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Changes in ambulatory knee adduction moment with lateral wedge insoles differ with respect to the natural foot progression angle

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ABSTRACT

Lateral wedge insoles (LWI) have been proposed to reduce the knee adduction moment (KAM) during walking; a biomechanical modification notably sought in case of medial knee osteoarthritis. However, the inter-individual inconsistency in KAM changes with LWI limits their therapeutic use. Although the foot progression angle (FPA) has been frequently discussed in KAM modifications literature, there is a lack of data regarding a possible relationship between this gait measure and changes in KAM with LWI. This study aimed to test if KAM changes with LWI differ with respect to the natural FPA and to compare KAM-related variables between individuals walking with smaller and larger natural FPA. Twenty-two healthy participants (14 males, 24 ± 3 years, 22.7 ± 2.7 kg/m^2) underwent gait analysis with and without LWI. They were divided into two groups based on their natural FPA, and changes in KAM 1st peak, KAM impulse, and KAM-related variables were compared between groups. KAM 1st peak and impulse decreased with LWI in the smaller natural FPA group ($p \leq 0.006$), while only KAM impulse decreased in the larger natural FPA group ($p < 0.001$). The difference in KAM 1st peak changes was explained by a less reduced lever arm in participants walking with larger natural FPA. In conclusion, this study brought new insight into the variability in KAM response to LWI. If the findings are confirmed in patients with medial knee osteoarthritis, the FPA could become a simple measure to help identify the patients more likely to reduce their KAM with LWI.

1. Introduction

Knee Osteoarthritis (OA) is a frequent disabling disease, inducing major socioeconomic burden. Indeed, about 45% of women and 33% of men aged 60 and above have radiographic knee OA, with a third of them experiencing symptoms (Pereira et al., 2011). Knee OA also affects younger individuals, especially those that have a history of traumatic knee injury or are obese (Ackerman et al., 2017). There is no known cure for this degenerative condition (McAlindon et al., 2014). Therefore, treatments for the earlier stages of the disease are badly necessary to alleviate symptoms and slow down disease progression in order to avoid or delay joint replacement procedures.

Ambulatory loading has been shown to play an important role in disease development (Andriacchi and Favre, 2014; Favre and Jolles, 2016). Medial-compartment knee OA is the most prevalent form of the disease (Ahlbäck, 1968), and consistent relationships have been reported between medial knee OA and the knee adduction moment (KAM), a surrogate measure for the medial–lateral distribution of loading at the knee (Schipplein and Andriacchi, 1991). During the stance phase of walking, the KAM presents a characteristic m-shape and the amplitude of the first bump (KAM 1st peak) as well as the area under the curve (KAM impulse) have been positively associated to medial knee OA severity, progression and pain (Chehab et al., 2014; Mündermann et al., 2004; Thorp et al., 2007). Thus, there is an interest to design gait interventions to reduce the KAM 1st peak and impulse as this could slow down disease progression and relieve symptoms (Reeves and Bowling, 2011).

Lateral wedge insoles (LWI) have been proposed to decrease the KAM. At first, this approach seemed promising, with multiple studies reporting KAM 1st peak and impulse reductions in groups of individuals with or without knee OA (Arnold et al., 2016; Shaw et al., 2018). However, literature failed to demonstrate clear improvements in disease outcomes (Penny et al., 2013; Zhang et al., 2018). The uncertainty of clinical benefits with LWI could

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find its origin in the fact that the KAM changes with LWI are inconsistent among individuals and that prior studies did not paid enough attention to inter-individual variations. Indeed, while a majority of individuals decreases both OA-related KAM variables with LWI, in some individuals, LWI increase these variables (Hinman et al., 2012; Jones et al., 2014; Kakihana et al., 2007). Additionally, the magnitude of the KAM changes strongly varies among persons (Hinman et al., 2012; Jones et al., 2014). The need to better understand these inter-individual variations is further supported by the fact that heterogeneous changes were consistently reported, independently of the LWI design and study population (Arnold et al., 2016; Hinman et al., 2008). Interestingly, a recent study defined patients as responder if they decreased their KAM 1st peak with the use of LWI, and showed significant pain reductions with LWI in these patients (Felson et al., 2019). Therefore, whereas earlier research showed that LWI are not a universal solution (Arnold et al., 2016; Kakihana et al., 2007), this recent work indicates that LWI could be clinically beneficial for the patients who actually decrease the KAM with this intervention. This observation of clinical improvements in case of KAM reductions is well supported by gait retraining studies where improvements in pain and function were also reported in patients who decreased the OA-related KAM variables (Cheung et al., 2018; Shull et al., 2013; Richards et al., 2018). Consequently, in view of the significant impact that LWI could make in the management of medial knee OA if recommended to the right (responder) patients, there are definite interests to develop screening procedures to differentiate between individuals who reduce sufficiently their KAM 1st peak and impulse with LWI and those who do not, without having to perform full instrumented gait analysis. To do so, a necessary first step is to better understand the underlying mechanism of LWI and identify easy-to-measure predictive variables.

