Overall Magnitude Of Loading And Inability To Unload During Stance Predict Progression To Total Knee Arthroplasty

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Introduction: Conservative interventions have been identified as the most important healthcare need for those with knee osteoarthritis (OA), with the majority of interventions focusing on decreasing the peak knee adduction moment (KAM), a surrogate measure of medial compartment loading. While the peak KAM and the KAM impulse have been associated with structural progression, both are discrete variables and therefore do not capture dynamic aspects of loading. Frontal plane biomechanics at the hip (decreased external hip adduction moments) and ankle (decreased toe out angle) have also been associated with knee OA structural progression, indicating that to fully understand how changes to the local biomechanical loading environment of the knee can be achieved, it is important to consider what changes are occurring at the other lower extremity joints in the kinetic chain as well. Three-dimensional, dynamic knee biomechanics during gait, including the, overall magnitude of the KAM, the difference between the early and mid-stance KAM magnitudes, and the difference between the knee flexion and extension moments have been shown to differ at baseline between those with moderate knee OA who progress to total knee arthroplasty (TKA) and those that do not. But, how well each of these gait variables predicts progression, how they interact with hip and ankle biomechanics, and which combination of lower extremity gait variables best predicts progression has not been evaluated. This follow up study determined how well individual (univariate) lower extremity biomechanical gait features discriminated between those who progressed to TKA versus those that did not, and whether a multivariate model including multiple gait features improved the discrimination ability of univariate models. The final study aim was to determine how well the gait biomechanical features that best discriminated between the groups predicted knee OA progression.

Methods: 55 patients with moderate medial compartment knee OA underwent gait analysis at baseline. Ground reaction forces (sampled at 1000 Hz) and segment motions (sampled at 100 Hz) were recorded during self-selected walking. Three-dimensional hip, knee, and ankle angles were expressed in the joint coordinate system. Three-dimensional lower extremity moments were calculated using inverse dynamics and also expressed in the joint coordinate system. All waveforms were time-normalized to percent of gait cycle, and moment waveforms were amplitude-normalized to body mass. Amplitude and temporal waveform characteristics were determined using Principal Component Analysis (PCA) for each gait variable separately. Additionally, discrete parameters were extracted from the KAM waveforms. The first peak was determined as the maximum value in the first 40% of the gait cycle. KAM impulses were calculated from non-time-normalized waveforms for each trial for each participant individually by calculating the area under the positive portion of the waveform during stance phase, and then averaged to get the mean KAM impulse for each participant. During follow up phone interviews 5-8 years later, 27 patients reported undergoing TKA surgery since baseline testing. Unpaired Student’s t-tests were used to test for differences in all baseline demographic and waveform characteristics (hip, knee, and ankle angle and moment PC scores, KAM peak, KAM impulse) between the group that had TKA and the group that did not (α=0.05). Receiver operating characteristic (ROC) curve analyses were used to determine how well each baseline gait biomechanical feature (i.e. univariate analysis) classified progressors (i.e. TKA group). The area under the curve (AUC) was calculated and used to quantify the overall “diagnostic accuracy” of each of the variables. Stepwise discriminate analyses between the TKA and no-TKA groups were performed to determine which combination of gait variables best distinguished between the two groups. The multivariate discriminant function that resulted in the best separation between the two groups was used to calculate discriminant scores for all participants, which were entered into logistic regression models to determine the predictive accuracy of the model.

Results: There were no between-group differences in age (60 years in TKA group vs. 58 years in no-TKA group), mass (92.7 kg vs. 95.4 kg), body mass index (30.7 kg/m2 vs. 30.8 kg/m2), and gait speed (1.2 m/s vs. 1.3 m/s), with similar static frontal plane alignment and radiographic disease severity (Kellgren-Lawrence score) distribution at baseline. The mean time between baseline and follow up was 7.8 yrs for each group. The mean time between baseline and TKA was 4 years. The group that progressed to TKA had higher KAM peaks (p<0.05), KAM impulses (p<0.05), overall magnitude of the KAM (KAMPC1, p<0.05), with less of a difference between the first peak KAM and the mid-stance KAM (KAMPC2, p<0.05), reduced early stance knee flexion and late stance knee extension moments (KFMPC1, p<0.05), decreased hip adduction angles (HAAPC2, p<0.05), decreased dorsiflexion angles in stance (AFAPC3, p<0.05), and decreased stance ankle dorsiflexion moments (AFMPC4, p<0.05) than the no-TKA group at baseline. The KAM impulse was best able to discriminate between the TKA and no-TKA groups (AUC of 0.79), and was the most specific gait variable (100.0%). The multivariate linear discriminant function that best discriminated between the two groups (AUC of 0.89) included the KAM impulse, KAMPC2, and frontal plane alignment. Lower KAM impulses, greater difference between the early and mid-stance KAM magnitudes, and more varus alignment was associated with decreased risk of progression to TKA. A one-unit increase in discriminant score for this model resulted in a seven-fold decrease in the risk of
progression to TKA (odds ratio 0.13, 95% confidence interval of 0.04-0.39, p<0.05).

**Discussion:** KAM features were best able to predict progression to TKA, despite the finding that three-dimensional gait biomechanics at the hip, knee, and ankle were altered in the TKA group. Importantly, the results indicate that two KAM features, one capturing magnitude and duration of loading and one capturing the ability to unload in mid-stance, had both high sensitivity and high specificity to discriminate between the two groups and predict risk of progression. Together, these factors give a more comprehensive indication of the local, dynamic biomechanical environment of the knee, in particular the medial compartment, during gait. Specifically, these two features address three different aspects of the KAM: overall loading magnitude, loading duration, and relative unloading. The results of this study suggest that conservative interventions should consider all three features as potential targets. Future work should determine how the components of the discriminant function can be altered conservatively, and what impact alterations have on the risk of disease progression.

**Significance:** This represents one of only three longitudinal studies to date that have examined knee OA progression and knee local biomechanical dynamic risk factors in an attempt to increase our knowledge on mechanical mechanisms of OA progression. This understanding is needed to guide the design of conservative interventions and could potentially help inform a patient specific implantation strategy at the time of TKA. This study identified two risk factors for progression to TKA that have not yet been identified, which may serve as effective conservative intervention targets.

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![Graph](Image)

**Figure 1:** Baseline ensemble average knee adduction moment waveforms for the TKA (red) and no-TKA (blue) groups. Positive values denote adduction moments.

**References:**

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