Knee OA, biomechanics, and progression to TKA

The frontal and sagittal plane gait biomechanics associated with progression to total joint replacement in patients with knee osteoarthritis, particularly variables related to sustained loading, may be promising new targets for conservative interventions.

By Cheryl Hubley-Kozey, PhD, and Gillian Hatfield, PT, PhD

Osteoarthritis (OA), the most prevalent type of arthritis, is characterized by damage to articular cartilage, a protective layer over the ends of bones, leading to changes in other joint structures (bones, ligaments, muscles, and nerves) that subsequently result in pain, stiffness, and functional disability in adults. OA is common at the knee joint, more so in the medial tibiofemoral compartment than the lateral compartment. For people older than 65 years knee OA results in more difficulties in performing activities of daily living, such as walking or climbing stairs, than any other medical condition. Currently, there is no cure for knee OA. Nonsurgical interventions have focused primarily on pain relief, and include pharmaceuticals, exercise, and various therapeutic modalities, with total knee arthroplasty (TKA) the main treatment for individuals with advanced OA.

Unfortunately, TKA rates are rising. In the US, the demand for primary TKA is projected to grow 673% between 2005 and 2030, to 3.48 million procedures, and five-year increases of 21.5% were reported for 2012 to 2013 in Canada. However, not all individuals with knee OA are suitable candidates for surgery, and not everyone is satisfied with the results of surgery. Furthermore, residual functional deficits exist after TKA. While more than 35% of patients receiving TKA are aged between 65 and 74 years, the cohort aged 55 to 64 years had the largest five-year percentage increase from 2008 to 2009 (14% and 16.5% increases for men and women, respectively). This is concerning because knee implants have a lifespan of 15 to 20 years, so TKA is not an ideal solution for younger people as they will likely require at least one revision, and patient satisfaction and clinical outcomes diminish following revision surgery. Alternative interventions aimed to slow knee OA progression and ideally delay or even prevent the demand for TKA are crucial.

OA processes have two components: the disease (structural damage) component and the illness (symptom) component, described by Lane et al, and these two components are not always well-correlated. Thus, TKA offers an identifiable clinical endpoint, with surgical decisions based on both components, ie, patient

Findings related to muscle activity during gait and progression to TKA may explain why interventions to improve joint stability can impact symptoms but not KAM.
Complaints of pain and functional deficits as well as radiographic evidence of joint structural damage.\textsuperscript{11} Developing interventions to reduce rates of TKA requires an understanding of the factors responsible for more rapid progression to TKA in some patients with moderate OA, specifically modifiable factors.

Pharmaceutical interventions represent the most commonly used category of nonsurgical interventions and, though effective at reducing pain and improving functional deficits,\textsuperscript{12} most are not designed to slow structural damage. In fact, masking knee OA pain with medications might accelerate progression, as decreased pain intensity is associated with increased dynamic knee joint loading in patients with mild to moderate knee OA, a change that can create a negative mechanical environment on the joint.\textsuperscript{13} Early research into disease-modifying osteoarthritis drugs that aim to inhibit destructive enzymes\textsuperscript{12} shows promise. However, OA is a mechanically induced disorder, so if the negative biomechanical environment is not addressed, any pharmaceutical treatment is unlikely to provide a long-lasting benefit.\textsuperscript{14}

Less used are conservative nonpharmaceutical interventions that target the biomechanical environment, such as braces, heel wedges, and exercise. Resistance to using these interventions has developed in part because the collective results of conservative interventional studies are equivocal for pain and symptom outcomes, which sometimes do not relate well with the biomechanical outcomes measured in these studies. Part of this disconnect can be explained by lack of correlation in the literature between structural damage and worsening of pain.\textsuperscript{10} Perhaps another explanation is that studies so far have focused on one biomechanical factor, the peak external knee adduction moment (KAM). KAM is a surrogate measure for the ratio of the medial-to-lateral load on the knee joint, as it has been significantly correlated with medial compartment contact force and the ratio of medial compartment to total knee force as measured by an instrumented knee prosthesis.\textsuperscript{6} Peak KAM has been identified as the key biomechanical target and hence the main outcome in interventional studies of medial compartment knee OA, based primarily on cross-sectional studies of OA and gait, as well as one well-cited longitudinal study.\textsuperscript{16}