Only a few studies so far investigated individual factors that could influence the KAM changes with LWI (Chapman et al., 2015; Sawada et al., 2016), and to the authors knowledge no study analyzed the effect the natural foot progression angle (FPA) could have on the KAM changes. The FPA is a classical spatio-temporal gait variable quantifying the amplitude of foot opening (toeing-in or toeing-out) during the stance phase of walking (Murray et al., 1964; Saggini et al., 1998; Scherer et al., 2006; Woolley, 2001). It significantly gained in interest during the last decades with advance in knee OA research. In fact, it is among the gait variables the most frequently associated to the KAM, with numerous studies reporting KAM changes with modifications of the FPA (Favre et al., 2016; Simic et al., 2013). Moreover, the reductions in KAM 1st peak and impulse with LWI were recently shown to be larger when the participants toed-in compared to when they walked with their natural FPA (Khan et al., 2018). Therefore, there is a possibility that the natural FPA influences the changes in KAM with LWI.

This study aimed at determining if the KAM changes induced by LWI differ with respect to the natural FPA. Specifically, it tested the hypothesis that individuals walking with smaller natural FPA have greater KAM 1st peak and impulse reductions than individuals walking with larger natural FPA. A second objective was to compare KAM-related gait variables between individuals walking with smaller and larger natural FPA to improve our understanding of the mechanism leading to KAM reductions.

2. Methods

2.1. Participants

Twenty-two healthy subjects (8 women) without history of serious lower extremity injury or gait impairments took part in this IRB-approved study after providing informed consent. Their mean (±standard deviation) age, height and weight were of 24 ± 3 years old, 1.76 ± 0.10 m and 70.8 ± 11.6 kg, respectively. A sample size calculation for the *t*-test used for the primary hypothesis indicated a minimum of 11 participants per group, considering an effect size (Cohen's d) greater than 1.2 (Felson et al., 2019; Radzimski et al., 2012), a power of 80% and an alpha level of 5% (G*Power, DE).

2.2. Experimental protocol

Participants performed a series of gait trials at normal self-selected speed with neutral frontal plane stability shoes (gel-beyond, Asics, JP), and with the same shoes in which custom full-length LWI (Fischer et al., 2018) were inserted bilaterally under the comfort insoles. Footwear order was random. LWI were made of high-density ethylene vinyl acetate (EVA) with a durometer of 60 (Shore C) and wedged at 5° following literature recommendations (Tipnis et al., 2014). Only the biomechanics of the right leg was recorded and analyzed in this study.

Gait trials consisted of straight-line walking across a 10 m-long gait lab instrumented with a motion capture system (Vicon, UK) and ground-embedded force plates (Kistler AG, CH) recording synchronously at 120 Hz and 1200 Hz, respectively. For both footwear conditions, three successful trials were recorded. A trial was considered successful when the right foot of the participant fully stepped on one force plate with no other step occurring on that force plate. The biomechanics of the participant was analyzed during these particular stance phases with the right foot on a force plate.

Prior to the gait trials, clusters of reflective markers were fixed on the participants following a common protocol (Chehab et al., 2017). The clusters were used to embed a technical frame in each lower-limb segment (Andriacchi et al., 1998). Anatomical landmarks, identified by palpation during a standing reference pose, were used to define the anatomical frame of the thigh, shank and foot segments (Favre et al., 2016), as well as the technical-to-anatomical transformations (Favre et al., 2016). During the gait trials, the position and orientation of the anatomical frames were cal-

Table 1
Definition of the additional biomechanical metrics related to the knee adduction moment (KAM).

