visit were included. Unilateral knee pain was defined as only one knee having at least mild pain with walking as reported on the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and the same knee having a score greater than zero on the Visual Analog Scale (VAS; 0–100). Individuals were excluded from all analyses for the following reasons: 1) incomplete or invalid gait data at the 60-month clinic visit, 2) had a VAS pain score greater than zero for their contralateral knee at the 60-month clinic visit, 3) reported buttock, hip, thigh, leg, ankle, or foot pain during the gait evaluation at the 60-month clinic visit, 4) underwent a hip or knee joint replacement surgery before the 60-month clinic visit, and 5) had missing covariate data. For longitudinal analyses, we additionally excluded those who:

1) withdrew or passed away before the 84-month clinic visit, 2) had missing outcome data, and 3) underwent a hip or knee joint replacement surgery before the 84-month clinic visit.

2.2. Measures

2.2.1. Temporal Asymmetry during Walking—Participants completed four self-selected and four fast walking trials over a 4.9-meter pressure-sensitive GAITRite walkway (CIR Systems, Inc., Franklin, NJ, USA) in their normal walking shoes. For the self-selected trials, participants walked at a comfortable and unhurried speed. After self-selected trials were completed, fast trials were performed. For the fast trials, participants walked as if they were late for an important meeting. All trials started and stopped 1.5 meters before and after the GAITRite walkway to avoid collecting data during acceleration and deceleration.

Mean stance, single limb support, and double limb support times were calculated for each limb by averaging the measures for each step on the GAITRite walkway. Stance time was defined as the duration between initial contact and terminal stance. Single limb support time was defined as the duration in stance where the contralateral limb was in swing (i.e., single limb on the ground). Double limb support time was defined as the duration in stance where the contralateral limb was also in stance (i.e., both limbs on the ground). Importantly, previous literature shows that the GAITRite walkway has excellent test-retest reliability (Intraclass correlation coefficients ≥ 0.89) and validity for temporal measures of gait (24, 25).

To quantify the degree of asymmetry in stance, single limb support, and double limb support, we calculated limb symmetry indices (LSI). For this, the measures from the non-painful limb were divided by the measures from the painful limb and then multiplied by 100 to transform the ratio into a percentage. This method of calculating LSI was used because it is common in clinical practice and easy to interpret. Although we kept LSI values continuous for all analyses, LSI values >100% indicated relatively longer times on the non-painful limb, LSI values <100% indicated relatively longer times on the painful limb, and LSI values of 100% indicated equal times.

Based on our hypotheses, we expected higher LSI values for stance and single limb support times to be associated with 1) more severe unilateral knee pain, 2) increased odds of knee pain in the non-painful limb two years later, and 3) decreased odds of still having knee pain in the painful limb two years later. Furthermore, we expected lower LSI values for double limb support time to be associated with these outcomes.

2.2.2. Unilateral Knee Pain Severity—To determine the cross-sectional relation of unilateral knee pain severity and temporal asymmetry during walking, VAS pain scores for the painful knee at the 60-month clinic visit were used. VAS pain scores were obtained by having participants mark an “X” on a zero to 100 scale in response to the question “How bad has the pain been in your knee, on average, in the past 30 days?” A score of zero indicated no pain, while a score of 100 indicated pain as bad as it could be. This same question was used for determining study eligibility and longitudinal outcomes.

2.2.3. Incident Contralateral Knee Pain—

Incident contralateral knee pain was defined as the non-painful knee at the 60-month clinic visit having at least mild pain with walking (WOMAC) or a VAS pain score of at least 20 at the 84-month clinic visit. Because individuals in the current study sample had contralateral VAS pain scores of zero at the 60-month clinic visit, a score of at least 20 at the 84-month clinic visit was used because a 20-point change in VAS is a clinically relevant increase in pain for those with knee OA (26).

2.2.4. Persistent Ipsilateral Knee Pain—

Persistent ipsilateral knee pain was defined when the painful knee at the 60-month clinic visit continued to have at least mild pain with walking (WOMAC) and a VAS pain score greater than zero at the 84-month clinic visit. In other words, the originally painful knee remained painful two years later.