More recently it has been recognized that, to understand the loading environment, one needs to consider 3D loads and muscle forces. New evidence suggests that dynamic knee loading characteristics, including frontal and nonfrontal plane moments, during gait are linked to knee OA progression, predominantly structural progression. These findings are fundamental, as structural progression is a component of TKA clinical decision-making.

**Gait and structural progression**

The hallmark longitudinal study by Miyazaki et al published in 2002 reported higher peak KAM in those who had increased medial joint space narrowing based on radiographic grades over six years than those who did not.\textsuperscript{16} Using logistic regression analysis, the risk of radiographic progression of knee OA increased more than six-fold with every 1% increase in peak KAM.\textsuperscript{16} As a result of its relationship with medial compartment loading,\textsuperscript{9} and particularly with knee OA progression,\textsuperscript{16} peak KAM has become the most common biomechanical gait variable used as a target for conservative interventions. Orthotic devices such as lateral wedge insoles\textsuperscript{7} and valgus unloader braces,\textsuperscript{18} muscle strengthening exercises,\textsuperscript{19} and gait modifications\textsuperscript{20} have all been recommended to reduce the magnitude of peak KAM.

Two recent studies using magnetic resonance imaging (MRI) have supported the predictive value of peak KAM in knee OA structural progression. In a small sample of 16 individuals with predominantly mild to moderate disease (Kellgren Lawrence [KL] grade 1-3), higher baseline KAM peaks were associated with five-year changes in the ratio of medial-to-lateral compartment cartilage thickness in the femur.\textsuperscript{21} A study using a large cohort (n = 391 knees) with a range of OA disease severities also found that higher peak KAM at baseline was associated with greater numbers of bone marrow lesions detected using MRI at two-year follow-up.\textsuperscript{22} However, another longitudinal MRI study found no predictive value for peak KAM in detecting medial cartilage volume loss at one-year follow-up in a cohort (n = 144) with moderate OA disease (KL grade 2-3).\textsuperscript{23} The latter finding might be explained by the shorter follow-up period, but also might reflect a potential limitation of peak KAM as a measure, as it represents only one point in the gait cycle (usually during weight acceptance), and thus only a fraction of the information within the entire waveform is being evaluated.

KAM impulse (the integral of the nontime-normalized KAM waveform) has been identified as an alternate outcome measure, as it considers both the magnitude and duration of knee loading throughout the gait cycle.\textsuperscript{24} KAM impulse is related to knee pain,\textsuperscript{25} and, importantly, has been found to be predictive of knee OA structural progression. In two MRI studies, higher KAM impulse at baseline was associated with greater cartilage volume loss over 12 months,\textsuperscript{23} as well as with both worsening of bone marrow lesions and medial cartilage volume loss at two-year follow-up.\textsuperscript{22}

Collectively, these results support that KAM characteristics (peak and impulse) are predictive of structural progression outcomes, but show that the specific variable assessed has an impact on the outcome. KAM, however, is limited as it provides a measure of the ratio of medial-to-lateral compartment loading, whereas the external knee flexion moment (KFM) is related to the overall loading environment.

Two longitudinal biomechanical studies have taken both moments into consideration in the past year. In the first study relating nonfrontal plane moments to knee OA structural progression, peak
Continued from page 26

KAM at baseline had a greater influence on the five-year change in the ratio of femoral medial-to-lateral compartment cartilage thickness than peak KFM at baseline; including the baseline peak KFM in the model added to the overall variance explained (40%). Furthermore, peak KFM at baseline was the most significant predictor of changes in the tibial medial-to-lateral compartment cartilage thickness ratio, explaining 40% of the variance. Interestingly, pain added to the prediction model (60% total variance explained) for the femoral changes, whereas walking velocity added to the tibial prediction model (49% total variance explained). This study sample was small, and the second, larger cohort study showed no predictive value for the KFM peak and MRI outcomes, but the follow-up time for the larger cohort was only two years.