Metric	Unit	Description
Frontal-plane GRF magnitude	%BW	Magnitude of the GRF in the frontal plane of the shank anatomical frame
Frontal-plane lever arm	mm	Perpendicular distance between the GRF and the knee joint center in the frontal-plane of the shank anatomical frame
Frontal-plane GRF-shank angle	degree	Angle between the GRF and the distal-proximal axis of the shank in the frontal plane of the shank anatomical frame (positive values indicate that the GRF is medial to the shank)
Medio-lateral COP position	mm	Medio-lateral position of the COP in the shank anatomical frame (positive values indicate that the COP is lateral to the knee joint center)

Three variables, corresponding to the values of the metrics at the time of the KAM 1st and 2nd peaks and to the average value of the metrics during stance, were used for statistical analysis.
GRF = Ground reaction force.
COP = Center of pressure.

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culated using the marker cluster trajectories and the technical-to-anatomical transformations (Andriacchi et al., 1998).

The KAM was calculated following a standard inverse dynamics approach based on the anatomical frame dynamics, force plate data and inertia properties of the segments (Zabala et al., 2013). The KAM was expressed as an external moment and normalized to percent bodyweight and height (%BW × Ht). Three variables were used to describe the KAM during the stance phase of interest of each trial: the maximum values during the first (1st peak) and second (2nd peak) halves of stance phase, as well as the impulse over the entire stance phase (Chehab et al., 2014). The foot progression angle variable (FPA) was calculated as the average horizontal-plane angle between the posterior–anterior axis of the foot anatomical frame and the forward axis of the walkway during the middle 50% of each stance phase of interest (Favre et al., 2016).

Four additional biomechanical metrics related to the KAM were computed to better understand the LWI mechanism. They included the magnitude of the ground reaction force (GRF), the lever arm, the angle between the GRF and the longitudinal shank axis, and the position of the center of pressure (COP), all measured in the frontal-plane of the shank anatomical frame (Table 1). Three variables, coinciding with the KAM variables, were used to analyze each of these additional metrics. They corresponded to the values of the metrics at the time of KAM 1st and 2nd peaks and to the average value of the metrics during stance phase.

Finally, the data were averaged over the three trials recorded with each footwear condition to have only one data point per participant, footwear condition and variable of interest. Computations were done using the software BioMove (Standford, CA, US) and custom scripts in Matlab (Mathworks, Natick, MA, USA).

2.3. Statistical analysis

Participants were divided in two groups of same size according to their FPA when walking without LWI. The split was done using the median FPA of the 22 subjects, yielding a group with the 11 "smaller natural FPA" participants and a group with the 11 "larger natural FPA" participants. For each group, two-sided paired t-tests were performed to compare the variables of interest between the two footwear conditions (with and without LWI). Unpaired two-sided t-tests were also done to compare the variables of interests and their changes with LWI between the two groups. To allow a thorough interpretation of these comparisons between conditions and groups, the unstandardized and standardized effect sizes were calculated. Cohen's d was used to report the standardized effect sizes (Cohen, 2013; Cooper et al., 2019). All data were previously tested for normality using Kolmogorov-Smirnov tests. Statistical significance level was set *a-priori* at 5%.

3. Results

When walking without LWI, the FPA was, on average, 9.6° larger in the larger natural FPA group (mean ± standard deviation: 20.0 ± 3.0°) than in the smaller natural FPA group (10.4 ± 3.1°). With this footwear condition, neither the speed nor the KAM variables differed statistically significantly between the two groups ($p \geq 0.47$) (Table 2).

Walking with LWI significantly decreased the KAM 1st peak in the smaller natural FPA group ($p < 0.01$; Cohen's d = -0.30), whereas no significant changes in the KAM 1st peak were observed in the larger natural FPA group ($p = 0.14$) (Fig. 1, Table 2). Furthermore, the changes in the KAM 1st peak were significantly different between both groups ($p = 0.04$; Cohen's d = -0.93). The LWI induced significant decreases in the KAM 2nd peak and impulse in both the smaller ($p = 0.01$; Cohen's d = -0.46 and $p < 0.01$; Cohen's d = -0.47, respectively) and larger ($p < 0.01$; Cohen's

Table 2
Foot progression angle (FPA), walking speed, and knee adduction moment (KAM) variables for the smaller and larger natural FPA groups with both footwear conditions.

