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Concurrent foot pain is common in people with knee osteoarthritis and impacts health and functional status: data from the Osteoarthritis Initiative

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Abstract

Objective—To document the prevalence of foot pain and foot pain laterality in people with knee osteoarthritis (OA), and to examine its impact on health and function.

Methods—Participants from the Progression subcohort (n=1255, aged 45-79 years) of the Osteoarthritis Initiative with symptomatic tibiofemoral knee OA were included. Prevalence of foot pain, defined as pain in the foot/ankle, and foot pain laterality was determined. Health status was evaluated using the Western Ontario and McMaster Universities Osteoarthritis Index, the Short Form-12 and the Centre for Epidemiological Studies Depression Scale. Function was assessed using the 20-meter walk test (20MWT) and a repeated chair stand test. Differences in health and functional measures were compared between groups with and without foot pain using multivariate analysis of covariance.

Results—One quarter (n=317, 25%) of people with knee OA experienced concurrent foot pain, with the majority (n=174, 55%) reporting pain in both feet. After adjusting for covariates, people with foot pain scored worse on all health measures and on the 20MWT compared to those without ($p<0.05$). Differences in health and function were found between the bilateral and ispilateral foot pain groups compared to those without foot pain ($p<0.05$), however no differences were found with the contralateral group.

Conclusion—Foot pain is common in people with knee OA, and bilateral and ipsilateral foot pain adversely affects health and function suggesting laterality is important. Further research is

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needed to establish the mechanism and interaction of pathology at these sites, and to evaluate foot pain treatment in this population.

Knee osteoarthritis (OA) is a highly prevalent disease affecting approximately 30% of people aged over 65 years (1). The primary symptom of knee OA is pain, and painful knee OA significantly reduces physical function (2) and quality of life (3). Foot pain, often defined as pain in the foot and/or ankle (4), is also very common amongst older people, with epidemiological studies reporting that approximately 40% of those over 50 years experience pain in their feet on most days in the last month (5) or year (6). Like knee OA, foot pain also reduces quality of life (7) and is a major cause of disability. Compared to those without foot pain, people with foot pain perform significantly worse during daily activities and basic functional tasks such as walking and balance activities (7, 8), and are also at a greater risk of falling (9). Concurrent foot pain in people with knee OA therefore has the potential to further exacerbate disability and symptom severity than if knee OA occurred in isolation.

Whilst it is recognized that multiple joint symptoms are both common and disabling in people with knee OA (10-12), concurrent foot and knee pain is rarely described and its prevalence is unclear. For instance, one study suggested the most common multi-joint pain presentation was foot and knee pain but did not report prevalence (13), whereas another reported prevalence rates (16.6%) but used a strict definition of isolated foot pain (i.e. not including the ankle) (14). No study has explored the relationship between foot pain and knee OA-specific symptoms or function. This information is important as it may provide insight into common clinical knee OA phenotypes, and has the potential to increase our knowledge of pain presentations at these two common sites. For instance, whilst increased foot pronation, a well- recognized biomechanical risk factor for many painful foot conditions (15-18), has been reported in people with medial knee OA compared to those without, studies have only explored associations between the foot and knee of the same limb (19, 20). With international guidelines now recommending clinicians identify and address different clinical OA phenotypes (21), a greater understanding of the clinical presentation of people with concurrent knee OA and foot pain, and their cumulative effects upon knee-OA symptoms and functional status, is needed.

This study sought to i) establish the prevalence of foot pain (defined as foot and/or ankle pain), and the laterality of foot pain to the most affected knee (bilateral, ispilateral or contralateral to the index knee), in people with symptomatic knee OA, and ii) evaluate differences in the clinical characteristics and functional abilities of those with and without foot pain. It was hypothesized that foot pain will be prevalent in people with symptomatic knee OA, and that those with concurrent knee OA and foot pain will experience greater knee OA-related pain and symptom severity, worse health-related quality of life and depressive symptoms, and will perform more poorly on objective measures of physical function, than those with knee OA but without foot pain.

