The effect of lateral wedge insoles in patients with medial compartment knee osteoarthritis : balancing biomechanics with pain neuroscience

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ABSTRACT

Results on the effects of lateral wedge insoles (LWIs) in patients with medial knee osteoarthritis (OA) are ambiguous and not fully understood. Because of the low cost of this intervention and its clinical utility, attention to LWIs is worth considering. Current insights on the efficacy of LWIs are mainly focused on changing biomechanical aspects, such as the external knee adduction moment, in an attempt to influence pain, functional ability and structural progression. It is however appropriate to interpret the effectiveness of LWIs in a broader concept than the pure biomechanical approach. Given our current understanding of OA-related pain, including the involvement of the central nervous system and nociception-motor interactions, concepts of pain neuroscience should be taken into account. The purpose of this review is to summarize the current state of knowledge regarding the biomechanical effect of LWIs. It aims to discuss the degree to which such biomechanical effect translates to clinical effects (symptom relief, function recovery and reduction of structural progression). In order to explain these clinical effects, this paper balances biomechanics with pain neuroscience. A literature search was performed and reviewed using a narrative approach. Many studies investigated the effect of LWIs on dynamic knee joint loading and beneficial biomechanical effects (reduction in knee adduction moment) were observed in patients with mild to moderate medial knee OA, in particular when using full-length LWIs. However, despite beneficial biomechanical effects, there is insufficient evidence for clinically important effects or significant reductions in disease progression. Evaluating the effects of LWIs, our current understanding of OA pain should be taken into account, as LWIs may be part of a comprehensive biopsychosocial treatment. Future work on all of the variables that could influence clinical outcomes in order to decide in which subgroups of patients LWIs are (most) effective is necessary.

Introduction

Knee osteoarthritis (OA) is the main cause of pain, disability and loss of quality of life in the elderly, with major implications on the individual and public health care level[1-3]. Despite the expected increase in prevalence[4], knee OA is still one of the few chronic diseases with no effective strategy to prevent disease onset or progression.

Traditional management is mainly symptomatic and involves a combination of non-pharmacological and pharmacological interventions[5-7]. Surgical interventions, such as total joint replacements, are reserved for severe clinical disease where conservative strategies have failed to relieve symptoms. The increased number of total joint replacements has provoked the identification of effective non-surgical conservative treatments as a high priority. Because the disease is chronic and characterized by progressive structural degeneration, more attention is drawn to the control of modifiable risk factors for progression in an attempt to delay structural degeneration[8].

In knee OA, the medial compartment is by far the most frequently affected as during the stance phase of gait the centre of mass is located medial to the joint centre, resulting in 70-80% of the knee joint load passing through the medial compartment [9]. Excessive medial tibiofemoral compartment loading during activity has been proposed as a significant contributing factor for progression of medial compartment knee OA[10,11]. Indirect methods to measure dynamic loading include movement analysis, that provides an accurate calculation of external joint moments, relative to internal joint loads[12].

In the recent decades, the external knee adduction moment (KAM) has been recognized as a clinically important measure to study indirectly the medial compartment knee joint loading during movement (Figure 1A)[13,14]. Throughout the entire stance phase of walking, this external KAM tends to adduct the tibia with respect to the femur. The most common KAM

parameter is the peak KAM, which typically occurs early in the stance phase during walking. More recently, the KAM impulse, defined as the integral of the KAM-time curve, has also been investigated because it incorporates not only the magnitude but also the duration of the KAM (Figure 1B)[15]. An increased external KAM during activities such as walking has been associated with pain[16] and progression of medial compartment knee OA[10,11].

[Figure 1(with reference [17])]

Recognition of this mechanical component influencing pain and structural progression has led to intervention strategies that seek to reduce dynamic knee joint loading. Knee braces, insoles and unloading footwear are popular non-invasive approaches that have the potential to reduce the external KAM during walking in patients with knee OA[18-21]. For instance, valgus bracing achieves effective unloading of the medial knee compartment in knee OA patients[22]. However, their long-term compliance seems to be problematic as they are often uncomfortable and not a practical daily solution for many patients.