2.3. Analytic Approach

Descriptive statistics were calculated for each variable. Continuous measures were reported as means and standard deviations. Categorical variables were reported as percentages and frequencies.

We determined the cross-sectional relation of unilateral knee pain severity and temporal asymmetry during walking with unadjusted and adjusted linear regression models. Adjusted models accounted for age (years), sex (female/male), body mass (kg), race (white/other), the presence of depressive symptoms (Center for Epidemiologic Studies Depression scale ≥16), gait speed (m/s), and Kellgren Lawrence (KL) grades for both knees. Associations were determined separately for self-selected and fast walking conditions. To assist with interpretation of effect estimates, beta coefficients were calculated per 20-unit increase in VAS pain scores.

To determine the longitudinal relations of temporal asymmetry during walking to 1) incident contralateral knee pain and 2) persistent ipsilateral knee pain, we used unadjusted and adjusted logistic regression models. Loess procedures were used to confirm the exposures were linearly associated with our outcomes. Similar to the cross-sectional analyses, adjusted models accounted for age, sex, body mass, race, the presence of depressive symptoms, gait speed, and KL grades. For each outcome, odds ratios (OR) and 95% confidence intervals (CI) were determined per 2.5-unit increase in exposure (i.e., 2.5% increase in LSI values). Because previous literature suggests that an absolute LSI >105% is a meaningful amount of asymmetry (27), we attempted to estimate our effects per 5-unit increase in exposure. However, in order to avoid estimating beyond the range of our data, a 2.5-unit increase was chosen. Since measures of temporal asymmetry were quantified during self-selected and fast walking trials, models were repeated for each exposure definition separately. In sensitivity analyses, we also adjusted for average steps per day, which was measured in the MOST Study with a StepWatch Activity Monitor (Orthocare Innovations, Mountlake Terrace, WA) worn for seven consecutive days.

All analyses were performed in SAS (version 9.4; SAS Institute Inc.; Cary, NC, USA). For cross-sectional analyses, significant level was set a priori to less than 0.05. For longitudinal analyses, significant associations were determined by confidence intervals not crossing 1.0.

3. RESULTS

3.1. Study Sample

Of the 3026 persons with or at risk for knee OA in the parent MOST Study, 127 were eligible for the cross-sectional analyses. Of those 127, 105 were subsequently eligible for the longitudinal analyses. Figure 1 shows the number of individuals excluded by study criterion. Participant characteristics can be found in Table 1 for those who were eligible. Additionally, a summary of the gait data collected at the 60-month clinic visit can be found in Table 2.

3.2. Cross-sectional relation of unilateral knee pain severity to temporal asymmetry during self-selected and fast walking

At both self-selected and fast walking speeds, unilateral knee pain severity was not significantly associated with LSIs for stance time, single limb support time, or double limb support time (Figure 2).

3.3. 2-year knee pain outcomes

Out of the 105 participants with unilateral knee pain at the 60-month clinic visit who were eligible for longitudinal analyses, 18 (17.1%) had contralateral knee pain (at least mild pain with walking or a VAS pain score of at least 20) and 54 (51.4%) had persistent ipsilateral knee pain (at least mild pain with walking and a VAS pain score greater than zero) at the 84-month clinic visit. Results for each longitudinal analysis are reported in Table 3. Notably, after adjusting for age, sex, body mass, race, depressive symptoms, gait speed, and KL grades, a 2.5% increase in stance and single limb support LSIs during self-selected walking were associated with a 51% (OR=0.49; 95% CI=0.27–0.91) and 37% (OR=0.63, 95% CI=0.41–0.96) decreased odds of incident contralateral knee pain, respectively. Double limb support time LSI was not significantly associated with incident contralateral knee pain (Table 3). Furthermore, temporal measures during fast walking were not associated with incident contralateral knee pain (Table 3).