MATERIALS AND METHODS

Participants

Clinical and functional data were obtained from the Osteoarthritis Initiative (OAI) database version 0.2.2, which is available for public access at http://www.oai.ecsf.edu/. The OAI is a prospective multicentre cohort study of 4,796 people aged 45-79 years with, or at- risk of, symptomatic knee OA. The database is comprised of three subcohorts including a Progression subcohort (n=1390), an Incident subcohort (n=3,284) and a Non-exposed Control group (n=122). The current study used baseline data from the Progression subcohort, defined as having both frequent knee symptoms (pain, aching or stiffness in and around the knee on most days of the month for at least one month in the past year) and radiographic evidence of knee OA (Kellgren and Lawrence [KL] grade >2) on a fixed flexion radiograph taken at baseline.

We selected the most painful knee as the index knee using the pain subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), however, in the event that the index knee did not have a KL grade of >2, or if participants were missing left or right WOMAC knee pain, foot pain or ankle pain data at baseline, they were excluded. This resulted in a final sample size of 1,255 people with symptomatic and radiographic knee OA. Details regarding exclusion criteria for the entire OAI cohort, study procedures and all self-report and functional performance measures are available on the OAI website (http://www.oai.ucsf.edu/datarelease/docs/StudyDesignProtocol.pdf).

Demographic information

We examined demographic characteristics collected from participants at baseline. Data included age, gender, body mass index (BMI), race, KL grade of disease severity (22) and comorbidities. Based on BMI, we also classified participants as obese (>30 kg/m^2), overweight (≥25 and ≤30 kg/m^2) or normal weight (<25 kg/m^2). Comorbidities were assessed using the Charlson comorbidity index (CCI), a validated self-administered questionnaire that determines the presence or absence of a number of comorbid conditions such as diabetes, heart attack and cancer (23). We dichotomized the cohort into those with ’no comorbidities’ and ‘one or more comorbidities’.

Self-reported clinical measures

Consistent with previous definitions (4, 13), the presence of foot pain was determined by asking participants if they experienced pain, aching or stiffness in the left or right foot and/or ankle on more than half of the days during the past 30 days.

Clinical symptoms were evaluated using the WOMAC (24), the Short Form-12 (SF-12) (25) and the Centre for Epidemiological Studies Depression Scale (CES-D) (26). The WOMAC is a disease-specific self-report questionnaire that was used to assess pain (five items, score range 0-20), stiffness (two items, score range 0-8) and function (17 items, score range 0-68). Responses were recorded on a 5-point Likert scale and scores for each sub-scale were summed, with higher scores indicating worse symptoms (24). Total WOMAC score was also calculated by summing the sub-scales (score range 0-96).The SF-12 is a generic health-

related quality of life measure comprised of 12 questions that were used to calculate two summary scales, the physical and mental component scales (25). Scores were combined and weighted to provide a range of 0 (extreme symptoms/poor health) to 100 (no symptoms/ perfect health) for each component, with higher scores indicating better health status. Depression was measured using the CESAD, a 20 item questionnaire that rates depressive symptoms on a scale of 0 (rarely or none of the time) to 3 (most or all of the time). Scores were summed and a score of ≥ 16 was used to indicate depression (26).

Objective functional measures

Physical function was assessed using two performance- based measures; 20 meter walk test (20MWT) pace (27), measured in meters per second (m/s), and repeated chair stand pace (28), measured in stands per second (stands/s) whilst standing up from sitting in a chair five times as quickly as possible. These measures were chosen as they represent commonly performed daily physical activities and have previously been used to assess function in community dwelling adults with foot pain (13). Both tests possess excellent intraA and inter-rater reliability in people with moderate to severe knee and/or hip OA (ICCs 0.93-0.97) (29).

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) version 22.0 was used for all analyses and an alpha level of $P<0.05$ was used for statistical significance. Participants were firstly categorized as having or not having any foot pain. Additionally, people with foot pain were further stratified in to those with foot pain that was ipsilateral, contralateral or bilateral to their index knee. Prevalence within each group was described using number (percentage).

