Universidade Estadual de Londrina

ALEXANDRE ROBERTO MARCONDES PELEGRINELLI

FORÇAS DE CONTATO NO JOELHO E ANÁLISE DA DEMANDA MUSCULAR DURANTE ATIVIDADES FUNCIONAIS EM PACIENTES COM OSTEOARTRITE DE JOELHO:

ANÁLISES COM MODELO MUSCULOESQUELÉTICO

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BANCA EXAMINADORA

Orientador: Prof. Dr. Felipe Arruda Moura
Universidade Estadual de Londrina – UEL

Prof. Dr. Karine Jacon Sarro
Universidade Estadual de Campinas – UNICAMP

Prof. Dr. Paulo Roberto Pereira Santiago
Universidade de São Paulo – USP

Prof. Dr. Paulo Roberto Garcia Lucareli
Universidade Nove de Julho – UNINOVE

Prof. Dr Victor Hugo Alves Okazaki
Universidade Estadual de Londrina – UEL

Londrina, 14 de abril de 2023.

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“O bom da ciência é que ela é verdade,
acredite você ou não.”

Neil deGrasse Tyson

RESUMO

Pelegrinelli, A. R. M. **Forças de contato no joelho e análise da demanda muscular durante atividades funcionais em pacientes com osteoartrite de joelho: análises com modelo musculoesquelético.** Defesa da Tese de Doutorado (Programa de Pós-Graduação em Educação Física UEM-UEL) – Universidade Estadual de Londrina, Londrina, 2023.

A intensidade da força de contato tibiofemoral e a distribuição entre os compartimentos do joelho são relacionados ao desenvolvimento e progressão da osteoartrite (OA). Estas forças de contato durante atividades funcionais podem ser estimadas de forma não-invasiva, utilizando modelos musculoesqueléticos (MSK). As tarefas de marcha, sentar e levantar são consideradas algumas das atividades funcionais mais relevantes e, quando afetadas pela OA, têm impacto na qualidade de vida dos pacientes. Para análises das forças tibiofemoral durante estas tarefas é importante a escolha e definição do modelo mais adequado. Desta forma, o objetivo geral da tese foi identificar as alterações nas forças de contato no joelho durante a marcha, o sentar e levantar em pacientes afetados pela OA. A tese foi dividida em três estudos. No primeiro, o objetivo foi de identificar o melhor modelo MSK para predizer a força de contato vertical no joelho e nos compartimentos medial e lateral. No segundo estudo, as alterações na força de contato no joelho e da demanda muscular durante a marcha foram comparadas entre pacientes com OA de joelho e indivíduos controles. Além disso, um modelo de predição baseado em aprendizagem de máquina foi empregado para identificar as variáveis cinemáticas e cinéticas mais relevantes e testar a capacidade de predizer os picos de força tibiofemoral. Por fim, no último estudo, foram analisadas as tarefas de sentar e levantar quanto às forças musculares e no joelho em pacientes com OA. No primeiro estudo, o modelo adaptado proposto foi o que melhor estimou as forças de contato vertical total e nos compartimentos medial e lateral para as atividades de sentar e levantar. Os resultados foram comparados com dados medidos *in vivo* em pacientes com uma prótese instrumentada de joelho. Para a marcha os resultados foram similares entre os modelos analisados. Diante desse resultado, o modelo adaptado foi empregado para as análises nos estudos 2 e 3, para a comparação entre pacientes com OA grave de joelho e controles saudáveis. No estudo 2, utilizando um modelo preditivo, *generalized linear model* (GLM), o primeiro pico de força vertical total no joelho e os dois picos no compartimento medial foram preditos com um erro em torno de 6 a 10% do pico calculado. O momento extensor do joelho e o abdutor do quadril foram as variáveis mais relevantes para predizer as forças total e no compartimento medial, respectivamente. Ainda, a comparação entre os grupos mostrou maiores valores de vale entre os picos para a força de contato vertical no grupo OA comparado aos controles. Adicionalmente, os pacientes com OA modificaram a marcha para reduzir a força no compartimento medial comparado aos controles. Por fim, no último estudo a tarefa de sentar foi a mais afetada na OA de joelho comparado ao levantar. A força muscular dos vastos foram reduzidas no grupo OA durante a atividade sentar, onde a contração é principalmente excêntrica. Para as duas tarefas, as força vertical total e no compartimento medial foram menores comparado aos controles. O grupo OA apresentou uma estratégia compensatória impondo maiores cargas no membro não afetado em comparação ao lesionado. Desta forma, concluímos que o modelo musculoesquelético, identificado como o que melhor estimava as forças de contato, foi capaz de encontrar diferenças durante as tarefas funcionais em pessoas com OA grave de joelho. Os resultados da tese indicam um grande potencial de, por meio de modelos de aprendizagem de máquina, predizer os resultados de força de contato tibiofemoral a partir de variáveis mais simples de serem calculadas. Por fim, os estudos indicam importantes modificações nas forças de contato tibiofemoral durante atividades funcionais em pessoas com OA grave de joelho. As alterações encontradas são associadas a diferentes estratégias de minimizar a compressão no compartimento medial. Dessa forma, exercícios de retreinamento da marcha e treino excêntrico da musculatura extensora do joelho devem ser estudados quanto à capacidade de minimizar as diferenças encontradas no presente estudo.

Palavras-chave: carga articular; força muscular; modelos musculoesqueléticos; OpenSim; marcha; sentar; levantar e *machine learning*.

ABSTRACT

Pelegrinelli, A. R. M. **Knee contact forces and muscle demands during functional tasks in knee osteoarthritis patients: musculoskeletal model analysis.** Ph.D. Thesis Defense. State University of Londrina, Londrina, 2023

The magnitude of the tibiofemoral contact force and its distribution between the knee compartments are related to the development and progression of osteoarthritis (OA). Joint contact forces during functional tasks can be estimated using a non-invasive approach with musculoskeletal (MSK) models. Gait, sitting down, and standing up are some of the most important functional tasks. When these tasks are affected by knee OA, they can have a significant impact on quality of life. To analyze the tibiofemoral forces during these tasks, it is important to choose and define the most appropriate model. Therefore, the main goal of this thesis was to identify differences in knee contact forces during gait, sitting down and, standing up in knee OA patients. The thesis was divided into three manuscripts. In the first manuscript, the main objective was to identify the best MSK model to predict the total vertical tibiofemoral force, and in the medial and lateral compartments. In the second study, differences in knee contact force and muscle demands during gait were compared between patients with knee OA and healthy controls. Additionally, a machine learning predictive model was used to identify the most relevant kinematic and kinetic variables and to test the model's ability to predict tibiofemoral peak forces. Finally, the third study analyzed differences in knee contact forces and muscle demands during the sit-to-stand and stand-to-sit tasks in knee OA patients. The first results showed that the proposed adapted model was the best to estimating total vertical forces and forces in the medial and lateral compartments during the sitting down and standing up tasks. The estimated results were compared to *in vivo* measured results with a knee instrumented prosthesis. For the gait, the results were similar among the models analyzed. Based on these results, the adapted model was used for the second and third studies. In manuscript 2, a generalized linear model was applied as a predictive model. The first peak of the total tibiofemoral force and both peaks in the medial compartment were predicted with an error of around 6 to 10% of the calculated peak. The knee extensor moment and the hip abductor moment were the most relevant features for predicting the total vertical tibiofemoral force and medial compartment, respectively. Moreover, the comparison between the groups showed higher values during the valley between the peaks for the total vertical force in the OA group compared to controls. Additionally, the OA patients showed a gait modification to minimize medial compartment forces compared to controls. In the final paper, the stand-to-sit task was found to be more affected by knee OA compared to the sit-to-stand task. The vastus muscle force was reduced in the OA group during the sitting down task, where eccentric contraction is more relevant. For both tasks, the total vertical force and medial compartment were reduced compared to controls. The OA group showed a compensatory strategy of increasing the higher load in the non-affected knee. We concluded that the selected model in the first study was able to found differences during functional tasks in patients with severe knee OA. The results of the thesis indicate a great potential for using machine learning models to predict tibiofemoral contact forces with simpler variables. Furthermore, the studies showed significant differences in knee contact force during functional tasks in patients with severe knee OA. The differences observed were associated with strategies to reduce medial compartment compressive force. Therefore, treatments involving gait retraining and eccentric muscle strengthening for the knee extensors should be tested for their capacity to modify the differences identified in this study.

Keywords: joint load, muscle force, musculoskeletal models, OpenSim, gait, sitting down, standing up, and machine learning.

LISTA DE FIGURAS

Estudo 1

Estudo 2

Estudo 3

LISTA DE TABELAS

Estudo 1

Estudo 2

Estudo 3

LISTA DE ABREVIATURAS E SIGLAS

OA	Osteoarthritis/ Osteoartrite
KCF	Knee Contact Force
MSK	Musculoskeletal/ Musculoesqueléticos
RMSE	Root Mean Square Error
RPE	Relative Peak Error
CTRL	Controls
MAE	Mean Absolute Error
GLM	Generalized Linear Model
BOPS	Batch OpenSim Processing Scripts
IK	Inverse Kinematics
ID	Inverse Dynamics
SO	Static Optimization
SnPM	Statistical nonparametric mapping
KOOS	Knee Injury and Osteoarthritis Outcome Score
GRF	Ground Reaction Forces
AP	Anteroposterior
ML	Mediolateral
ADLs	Activities of daily living

SUMÁRIO

1 INTRODUÇÃO

Doenças degenerativas articulares são comumente associadas à perda de função para as atividades de vida diária, comprometendo a capacidade funcional e qualidade de vida destes pacientes (Michael *et al.*, 2010). As transições entre o sentar e levantar e a marcha são três das atividades funcionais mais realizadas durante um dia (Dall e Kerr, 2010; Baker *et al.*, 2016). A marcha é realizada em diferentes atividades básicas envolvendo curtas distância, assim como para longas distâncias como um meio de transporte (Manickam e Gardiner, 2021). As tarefas de sentar e levantar são realizadas cerca de 60 vezes ao longo do dia. Sua relevância funcional é destacada considerando que a versão curta do questionário Knee and Osteoarthritis Outcome Score (KOOS) apresenta apenas três questões sobre o domínio função e duas dessas são sobre o sentar e levantar (Gandek *et al.*, 2019).