	Smaller natural FPA group			Larger natural FPA group			Inter-group differences in gait without LWI		Inter-group differences in changes with LWI	
	Value without LWI	Changes with LWI: Unstandardized (U) and standardized (S) changes	p-value	Value without LWI	Changes with LWI: Unstandardized (U) and standardized (S) changes	p-value	Unstandardized (U) and standardized (S) differences	p-value	Unstandardized (U) and standardized (S) differences	p-value
FPA (°)	10.4 ± 3.1	U: 0.9 (0.3, 1.4) S: 0.27 (-0.57, 1.11)	**0.014**	20.0 ± 3.0	U: 1.5 (0.5, 2.5) S: 0.49 (-0.36, 1.34)	**0.015**	U: 9.6 (7.0, 12.1) S: 3.11 (1.87, 4.35)	**< 0.001**	U: 0.6 (-0.5, 1.8) S: 0.45 (-0.40, 1.30)	0.30
Speed (m/s)	1.47 ± 0.17	U: 0.01 (-0.04, 0.05) S: 0.04 (-0.80, 0.87)	0.81	1.48 ± 0.21	U: 0.00 (-0.04, 0.04) S: 0.01 (-0.82, 0.85)	0.90	U: 0.01 (-0.15, 0.17) S: 0.06 (-0.78, 0.90)	0.89	U: −0.00 (-0.07, 0.06) S: 0.05 (-0.79, 0.89)	0.91
KAM 1st peak (%BW*Ht)	2.73 ± 1.09	U: −0.32 (-0.50, −0.15) S: −0.30 (-1.14, 0.54)	**0.005**	2.96 ± 0.65	U: −0.09 (-0.02, 0.20) S: −0.14 (-0.98, 0.70)	0.14	U: 0.23 (-0.53, 0.98) S: 0.25 (-0.59, 1.09)	0.56	U: 0.23 (0.02, 0.44) S: 0.93 (0.05, 1.81)	**0.042**
KAM 2nd peak (%BW*Ht)	1.86 ± 0.62	U: −0.29 (-0.47, −0.10) S: −0.46 (-1.31, 0.38)	**0.012**	1.85 ± 0.60	U: −0.33 (-0.43, −0.24) S: −0.56 (-1.41, 0.29)	**< 0.001**	U: −0.02 (-0.52, 0.49) S: −0.03 (-0.87, 0.81)	0.95	U: −0.05 (-0.26, 0.16) S: −0.19 (-1.03, 0.65)	0.67
KAM impulse (%BW*Ht*s)	0.79 ± 0.28	U: −0.13 (-0.21, −0.06) S: −0.47 (-1.32, 0.37)	**0.006**	0.89 ± 0.34	U: −0.11 (-0.15, −0.07) S: −0.32 (-1.34, 0.36)	**< 0.001**	U: 0.10 (-0.16, 0.36) S: 0.32 (-0.52, 1.16)	0.47	U: 0.02 (-0.06, 0.11) S: 0.23 (-0.61, 1.07)	0.59

Measures are reported as 'mean ± one standard deviation'.
Changes and differences are reported as 'effect size (95% confidence interval)'. Standardized effect sizes are Cohen's d.
Bolded numbers indicate significant p-values ($p < 0.05$).
LWI = Lateral wedge insoles.

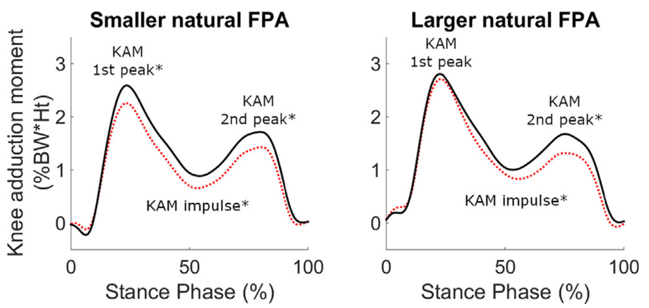

Fig. 1. Mean knee adduction moment (KAM) over stance phase for the smaller (left) and larger (right) natural foot progression angle (FPA) groups. In both plots, the continuous black and the dotted red lines correspond to the walking conditions without lateral wedge insole (LWI) and with LWI, respectively. Stars (*) indicate significant difference between LWI conditions ($p \leq 0.02$; Table 2).

d = -0.56 and p < 0.01; Cohen's d = -0.32, respectively) natural FPA groups, without significant differences in the changes between the groups ($p \geq 0.59$). Walking with LWI also changed the FPA, with significant increases in both the smaller (p = 0.014; Cohen's d = -0.27) and the larger (p = 0.015; Cohen's d = -0.49) natural FPA groups. The FPA increases induced by the LWI did not significantly differ between the groups (p = 0.30). Finally, speed was not significantly different when walking with or without LWI for neither groups ($p \geq 0.81$).