To test the hypothesis that concurrent foot pain and knee OA impacts health and physical function, we compared subgroups with and without each category of foot pain. Initial data exploration showed that subgroup data were not normally distributed, and therefore continuous variables were described using the median (interquartile range (IQR)) and categorical variables using number (percentage). To test for differences in demographic data across groups, chi square tests, Kruskal-Wallis and/or Mann Whitney U tests were used as appropriate. To evaluate differences in the clinical characteristics and physical function of people with and without concurrent foot pain, we then performed multivariate analysis of covariance (MANCOVA), with group allocation as the fixed factor, and age, gender and BMI entered as covariates. Any additional demographic variables that were found to differ significantly between the groups were also entered as covariates (30). Two separate MANCOVAs were conducted to firstly compare participants with and without concurrent foot pain, and then to compare people with bilateral, ipsilateral or contralateral foot pain to those without foot pain. MANCOVA has been shown to be robust to non-normality and unequal sample sizes in much smaller subgroups than in our study (31, 32). To be conservative, we used the sequential approach to adjust for the unequal subgroup numbers and interpreted significance using the more stringent Pillai's criterion (30).

RESULTS

One quarter (n=317, 25.3%) of people with symptomatic knee OA reported pain in one or both feet (Table 1). People with knee OA and concurrent foot pain were significantly more likely to be younger (P=0.025), female (P<0.001) and have a higher BMI (P<0.001). A higher proportion of people with foot pain had a KL grade of 3 whilst fewer had a KL grade of 4 (P=0.007), and more people with foot pain reported one or more comorbid conditions than those without foot pain (P=0.002). Bilateral foot pain was found to be the most prevalent foot pain presentation (54.9% of people with foot pain) and contralateral foot pain the least (17.7% of people with foot pain). People with knee OA and bilateral foot pain were also significantly more likely to be female (P<0.001) and have a higher BMI (P=0.001). More people with bilateral foot pain had a KL grade of 3 and fewer had a KL grade of 4 (P=0.006), and people with bilateral foot pain also reported more comorbidities (P=0.001). With the exception of a higher BMI in those with ipsilateral foot pain compared to no foot pain (P=0.001), there were no demographic differences between the ipsilateral and contralateral subgroups compared to the no foot pain group.

Clinical characteristics and physical function of people with and without foot pain are reported in Table 2. MANCOVA revealed a significant difference (P<0.001) between the foot pain and no foot pain groups after controlling for age, gender, BMI, KL grade and comorbidities, with the foot pain group performing significantly worse on the CESAD (P=0.007), the SFA12 mental (P=0.017) and physical (P<0.001) component scales, the WOMAC subscales of pain (P<0.001), stiffness (P=0.003) and function (P<0.001), WOMAC total score (P<0.001), and on 20m walk pace (P=0.024). A second MANCOVA was performed to compare dependent variables between the foot pain subgroups and those without foot pain (Table 2), with results also demonstrating significant betweenAgroup differences (P<0.001). After controlling for age, gender, BMI, KL grade and comorbidities, the bilateral foot pain subgroup had a significantly higher CESAD score (P<0.015), worse SFA12 mental (P=0.025) and physical component scores (P<0.001) and poorer WOMAC pain (P<0.001), stiffness (P=0.012), function (P<0.001) and total scores (P<0.001) when compared to people without foot pain. Additionally, the ipsilateral foot pain subgroup reported significantly worse SF-12 physical scores (P=0.004), higher WOMAC pain (P=0.029) and stiffness (P=0.017) scores, walked significantly more slowly (P=0.049) and performed significantly slower on the repeated chair stand test (P=0.042), when compared to people without foot pain. No differences were found between the contralateral foot pain subgroup compared to the no foot pain group on any of the measures.

DISCUSSION

Our results demonstrated that concurrent foot pain is common in people with symptomatic and radiographic knee OA, and the presence of bilateral or ipsilateral foot pain adversely affects knee OA-related pain and symptom severity, health-related quality of life and depressive symptoms, and objective measures of physical function. Of note, no differences were found between people with contralateral foot pain and those without foot pain, suggesting that the laterality of foot pain is important in people with knee OA.