A simpler, less expensive and probably more comfortable approach for reducing medial knee loading is the use of lateral wedge insoles (LWIs). These insoles fit comfortably inside the shoes and are thicker at the lateral than at the medial side, transferring load from the medial to the lateral knee compartment during weight bearing. LWIs have been strongly recommended in previous clinical guidelines for knee OA management[23]. However, the most recently published guidelines for non-pharmacological knee OA management rejected their use[5,24]. Results on the effects of these insoles are still ambiguous and not fully understood with different research groups declaring different recommendations. Given the low cost of this intervention and its clinical utility attention to LWIs is still worth considering.

From a clinical perspective, symptom reduction and functional improvement are the ultimate goal of interventions such as LWIs. In addition, the effect of LWIs on the reduction of structural

progression is very important in the context of secondary prevention. Given the assumption that a significant effect of LWIs on knee joint loading would translate to pain relief, functional recovery and reduction of structural progression, current insights on the efficacy of LWIs are often focused on changing biomechanical aspects such as the KAM (input mechanisms) in an attempt to influence OA-related pain.

It is however important to realize that OA pain experience is multidimensional in nature. This implies that in the management of chronic OA-related pain it is crucial to consider the broader concept of pain mechanisms[25]. Pain mechanisms can be categorized into input, output and processing mechanisms. Input mechanisms include nociceptive and peripheral neurogenic pain, output mechanisms entail the motor, autonomic, immune and neuroendocrine systems, while processing mechanisms include central sensitization (CS) and cognitive-affective mechanisms of pain[26]. In recent years, there is increasing evidence that altered central pain processing mechanisms, such as CS or hyperexcitability of the central nervous system, play a significant role in a subgroup of patients with knee OA[27,28]. In addition, neurophysiological research has provided us with an increased understanding of nociception-motor interaction in patients with (chronic) pain[29-31]. Nociception impairs motor output through central mechanisms (e.g. decreased excitability of the motor cortex, altered motor unit recruitment during movements). This way, nociception may prevent normal movement coordination and possibly increased knee joint loading. Both concepts of pain neuroscience and motor adaptation to pain should be considered consequently when interpreting the effects of LWIs.

The purpose of this review is 1) to summarize the current state of knowledge regarding the biomechanical effect of LWIs, 2) to discuss whether and to what extend such biomechanical effect results in clinical effects such as symptom relief, functional recovery and reduction of structural disease progression, 3) to explain and interpret these clinical effects by balancing a

biomechanical with a neuroscientific framework, and 4) to identify if there is evidence to predict those patients who will benefit from LWIs and those who will not.

Method

Papers were selected from the electronic databases PubMed and Web of Science using keywords for knee OA (”Osteoarthritis, Knee”[MeSH]) and for LWIs (“Foot Orthoses”[MeSH] or “Insoles”). To focus the search results, these keywords were combined with other keywords (“Knee Joint Loading”, “Knee Load”, “Knee Adduction Moment”, or “Pain”[MeSH], “Activities of Daily Living”[MeSH], “Functional Ability” or “Disease Progression”[MeSH], “Structural Degeneration”, “Magnetic Resonance Imaging”[MeSH], “Radiography”[MeSH]). Relevant studies related to the biomechanical or clinical effect of LWIs in patients with medial knee OA were included in this review.

Effect of lateral wedge insoles

Studies investigating the effect of LWIs in medial knee OA are heterogeneous in nature, using different insole properties or comparison treatments, varying patient characteristics, outcome measures and follow-up periods.

First, the biomechanical effect of LWIs on dynamic knee joint loading will be reviewed. Next, the assumption that a significant effect on knee joint loading would also translate to symptom relief and functional recovery will be addressed. From a clinical perspective, symptom reduction and functional improvement are the ultimate goal. However, in the context of secondary prevention, the effect of LWIs on structural disease progression is important as well

and will be discussed. The effects on symptom relief, functional improvement and structural disease progression will be interpreted by balancing biomechanics with pain neuroscience.

Biomechanical effect

The immediate effect of LWIs on the external KAM has been examined in both healthy and knee OA patient populations. In healthy subjects, the use of 5° or 6° inclined LWIs significantly reduced the peak KAM during walking[32,33], but no significant reductions in KAM were observed when using 10° inclined insoles[34]. In knee OA patients, multiple studies[35-40], including a systematic review[41], have shown that LWIs with an inclination between 5° and 15° significantly reduced the peak KAM during walking when compared to walking with no insoles or non-wedge insoles. More recently, a decreased KAM impulse during walking has also been shown in patients with medial compartment knee OA using LWIs[38,42,39]. This effect on the reduction in KAM does not appear to decline after continuous use of the insoles over 1 month or 1 year[38,43].