Analyzing the additional KAM-related metrics at the time of the KAM 1st peak allowed better understanding the differences between the two groups in the KAM 1st peak changes with LWI (Table 3, Fig. 2). First, when comparing the two main components of the KAM, this analysis indicated statistically significant differences in the lever arm changes between groups (p = 0.04; Cohen's d = 0.93), but no group differences in the GRF magnitude changes (p = 0.63). Indeed, while the lever arms were reduced with the LWI in both groups, the reductions were larger in the smaller (p < 0.01; Cohen's d = -0.31) than in the larger (p = 0.04; Cohen's d = -0.19) natural FPA group. Second, when comparing the main components of the lever arm, statistically significant group differences were observed in the GRF-shank angle changes (p = 0.04; Cohen's d = 0.97), whereas the changes in the COP position were not significantly different between groups (p = 0.75). The differences in the GRF-shank angle changes are explained by significant increases in the GRF-shank angle with LWI in the larger natural FPA group (p = 0.01; Cohen's d = 0.29), with non-significant changes in the smaller natural FPA group (p = 0.31).

4. Discussion

This study showed that the changes in KAM 1st peak with LWI are related to the natural FPA. Specifically, a statistically significant decrease in this peak was only observed in the group of participants walking with smaller natural FPA, and the standardized effect size of the changes with LWI was twice as large in the smaller natural FPA group than in the other group (Cohen's d of −0.30 vs. −0.14). While no effect size recommendation exist regarding KAM 1st peak decreases in the case of medial knee OA, mainly because there has been too few longitudinal studies on gait intervention with KAM measurement, the difference in effect size with respect to the FPA is certainly clinically relevant. In fact, the effect sizes in prior studies that reported clinical improvements with LWI were comprised between −0.25 and −0.20 (Hinman et al., 2008; Felson et al., 2019), and gait retraining studies aimed for reductions equivalent to effect sizes between −0.45 and −0.30 (Shull et al, 2013; Richards et al., 2018). Comparing the present results with the literature thus suggests an adequate effect size in the smaller

Table 3
Additional biomechanical metrics at the time of knee adduction moment (KAM) 1st peak for the smaller and larger natural foot progression angle (FPA) groups with both footwear conditions.

	Smaller natural FPA group			Larger natural FPA group			Inter-group differences in gait without LWI		Inter-group differences in changes with LWI	
	Value without LWI	Changes with LWI		Value without LWI	Changes with LWI					
		Unstandardized (U) and standardized (S) changes	p-value		Unstandardized (U) and standardized (S) changes	p-value	Unstandardized (U) and standardized (S) differences	p-value	Unstandardized (U) and standardized (S) differences	p-value
Frontal-plane GRF magnitude (%BW)	112.78 ± 11.96	U: 0.04 (-3.03, 3.12) S: 0.00 (-0.83, 0.84)	0.98	111.83 ± 7.00	U: 1.09 (-1.78, 3.97) S: 0.16 (-0.68, 0.99)	0.47	U: −0.95 (-9.14, 7.23) S: −0.10 (-0.93, 0.74)	0.82	U: 1.05 (-3.16, 5.26) S: 0.21 (-0.63, 1.05)	0.63
Frontal-plane lever arm (mm)	42.62 ± 15.90	U: −4.87 (-6.63, −3.11) S: −0.31 (-1.15, 0.53)	**< 0.001**	49.00 ± 11.14	U: −2.10 (-3.86, −0.33) S: −0.19 (-1.03, 0.65)	**0.042**	U: 6.38 (-5.10, 17.85) S: 0.46 (-0.38, 1.31)	0.29	U: 2.77 (0.28, 5.27) S: 0.93 (0.05, 1.81)	**0.041**
Frontal-plane GRF-shank angle (°)	7.09 ± 2.16	U: 0.07 (-0.06, 0.21) S: 0.03 (-0.80, 0.87)	0.31	7.74 ± 1.47	U: 0.42 (0.15, 0.69) S: 0.29 (-0.55, 1.13)	**0.012**	U: 0.65 (-0.90, 2.20) S: 0.35 (-0.49, 1.19)	0.42	U: 0.35 (0.05, 0.65) S: 0.97 (0.08, 1.85)	**0.035**
Medio-lateral COP position (mm)	15.85 ± 3.33	U: 6.15 (4.06, 8.24) S: 1.84 (0.85, 2.84)	**< 0.001**	18.82 ± 7.23	U: 6.62 (4.68, 8.56) S: 0.92 (0.04, 1.79)	**< 0.001**	U: 2.96 (-1.74, 7.67) S: 0.53 (-0.32, 1.38)	0.23	U: 0.48 (-2.37, 3.33) S: 0.14 (-0.70, 0.98)	0.75