Our finding of concurrent foot pain in a quarter of people with symptomatic knee OA aged between 45 and 75 years is higher than that reported for the general population. Using comparable between-study case definitions of frequent foot pain (including ankle pain) in adults aged over 58 years, a recent systematic review reported the estimated point prevalence of foot pain to be 20% (4). However, the overwhelming majority of participants from the studies included in the analysis were aged over 65, and given the strong positive association between foot pain and age (33), it is likely that the rate would be lower if younger participants such as ours were included. The fact that the only study in the analysis that included participants younger than 65 years reported a lower prevalence rate of 14.5% would appear to support this assumption (34).

A number of previous studies have shown that foot pain is disabling and reduces health-related quality of life (7, 8, 13, 33), however this is the first study to show that knee OA-specific symptoms, in addition to general measures of health and function, are worse in people with concurrent foot pain. Specifically, compared to the no foot pain group, people with foot pain reported scores that were up to 39% worse on all WOMAC subscales including the total score, and these differences were even larger in people with ipsilateral or bilateral foot pain. The between-group differences of 2 points (ipsilateral and bilateral foot pain versus no foot pain) on the WOMAC pain subscale, and of 0.06 m/s (foot pain versus no foot pain) and 0.08 m/s (ipsilateral versus no foot pain) on the 20m walk test, exceed minimal clinically important difference values (35, 36), suggesting these changes are clinically meaningful. This is important given people with symptomatic knee OA already suffer from worse selfAreported health outcomes (3) and functional disability (2), and consequently concurrent foot pain may further compound these existing deficits. This finding highlights that clinicians should consider evaluating the foot and ankle in people with knee OA, and provide interventions for foot pain if present, to improve general and kneeAspecific outcomes in this patient population. Given that footwear and insole/orthotic interventions are often used to manage knee OA, our findings also suggest clinicians need to be cognizant of the effects of such interventions on ipsilateral foot pain.

Consistent with previous research in the general population (33), we found that bilateral foot pain was the most common clinical presentation, accounting for over half of the knee OA patients with foot pain. Additionally, whilst between-group differences in health and function were found in the bilateral and ipsilateral foot pain groups compared to the no foot pain group after controlling for covariates, there were no differences in the contralateral compared to the no foot pain group. This suggests that foot pain that is ipsilateral to the most painful knee may be the driver of these adverse outcomes in people with knee OA, whereas contralateral foot pain does not appear to affect health or functional status.

Aberrant foot posture and function has previously been shown to influence knee biomechanics and joint load, and therefore offers a theoretical mechanism through which foot and knee pain may be linked in people with symptomatic knee OA. Specifically, a more pronated, less mobile foot type has been reported in those with medial knee OA (20, 37, 38), and this finding has also been associated with a number of painful musculoskeletal foot conditions (15-18). Through this mechanism, foot pain due to excessive pronation or other biomechanical factors may occur following, in concert with, or prior to knee OA-related

pain. For example, foot pronation (and subsequent pain) could be a compensatory response to OA-related knee pain, whereby the foot pronates to shift the centre of pressure and ground reaction force-knee joint lever arm more laterally, in an attempt to reduce medial knee load and pain (19). Alternatively, both foot and knee pain may be related to the presence of varus knee malalignment, which may occur with or without knee OA. Increased knee varus may increase the risk of knee OA by increasing medial knee compartmental loading (39, 40), and may also lead to increased foot pronation (contributing to subsequent pathology and pain) to ensure the foot is plantigrade to the ground during the stance phase of walking. Future research should consider examining potential mechanisms underpinning the relationship between foot pain and knee OA, and investigate the effects of interventions targeted towards the treatment of aberrant foot posture and/or pain in this population. It would also be of interest to examine the interaction between proximal and distal mechanics in people with knee OA given abnormal hip mechanics adversely affect loading conditions at the knee in this population (41), and modified footwear with lateral wedges reduce knee load partly by altering the hip-knee-ankle angle (42).