Although different predictor variables, follow-up times, and progression outcomes were used in these four longitudinal studies, all showed that external knee joint moment features were related to structural progression. Thus, these results suggest that focusing only on one biomechanical target (e.g., peak KAM) may be an oversimplification, and the effect of changing one feature on other mechanical factors should be addressed when identifying biomechanical targets. For example, Chehab et al’s finding of higher early peaks for both moments supports a higher overall peak joint load in patients who experienced cartilage changes; therefore, determining how to alter both moments simultaneously should be considered. Predictive models provide the basis for identifying potential targets, but establishing validity will require interventional studies that include quantitative measures of structural progression as opposed to using only pain as the main outcome.

Because structural changes are poorly correlated with patient symptoms, the biomechanical factors driving structural progression may differ from factors driving symptom progression. Differences in mechanisms may explain why interventions aimed at reducing KAM variables might not always be accompanied by decreases in pain. TKA is a clear progression endpoint that includes both symptom and structural aspects of progression, with both aspects considered in TKA surgical decision-making. Determining whether biomechanical factors are predictive of progression to TKA could refine the identification of biomechanical targets and outcome measures for developing conservative interventions with clinically important outcomes.

Gait biomechanics and progression to TKA

Less work has been done on symptom progression, with one longitudinal study finding a higher peak KAM at baseline during a variety of activities in a group of older adults who developed chronic knee pain at three- to four-year follow-up than in those whose pain did not progress. In Miyazaki et al’s hallmark study, a subset of participants went on to have TKA. These participants were not analyzed subsequently in the structural progression aspect of the study; however, their descriptive data showed they were older and had greater varus knee joint angles and higher pain scores than the nonsurgical group, indicating that their OA was indeed more severe at baseline. Consequently, the higher peak KAM also found in the group that progressed to TKA is likely not an independent predictor of the need for surgery.

In a recent study of 54 participants with moderate medial compartment knee OA, we found that 3D gait biomechanics differed at baseline between those who progressed to TKA within seven years and those who did not, despite similarities in other factors related to knee OA progression, such as age, sex, body mass index, frontal plane angle, radiographic disease severity, pain, and physical activity level. Both KAM and KFM dynamic characteristics, determined using principal component analysis, were significantly different at baseline between those who progressed to TKA (n = 26) and those who did not. Specifically, a higher overall KAM magnitude, a smaller difference between the early stance and midstance KAM magnitudes, and a smaller knee flexion/extension moment range were found in those who progressed to TKA. The higher overall KAM magnitude indicates an increased ratio of medial compartment loading relative to lateral compartment loading throughout the entire gait cycle, and is consistent with the previous studies linking higher KAM impulses and peaks to structural progression. This is not surprising, since structural progression is part of TKA decision-making, and these magnitude features are highly correlated.

The novel finding of our study was that the dynamic patterns capturing the differences in early to mid- and late-stance magnitudes for both KAM and KFM differed between the TKA and no-TKA groups. Although these features had been previously associated with knee OA severity, they had not been related to progression. The smaller difference between the early and midstance KAM at baseline in the group that progressed to TKA is indicative of a greater ratio of sustained compressive loading pattern on the medial compartment during midstance, which may be detrimental to cartilage. The smaller knee flexion/extension moment range at baseline in the group that progressed to TKA is consistent with a “stiff-knee” gait and sustained loading.