Measures are reported as 'mean ± one standard deviation'.
Changes and differences are reported as 'effect size (95% confidence interval)'. Standardized effect sizes are Cohen's d.
Bolded numbers indicate significant p-values (p < 0.05).
LWI = Lateral wedge insoles.
GRF = Ground reaction force.
COP = Center of pressure.

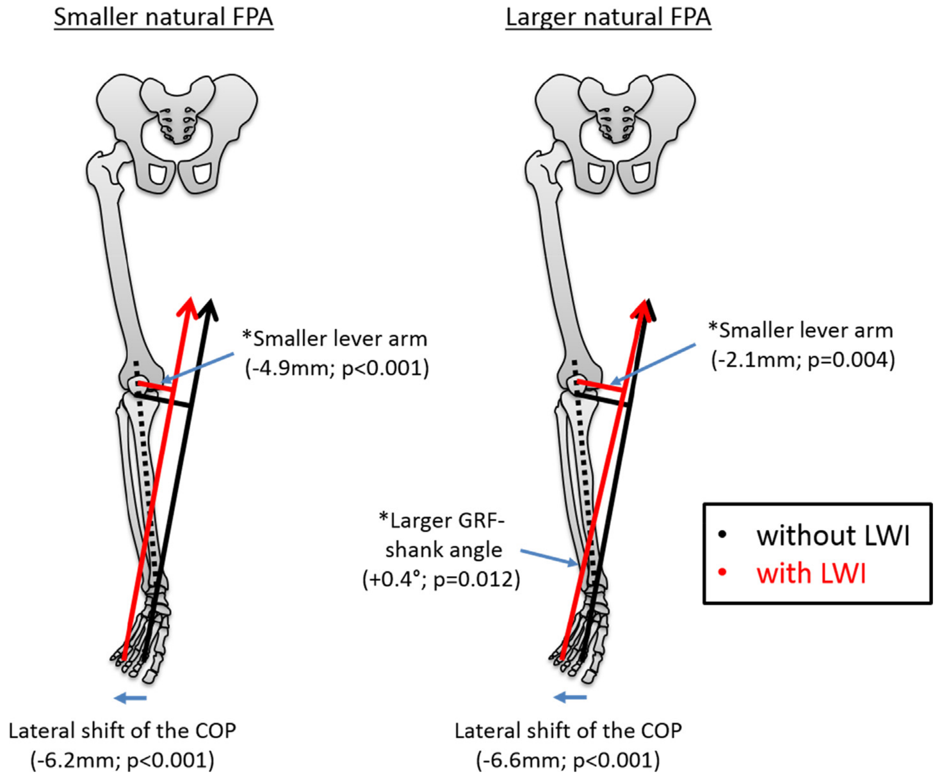

Fig. 2. Illustration of the significant changes in KAM-related biomechanical metrics at the time of KAM 1st peak with lateral wedge insoles (LWI) in the smaller (left) and larger (right) natural foot progression angle (FPA) groups. Numbers reported into brackets correspond to the mean changes with LWI (Table 3). Stars (*) indicate changes that are statistically significantly different from the changes occurring in the other group ($p \leq 0.04$). GRF = Ground reaction force. COP = Center of pressure.

natural FPA group and a questionable effect size in the other group. Consequently, the natural FPA could help to screen patients who should be more likely to decrease their KAM 1st peak with LWI and therefore for who LWI could improve clinical outcomes. In this regard, it should be noted that the FPA could be measured using much simpler instrumentation than in the present study, therefore making its use in routine practice totally possible. For example, the FPA can be measured using pressure mats (Menz et al., 2004) or inertial sensors (Huang et al., 2016).