Temporal asymmetry measures were not associated with persistent ipsilateral knee pain, except for single limb support LSI during fast walking when adjusting for average steps per day (Table 3). This relation showed that a 2.5% increase in single limb support LSI is associated with a 59% (OR=1.59, 95% CI=1.05–2.41) increased odds of persistent ipsilateral knee pain.

When adding average steps per day to the models in sensitivity analyses, confidence intervals widened and point estimates changed slightly for each outcome (Table 3). The only exceptions where the point estimates appeared to change more than slightly were for relations of single limb support time and for stance time during fast walking (Table 3).

4. DISCUSSION

The objectives of this study were to determine if unilateral knee pain is associated with temporal asymmetry while walking, and subsequently if the degree of temporal asymmetry influences knee pain outcomes two years later. Our findings indicate that the severity of unilateral knee pain is not related to temporal asymmetry while walking at self-selected or fast speeds in persons with mostly mild or moderate knee pain. In other words, individuals with moderate unilateral knee pain do not spend more time on their contralateral limb during walking any more than those with mild pain. Because our sample for cross-sectional analyses included only one individual with severe knee pain with walking, further work is needed to determine if more severe knee pain has a greater effect on temporal asymmetry. From our longitudinal analyses, we found that relatively longer stance and single limb support times on the non-painful limb were protective against developing contralateral knee pain in those with unilateral knee pain. On the other hand, spending relatively more time in single limb support on the contralateral limb during fast walking was associated with persistent pain in the originally painful knee. Taken together, measures of temporal asymmetry during self-selected and fast walking may be useful for predicting knee pain outcomes.

Prior to determining if temporal asymmetry during walking influenced knee pain outcomes two years later, we were interested in understanding how unilateral knee pain severity affects temporal asymmetry. Because antalgic gait (i.e., a pain-avoidant walking pattern defined by spending more time on the non-painful limb compared to the painful limb) is a hallmark sign of unilateral lower body pain that seems more pronounced in those with worse pain, we hypothesized that more severe unilateral knee pain would be associated with relatively longer stance and single limb support times on the non-painful limb and relatively shorter double limb support times on the non-painful limb. Surprisingly, we found that unilateral knee pain severity was not associated with measures of temporal asymmetry. The lack of association may be a result of how the walking evaluation was performed and who was included in the sample. Specifically, because the walking evaluation was brief, it may not have triggered pain or gait modifications. As for the sample, relationships may have been more evident if individuals with severe or extreme unilateral knee pain with walking were included. Upon further analysis, we determined that our sample was predominantly individuals with mild or moderate unilateral knee pain because persons in the MOST cohort with severe or extreme knee pain with walking had at least some pain in their contralateral knee, which made them ineligible for the current study. Another characteristic of the sample that may have affected our results is chronicity of pain. Little is known in this area, but chronic knee pain may affect walking patterns differently than acute knee pain.

We expected the non-painful limb to have longer stance and single limb support times and shorter double limb support times relative to the painful limb and be associated with greater odds of developing knee pain in the non-painful limb. This hypothesis was grounded in prior research showing that increased loading contributes to knee OA progression (14–18). Our results indicate that relatively longer stance and single limb support times on the non-painful limb do not increase the likelihood of developing contralateral knee pain in those with mild-to-moderate unilateral knee pain. In fact, the directionality of the associations suggest that spending relatively more time on non-painful limb is protective against developing contralateral knee pain. This raises the possibility that increased stance and single limb support times could be associated with loading the knee in a way that is beneficial to the joint. For example, longer stances times may be associated with greater overall load (i.e., total impulse) per step, but reduced peak forces and loading rates, which have been historically considered harmful to the knee joint (28, 29). On the other hand, our assumption that increased loading is harmful to the joint should be challenged in future research. The idea, however, that increased loading may be beneficial should not be considered novel as physical therapy, physical activity, and walking programs increase loading and are recommended for the management of knee OA (19–21).

