ASSOCIATION OF MRI-DEFINED STRUCTURE FEATURES AT BASELINE WITH KNEE PAIN TRAJECTORIES

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INTRODUCTION: Characterizing knee pain trajectories and understanding differences among knee pain trajectories have enormous potential to enhance our understanding of knee pain mechanisms and promote the development of customized treatment and management plans. In addition, identifying different knee pain trajectories can facilitate more efficient and effective clinical trial designs by identifying subgroups of patients who have worse knee pain trajectories and should be targeted for treatment vs. those who have minimal or mild disease trajectories who may not need treatment. The complexity of knee pain reporting has not been systematically considered in prior studies, however. Thus, there is an urgent need to conduct knee pain phenotyping in large longitudinal cohort studies in order to better understand the etiology of knee pain in OA.

OBJECTIVES: 1) To identify diverse knee pain trajectories in the OAI studies using different knee pain measurements over time; and 2) To investigate the potential association between baseline MRI-detected structural changes and distinct temporal knee pain phenotypes.

METHODS: To achieve our objectives, we employed a two-stage strategy. In Stage 1, we initially identified 2560 knees with a baseline WOMAC pain score of 0 from the OAI study. Employing Group-Based Multi-Trajectory Modeling (GBMTM), a maximum likelihood statistical technique rooted in finite mixture modeling, we categorized these knees into three subgroups, each of which demonstrates distinct trajectories over ten years across four key variables: Numerical Rating Scale (NRS) for severity, KOOS knee pain frequency (i.e., none, monthly, weekly, daily), WOMAC disability score, and WOMAC pain score. Subsequently, in Stage 2, we utilized a logistic regression model to examine the relationship between the Group 3 knee pain trajectory identified in Stage 1 vs. Group 1 and Group 2 combined into a reference group, and various MRI-defined features independently, including BML (sum of size scores in 15 sub-regions), cartilage (sum of surface scores and sum of depth scores in 14 sub-regions), Hoffa-synovitis, and effusion-synovitis (ES), as graded by the MRI Osteoarthritis Knee Score (MOAKS). Adjustments were made for age, gender, race, and BMI. This analysis involved a subsample size of 716 knees for which MOAKS readings were available.

RESULTS: Figure 1 illustrates the outcomes of GBMTM analysis, revealing three distinct knee pain phenotypes: Group 1 (1114 knees; depicted in red) and Group 2 (989 knees; depicted in green) exhibit non-progressive and slowly progressive patterns, respectively, while Group 3 (457 knees; depicted in blue) demonstrates a rapid progression trajectory. Figure 2 a) displays the bivariate results. Females exhibit an odds ratio (OR) of 1.39 (95% confidence interval [CI]: 1.02, 1.89) for belonging to the fast progressive phenotype. Furthermore, each unit increase in BML total size scores corresponds to an OR of 1.32 (95% CI: 1.20, 1.45). Conversely, both cartilage and BMI show significant ORs closer to 1. Figure 2 b) displays the multivariate logistic regression findings that include all the variables in the model. Females show a higher OR of 1.57 (95% CI: 1.12, 2.19) for being in the fast progressive phenotype. Furthermore, each unit increase in BML total size scores corresponds to an OR of 1.23 (95% CI: 1.09, 1.39). Results for the other variables are similar to the bivariate analysis except for Hoffa-synovitis, ES, and the fact that both cartilage scores become insignificant. Additionally, advancing age appears to lean towards a higher probability of being classified in the non-fast progressive phenotype.

CONCLUSION: We delineated three distinct knee pain phenotypes using longitudinal OAI data extending over ten years. Our findings consistently reveal knee pain patterns over time across all four distinct knee pain measurements. Moreover, the results indicate a notable gender disparity in knee pain progression. The observed inverse correlation with age may stem from the exclusion of older individuals with non-zero WOMAC pain scores at baseline. Importantly, the presence of structural abnormalities at baseline, such as BMLs and cartilage issues, may serve as a robust indicator of rapid knee pain development.

SPONSOR: Research reported in this abstract was supported by the National Institute of Arthritis and Musculoskeletal and Skin Disease sunder Award Number RO1AR080742. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.
DISCLOSURES: No relevant disclosures
ACKNOWLEDEMENT: OAI investigators, clinic staff and participants
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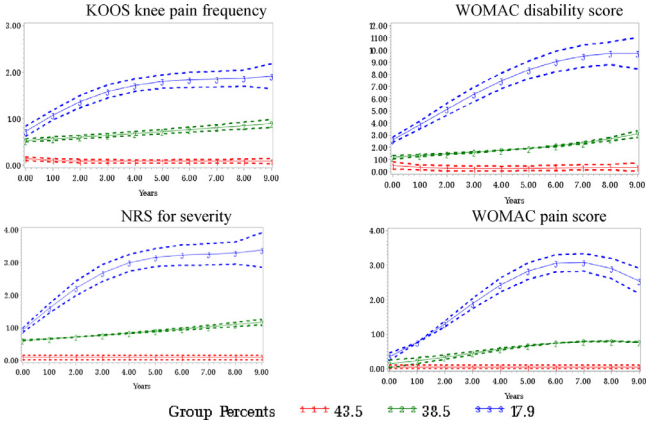

Figure 1. Knee pain phenotypes (three groups) identified using the GBMTM method.

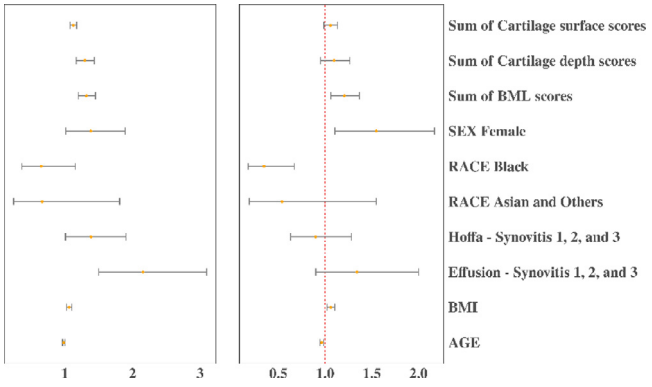

Figure 2. Association results in the bivariate a) and multivariate b) analysis.

doi: 10.1016/j.ostima.2024.100187