Several mechanisms explaining this KAM reduction have been postulated. It was assumed that the reduced KAM is not simply the result of a slower walking speed or reduced stride length secondary to walking with LWIs, as no differences in these parameters were found between walking with wedge insoles, non-wedge insoles or no insoles[35]. In addition, the significant reduction in KAM walking with LWIs compared to non-wedge insoles suggests that the effect of the wedge is not merely the result of insole cushioning, but rather the result of directly altering knee joint biomechanics[35].

The key mechanism explaining this decrease in KAM and load-reducing effect seems to be a reduction in knee-ground reaction force moment arm[39]. LWIs are indeed designed to alter the position of the centre of pressure under the foot[36,20,44], which moves the ground reaction

force laterally with respect to the knee, reducing the ground reaction force moment arm around the knee in the frontal plane. Computer modelling and simulation has shown that 1mm lateral displacement of the centre of pressure under the foot decreases the peak KAM by 2%, resulting in a 1% reduction in peak medial compartment knee joint loading[45].

Although there is a vast amount of literature confirming significant reductions in KAM walking with LWIs, this biomechanical effect is not consistently observed in all studies. In fact, some studies showed no effect on the KAM during walking[46,34] and, in some cases, LWIs even increased the KAM[20,47,35,48].

Reasons for this inconsistency may be related to LWIs properties or shoe characteristics. Most studies demonstrating a beneficial effect on the KAM used full-length insoles that wedged the foot from heel to forefoot[15,32,33,36]. In contrast, studies demonstrating no effect on the KAM used insoles that wedged only the heel[46,34]. One study actually compared the effect of full-length LWIs on the KAM with that of heel wedges in patients with medial knee OA. Full-length wedges were more effective at reducing the KAM than heel wedges[36]. The optimal degree of inclination should be further investigated, as well as the choice between custom-made and off-the-shelf insoles. Individualization of the degree of inclination might optimally balance the biomechanical effect (KAM reduction) and the discomfort reported by the patient[37,35]. A study comparing 5° and 10° LWIs with comparable thickness non-wedge insoles in patients with knee OA showed that 5° wedges reduced the KAM by approximately 6% and 10° wedges by approximately 8%. However, 10° wedges were less tolerated by patients due to pain[35]. Footwear used in combination with LWIs needs to accommodate for such insoles in benefit of optimal comfort so that patients want to use them together. Different types of footwear may alter the effectiveness of LWIs due to different biomechanical effects, which should be considered in future studies.

The addition of subtalar strapping or medial arch support to LWIs can also influence biomechanical effects in knee OA patients. The addition of subtalar strapping seems to reduce the KAM more during walking compared to conventional LWIs[49]. Strapping causes valgus angulation of the talus which corrects the femorotibial knee angle[50]. The addition of a medial arch support to LWIs also reduced the KAM more efficiently, possibly because of elimination of potential negative effects of LWIs[51].

Inconsistency in the results on the effect of LWIs on the KAM also suggests that patient characteristics may mediate these biomechanical effects. Disease severity may be important as LWIs seem to reduce the KAM significantly in patients with early to mild knee OA (Kellgren & Lawrence (K&L) grades 1–2), but not in patients with moderate to severe knee OA (K&L grades 3–4)[52]. Previous studies suggest that certain patient groups are more likely to respond to treatment with LWIs[44,48,53], but studies evaluating the role of specific patient characteristics are scarce. Characteristics that could mediate biomechanical responsiveness to LWIs include foot alignment and motion, frontal plane knee alignment and baseline KAM. For example, greater reductions in KAM are seen in subjects with more frontal plane rear foot motion[48]. Prescription and casting methods seem to differ between studies as well depending on the practitioner involved, which can also, in part, explain conflicting results. In fact, inter-practitioner variability seems to be a major factor in orthotic interventions when treating a single patient[54].

Taken together, although several studies investigating the effect of LWIs on dynamic knee joint loading show methodological heterogeneity[41], there seems to be evidence to confirm beneficial biomechanical effects. A systematic review shows that most studies that included subjects with medial knee OA using LWIs reported significant reductions in the external KAM, certainly when patients had mild to moderate medial knee OA and when full-length LWIs were used[41].