As for the originally painful knee, we expected the odds of persistent pain to be reduced for those who walk with relatively longer stance and single limb support times as well as shorter double limb support times on the non-painful limb. We hypothesized that pain would improve because these temporal patterns suggest that load is being shifted away from the painful knee. Contrary to our expectations, the results showed that measures of temporal asymmetry at self-selected walking speed are not associated with the originally painful knee still being painful two years later. This finding is surprising because it suggests that individuals with mild-to-moderate unilateral knee pain who spend more time on their non-painful limb while walking are just as likely to have continued pain as those who spend more time on their painful limb or neither limb (i.e., relatively symmetric). When considering this alongside the fact that 51% of our sample no longer had pain in their originally painful limb 2 years later, it seems possible that our results could have been affected by including those with persistent or transient knee pain. Future work in this area is needed to understand how different pain patterns influence walking patterns and their downstream effects. It is worth noting, however, that spending more relative time in single limb support on the contralateral limb during fast walking increased the odds of having continued ipsilateral knee pain when accounting for physical activity.

There are several limitations to consider for this study. Our primary limitation is that our sample included only individuals with mild or moderate pain with walking. We expected that more persons from the MOST cohort would have severe or extreme unilateral knee pain with walking. Likely because of this, our sample largely demonstrated only subtle temporal asymmetries. With only limited distributions, we were limited in our ability to evaluate its relation to the pain outcomes of interest, which themselves had low incidence over two years. To advance our understanding about the pathway from unilateral to bilateral knee OA, future research may need to either evaluate walking differently or include individuals with more severe pain. Another limitation is that temporal measures of gait may not be good surrogates for knee joint loading, and therefore may not capture the construct we are trying to assess. Future research should aim to elucidate relations between gait metrics that are simple to obtain in clinical and real-world settings (i.e., spatiotemporal measures) and estimates of knee joint loading. Without a better understanding of these relations, we may fail to leverage metrics provided by wearable and portable technologies for improving outcomes for individuals with knee OA. Another limitation of our study is that two years may not be enough time for gait modifications to influence outcomes. Additionally, the gait assessment may have been too short for asymmetric stance time to be identified since it may require longer duration of walking before such asymmetry may become evident. Regardless, this is the first study to leverage longitudinal, prospective data to assess cross-sectional and longitudinal relations of temporal asymmetry to pain outcomes in those with unilateral knee pain. Another limitation is that our sensitivity analyses that included physical activity may have been underpowered. Only 79% (n=84) of our sample had valid physical activity data, which lowered our sample size and limited our power by adding it as a covariate.

Future biomechanics research in knee OA should strongly consider not only the quality of movement, but also the quantity.

In conclusion, for those with mild-to-moderate unilateral knee pain, spending relatively more time in stance and single limb support on the non-painful limb can be considered a biomarker associated with the contralateral knee remaining pain-free. However, it does not appear to be a biomarker for having persistent pain in the already painful knee. These findings suggest that measures of temporal asymmetry hold little value in explaining the progression from unilateral to bilateral knee OA. Further research is needed to elucidate the mechanisms that explain why nearly every individual with unilateral knee OA progresses to bilateral disease.

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Significance and Innovations

1. Temporal measures of gait may be surrogates of limb loading that clinicians can use to detect aberrant gait patterns in those with knee pain or osteoarthritis.
2. Temporal asymmetry during walking is not associated with pain severity in those with unilateral knee pain.
3. For those with unilateral knee pain, spending relatively more time on the non-painful limb while walking is associated with a decreased risk of developing contralateral knee pain and an increased risk of continuing to have ipsilateral knee pain.