The discriminate analysis indicated that both KAM and KFM features were significant predictors for progression to TKA. The gait model was adjusted by including frontal plane alignment, KL grade, and medial joint space narrowing scores from radiographs, self-reported pain scores, stiffness and function, age, sex, and mass. The same gait variables (and no other demographic or clinical variables) emerged as significant discriminators. Logistic regression analyses determined that a one-unit increase in model score increased the odds of progression to TKA six-fold.

The finding that a smaller knee flexion/extension moment range, as opposed to a higher peak KFM (as seen in the Chehab et al study) was associated with progression to TKA lends support to the idea that some biomechanical factors for structural progression versus progression to TKA may differ. The frontal and sagittal plane gait biomechanics associated with knee OA progression, particularly those related to sustained loading, may be promising new targets for conservative interventions. How these variables can be altered, however, requires an understanding of the underlying cause of these altered gait patterns.

Future research

We are presently focusing on the relationship between soft tissue envelope and knee joint mechanics, specifically muscle strength and activation patterns, to offer insight on potential modifiable variables in those with knee OA who progress both structurally and to TKA. Higher and prolonged agonist and antagonist muscle activity is seen in those with knee OA and is related to disease severity, with preliminary findings showing these patterns exist in those who progress to TKA. The higher activity might reflect a strength deficit or more severe pain, but quadriceps and hamstring muscle strength was not significantly different between groups at baseline, nor did
pain scores differ between the groups that progressed compared with those that did not. Prolonged muscle activation and coactivation is thought to increase joint stability, suggesting more instability in the TKA progression group, though joint space narrowing scores were not different.

Together these activation patterns, however, have the potential to increase and sustain compressive joint contact loads, consistent with the dynamic loading changes observed in those who progress to TKA. In fact, prolonged activity of both hamstrings and quadriceps during midstance was correlated with both the KFM and KAM unloading features in a preliminary analysis (ie, more prolonged activity was correlated with less unloading). These results suggest that simply increasing muscle strength may not be the optimal target for knee OA interventions; potentially, finding a solution to the instability problem through bracing or other methods may be warranted.

Essentially, confirming that higher, more prolonged muscle activity during gait is related to the gait biomechanics predictive of progression to TKA provides a better explanation as to why interventions such as neuromuscular training, muscle strengthening programs, or bracing to improve joint stability can impact symptoms but not KAM magnitude. The gold standard to establish clinical validity for these biomechanical metrics will require long-term follow-up interventional studies to determine if alterations are associated with reduced risk of progression both structurally and symptomatically using TKA as an outcome.

**Clinical implications**

Much of the longitudinal research has focused on structural progression, with evidence emerging that frontal and sagittal plane knee biomechanics during gait play a role in knee OA disease progression. Thus, loading in both frontal and sagittal planes of motion may be important targets to consider in the development and assessment of conservative interventions. At present, there is little research quantifying the role of gait biomechanics in the progression of knee OA symptoms or progression to TKA. Based on previous studies on knee OA structural progression, and the one study on progression to TKA, KAM magnitude offers a potential biomechanical target for interventions, but basing conservative interventions on a single biomechanical target is likely too simplistic.

Although some variability associated with the type of healthcare system and the patient’s willingness to undergo surgery may impact surgical decisions, our statistically validated TKA prediction model was robust, and a next step is to validate a new test set to establish clinical value. Similar validations are needed for the structural progression studies, as no statistical or test set evaluations were performed in the four main studies presented. However, consistency in the general findings supports the integration of features other than peak KAM into the development and evaluation of conservative treatments aimed to delay or prevent TKA.

Cheryl Hubley-Kozey, PhD, is a professor in the schools of physiotherapy, biomedical engineering, and health and human performance, faculties of health professions, medicine, and engineering at Dalhousie University in Halifax, Nova Scotia, Canada. Gillian Hatfield, PT, PhD, is a licensed physiotherapist and postdoctoral fellow in the Motion Analysis and Biofeedback Laboratory at the University of British Columbia in Vancouver, Canada.

References are available at lermagazine.com.