A osteoartrite (OA) é a doença progressiva articular mais comum e acomete em todo o mundo cerca de 250 milhões de pessoas. O joelho é a articulação mais acometida, em torno de 83% de todos os casos (Vos *et al.*, 2012). A prevalência varia entre os países. Nos Estados Unidos a prevalência é de cerca de 12%, enquanto no Japão em torno de 5% (Cross *et al.*, 2014). No Brasil não existem dados precisos de prevalência na população comum. A prevalência apresenta um aumento contínuo a cada ano em diversos países, relacionado ao envelhecimento da população, aumento da obesidade e maior número de lesões articulares prévias (Hunter e Bierma-Zeinstra, 2019). A OA é também considerada um problema de saúde pública considerando o alto custo de tratamento e o absenteísmo no trabalho. Nos Estados Unidos é estimado um gasto médio de 140.300 dólares para o tratamento de um paciente durante sua vida (Losina *et al.*, 2015; Gupta *et al.*, 2022)

A osteoartrite é considerada multifatorial, influenciada por fatores como a obesidade, idade, lesões prévias articulares, aspectos mecânicos, bioquímico e genéticos (Deasy *et al.*, 2016; Hunter e Bierma-Zeinstra, 2019). Fortes evidências consideram que mudanças estruturais e mecânicas nas articulações são responsáveis pelo desenvolvimento e progressão da osteoartrite (Tanzer e Noiseux, 2004; Astephen Wilson *et al.*, 2019). A intensidade e distribuição da força nas regiões do joelho durante toda a vida são relacionadas à degeneração da cartilagem articular (Eckstein *et al.*, 2002; Wong e Carter, 2003). A osteoartrite é classificada em acordo com o nível de degeneração (Kellgren e Lawrence, 1957), e no estágio final a artroplastia é recomendada. Nos Estados Unidos é estimado que até 2030, considerando a progressiva demanda para artroplastia de joelho, serão realizadas 3,48 milhões de cirurgias (Kurtz *et al.*, 2007).

A OA de joelho acomete em diferentes graus os compartimentos tibiofemoral e patelofemoral. A região medial do compartimento tibiofemoral é a mais acometida, principalmente no estágio inicial (Misir *et al.*, 2020). Cerca de 27% dos pacientes apresentam OA apenas no compartimento medial e em 23% dos casos a lesão é na região medial e patelofemoral (Stoddart *et al.*, 2021). O maior acometimento desta região é relacionado ao desalinhamento em varo do joelho. Wei et al. (2019) encontraram que o desalinhamento é associado a 466% mais incidência de osteoartrite medial em relação a lateral (Wei *et al.*, 2019). Uma assimetria no alinhamento tibiofemoral afeta a distribuição de carga entre os componentes medial e lateral, aumentando o risco do desenvolvimento da OA (Jackson *et al.*, 2004).

Considerando a intensidade e distribuição de força no joelho como um dos responsáveis pelo surgimento e progressão da OA, estas forças devem ser analisadas. Para uma análise de forma não invasiva das forças de contato articular, as simulações com modelos musculoesqueléticos (MSK) têm sido empregadas. Estas análises permitem extrair variáveis cinemáticas e dinâmicas, bem como simular as forças musculares e de contato articular (Hicks *et al.*, 2015; Weinhandl e Bennett, 2019). Diferentes *softwares* são utilizados para análises com modelos MSK, mas os dois principais são o OpenSim e o Anybody (Delp *et al.*, 2007b; Lee e Umberger, 2016). Nos últimos anos (2015 - 2023), as publicações com OpenSim aumentaram consideravelmente e, somado ao fato de ser um *software open source*, modelos mais complexos e reprodutíveis têm sido desenvolvidos (Seth *et al.*, 2018).

Para a correta aplicação das simulações com modelos MSK, a escolha do modelo deve ser criteriosa, considerando as variáveis de interesse e a capacidade do modelo em estimar as forças de contato (Roelker *et al.*, 2020). Para a análise do joelho, existem modelos publicados na literatura que permitem analisar as forças de contato medial e lateral. Tal distribuição é importante para o tratamento focado na redução da força na região do joelho mais afetada pela OA. Estes modelos permitem avaliar atividades como a marcha, corrida, agachamento, entre outros com reduzida ou grandes amplitudes de movimentos do membro inferior (Lerner *et al.*, 2015; Lai *et al.*, 2017; Bedo *et al.*, 2020).

Embora diversos modelos tenham sido publicados, ainda faltam estudos analisando a eficiência em estimar as forças de contato. Apenas o estudo de Imani Nejad *et al.* (2020) comparou a capacidade dos modelos MSK genéricos em estimar as forças de contato, utilizando pacientes com uma prótese de joelho instrumentada para adquirir medidas em *in vivo*. Neste estudo, as forças de cisalhamento apresentaram uma baixa capacidade de serem preditas com o modelo de Rajagopal e colaboradores (Rajagopal *et al.*, 2016) para a marcha e o agachamento, assim como a força vertical durante o agachamento apresentou uma importante diferença de magnitude entre o medido e o estimado. Erros da magnitude das forças de contato são associados a falhas na estimativa da ativação muscular, causada pela capacidade limitada do método de optimização utilizado, ou por inconsistências na geometria e parâmetros musculares do modelo. Uhlrich *et al.* (2022) modificaram parâmetros musculares do modelo Rajagopal (Rajagopal *et al.*, 2016), que apresentavam inconsistências. Os resultados mostraram uma redução das forças de contato vertical no joelho, que devem promover um resultado mais próximo ao medido *in vivo*.

O resultado das forças de contato no joelho é uma combinação dos resultados de força muscular e das forças de reação ao solo durante a execução da tarefa. Neste sentido, para uma efetiva análise e posterior interpretação para o desenvolvimento de tratamentos o desempenho muscular durante a tarefa deve também ser analisado. Pacientes com OA de joelho comumente apresentam fraqueza nas musculaturas abdutora de quadril e para os flexores e extensores de joelho (Deasy *et al.*, 2016; Messier *et al.*, 2021). Estes grupos musculares são diretamente relacionados às forças de compressão tibiofemoral e com a distribuição da força entre os compartimentos medial e lateral (Chang *et al.*, 2005; Iijima *et al.*, 2020). Neste sentido, as comparações entre diferentes níveis da OA e com indivíduos controles devem analisar todas as variáveis envolvidas com as forças de contato, assim como a relação entre elas.

Diferentes análises de correlação ou regressão podem ser empregadas para testar a relação entre as variáveis. Atualmente, modelos de aprendizagem de máquina têm sido amplamente utilizados em diferentes áreas de estudo para análises envolvendo predição, classificação e seleção das variáveis relevantes (Saxby *et al.*, 2020). Estas análises podem auxiliar na predição de uma variável que envolve maior complexidade de processamento utilizando apenas variáveis relativamente mais simples, como os ângulos articulares durante o movimento (Burton *et al.*, 2021). Também, entender as variáveis preditoras pode promover um conhecimento inicial de qual modificação biomecânica deve ser promovida com o objetivo de modificar a magnitude e a distribuição das forças de contato no joelho.

A marcha é amplamente estudada em pessoas com OA de joelho, entretanto outras tarefas funcionais ainda foram pouco analisadas. As tarefas de sentar e levantar tem uma grande importância funcional como citado anteriormente e é afetada na OA de joelho. Estas tarefas são bilaterais o que pode resultar em compensações, como aumentar a descarga de peso no lado não afetado (Christiansen e Stevens-Lapsley, 2010; Duffell *et al.*, 2013). Estas compensações devem ser estudadas e analisadas, considerando o alto risco de desenvolvimento da OA em outras articulações após o primeiro diagnóstico. Neste sentido e considerando a grande força de contato imposta no joelho nestas tarefas (Kutzner *et al.*, 2010; Taylor *et al.*, 2017), elas devem ser analisadas com modelos MSK, afim de analisar a magnitude e distribuição da força entre os compartimentos durante a execução.

Diante do exposto, torna-se inevitável destacar a importância da magnitude das forças de contato no joelho e de sua distribuição entre os compartimentos para a progressão da OA de joelho. Também, a possibilidade de modificar estas forças impostas durante atividades funcionais através do retreinamento do movimento, uso de órteses ou treinamento muscular ressalta a importância da caracterização das forças atuantes no joelho. Embora as pesquisas apresentadas sejam de suma importância, algumas lacunas foram identificadas e consideramos que os modelos MSK para análise das forças de contato no joelho deveriam ser testados quanto ao erro da estimativa das forças e um possível aperfeiçoamento dos modelos. Também, identificado a complexidade dos modelos, do processamento e da instrumentação, foi compreendido que um modelo preditivo para as forças de contato no joelho a partir de variáveis de menor complexidade apresenta um grande potencial para o aumento da avaliação destes desfechos em outros estudos. Por fim, a maioria dos estudos sobre o tema são focados na marcha, emergindo a necessidade de investigar como as forças de contato no joelho são afetadas com a OA em outras atividades funcionais, como no sentar e levantar.

A partir da contextualização e lacunas apresentadas na introdução geral, a sequência da tese foi estruturada com a definição dos objetivos, resultados com a apresentação de três artigos originais, e por último as considerações finais.

A partir da análise dos modelos MSK e dos artigos publicados para análise das forças de contato no joelho, em conjunto com o processamento inicial dos dados, a seguinte questão foi levantada para ser respondida no estudo 1: qual a capacidade dos modelos MSK genéricos em estimar as forças de contato no joelho durante as tarefas de marcha, sentar e levantar? Para responder a esta questão, uma base de dados publicada na literatura, composta por pacientes submetidos a artroplastia de joelho com uma prótese instrumentada, realizando diferentes atividades funcionais foi solicitada ao laboratório responsável. Utilizando esses dados, dois modelos previamente publicados e um modelo adaptado foram testados quanto à capacidade de estimar as forças de contato tibiofemoral.

Nos últimos anos, diferentes modelos preditivos de aprendizagem de máquina têm sido testados para predizer desfechos muitas vezes complexos. Após a análise das publicações e compreensão da complexidade do processamento das forças de contato, as seguintes questões foram formuladas para o estudo 2: é possível predizer os picos de força de contato no joelho com um modelo de regressão utilizando variáveis com menor complexidade de processamento? Quais seriam as variáveis mais relevantes? Existem diferenças nas forças de contato de joelho em pacientes com OA comparados a controles saudáveis? Para responder às questões, o melhor modelo MSK encontrado no estudo 1 foi aplicado para o processamento das forças de contato em pacientes com OA grave de joelho e controles saudáveis. Assim, uma análise descritiva e comparativa foi realizada entre os grupos. Também, um modelo de aprendizagem de máquina foi empregado para predizer os picos de força de contato no joelho e identificar as variáveis mais relevantes para as forças atuantes no joelho.

Por fim, considerando os limitados estudos de força de contato no joelho na OA durante as tarefas de sentar e levantar. Estas tarefas que são realizadas diversas vezes ao longo do dia e envolvem uma importante carga na articulação, as seguintes questões foram levantadas para o estudo 3: as forças compressivas nos joelhos e a demanda muscular são afetadas na OA durante as tarefas de sentar e levantar? Ainda, são realizadas compensações de forma a minimizar as forças no joelho afetado? Para responder a estas questões, pacientes com OA grave de joelho e controles foram analisados durante as duas tarefas e os resultados de força de contato no joelho e demanda muscular foram comparados e analisados entre os grupos. Também, foram realizadas comparações entre os membros com objetivos de identificar assimetrias e compensações.

2 OBJETIVOS

Objetivo Geral:

O objetivo geral da tese foi caracterizar as forças de contato tibiofemoral em pacientes com OA de joelho durante tarefas de marcha, sentar e levantar.