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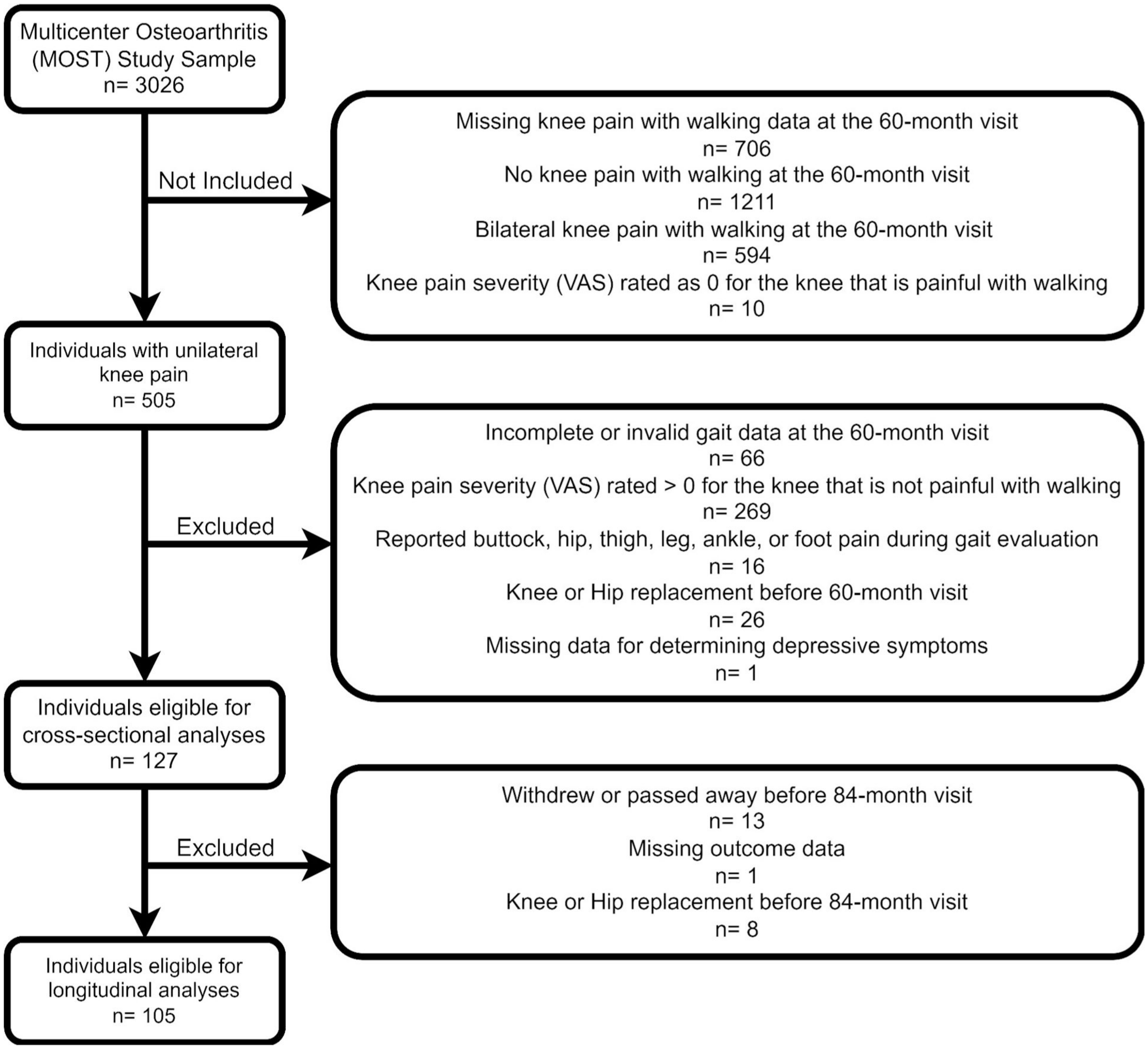