In patients with unilateral medial knee OA, the medial unloading effects of LWIs seem to occur not only in the affected knee, but also in the contralateral knee. This contralateral reduction seems to be as great as or even greater than that in the affected limb[42]. In obese individuals (average BMI 37.2 kg/m^2) without knee OA, the use of LWIs also reduced the peak KAM and KAM impulse in both knees[55]. Both the contralateral knee in patients with unilateral knee OA and the knees in obese individuals are at high risk of future medial knee OA[56,57]. As an increased KAM has been associated with development of medial knee OA, these findings may have important implications for disease prevention. This non-invasive intervention may be able to prevent or delay disease onset, but future randomized controlled trials (RCTs) should determine if LWIs can effectively postpone or prevent disease development.

Clinical effect

Effect on pain and functional ability

Given the effectiveness of LWIs at reducing medial knee joint loading during activity, it is often assumed that this effect will also translate to pain and symptom relief and to functional recovery.

However, studies examining clinical outcomes following treatment with LWIs have shown inconsistent findings. Some literature overviews report positive clinical outcomes such as symptom improvement and particularly reductions in the use of non-steroidal anti-inflammatory drugs (NSAIDs)[58-60]. In contrast, a review by Reilly et al.[61] suggests no major or long-term beneficial effects when using LWIs. It is suggested that, because of the heterogeneity in study design and poor quality of some studies, conclusive evidence for positive clinical effects of LWIs cannot be stated[62,63]. The most recent systematic reviews, including

comprehensive meta-analysis, published results on the efficacy of using LWIs on pain and function in medial knee OA[64,65]. They concluded that LWIs have no significant or clinically important effects on knee pain compared to non-wedge insoles[64,65]. Both types of insoles were similar with regard to functional outcomes, analgesic requirements, adherence to insoles or complications[65]. There was only evidence to suggest that LWIs do significantly reduce NSAIDs requirements[65]. Results of these meta-analyses suggest that compared with control interventions, LWIs are not efficacious for the treatment of knee pain and functional disability in knee OA[64,65].

Given some inconsistency in biomechanical effects of LWIs due to differences in study design - including insole properties, shoe characteristics or patient characteristics - it is reasonable that not all types of LWIs do provide good clinical outcome and that not all patients with medial knee OA do benefit clinically[66]. Specific characteristics can influence both beneficial as well as adverse effects.

Taken together, despite the beneficial biomechanical effect of LWIs in medial knee OA, results of systematic reviews with meta-analysis show that there is no evidence to prove clinical effects[64,65]. It is often suggested that the amount of KAM reduction might not be sufficient to reduce pain[64]. Other factors such as sagittal knee joint moments, muscle co-contractions and passive soft tissue tension in and around the knee also contribute importantly to medial knee joint loading, so that reducing the KAM alone may be insufficient to reduce pain[64].

Additionally, it is important to realize that multiple mechanisms are involved in pain experience or functional disability in knee OA. OA pain has historically been related to peripheral joint pathology. The traditional biomedical model, which underlies training and education of the majority of physical therapists[67], has favored the formulation of direct correlations between joint pathology and symptoms. A greater expression of symptoms in patients with knee OA

would therefore indicate greater underlying pathology. However, knee OA is a disease characterized by chronic pain. Similar to other chronic pain conditions (i.e. fibromyalgia[68]), there is growing body of research suggesting that in a subgroup of patients with knee OA (particularly those with moderate to severe symptomatic OA[69]), the clinical picture is dominated by sensitization of central nervous system pain pathways (i.e. CS) rather than by biomechanical or structural factors causing nociceptive pain (reviewed by Lluch Girbes et al.[27]).

Pathophysiological mechanisms underlying CS are complex and numerous, but the net effect is an amplification of neural signalling within the central nervous system that elicits pain hypersensitivity[70]. It is a broad concept reflecting not only spinal cord sensitization, but also an alteration of sensory processing in the brain[71], loss of descending anti-nociceptive mechanisms[72], enhanced facilitory pain mechanisms[71,73], increased temporal summation or wind-up[73] and long-term potentiation of neuronal synapsis in the anterior cingulate cortex[74]. The outcome of the processes involved in CS is an increased responsiveness to a variety of stimuli. When the central nervous system is sensitized, either no or minimal and undetectable tissue damage is required to induce pain.