Para que o objetivo geral fosse alcançado, os seguintes objetivos específicos foram estabelecidos:

Objetivos específicos:

- Comparar dois modelos MSK previamente publicados e um modelo modificado para estimar as forças de contato durante as tarefas de marcha, sentar e levantar com dados medidos *in vivo*.

- Predizer os picos de força de contato tibiofemoral total e no compartimento medial, bem como identificar as variáveis mais relevantes para estes desfechos durante a marcha.

- Comparar e descrever os resultados de força de contato e muscular durante a marcha em pessoas com OA de joelho e grupo controle.

- Comparar e descrever as forças de contato no joelho e as forças musculares durante as tarefas de sentar e levantar em pessoas com OA de joelho e grupo controle.

3 RESULTADOS

Este capítulo está dividido em três estudos originais:*

Estudo 1:

Comparison between three musculoskeletal models to estimate the knee joint contact forces during gait and sit-to-stand tasks

Estudo 2:

Tibiofemoral contact forces during gait in knee osteoarthritis patients: descriptive and predictive analysis

Estudo 3:

Tibiofemoral contact forces and muscle demands in knee osteoarthritis patients during the stand-to-sit and sit-to-stand tasks

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* Os resultados da presente tese, no modelo escandinavo, foram apresentados na língua inglesa juntamente ao orientador brasileiro e o orientador da Universidade de Ottawa onde o doutorado foi desenvolvido parcialmente. Essa foi também uma exigência da Universidade de Ottawa para autorizar que os dados coletados e tratados pudessem ser apresentados na tese. Assim, os artigos aqui serão apresentados em língua inglesa para garantir isonomia e entendimento de ambas as partes nesse processo documental, além de fato sustentar as ações institucionais de internacionalização.

3.1 ESTUDO 1

Comparison between three musculoskeletal models to estimate the knee joint contact forces during gait and sit-to-stand tasks

Abstract

The choice of musculoskeletal (MSK) model is crucial to perform MSK estimations to evaluate the muscle demands and the joint forces during different tasks. This study compared two previously published generic-MSK models and a modified MSK model to estimate knee contact forces (KCF) during gait, sit-to-stand, and stand-to-sit. It compared their results with an *in vivo* dataset obtained from six patients using an instrumented knee prosthesis. The estimated tibiofemoral forces were evaluated by comparing them to the *in vivo* data using a correlation and root mean square error (RMSE) in the time-series analysis and a relative peak error (RPE). The results showed that three MSK models were similar in estimating the vertical forces, both in total and for the medial compartment, a with large correlation and RPE around 20% during the gait. The correlation was large high for all three models in estimating the vertical forces for the sit-to-stand and stand-to-sit tasks. However, the RMSE and the RPE indicated that the modified model had lower total and lateral compartment forces errors. The shear forces for all tasks and models showed large errors and lacked reliability. Future MSK studies should consider these findings when researching gait and tasks with high knee flexion. The modified MSK model was found to be more effective in estimating the vertical tibiofemoral forces in tasks that are more demanding on the muscle forces and require high knee and hip flexion. Ultimately, none of the three models successfully estimated the shear forces.

Keywords: OpenSim; musculoskeletal modelling; sit-to-stand; gait; joint loading.

Introduction

Musculoskeletal (MSK) models are helpful tools to non-invasively estimate the joint contact forces in different injuries during functional tasks (Delp *et al.*, 2007a; Seth *et al.*, 2018). A good, simple, and reliable method to estimate the knee contact forces (KCF) with MSK simulations is important to the diagnosis, rehabilitation process, and development of joint implants or surgery techniques (Bergmann *et al.*, 2014; Xu *et al.*, 2016). Few studies compared the reliability of MSK models to estimate the KCF using *in vivo* results with an instrumented knee prosthesis for limited tasks (Schellenberg *et al.*, 2018; Imani Nejad *et al.*, 2020; Curreli *et al.*, 2021).

Some MSK models segment the vertical force into the medial and lateral compartments and have been employed to examine the distribution of the contact forces between compartments during the activities of daily living. This knowledge is relevant to evaluate the progress of degenerative or load-dependent knee injuries (Manal e Buchanan, 2013). Models that simulate the loading of medial and lateral compartments were implemented and adjusted for use during gait (Lerner *et al.*, 2015) and tasks with a high knee and hip flexion (Bedo *et al.*, 2020). These models can be improved by using different optimization approaches and a subject-specific scaling process, but these improvements are limited (Marra *et al.*, 2015; Dumas e Moissenet, 2020). An automated process has been developed for personalized MSK models with good results (Killen *et al.*, 2021). Still it demands higher cost, complexity, and time to process compared to generic models (Saxby *et al.*, 2020). So, it is important to identify how efficient and reliable a generic MSK modelling is for estimating the KCF.

To the best of our knowledge, the estimated KCF using MSK modelling during sit-stand transitions has not yet been compared to KCF measured from instrumented prosthesis. The aim of the study was to compare two (previous published) generic models and a modified generic model on the estimation of the KCF resultant of mediolateral, anteroposterior, and vertical forces, as well as the medial and lateral compartments of the KCF during gait, sit-to-stand, and stand-to-sit tasks, compared to measured results of an instrumented prosthesis.

Methods

The experimental data were obtained from the CAMS-Knee dataset (Taylor *et al.*, 2017; Damm e Taylor, 2019). Six patients from this dataset who received a total knee arthroplasty with a tibial component instrumented with six load components (forces and moments, 90-100 Hz acquisition frequency) were analyzed (Heinlein *et al.*, 2007). The sample was represented by five males and one female (74 ± 5 years old, 88.9 ± 13.7 kg and 1.71 ± 0.04 m height). The data collection was performed in the Laboratory for Movement Biomechanics at ETH Zurich, 64-87 months postoperatively.

The prosthesis data was synchronized with the kinematic (Vicon system, 100 Hz) and kinetic systems (8 Kistler force plates, 2000 Hz). For the kinematics capture, a full-body model with 75 skin markers was used (Taylor *et al.*, 2017). Three trials of sit-to-stand and stand-to-sit, and five gait cycles were analyzed. The sit-to-stand and the stand-to-sit tasks were performed in sequence, starting in the sitting position moving to stand and sitting down again. Both tasks were performed at a self-selected speed. The tasks were time normalized (0-100 %).

Using OpenSim 3.3 software (Delp *et al.*, 2007a), the inverse kinematics and dynamics, static optimization approach, and joint reaction analysis were employed for all models using a batch process toolbox (Bedo *et al.*, 2021). The same scale process and factors were used for all models using the skin marker positions to scale the segments for each subject. Three full-body models were analysed (for a detailed description, see the supplementary material):

- Rajagopal *et al.* (2016), with an equation to subdivide the medial and lateral compartments of the KCF;
- Bedo *et al.* (2020), with segmented the medial and lateral compartments (Lerner *et al.*, 2015) and allows high hip and knee flexions (Lai *et al.*, 2017; Catelli *et al.*, 2019).
- Modified model, used the Bedo model (Bedo *et al.*, 2020) with updated muscle-tendon parameters proposed by Uhlrich *et al.* (2022).

For the *in vivo* data, the medial and lateral compartment forces were calculated with the equations: $F_{med}=0.5*F_{vert}+0.02*M_{var}$ and for $F_{lat}=0.5*F_{vert}-0.02*M_{var}$. The force is expressed in Newtons and the moment in Nmm. This equation is for the right side. The equation was proposed by Kutzner et al. (2013) and the condyle distance (0.02) was the same employed in Modified and Bedo models. The mediolateral and anteroposterior shear forces, and the vertical forces for the medial and lateral compartments, were extracted. To calculate the total vertical force for Modified and Bedo models, the forces of the medial and lateral compartments were summed. All results from the KCF were normalized by body weight.

The estimated KCF obtained from the models were then compared to the data extracted from the instrumented prosthesis (Taylor *et al.*, 2017). The root means square error (RMSE) and Pearson correlation coefficients were computed between the measured and estimated results for the temporal series. The Pearson coefficients between 0.1-0.3 indicates a small correlation, 0.3-0.5 medium and higher than 0.5 a large correlation. The differences between the peaks were compared using the relative peak error (RPE) as equation (1) (Schellenberg *et al.*, 2018; Imani Nejad *et al.*, 2020):

$$\mathrm{RPE}=\frac{\text{peak measured-peak estimated}}{\text{peak estimated}}*100 \quad (1).$$

The RPE and the RMSE results were tested between the models using a One-Way ANOVA. First, the homogeneity of the data was tested using Levene’s test. When differences between the models were identified, *post hoc* comparison using Bonferroni corrections was performed. The statistical analyses were performed in SPSS version 19 (IBM Corporation, Armonk, USA) and Matlab R2018b (MathWorks, Natick, USA). The significance level was set at 5%.

Results

In table 1, the correlation coefficients for each model are described. The gait results showed that all three models had a large correlation between the total vertical force and the medial compartment. For the total vertical, Modified and Rajagopal models had a correlation >0.9. The lateral compartment showed a medium correlation for Rajagopal model, and a small correlation for Modified and Bedo models. The anteroposterior component showed a medium correlation for Bedo model and a small correlation for Modified and Rajagopal models. The mediolateral component showed a small and negative correlation for all three models.

All vertical forces showed large correlations for the three models during the stand-to-sit task. Modified model had higher correlation values compared to the other two models. For the anteroposterior, the correlation was medium, and for mediolateral, there was a small negative correlation for the Modified model and a medium correlation for Bedo and Rajagopal models. Finally, for the stand-to-sit task, all vertical forces showed large correlations for the three models, with higher values for the Modified model. The three models had a small correlation for both the anteroposterior and mediolateral components.

Table 1. Pearson correlation coefficient results for each model in relation to the *in vivo* results.

	Modified Mean ± SD	**Bedo** Mean ± SD	**Rajagopal** Mean ± SD
Gait			
Total vertical	0.907 ± 0.033	0.891 ± 0.053	0.908 ± 0.049
Medial compartment	0.947 ± 0.034	0.941 ± 0.039	0.942 ± 0.033
Lateral compartment	0.213 ± 0.373	0.337 ± 0.409	0.504 ± 0.142
Anteroposterior	0.232 ± 0.355	0.360 ± 0.278	0.226 ± 0.362
Mediolateral	-0.194 ± 0.361	-0.142 ± 0.470	-0.161 ± 0.518
Stand-to-sit			
Total vertical	0.933 ± 0.105	0.900 ± 0.121	0.911 ± 0.114
Medial compartment	0.831 ± 0.237	0.780 ± 0.253	0.806 ± 0.237
Lateral compartment	0.964 ± 0.025	0.942 ± 0.031	0.952 ± 0.027
Anteroposterior	0.389 ± 0.608	0.384 ± 0.609	0.381 ± 0.615
Mediolateral	-0.264 ± 0.535	-0.421 ± 0.660	-0.377 ± 0.620
Sit-to-stand			
Total vertical	0.956 ± 0.039	0.926 ± 0.037	0.934 ± 0.034
Medial compartment	0.859 ± 0.130	0.835 ± 0.167	0.836 ± 0.176
Lateral compartment	0.970 ± 0.026	0.941 ± 0.032	0.949 ± 0.032
Anteroposterior	0.220 ± 0.508	0.221 ± 0.511	0.221 ± 0.511
Mediolateral	-0.244 ± 0.578	-0.307 ± 0.604	-0.273 ± 0.593

SD: standard deviation; Pearson coefficients 0.1-0.3: small correlation; 0.3-0.5: medium; higher than 0.5: large.