Figure 1.
Study Eligibility Flow Chart

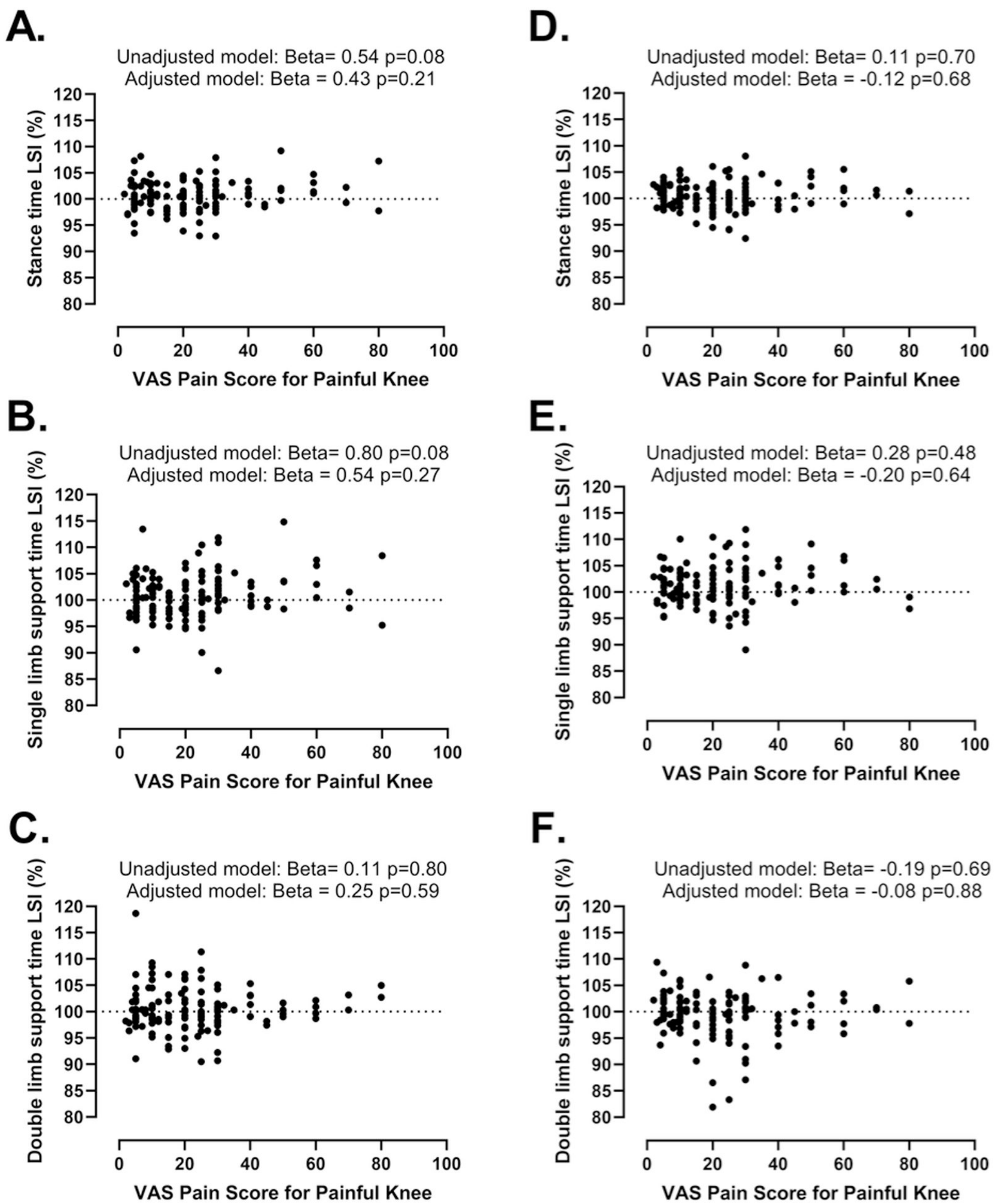

Figure 2.

Cross-sectional relations of unilateral knee pain severity to measures of temporal asymmetry in stance (A&D), single limb support (B&E), and double limb support (C&F) during self-selected (A-C) and fast (D-F) walking. Beta coefficients are reported per 20-unit increase in Visual Analog Scale (VAS) pain score. Adjusted models included age, sex, body mass, race, the presence of depressive symptoms, gait speed, and KL grades as covariates.

Table 1.