Although foot pain adversely affected knee OA symptoms and physical function, the data used in the analysis were cross-sectional, and as highlighted, it is not possible to infer whether foot pain developed subsequent to knee OA, simultaneously, or in fact preceded disease incidence. Longitudinal studies evaluating the temporal sequence between pain locations and knee OA onset and progression are required. It would also be of interest to examine whether the definition of foot pain influences the relationship between pain and function. For example, Mickle and colleagues (7) found differences in both the prevalence of foot pain and in measures of disability when using two alternate definitions of foot pain. The definition used in our study was consistent with questionnaire items used to characterize pain at other anatomical sites, including those used in research investigating the association between low back pain and knee OA (14). It is also comparable to the case definition used in recent epidemiological studies to calculate overall ankle/foot/toe pain prevalence (4, 33).

There are some limitations that should be considered when interpreting the results of our study. For instance, study participants were excluded if they possessed any comorbid condition that might affect the outcomes of the broader OAI study, which explains why the majority of our participants reported having no comorbidities. It is possible therefore that this may have resulted in some bias our sample. Additionally, we did not examine foot pain prevalence according the knee joint compartment affected by OA. People with medial tibiofemoral OA exhibit biomechanical characteristics that increase their risk of painful foot conditions (19, 20, 37), and therefore it is possible that prevalence of foot pain may be higher in this subgroup. Future studies may wish to examine whether foot pain prevalence differs depending on knee OA compartment.

The findings of our study highlight that the foot is a common concurrent location of pain in people with symptomatic knee OA, and people with foot pain, and in particular bilateral or ipsilateral foot pain, have reduced measures of health and physical function, including worse knee-specific measures of symptom severity. As such, clinicians should consider assessing and treating foot pain in people with symptomatic knee OA. Longitudinal research is needed to establish causative factors and the inter-relationship of pathology at these two sites.

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Significance & Innovations

- Foot pain is common in people with symptomatic and radiographic knee OA, and the most common clinical presentation is bilateral foot pain.
- The presence of foot pain significantly impacts the health and functional status of people with knee OA, including knee-specific measures of symptom severity.
- People with foot pain that is ipsilateral to their most affected knee also perform significantly worse than those without foot pain on measures of health and function, whereas those with contralateral foot pain do not, suggesting that foot pain laterality is important in people with knee OA.

Table 1

Descriptive characteristics of people with symptomatic knee OA (n=1255) based on the presence or absence of foot pain, reported as number (percentage) unless otherwise indicated.

	No foot pain (n=938)	Any foot pain (n=317)	*P* *	Ipsilateral foot pain (n=87)	Contralateral foot pain (n=56)	Bilateral foot pain (n=174)	*P* *
Age, median (IQR) years	61.0 (45.0-77.0)	60.0 (47.5-72.5) †	.025	61.0 (49.0-73.0)	57.5 (46.8-68.3)	60 (48.0-72.0)	0.056
Gender, women	500 (53.3)	211 (66.6) †‡	<0.001	58 (66.7)	33 (58.9)	120 (69.0) †‡	<0.001
Race			0.150				0.165
White	672 (71.7)	211 (66.6)		54 (62.1)	40 (71.4)	117 (67.2)	
African American	234 (25.0)	96 (30.3)		32 (36.8)	14 (25.0)	50 (28.7)	
Asian	10 (1.1)	1 (0.3)		1 (11)	0 (0.0)	0 (0.0)	
Other nonwhite	21 (2.2)	9 (2.8)		0 (0.0)	2 (3.6)	7 (4.0)	
BMI, median (IQR) kg/m^2	29.6 (23.0-36.2)	31.1 (24.2-37.9) †	<0.001	31.8 (26.0-37.6) †	29.3 (21.2-37.4)	31.2 (24.3-38.1) †	0.001
BMI category			0.018				p<0.042
obese	433 (46.3)	172 (54.3)		52 (59.8)	24 (42.9)	96 (55.2)	
overweight	371 (39.7)	116 (36.6)		26 (29.9)	25 (44.6)	65 (37.4)	
normal	131 (14.0)	29 (9.1) †		9 (10.3)	7 (12.5)	13 (7.5) †	
KL grade			0.007				0.006
2	298 (31.8)	91 (28.7)		29 (33.3)	18 (32.1)	44 (25.3)	
3	385 (41.0)	161 (50.8) †		39 (44.8)	22 (39.3)	100 (57.5) †	
4	255 (27.2)	65 (20.5) †		19 (21.8)	16 (28.6)	30 (17.2) †	
CCI score			0.002				0.001
0	652 (69.5)	191 (60.3)		51 (58.6)	42 (75.0)	98 (56.3)	
≥1	286 (30.5)	126 (39.7) †		36 (41.4)	14 (25.0)	76 (43.7) †	

