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Letter to the Editor

Expanding the Horizon of Multidisciplinarity: Incorporating Biomechanical, Metabolic, and Functional Factors Into Registry-Based Research to Predict Subsequent Risk for Total Knee Arthroplasty

Dear Editor,

We read with great interest the recent study by Concoff et al., "*Association of Knee Osteoarthritis Treatment Types, Patient Characteristics, and Medical History With Subsequent Risk for Total Knee Arthroplasty: Data From a New Real-World Registry. Arthroplasty Today.2025;32:101643.* https://doi.org/10.1016/j.artd.2025.101643," which investigates predictors of total knee arthroplasty (TKA) within 6 months following nonoperative interventions for knee osteoarthritis (OA).

This research provides valuable insights into the role of obesity and Kellgren-Lawrence (KL) grade IV in predicting the need for TKA and contributes significantly to refining clinical decision-making. The findings are particularly relevant for improving patient stratification and early identification of high-risk individuals, offering an important step toward enhancing registry-based predictive models.

However, we would like to highlight additional dimensions that could further strengthen the predictive framework proposed by the authors.

Emerging evidence suggests that biomechanical factors, metabolic conditions, and muscle composition also play critical roles in OA progression, and their inclusion could improve risk stratification models. Among these, mechanical alignment abnormalities such as varus deformity have been widely recognized as independent predictors of TKA [1], yet the study primarily emphasizes radiographic severity (KL grade IV) without fully accounting for these structural factors. Varus malalignment increases medial compartment loading, accelerating cartilage degeneration and structural deterioration, ultimately leading to earlier surgical intervention. Including these biomechanical variables in future registry-based models could provide a more comprehensive prediction of OA progression.

Sarcopenic obesity as a key tissue-cross-talk factor in OA progression is an important consideration, as obesity is rightly emphasized in the study as a major predictive factor for TKA, yet sarcopenic obesity, a condition characterized by high adiposity with reduced muscle mass, is an emerging concept that deserves attention [2]. Studies suggest that sarcopenic obesity not only increases joint load but also contributes to systemic inflammation and impaired muscle support, leading to faster functional decline in OA patients [2]. Given that weight loss strategies may affect fat and muscle mass differently, distinguishing between general obesity and sarcopenic obesity could provide more tailored treatment approaches to delay TKA.

Obesity and hyperlipidemia as independent contributors to OA severity extend beyond mechanical overload, as obesity is increasingly recognized as a metabolic driver of OA. Recent research has demonstrated that hyperlipidemia is associated with increased synovitis and cartilage degradation, independent of body mass index [3]. This reinforces the concept that OA is not purely a wear-and-tear disease but is also influenced by systemic factors.

Future studies incorporating biochemical markers of metabolic dysfunction could improve the accuracy of TKA risk prediction models [4].

Sarcopenia, characterized by muscle atrophy and weakness, is frequently overlooked in OA risk assessments. However, a recent meta-analysis has shown that nearly 1 in 2 OA patients also has sarcopenia (osteosarcopenia), a significantly higher prevalence than in non-OA controls [4]. Given its impact on joint stability and mobility, osteosarcopenia should be considered not just as a coexisting condition but as a potential predictive factor for TKA candidacy [5].

The authors' work represents a significant step toward enhancing registry-based predictive models for TKA by identifying key risk factors such as obesity and KL grade IV severity. To further advance this initiative, a multidimensional approach that integrates biomechanical, metabolic, and functional factors could provide a more comprehensive predictive framework. Incorporating radiographic severity alongside mechanical alignment abnormalities such as varus deformity, distinguishing general obesity from sarcopenic obesity to account for differences in muscle mass and metabolic impact, and considering metabolic indicators such as hyperlipidemia and systemic inflammation would improve risk stratification. Additionally, functional assessments of muscle strength and sarcopenia could enhance patient evaluation, allowing for more tailored interventions. Expanding the predictive model in this way would improve clinical orientation and decision-making. Such an interdisciplinary registry would provide a more comprehensive and realistic tool for predicting OA progression, guiding personalized treatment strategies, and improving the accuracy of estimating the timing of disease progression and the need for surgical intervention, ultimately allowing for more proactive and individualized patient management.

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In conclusion, the study by Concoff et al. is an important and innovative contribution to the field of arthroplasty research. It lays the foundation for refining predictive models for TKA and improving early intervention strategies. By incorporating biomechanical, metabolic, and functional factors into future registry-based research, we can further enhance the accuracy and clinical utility of these predictive models, ultimately leading to a more precise assessment of the risk and timing of TKA within the framework of a real-world registry.

Conflicts of interest

The authors declare there are no conflicts of interest.

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CRediT authorship contribution statement

Francesco Pegreffi: Conceptualization, Writing – original draft. **Maria Tiziana Di Leo:** Conceptualization, Writing – review & editing. **Giuseppe Fanzone:** Conceptualization, Writing – review & editing. **Arcangelo Russo:** Conceptualization, Writing – review & editing. **Sara Bravaccini:** Conceptualization, Writing – review & editing. **Raoul Saggini:** Conceptualization, Writing – review & editing.

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