Participant Characteristics

	Cross-sectional Analyses (n=127)	Longitudinal Analyses (n=105)
Age (years); mean (SD)	66.4 (7.2)	65.5 (6.6)
Height (cm); mean (SD)	169.8 (9.6)	170.2 (9.0)
Body mass (kg); mean (SD)	85.7 (18.1)	86.3 (17.9)
Female; n (%)	68 (53.5)	57 (54.3)
White; n (%)	115 (90.6)	95 (90.5)
Depressive Symptoms; n (%)	14 (11.0)	10 (9.5)
Average Steps per day; mean (SD)	7224 (2777) *	7335 (2841) †
Kellgren Lawrence Grades for the Painful Knee		
0; n (%)	35 (27.6)	33 (31.4)
1; n (%)	15 (11.8)	12 (11.4)
2; n (%)	25 (19.7)	19 (18.1)
3; n (%)	34 (26.8)	29 (27.6)
4; n (%)	18 (14.2)	12 (11.4)
Kellgren Lawrence Grades for the Nonpainful Knee		
0; n (%)	61 (48.0)	56 (53.3)
1; n (%)	31 (24.4)	23 (21.9)
2; n (%)	18 (14.2)	15 (14.3)
3; n (%)	17 (13.4)	11 (10.5)
4; n (%)	0 (0)	0 (0)
VAS for the Painful Knee (0–100):		
Baseline; mean (SD)	22.5 (16.8)	19.8 (13.7)
2-year Follow-up; mean (SD)	N/A	17.6 (19.1)
VAS for the Nonpainful Knee (0–100)		
Baseline; mean (SD)	0 (0)	0 (0)
2-year Follow-up; mean (SD)	N/A	5.0 (11.1)
Pain with Walking for the Painful Knee (WOMAC):		
Baseline:		
None; n (%)	0 (0)	0 (0)
Mild; n (%)	106 (83.46)	90 (85.71)
Moderate; n (%)	20 (15.75)	15 (14.29)
Severe; n (%)	1 (0.79)	0 (0)
Extreme; n (%)	0 (0)	0 (0)
2-year Follow-up:		
None; n (%)	N/A	50 (47.62)
Mild; n (%)	N/A	42 (40.00)
Moderate; n (%)	N/A	12 (11.43)
Severe; n (%)	N/A	1 (0.95)
Extreme; n (%)	N/A	0 (0)
Pain with Walking for the Nonpainful Knee (WOMAC):		

	Cross-sectional Analyses (n=127)	Longitudinal Analyses (n=105)
Baseline:		
None; n (%)	127 (100)	105 (100)
Mild; n (%)	0 (0)	0 (0)
Moderate; n (%)	0 (0)	0 (0)
Severe; n (%)	0 (0)	0 (0)
Extreme; n (%)	0 (0)	0 (0)
2-year Follow-up:		
None; n (%)	N/A	90 (85.71)
Mild; n (%)	N/A	14 (13.33)
Moderate; n (%)	N/A	0 (0)
Severe; n (%)	N/A	1 (0.95)
Extreme; n (%)	N/A	0 (0)

* – sample size of 100 due to missing or invalid physical activity data

† – sample size of 84 due to missing or invalid physical activity data

VAS – Visual Analog Scale

WOMAC – Western Ontario and McMaster Universities Arthritis Index

Table 2.

Temporal measures of gait during self-selected and fast walking in adults with unilateral knee pain