Chronic pain is also influenced by cognitive, affective and psychosocial variables (i.e. mood, coping and social support), which can vary between patients and within a patient over time. Several psychosocial variables (i.e. catastrophizing, high level of depression, cognition about pain) have been suggested as influencing OA pain and disability[75]. Maladapted pain cognitions might dominate pain experience and functional disability in some patients with knee OA. Within this context, previous reports showed inconsistent results investigating the association between structural joint abnormalities, measured by radiography or Magnetic Resonance Imaging (MRI), and clinical features of knee OA[76-79]. These findings might be explained by the presence of altered pain processing in some patients with knee OA. In line

with this thinking, it is not surprising that beneficial biomechanical changes, such as KAM reductions, do not always guarantee pain reduction or functional recovery.

Moreover, given our current understanding of nociception-motor interactions[29-31], it seems rational to look at it from a different angle. LWIs are expected to reduce pain due to their effects on KAM reduction, which imparts a pure biomechanical viewpoint. Pain neuroscience, and more specifically the effects of pain on movement, suggests that LWIs or any other analgesic intervention leads to improved movement control (due to the diminished detrimental effects of nociception on motor output). Hence, LWIs and consequent pain reduction might lead to KAM reduction rather than vice versa. Still, further study is required to either refute or confirm these hypotheses as often the truth might lie in between both options, or a combination effect might even occur.

Effect on structural progression

Given the significant reduction in KAM when using LWIs and considering the established relation between compartmental knee joint loading and structural deterioration over time, it would seem logical to expect an influence of LWIs on structural progression in medial knee OA.

However, a RCT failed to show structural benefits in patients with medial knee OA wearing LWIs for 6 months and 2 years compared to control insoles[80,18]. The non-significant effect on structural progression could be related to the use of heel wedges in the 2 year follow-up study[80], as heel wedges do not reduce medial load as much as full-length wedges[36]. Moreover, in both studies structural joint changes were measured with conventional radiography, which is not sensitive enough to detect small structural changes.

Although knee OA has traditionally been characterized by progressive articular cartilage loss and new bone formation, it is now generally accepted that knee OA can be regarded as a "whole organ" disorder, also including events in ligaments, menisci and synovial and adipose tissues[81,82]. Therefore, in recent decades, MRI has been proposed as an important tool in the evaluation of structural joint changes over time, since MRI allows not only direct visualisation of cartilage loss, but also identifies non-cartilage structures. For that reason, Bennell and colleagues carried out a RCT to assess the efficacy of full-length LWIs compared with control insoles worn daily for 12 months on slowing structural progression (measured on MRI), in medial knee OA[83]. Results of this study showed no reduction in rate of cartilage loss or size of bone marrow lesions over time. So, although they used LWIs that had proved effectiveness in reducing knee load[20] and incorporated a sensitive outcome measure to assess structural joint changes (MRI), no structural benefits were observed after using LWIs.

As knee OA usually progresses slowly[84,85], it is possible that the duration of these follow-up studies was still insufficient to observe a significant effect on structural progression. It is also conceivable that LWIs are only effective in slowing down structural degeneration in subgroups of OA patients, but this needs further investigation. For example, one could argue that LWIs might be more effective on structural progression in patients with isolated medial compartment OA than in those with multiple compartment knee OA. However, associated patellofemoral or lateral compartment OA did not affect results on structural progression[18].

Importantly, structural progression of knee OA is likely to be a multifactorial issue, for which nociception-motor interactions may be taken into account as well. The interaction between nociception and motor output is very complex, especially in cases of chronic nociception as in knee OA. Indeed, knee OA implies chronic nociceptive input, which is likely to result in altered movement patterns. Our current understanding of nociception-motor interactions[29-31] has informed us that nociceptive stimuli result in cortical delay of motor output in humans and

reduced activity of the painful muscle. Nociception impairs motor output through central mechanisms: activated neurons in the somatosensory-cortex produce a pain-dependent inhibitory input to the primary motor cortex (both ipsilateral and contralateral)[86,87], and tonic human muscle nociception results in long-lasting inhibition of the primary motor cortex[88]. In addition, the nervous system employs a different (i.e. compensatory) motor unit recruitment strategy to maintain force during pain, which includes the inhibition of one population of motor units and the concurrent recruitment of a new population of motor units[89], resulting in an altered movement pattern[90].