OA = osteoarthritis; IQR = interquartile range; BMI = body mass index; KL = Kellgren Lawrence; CCI = Charlson comorbidity index.

*Significance of Chi Square test, with the exception of age and BMI which used either a Mann Whitney U test (foot pain and no foot pain groups) or Kruskal-Wallis test (ipsilateral, contralateral, bilateral and no foot pain subgroups).

†Significantly different to no foot pain group.

‡Significant difference between males and females.

Table 2

Clinical characteristics and physical function compared across subgroups with and without foot pain, reported as median (interquartile range).*

	No foot pain (n=938)	Foot pain (n=317)	*P**	Ipsilateral foot pain (n=87)	Contralateral foot pain (n=56)	Bilateral foot pain (n=174)	*P**
Depression, CES-D score	5.0 (−3.0−13.0)	6.0 (−3.0-15.0) †	0.007	7.0 (−3.0−17.0)	5.0 (−3.8-13.8)	6.0 (−4.0−16.0) †	0.002
SF-12 score							
Mental	56.3 (46.6-66.1)	54.6 (42.4-66.8) †	0.017	54.4 (41.0-67.8)	54.9 (45.3-64.4)	54.4 (42.1-66.6) †	0.019
Physical	47.3 (34.5-60.1)	43.5 (27.7-59.2) †	<0.001	41.6 (23.1-60.0) †	48.9 (37.1-60.7)	42.6 (27.0-58.2) †	<0.001
WOMAC							
Pain	5.0 (−1.0-11.0)	6.0 (0.3-11.6) †	<0.001	7.0 (3.0-11.0) †	6.0 (0.0-12.0)	7.0 (1.0-13.0) †	<0.001
Stiffness	3.0 (1.0-5.0)	3.0 (0.0-6.0) †	0.003	4.0 (1.0-7.0) †	2.5 (0.5-4.5)	4.0 (1.0-7.0) †	0.012
Function	14.9 (−2.5-32.3)	20.2 (−1.7-42.1) †	<0.001	20.2 (−2.7-43.1)	20.1 (−0.2-40.4)	21.0 (−0.5-42.5) †	<0.001
Total	22.0 (−1.0-45.0)	30.6 (0.7-60.5) †	<0.001	31.0 (2.1-59.9)	28.5 (−0.9-57.9)	32.0 (2.0-62.0) †	<0.001
20m walk pace, m/s	1.30 (1.03-1.57)	1.24 (0.96-1.52) †	0.024	1.22 (0.99-1.46) †	1.29 (0.94-1.64)	1.25 (0.94-1.55)	0.019
Repeated chair stand pace, stand/s	0.46 (0.29-0.63)	0.42 (0.23-0.61)	0.057	0.40 (0.23-0.57) †	0.46 (0.24-0.68)	0.42 (0.24-0.61)	0.014

CES-D = Centre for Epidemiologic Studies Depression Scale; SF-12 = Short Form-12; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

*Significance of MANCOVA between the foot pain and no foot pain groups, and between foot pain subgroups and the no foot pain group, adjusted for age, gender, BMI, KL grade and co-morbidities.

†Significantly different to no foot pain group