	Cross-sectional Analyses (n=127)	Longitudinal Analyses (n=105)
Self-Selected Walking		
Gait speed (m/s); mean (SD)	1.20 (0.16)	1.21 (0.16)
Stance time for painful limb (ms); mean (SD)	702.7 (66.3)	703.1 (68.8)
Stance time for non-painful limb (ms); mean (SD)	706.8 (65.6)	706.5 (68.4)
Stance time LSI (%); mean (SD)	100.6 (2.9)	100.5 (2.8)
Single limb support time for painful limb (ms); mean (SD)	423.9 (39.7)	423.8 (39.6)
Single limb support time for non-painful limb (ms); mean (SD)	427.6 (38.9)	427.0 (39.2)
Single limb support time LSI (%); mean (SD)	101.0 (4.3)	100.8 (4.1)
Double limb support time for painful limb (ms); mean (SD)	278.8 (48.1)	279.2 (49.4)
Double limb support time for non-painful limb (ms); mean (SD)	279.3 (46.3)	279.5 (47.7)
Double limb support time LSI (%); mean (SD)	100.4 (4.1)	100.3 (4.2)
Fast Walking		
Gait speed (m/s); mean (SD)	1.62 (0.21)	1.64 (0.21)
Stance time for painful limb (ms); mean (SD)	581.0 (61.7)	577.4 (63.7)
Stance time for non-painful limb (ms); mean (SD)	583.7 (63.1)	580.6 (64.9)
Stance time LSI (%); mean (SD)	100.5 (2.6)	100.6 (2.4)
Single limb support time for painful limb (ms); mean (SD)	373.8 (35.1)	372.4 (35.3)
Single limb support time for non-painful limb (ms); mean (SD)	378.0 (36.0)	376.9 (36.2)
Single limb support time LSI (%); mean (SD)	101.2 (3.7)	101.2 (3.6)
Double limb support time for painful limb (ms); mean (SD)	207.2 (41.2)	205.0 (42.4)
Double limb support time for non-painful limb (ms); mean (SD)	205.7 (41.1)	203.7 (42.0)
Double limb support time LSI (%); mean (SD)	99.4 (4.4)	99.5 (4.3)

LSI – Limb symmetry index (non-painful/painful*100)

Table 3.

Relation of temporal asymmetry measures during self-selected and fast walking to 2-year knee pain outcomes

	Incident Contralateral Knee Pain			Persistent Ipsilateral Knee Pain		
	Unadjusted OR (95%CI)	**Adjusted OR (95%CI)***	**Adjusted OR (95%CI)†**	**Unadjusted OR (95%CI)**	**Adjusted OR (95% CI)***	**Adjusted OR (95%CI)†**
Self-Selected Walking						
Stance time LSI	**0.57 (0.35–0.94)**	**0.49 (0.27–0.91)**	0.46 (0.17–1.23)	1.11 (0.79–1.56)	1.07 (0.75–1.53)	1.22 (0.79–1.89)
Single limb support time LSI	0.78 (0.56–1.08)	**0.63 (0.41–0.96)**	**0.37 (0.14–0.98)**	1.25 (0.97–1.60)	1.22 (0.95–1.58)	1.30 (0.93–1.82)
Double limb support time LSI	0.76 (0.54–1.09)	0.86 (0.59–1.25)	0.92 (0.58–1.44)	0.79 (0.61–1.02)	0.77 (0.58–1.00)	0.87 (0.65–1.17)
Fast Walking						
Stance time LSI	0.58 (0.33–1.00)	0.52 (0.25–1.11)	0.59 (0.20–1.75)	1.24 (0.83–1.86)	1.33 (0.86–2.08)	1.68 (0.97–2.91)
Single limb support time LSI	0.72 (0.49–1.05)	0.67 (0.41–1.09)	0.67 (0.41–1.09)	1.27 (0.96–1.68)	1.32 (0.96–1.82)	**1.59 (1.05–2.41)**
Double limb support time LSI	0.97 (0.73–1.30)	1.05 (0.75–1.48)	0.97 (0.60–1.58)	0.93 (0.74–1.16)	0.97 (0.76–1.25)	1.00 (0.76–1.31)

All odds ratios and 95% confidence intervals are reported per 2.5% increase in exposure.

* – Models adjusted for age, sex, body mass, race, the presence of depressive symptoms, gait speed, and Kellgren Lawrence grades;

† – Models additionally adjusted for average steps per day. Sample size of 84 due to missing or invalid physical activity data.

LSI – Limb symmetry index (non-painful/painful*100)