The relationship between the natural FPA and the KAM 1st peak changes with LWI highlighted in the present study could also shed light on the inter-individual variability in the KAM changes with LWI reported in literature (Arnold et al., 2016; Kakihana et al., 2007). In fact, to the authors' knowledge, none of the prior studies on LWI accounted for participants variations in natural FPA. While this is unfortunate, it might also be very encouraging for the treatment of medial knee OA. Indeed, this supports a shift toward personalized management where the differences among patients are acknowledged and each patient is proposed the best biomechanical intervention for him/herself. With this approach, as shown in this work, the effect size of existing interventions could be significantly improved. Additional research will nonetheless be required to establish which intervention suits better which patient profile.

Analyzing the underlying mechanism of the changes in KAM 1st peak with LWI showed that the decreases in the smaller natural FPA group were related to decreased lever arms and not to decreased GRF magnitudes. The analysis further indicated that the lever arms were decreased by lateral shifts of the COP (Fig. 2 left). In the larger natural FPA group, the lever arms were also decreased with the wear of LWI, but the decreases were smaller than in the other group. The smaller decreases in lever arm in the larger natural FPA group were explained by increases in the frontal-plane GRF-shank angles with LWI (Fig. 2 right). Consequently, the difference of changes in KAM 1st peak with LWI between groups was related to less decreased lever arms induced by increased frontal-plane GRF-shank angles in the larger natural FPA group. Further research will be necessary to determine if other interventions could be combined with LWI to avoid the increase of the frontal-plane GRF-shank angle. For example, in the future, we could imagine that LWI will not simply be given to the patients, but that a clinician will help the patients improve their gait patterns when walking with LWI. Interestingly, a recent study showed that the effect of LWI can be improved if walking instructions are given to the patients (Khan et al., 2018).

Medial knee OA literature suggests reducing the KAM impulse, in addition to the KAM 1st peak (Chehab et al., 2014; Mündermann et al., 2004; Thorp et al., 2007). However, when discussing the effect of the FPA, the KAM impulse appears of lesser importance since this variable statistically significantly decreased in both groups, without difference between groups. Consequently, there is no counter-argument between the two KAM variables associated with medial knee OA, and screening for smaller FPA could help identify patients more likely to improve their ambulatory loading with LWI and thus benefit from this intervention.

This study has a few limitations that should be discussed. First, while testing healthy, young, normal weight subjects was justified by the aim to understand the biomechanics of LWI, the finding that FPA could be used to determine which individuals are more likely to have KAM reductions with LWI should be confirmed with medial knee OA patients. Second, this study separated participants in two groups of same size according to their natural FPA, which led to a separation value of about 15° of natural FPA. Further works are needed to determine if a strict threshold is the most effective method to differentiate individuals. Third, additional studies are also necessary to determine whether the response to LWI is equivalent between an individual naturally walking with a small FPA

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and someone with a larger natural FPA but toeing-in to actually walk with the same smaller FPA. Finally, while the number of subjects was sufficient for the primary objectives and provided valuable insights on LWI mechanism, further studies on larger populations will be necessary for more precise estimation of the effect sizes, as well as to analyze multiple factors simultaneously and establish a responder profile. Indeed, while this study focused on FPA, other factors have been suggested to influence the KAM changes induced by LWI, including foot posture, ankle kinematics and OA severity (Chapman et al., 2015; Sawada et al., 2016; Shimada et al., 2006), and it is likely that other factors, for example describing demographics, alignment and/or walking mechanics, will be associated to the KAM changes in the future. Nevertheless, later, when the questions of comparing factors and building a responder profile will come, it will be important to take into account the possibility to estimate the natural FPA in routine practice (Huang et al., 2016; Menz et al., 2004)

5. Conclusion

This study showed a relationship between the natural FPA and the changes in KAM 1st peak occurring with LWI. Specifically, statistically significant decreases, of adequate effect size, in KAM 1st peak were only observed in the group walking with smaller natural FPA. The different response in the larger natural FPA group was related to an increased frontal-plane GRF-shank angle. Consequently, this study suggested that screening based on the natural FPA could become a simple procedure to identify medial knee OA patients more likely to benefit from LWI. More generally, this study highlighted the needs to better understand the factors influencing the response to LWI and determine if the biomechanical and clinical outcomes could be enhanced by combining LWI with walking rehabilitation.

Declaration of Competing Interest

The authors confirm that none of the authors has any conflict of interest regarding the work presented in this manuscript.

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