Table 2 presents the RMSE and RPE values for evaluating the error magnitudes of the peaks and the time series. During the gait, no significant differences were identified between the models. The total vertical force had an RMSE of around 39% of BW and a peak error of 18%. The medial compartment showed lower errors compared to the lateral. The RPE for the anteroposterior shear force had errors over 100% for all three models. The mediolateral shear force had peak errors ranging from 670 to 1341%.

During the stand-to-sit, the RMSE error for the total vertical force was 22% BW lower for the Modified model compared to Rajagopal model (*p*=.002), and the RPE was 37% lower (*p*=.031). In the lateral compartment, the RMSE and RPE were lower for Modified model compared to Rajagopal model (RMSE: *p*=.007, RPE: *p*=.008). No significant differences were identified among the models for the medial compartment, as the RPE was small for all three models. For the mediolateral force, the RMSE was higher in Bedo model compared to the Modified (*p*=.001) and

Rajagopal models (*p*=.009). Despite the differences, Modified and Rajagopal models showed an RPE of about 804% and 1344%, respectively. The anteroposterior force showed no significant differences, with all three models presenting a large RPE.

For the sit-to-stand task, the RMSE of the total vertical force was lower in Modified model compared to both Bedo (*p*=.014) and Rajagopal models (*p*=.002), and the RPE was lower compared to Bedo (*p*=.023) and Rajagopal models (*p*=.002). No significant differences were identified for the medial compartment, with small RPE and RMS for all three models. For the lateral compartment, the RMSE was higher for the Rajagopal model compared to the Modified (*p*<.001) and Bedo models (*p*=.012), and the RPE was also higher for the Rajagopal model compared to the Modified (*p*=.001) and Bedo models (*p*=.034). Regarding the anteroposterior force, Modified model showed a lower RMSE compared to Rajagopal model (*p*=.002), but all three models had a large RPE. The mediolateral force had a higher RMSE for Bedo model compared to both Modified (*p*<.001) and Rajagopal models (*p*=.001), and all three models had a large RPE. Individual participant results, correlations, RMS, and RPE are all available in the supplementary tables.

Table 2. Comparison between the models for RMSE and RPE.

		Modified	**Bedo**	**Rajagopal**
		Mean ± SD	Mean ± SD	Mean ± SD
		Gait		
Total vertical	RMSE (% BW)	37.2 ± 11.5	42.0 ± 11.6	39.0 ± 9.7
	RPE (%)	17.6 ± 11.0	18.8 ± 14.6	19.1 ± 12.3
Medial compartment	RMSE (% BW)	24.7 ± 11.3	28.7 ± 15.8	25.5 ± 7.8
	RPE (%)	18.1 ± 12.2	20.5 ± 17.7	16.8 ± 8.2
Lateral compartment	RMSE (% BW)	33.9 ± 26.6	34.3 ± 26.8	30.7 ± 19.8
	RPE (%)	40.5 ± 17.9	41.0 ± 24.1	42.7 ± 34.0
Anteroposterior	RMSE (% BW)	16.6 ± 1.5	16.1 ± 1.8	17.7 ± 2.3
	RPE (%)	144.6 ±107.0	131.4 ± 90.3	123.1 ± 64.7
Mediolateral	RMSE (% BW)	18.1 ± 8.2	27.0 ± 16.4	33.6 ± 11.6
	RPE (%)	670.5 ± 737.5	1296.0 ± 1730.5	1341.3 ± 1340.5
		Stand-to-sit		
Total vertical	RMSE (% BW)	**48.5 ± 15.7 ‡**	**65.5 ± 6.3**	**70.6 ± 5.9**
	RPE (%)	**13.8 ± 11.5 ‡**	**39.5 ± 21.0**	**50.8 ± 24.8**
Medial compartment	RMSE (% BW)	26.8 ± 13.2	23.8 ± 11.1	30.6 ± 12.3
	RPE (%)	17.7 ± 9.43	16.3 ± 7.9	17.6 ± 12.4
Lateral compartment	RMSE (% BW)	**31.7 ± 7.4 ‡**	**44.9 ± 11.6**	**64.1 ± 22.4**
	RPE (%)	**29.5 ± 25.1 ‡**	**57.1 ± 34.1**	**103.0 ± 44.0**
Anteroposterior	RMSE (% BW)	18.0 ± 5.3	23.2 ± 9.3	31.0 ± 10.7
	RPE (%)	779.4 ± 1035.0	1089.3 ± 1315.1	1509.2 ± 1800.1
Mediolateral	RMSE (% BW)	**13.7 ± 4.2 †**	**44.4 ± 15.7 ϯ**	**22.3 ± 5.3**
	RPE (%)	804.3 ± 905.8	2841.8 ± 2328.3	1344.3 ± 1485.1
		Sit-to-stand		
Total vertical	RMSE (% BW)	**43.8 ± 12.4 † ‡**	**68.8 ± 11.7**	**76.4 ± 11.5**
	RPE (%)	**15.6 ± 12.6 † ‡**	**47.3 ± 14.2**	**59.9 ± 20.8**
Medial compartment	RMSE (% BW)	21.3± 9.7	19.9 ± 6.6	25.7 ± 8.3
	RPE (%)	16.7 ± 11.9	16.1 ± 10.0	15.4 ± 10.9
Lateral compartment	RMSE (% BW)	**35.1 ± 9.1 ‡**	**52.9 ± 11.0 ϯ**	**76.0 ± 14.5**
	RPE (%)	**40.1 ± 21.5 ‡**	**70.7 ± 24.8 ϯ**	**116.0 ± 33.8**
Anteroposterior	RMSE (% BW)	**20.5 ± 4.5 ‡**	**26.7 ± 5.9**	**35.3 ± 6.0**
	RPE (%)	742.8 ± 433.0	1070.7 ± 575.2	1500.6 ± 825.0
Mediolateral	RMSE (% BW)	**17.5 ± 6.4 †**	**50.2 ± 11.0 ϯ**	**25.8 ± 6.6**
	RPE (%)	1963.0 ± 2468.2	8900.0 ± 13583.6	3450.2 ± 4526.2

‡: significant difference between Modified model and Rajagopal model; †: significant difference between Modified model and Bedo model; ϯ: significant difference between Bedo model and Rajagopal model; RMSE: root means square error in % of the BW; RPE: relative peak error in % of the measured peak.

The results for each participant and the three models in the gait task are presented in figure 1. For the total vertical force and the medial compartment, the second peak showed greater differences between the *in-vivo* data and the models results. In most cases, the models underestimated the forces compared to the *in vivo* data. In general, the lateral compartment force was underestimated by Modified and Bedo models.

Figure 2 compares the results for the stand-to-sit task. For both the vertical and lateral compartment forces, Modified model showed closer results to the *in vivo* data in magnitude and shape compared to the other models. Modified and Bedo models underestimated the medial compartment forces compared to the *in vivo* results. The results for the sit-to-stand task are presented in figure 3. The results were similar to the stand-to-sit task. However, the medial compartment force was better estimated by Modified and Bedo models. The error and correlations for the mediolateral and anteroposterior forces were bad for all tasks. The curve analysis for each participant in both directions is available in the supplementary figures and shows differences compared o *in vivo* in magnitude and shape.

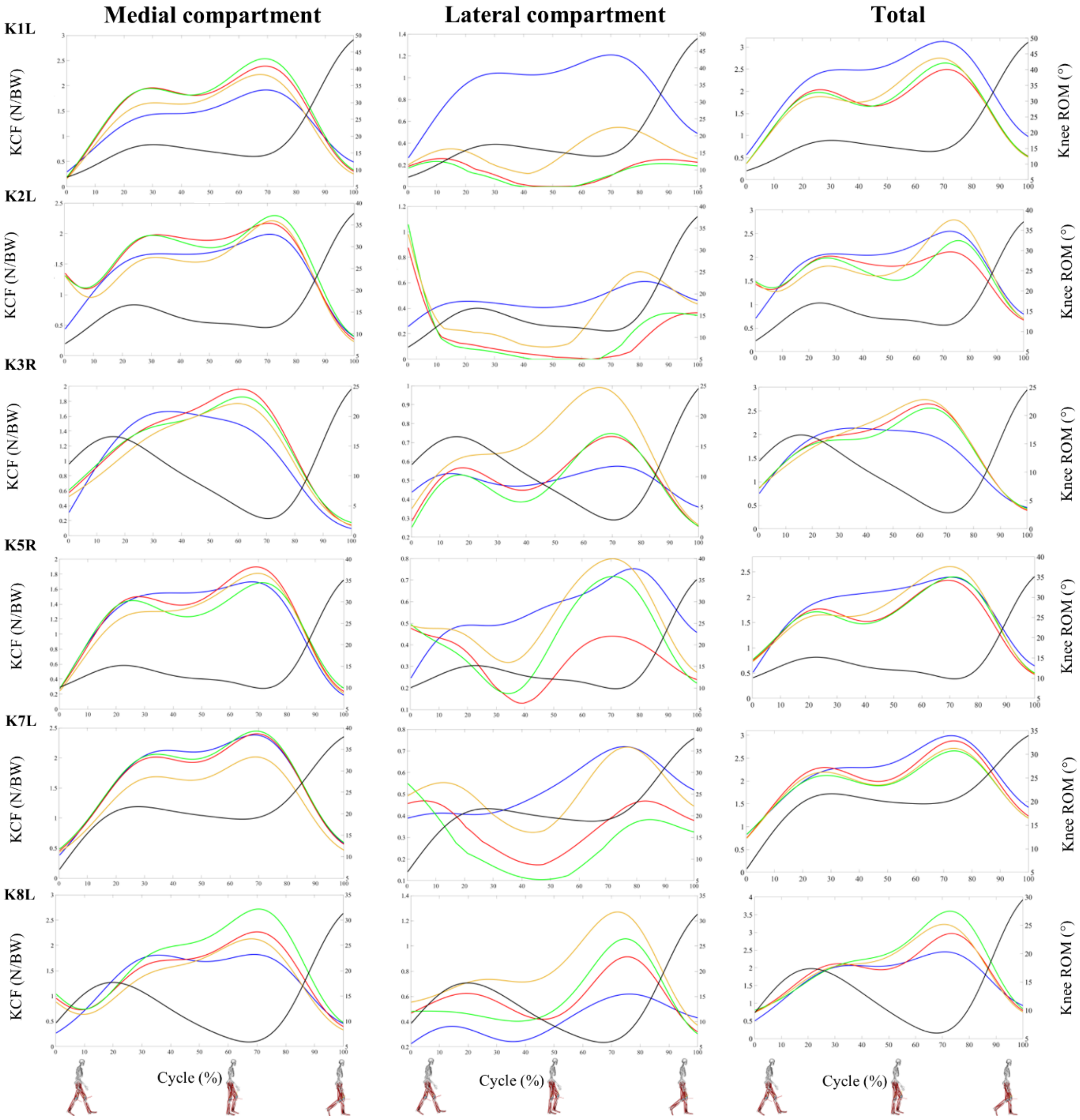

Figure 1. Gait comparisons between the measured and the models for each subject. The black line is referent to the knee angle (right y-axis). In the left y-axis: blue is the measured results (in vivo), red for Modified model, green for Bedo model, and yellow for Rajagopal model. KCF: knee contact force; N/BW: Newton/body weight; ROM: range of motion.