If one translates these findings to knee OA, a broader picture appears. Studies that report relationships between an increased KAM and pain[16] or structural progression[10,11] often suggest that the increased knee joint loading is the main factor contributing to pain and structural degeneration. However, understanding how pain affects motor output makes us wonder whether the reverse could be true as well. Could knee OA pain change, for example, muscle recruitment in and around the OA affected knee and thus alter biomechanical stress, resulting in faster structural degeneration? Future research should investigate these promising avenues.

Likewise, in clinical practice it might be worthwhile using LWIs for patients with OA as long as they impart analgesic effects, regardless of their (immediate) biomechanical effects. If they reduce nociception in the short term, then they are likely to diminish the negative effects of nociception on central movement control as outlined above. This in turn might allow neuromuscular retraining to occur, which in turn might lead to slowing down cartilage destruction. Hence, LWIs combined with neuromuscular training might impart a synergistic effect.

Conclusions

Multiple studies provided biomechanical evidence for a KAM reduction due to LWIs in medial knee OA. However, despite this biomechanical effect, LWIs produce no significant or clinically relevant symptom relief or functional improvement. Moreover, although excessive dynamic knee joint loading has been proposed as a significant contributing factor for progression of knee OA, no long term structural benefits were shown in medial knee OA using LWIs. At present, there is insufficient evidence to guide clinicians regarding which knee OA patients are most likely to benefit from LWIs.

As LWIs offer great potential as simple, inexpensive treatment strategies for medial knee OA, further research on all of the variables that could influence the outcome is needed. Potential areas for further research are for example determining the difference between custom-made and off-the-shelf insoles, optimal degree of wedging, effect of different types of footwear used in conjunction with LWIs, influence of disease severity and the effect of combining treatment interventions. In addition, there is a need for RCTs with longer follow-up which establish definite conclusions on the effect of LWIs on disease progression. Moreover, further research is needed to determine the optimal outcome, determining for example pain or disease progression, when evaluating the effect of LWIs.

It is important to realize that LWIs could be effective in some subgroups of patients rather than in the whole knee OA population. In order to understand why some patients do show beneficial effects using LWIs and others do not, future evaluation of patient characteristics that mediate lateral wedge effects is required. In this context, our current understanding of OA pain, including the involvement of the central nervous system and nociception-motor interactions, should be taken into account.

Recent guidelines recognize that diseases such as knee OA must be studied and treated within a biopsychosocial perspective[24]. As it has been shown that altered pain processing mechanisms are present in some knee OA patients, it is important to identify this subgroup of patients[27,91]. In those with altered pain processing or CS, pain is disproportional to the tissue damage, due to hyperexcitability of the central nervous system. A non-significant effect of LWIs on knee OA symptoms would be expected in this subgroup, as there is no longer a clear relationship between peripheral input and perceived pain. So, the presence of altered pain processing in some patients with knee OA may, in part, explain the discrepancy in the results on the effect of LWIs. However, the role of interventions such as LWIs in patients with CS or altered pain processing needs to be explored.

In addition, nociception-motor interactions should be considered when treating patients with knee OA. It might be relevant to stop trying to restore normal motor control and decrease knee joint loading in case of chronic nociception in patients with knee OA. It seems more reasonable to search for treatment strategies that reverse the effects of chronic nociception on motor performance. However, clinical studies are required to examine whether activating nociceptive inhibitory pathways might address nociception-motor interactions. These are important avenues for future work in this area.

Optimal treatment for people with knee OA requires determination of how peripheral and central factors contribute to the clinical expression in each patient in order to enable tailored treatment strategies. Altered pain processing seems to be driven by ongoing peripheral joint pathology[92,93], which stresses the importance of reducing nociception in OA by means of locally applied interventions. So, LWIs may be part of a more comprehensive biopsychosocial treatment in which the insoles serve as a manner to reduce the nociceptive barrage of the central nervous system in order to slow down the process of CS.

Finally, when investigating the effect of LWIs it is very important that researchers clearly state in as much detail as possible insole properties, shoe and patient characteristics. Including more detailed description of these variables would facilitate comparisons across studies and enable clinicians to decide in which subgroups of patients LWIs are (most) effective.

Disclosures None

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FIGURE LEGENDS

Figure 1. (A) Illustration of the external knee adduction moment (KAM), representing medial compartment loading. The load depends on the magnitude of the ground reaction force vector and the perpendicular moment arm from its line of action to the knee joint centre[17]. **(B)** Representative KAM waveform during gait. The peak KAM typically occurs early in the stance phase. The KAM impulse is represented by the area under the curve.

FIGURES

Figure 1