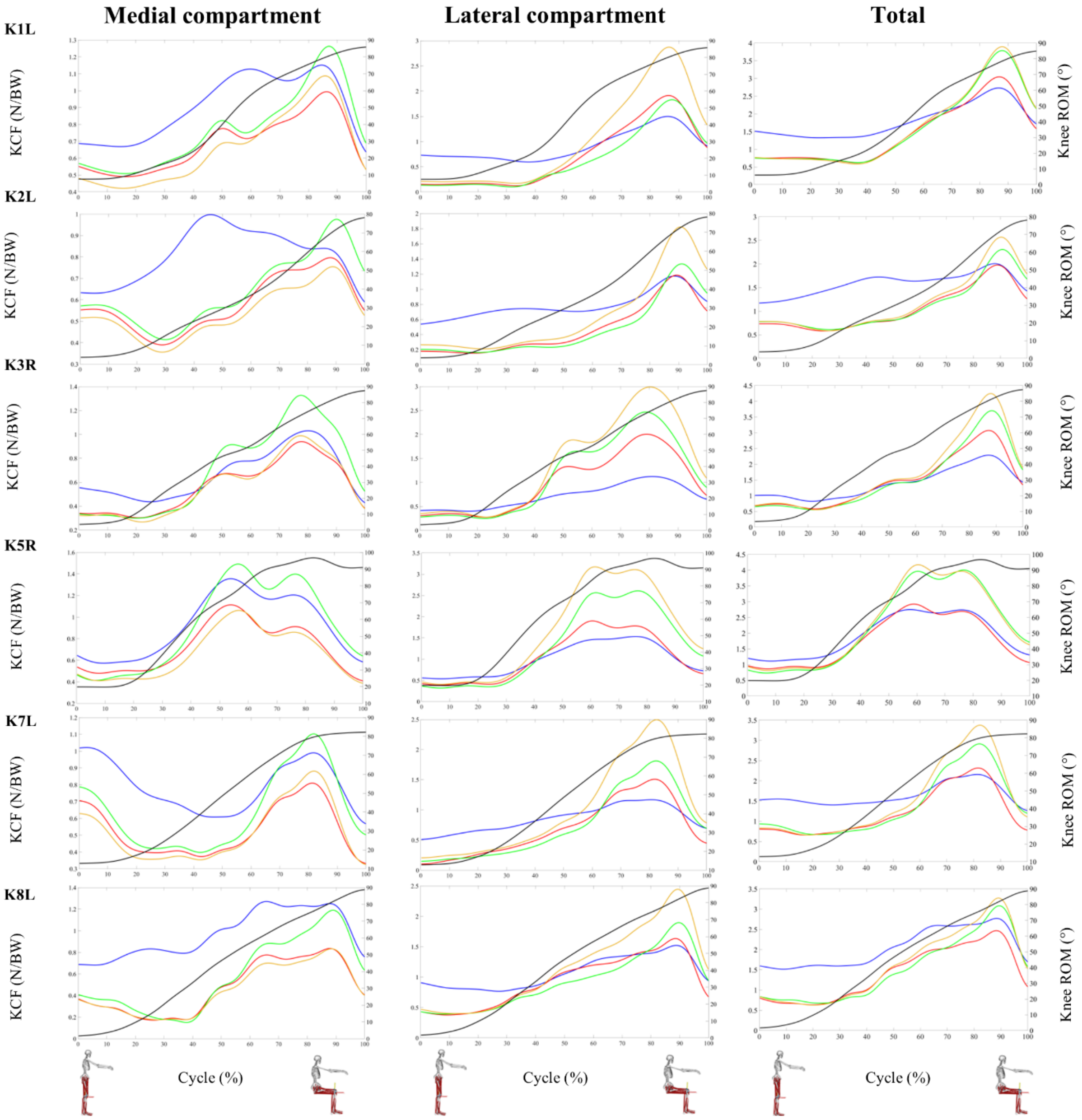

Figure 2. Stand-to-sit comparisons between the measured and the models for each subject.

The solid black line is referent to the knee angle (right y-axis). In the left y-axis: blue is the measured results (in vivo), red for Modified model, green for Bedo model, and yellow for Rajagopal model. KCF: knee contact force; N/BW: Newton/body weight; ROM: range of motion.

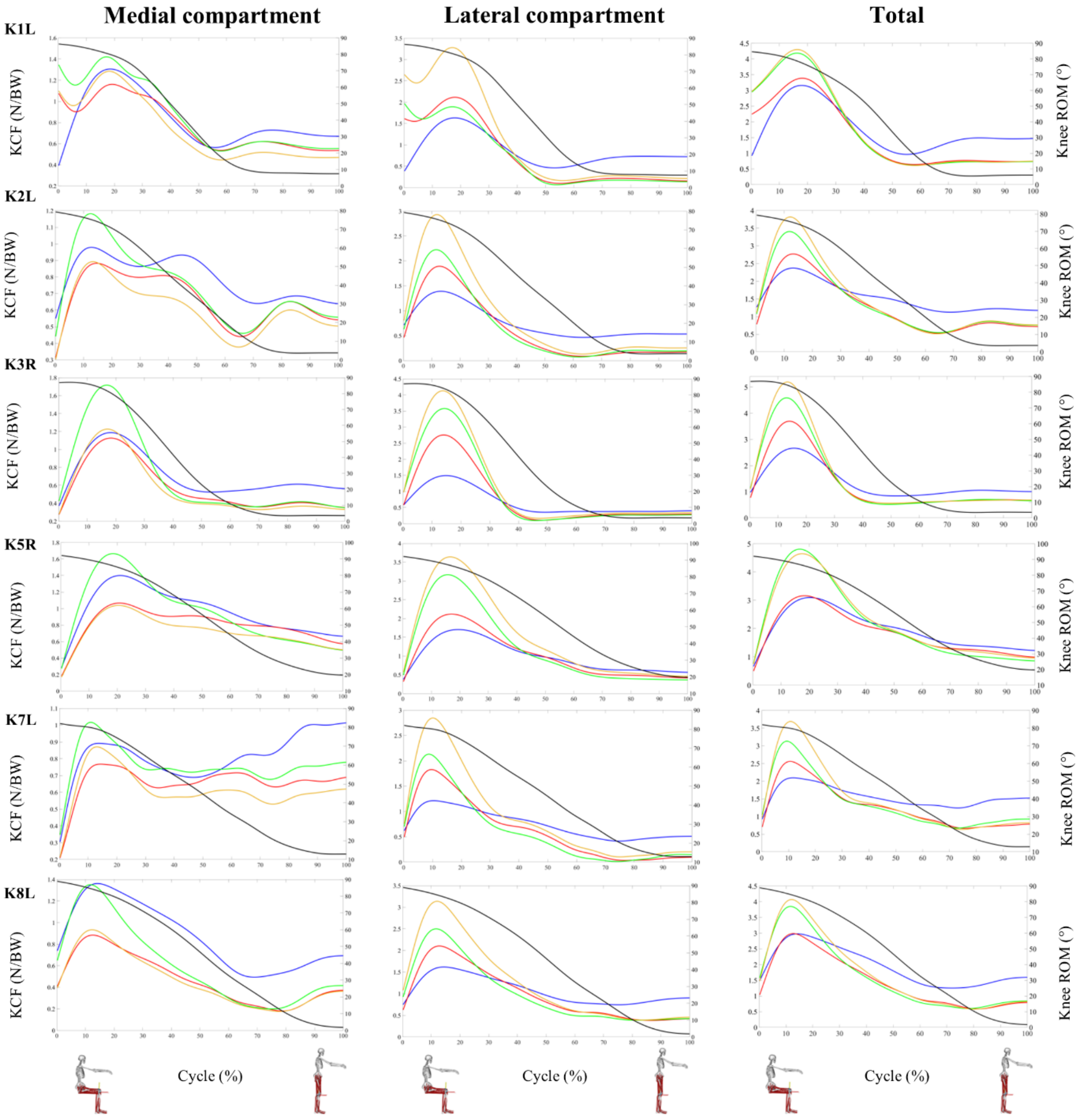

Figure 3. Sit-to-stand comparisons between the measured and the models for each subject.

The solid black line is referent to the knee angle (right y-axis). In the left y-axis: blue is the measured results (in vivo), red for Modified model, green for Bedo model, and yellow for Rajagopal model. KCF: knee contact force; N/BW: Newton/body weight; ROM: range of motion.

The average plots comparing Modified model the best-performed model as presented in previous results, and *in vivo* data for the three tasks are presented in figure 4 with the mean and standard deviation for reference. The mediolateral and anteroposterior shear forces showed large differences between the *in vivo* and the estimated force curves. The vertical forces for total KCF showed a similar shape and magnitude compared to *in vivo* measured results. The same was noted for the medial and lateral compartments. For the medial compartment, the models underestimated sit-to-stand results, and overestimated gait outcomes, when compared to in vivo data. For the lateral compartment, results were underestimated during gait, and overestimated for the sit-to-stand tasks, when compared to in vivo data. In general, for the vertical forces, during the sit-to-stand transitions, there were higher differences between the *in vivo* and estimated outcomes in the moment with full or close to full knee extension, and at the start or end of the cycle.

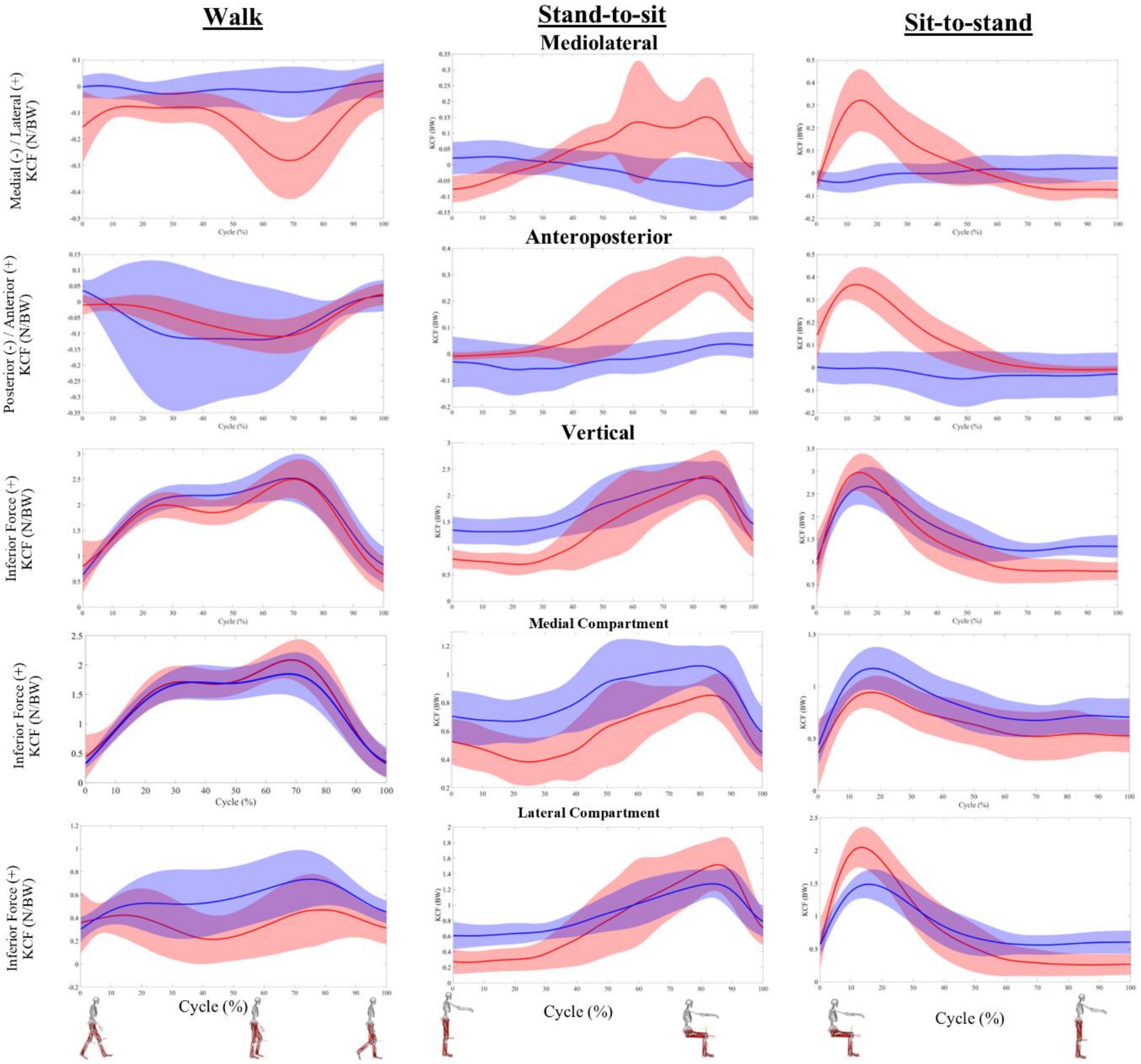

Figure 4. Mean group curves comparing the ***in vivo*** and Modified **model** results.
The solid line is the average between all subjects, and the shaded area is the standard deviation. The blue line is ***in vivo*** results and red line is the **Modified model**. KCF: knee contact force; BW: body weight.

Discussion

The study aimed to compare the accuracy between three MSK models to estimate the mediolateral, anteroposterior, and vertical forces, and medial and lateral compartments KCF. Considering the three tasks, the Modified model showed higher correlation and lower RMSE for the time series and peaks, presenting closer results to the measured in vivo data than the other two generic models. During the gait, the results for the vertical forces were similar among the models. However, during sit-to-stand tasks, the results for Modified model were superior compared to the other two models. The shear forces in all three models showed inconsistent results in the anteroposterior and mediolateral directions compared to the *in vivo* results. Shear force estimations lacked reliability as there were large errors and peak differences between the MSK and *in vivo* measurements.

The three models presented satisfactory results in estimating vertical KCF during gait. The correlations were high for the total knee and medial compartment, with a peak error of around 20% in relation to in-vivo results. For the lateral compartment, the correlations were low for Modified and Bedo models and moderate for Rajagopal model, with similar errors among the models (RPE ~40%). It is important to consider that the knee varus-valgus moment, used to split the forces between the medial and lateral compartments, was computed in different positions between Rajagopal model and in-vivo (the tibial plateau) compared to Modified and Bedo models (center of femoral condyles). The difference in the vertical position of the joint center can potentially modify the magnitude of the knee moment. The reduced forces in the lateral compartment were noted in another study (Saliba *et al.*, 2017), using a contact point model in patients with neutral frontal plane alignment. This problem increased in patients with significant varus deformity.

Despite similar results among the models during the gait task, for the sit-to-stand transitions, Modified model was superior in estimating the KCF. For the stand-to-sit task, the peak errors ranged between 13 to 29 % of the RPE for total and medial/lateral compartments. For sit-to-stand, the results were similar, but the lateral compartment presented a 40% peak error. For both tasks, the RMSE relative to the entire cycle was around 40%, but it is important to consider a higher difference close to the standing position with a full knee extension and no movement.

For the total vertical peak forces during the gait, the results were similar to those reported by Imani Nejad *et al.* (2020), that also used the Rajagopal model. The same study analyzed the squat and the vertical peak forces and showed significant differences between measured and estimated KCF. The results of the present study showed that the peak error for the Rajagopal model was around 60%, and for the Modified model was around 15% for sit-to-stand tasks. Two modifications possibly improved these results. One is the modifications proposed and implemented in Modified and Bedo models which allowed movements with a high knee and hip flexions (Catelli *et al.*, 2019). For the Modified model, the muscle and tendon properties implementations by Uhlrich *et al.* (2022) resulted in more physiological results for the muscle forces and activations, that allows reducing the KCF magnitudes.

Regarding the shear forces in the anteroposterior and mediolateral directions, the results for all three models presented poor correlations and high differences in the temporal series and peaks for all tasks, compared to the *in vivo* data. Poor results for the shear forces were identified for gait and squat using the Rajagopal model (Imani Nejad *et al.*, 2020). It is important to consider that the ligaments have an essential role in maintaining knee stability and reduce shear forces (Marra *et al.*, 2015; Ding *et al.*, 2016). However, some generic models, such as the ones used in this study, do not implement ligament structures because of their scaling and bone attachment. Another factor is the problem of measuring the translation movements between the tibia and femur with kinematic systems, as this movement is generally overestimated during the gait (Benoit *et al.*, 2006; Garling *et al.*, 2007; Andersen *et al.*, 2010).

Only generic models with a simple scale process were included in this paper. The results for the vertical forces were considered satisfactory, and the magnitude of errors between the measured and estimated were identified. Other modeling approaches with subject-specific or more sophisticated scaling and optimization processes can potentially improve the reliability of the results (Saxby *et al.*, 2020; Killen *et al.*, 2021). Still, Dumas e Moissenet (2020) reported an inconsistent improvement in estimating the KCF using subject-specific contact point scaling compared to *in vivo* data.

Future studies using musculoskeletal modeling with generic models and static optimization approaches should consider the magnitude of error for interpreting the results. Also, with these generic models, the shear forces showed high errors between the measured and estimated forces, therefore lacking reliability. In conclusion, the results for the vertical force components were similar among the three models compared to the in-vivo data during the gait. Meanwhile, the Modified model showed better estimated vertical knee contact forces in total, medial and lateral compartments for the sit-to-stand task.

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Declaration of interest statement

The authors declare no conflict of interests.

Supplementary Methods

Modified model detailed description

For the Modified and Bedo models, the point-contact method was used to divide the knee into medial and lateral compartments. All information about the medial and lateral compartment forces are described in Lerner *et al.* (2015) and Bedo *et al.* (2020). This model (Bedo *et al.*, 2020) included the adaptations in the wrap surfaces for the lower limb muscles proposed by Catelli *et al.* (2019) to ensure the model can perform analysis with high hip (138 deg) and knee flexion (145 deg). The lower limb model used in Modified model was proposed by Uhlrich *et al.* (2022) that improved the Rajagopal model (Rajagopal *et al.*, 2016), calibrating the passive muscle forces curves to reduce and closely match the experimental data, especially at the large knee or hip flexion angles (Silder *et al.*, 2007). The passive muscle force changes helped reduce large hip flexor muscle activations during the stance phase and for the quadriceps-hamstring co-activation when the knee is flexed during the swing phase. Also, the muscle paths of the hip abductors were altered, including the origin and insertion points, in order to the anterior fibres of the gluteus mediums and minimum generate a hip flexion moment when the hip is in an extended position (Blemker e Delp, 2005; De Pieri *et al.*, 2018; Uhlrich *et al.*, 2022). By the end, in this model, tendon compliance was included to reduce the muscle activation and match closely to the muscle activation measured with the electromyography (Uhlrich *et al.*, 2022). In this model, the knee has only flexion and extension rotations. Also, the anteroposterior and superior-inferior translations were in the function of the knee flexion, and the mediolateral translation was locked (Lerner *et al.*, 2015).

Supplementary figures

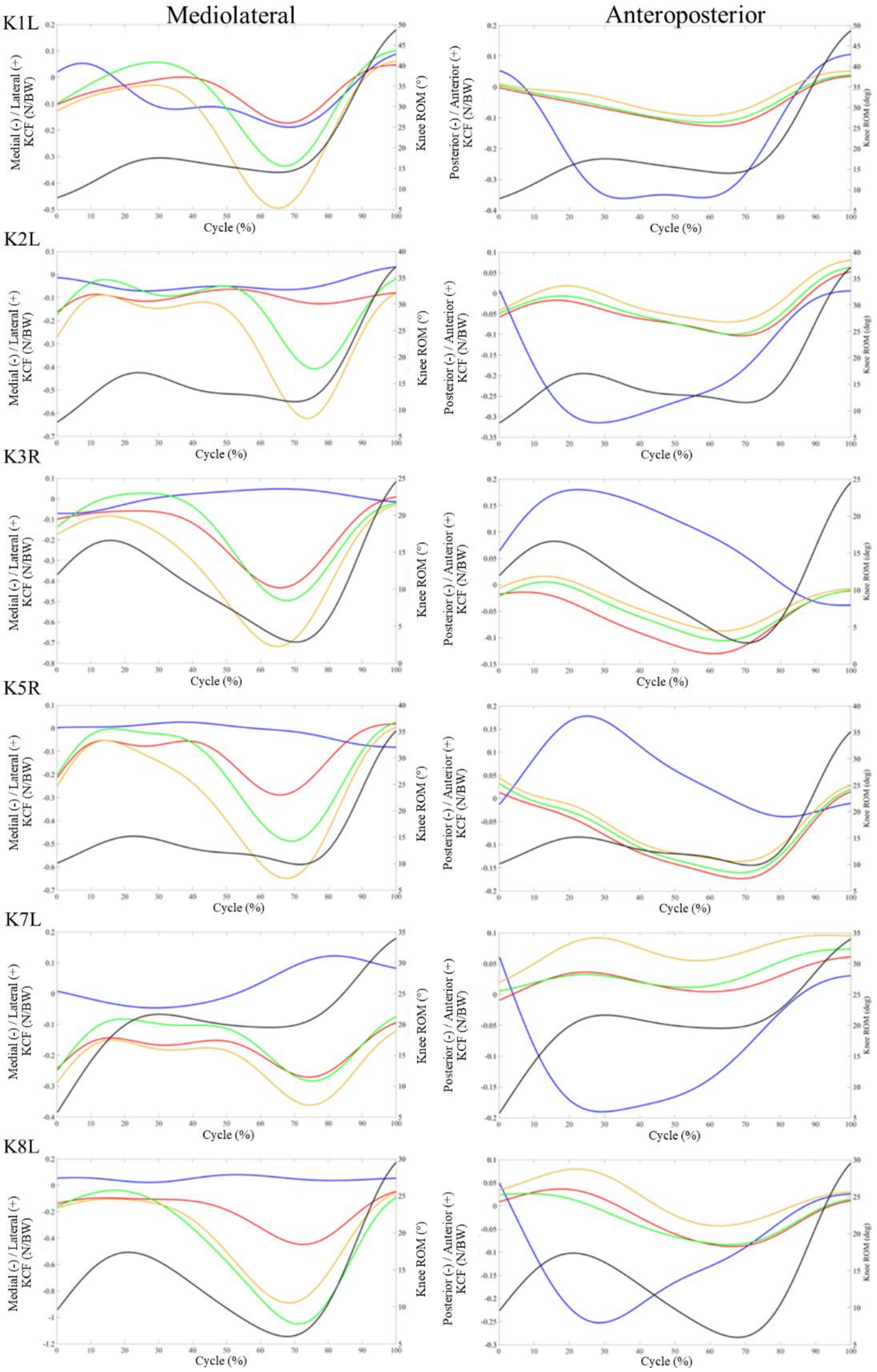

Figure 1. Gait comparisons between the measured and the models for each subject for the mediolateral and anteroposterior forces.

The black line is referent to the knee angle (right y-axis). In the left y-axis: blue is the measured results (in vivo), red for Modified model, green for Bedo model, and yellow for Rajagopal model. KCF: knee contact force; N/BW: Newton/body weight; ROM: range of motion.

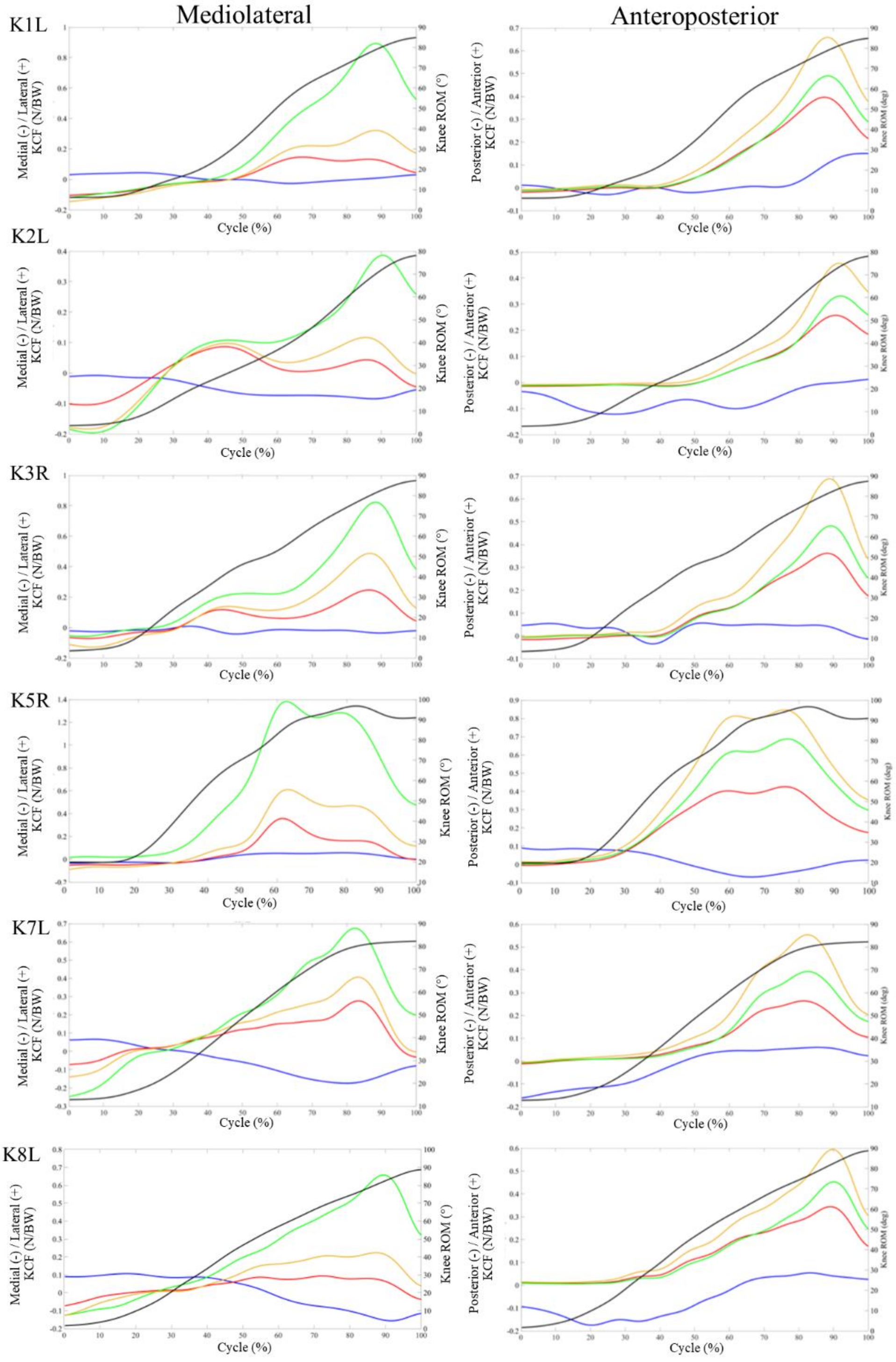

Figure 2. Stand-to-sit comparisons between the measured and the models for each subject for the mediolateral and anteroposterior forces.

The black line is referent to the knee angle (right y-axis). In the left y-axis: blue is the measured results (in vivo), red for Modified model, green for Bedo model, and yellow for Rajagopal model. KCF: knee contact force; N/BW: Newton/body weight; ROM: range of motion.

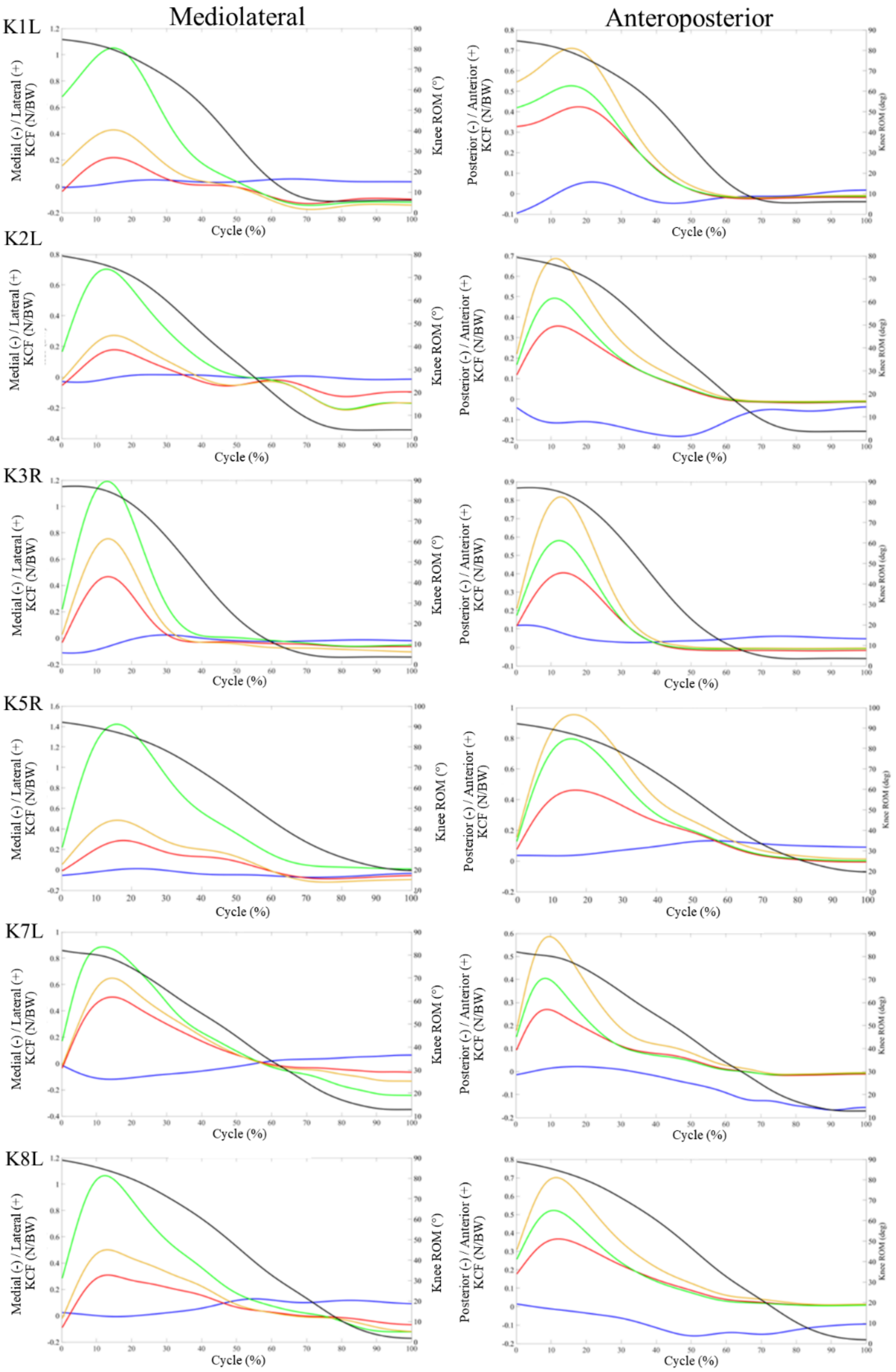

Figure 3. Sit-to-stand comparisons between the measured and the models for each subject for the mediolateral and anteroposterior forces.

The black line is referent to the knee angle (right y-axis). In the left y-axis: blue is the measured results (in vivo), red for model 1, green for model 2, and yellow for model 3. KCF: knee contact force; N/BW: Newton/body weight; ROM: range of motion.

Supplementary tables

Table 1. Comparison between the models for each subject during the **gait**.

Sub	Md	Total				Medial compartment				Lateral compartment				Anteroposterior				Mediolateral			
		Peak Inf	RPE	RMS	R^2	Peak Inf	RPE	RMS	R^2	Peak Inf	RPE	RMS	R^2	Peak Post	RPE	RMS	R^2	Peak Med	RPE	RMS	R^2
K1L	V	3.13				1.92				1.23				-0.39				-0.19			
	M	2.50	19.9	59.5	.943	2.39	25.1	37.9	.951	0.27	73.7	85.2	-.440	-0.12	67.2	18.3	.888	-0.17	10.6	8.0	.458
	B	2.64	15.3	56.1	.947	2.54	32.8	42.6	.960	0.25	75.9	86.9	-.423	-0.11	70.3	19.0	.896	-0.34	75.1	10.7	.625
	R	2.76	11.7	51.2	.965	2.22	18.2	28.1	.959	0.56	50.2	65.9	.231	-0.09	75.8	20.8	.867	-0.49	159.1	15.9	.737
K2L	V	2.55				2.00				0.61				-0.31				-0.07			
	M	2.12	16.6	32.8	.863	2.16	8.16	20.7	.971	0.43	40.8	35.7	-.046	-0.10	66.3	17.1	.437	-0.17	129.4	7.7	-.086
	B	2.36	7.4	36.6	.802	2.26	13.0	21.2	.977	0.45	35.4	35.3	.103	-0.10	67.3	17.8	.449	-0.41	424.0	15.8	.101
	R	2.81	12.4	33.7	.826	2.20	10.2	15.3	.954	0.75	24.4	20.5	.571	-0.07	76.7	19.7	.450	-0.63	723.6	27.8	.170
K3R	V	2.14				1.58				0.58				-0.04				-0.06			
	M	2.68	28.3	37.3	.865	1.99	25.7	29.9	.886	0.74	29.9	11.3	.646	-0.13	222.6	18.3	-.121	-0.44	659.0	25.4	-.696
	B	2.59	23.9	34.6	.849	1.88	18.9	26.7	.889	0.76	32.2	12.0	.620	-0.10	164.3	16.1	.136	-0.51	772.5	27.7	-.652
	R	2.77	32.3	41.7	.859	1.79	13.1	24.6	.889	1.00	74.4	24.7	.525	-0.09	119.6	14.8	.175	-0.73	1131.7	42.4	-.772
K5R	V	2.40				1.70				0.75				-0.04				-0.08			
	M	2.34	3.9	32.0	.906	1.90	11.9	13.8	.967	0.45	39.2	29.9	.185	-0.17	349.2	16.7	.172	-0.29	253.1	15.4	-.231
	B	2.40	6.5	33.8	.880	1.68	7.3	18.7	.941	0.72	7.6	21.7	.559	-0.16	318.3	15.8	.185	-0.49	497.6	24.1	.090
	R	2.61	9.0	28.1	.918	1.81	7.3	16.8	.951	0.80	8.8	16.4	.625	-0.13	261.5	14.5	.169	-0.65	694.7	35.0	-.068
K7L	V	3.00				2.24				0.80				-0.19				-0.04			
	M	2.89	4.1	21.3	.946	2.31	2.95	8.20	.986	0.64	21.0	16.7	.356	-0.002	98.1	14.6	.178	-0.27	749.9	23.0	-.488
	B	2.67	10.9	30.5	.948	2.29	1.66	7.61	.989	0.53	33.4	26.6	.335	0.005	102.1	14.9	.427	-0.28	884.8	22.1	-.729
	R	2.73	9.0	28.1	.943	1.91	14.8	30.3	.989	0.85	9.66	14.6	.423	0.04	122.1	19.1	-.015	-0.36	1083.2	27.8	-.689
K8L	V	2.45				1.84				0.65				-0.25				0.02			
	M	2.98	33.0	40.0	.920	2.14	34.7	37.7	.921	0.90	38.6	24.3	.578	-0.08	64.1	14.4	-.160	-0.45	2209.8	28.7	-.121
	B	3.63	48.8	60.2	.917	2.63	49.5	55.2	.888	1.05	61.6	23.2	.832	-0.08	66.0	13.2	.065	-1.06	5122.0	61.6	-.291
	R	3.22	40.1	51.3	.939	2.04	30.8	37.9	.907	1.22	89.0	42.4	.650	-0.04	82.7	17.5	-.285	-0.89	4252.6	52.4	-.344

Subj: subject; Md: model; V: *in vivo* (measured); M: Modified model; B: Bedo model; R: Rajagopal model; Peak: maximum or minimum value during the cycle in BW; Inf: inferior; Post: posterior; Med: medial; RPE: relative peak error in % of the measured; RMS= root mean square error in % of the N/BW; R^2 = Pearson correlation coefficients.

Table 2. Comparison between the models for each subject during the **stand-to-sit**.

Subj	**Md**	**Total**				**Medial compartment**				**Lateral compartment**				**Anteroposterior**				**Mediolateral**			
		Peak Inf	RPE	RMS	R^2	Peak Inf	RPE	RMS	R^2	Peak Inf	RPE	RMS	R^2	Peak Ant	RPE	RMS	R^2	Peak Lat	RPE	RMS	R^2
K1L	V	2.73				1.19				1.55				0.15				0.05			
	M	3.04	11.6	49.7	.984	1.12	6.2	16.5	.949	1.92	23.4	37.3	.971	0.39	158.7	15.7	.636	0.16	225.7	10.7	-.621
	B	3.78	38.6	63.9	.968	1.54	28.6	20.0	.864	2.24	44.1	44.9	.974	0.49	219.5	18.7	.702	0.89	1667.6	42.5	-.478
	R	3.90	42.7	66.6	.970	1.11	7.02	24.3	.908	2.78	78.7	57.6	.972	0.65	329.7	26.3	.695	0.32	525.0	18.0	-.541
K2L	V	2.00				1.06				1.17				0.01				-0.00			
	M	1.97	3.0	64.7	.699	0.83	21.2	29.6	.304	1.18	6.8	37.0	.921	0.25	3085.8	14.4	.675	0.09	904.3	9.8	-.496
	B	2.30	14.8	65.6	.631	0.97	10.3	27.5	.224	1.33	14.5	40.0	.895	0.33	4014.0	16.2	.697	0.38	3769.9	24.2	-.828
	R	2.56	27.8	65.4	.657	0.76	27.5	32.7	.290	1.82	55.4	39.8	.905	0.45	5514.9	21.4	.697	0.12	1294.4	13.9	-727
K3R	V	2.31				1.10				1.20				0.07				0.01			
	M	3.11	38.8	34.3	.991	1.00	9.5	14.6	.969	2.12	75.9	38.7	.989	0.36	315.4	15.1	.194	0.25	2748.0	13.0	-.167
	B	3.75	72.8	56.1	.976	1.34	21.1	14.4	.967	2.42	100.9	46.7	.977	0.48	495.3	19.2	.144	0.84	7536.5	38.7	-.251
	R	4.31	95.0	77.5	.978	1.06	3.9	16.7	.965	3.26	170.4	82.6	.978	0.69	738.3	28.3	.131	0.50	4569.5	23.3	-.201
K5R	V	2.87				1.37				1.55				0.10				0.06			
	M	3.02	7.8	22.7	.994	1.13	18.5	21.8	.977	1.98	27.2	21.5	.991	0.43	321.5	29.2	-.875	0.36	455.6	12.1	.834
	B	4.53	56.8	77.1	.953	1.62	17.7	15.2	.952	2.96	90.1	65.0	.961	0.73	610.2	43.6	-.874	1.56	2325.5	76.4	.937
	R	4.54	56.6	78.5	.965	1.08	22.2	27.5	.976	3.50	124.4	97.2	.976	0.91	780.1	54.3	-.886	0.66	912.0	27.8	.915
K7L	V	2.34				1.08				1.27				0.07				0.06			
	M	2.59	10.8	53.2	.952	0.88	17.9	27.5	.885	1.71	34.7	32.1	.971	0.30	342.2	13.6	.780	0.28	413.5	22.6	-.830
	B	3.31	41.2	62.4	.944	1.22	13.3	21.4	.837	2.09	64.1	44.1	.914	0.45	559.2	18.9	.738	0.72	1227.5	44.1	-.954
	R	3.81	62.8	72.3	.946	0.97	10.2	29.3	.816	2.84	124.0	64.5	.925	0.64	825.9	26.3	.746	0.41	628.1	29.4	-.905
K8L	V	2.84				1.32				1.54				0.06				0.11			
	M	2.54	10.6	66.6	.978	0.89	33.0	51.1	.900	1.68	8.98	23.6	.943	0.36	452.7	20.1	.925	0.15	78.8	14.0	-.304
	B	3.22	13.3	68.1	.928	1.24	7.01	44.5	.837	1.98	28.8	29.1	.927	0.47	637.4	22.6	.898	0.69	523.8	40.3	-.956
	R	3.40	19.6	63.3	.953	0.86	34.9	53.2	.884	2.54	65.3	42.8	.956	0.62	866.3	29.7	.904	0.26	136.5	21.2	-.802

Subj: subject; Md: model; V: *in vivo* (measured); M: Modified model; B: Bedo model; R: Rajagopal model; Peak: maximum or minimum value during the cycle in BW; Inf: inferior; Post: posterior; Med: medial; RPE: relative peak error in % of the measured; RMS= root mean square error in % of the N/BW; R^2 = Pearson correlation coefficients.

Table 3. Comparison between the models for each subject during the **sit-to-stand**.

Subj	Md	Total				Medial compartment				Lateral compartment				Anteroposterior				Mediolateral			
		Peak Inf	RPE	RMS	R^2	Peak Inf	RPE	RMS	R^2	Peak Inf	RPE	RMS	R^2	Peak Ant	RPE	RMS	R^2	Peak Lat	RPE	RMS	R^2
K1L	V	3.17				1.34				1.83				0.06				0.06			
	M	3.48	9.6	55.5	.902	1.28	4.34	14.7	.862	2.21	20.8	45.2	.916	0.44	646.5	22.2	.281	0.21	258.3	12.5	-.171
	B	4.28	35.0	81.6	.876	1.71	28.0	26.4	.850	2.58	40.8	58.8	.889	0.54	814.5	26.9	.259	1.06	1659.9	49.5	-.290
	R	4.39	38.5	84.2	.880	1.24	7.06	19.4	.866	3.16	72.4	75.1	.889	0.72	1129.8	35.9	.266	0.43	610.9	21.4	-.254
K2L	V	2.37				1.01				1.39				-0.03				0.02			
	M	2.77	16.8	42.8	.989	0.95	6.51	15.6	.872	1.89	36.0	33.5	.998	0.35	1512.9	25.9	-.345	0.18	772.6	9.6	.106
	B	3.40	43.3	54.3	.971	1.18	15.9	14.5	.880	2.22	59.6	41.3	.988	0.49	2067.6	30.2	-.280	0.70	3276.0	32.6	-.027
	R	3.81	60.8	66.5	.970	0.89	12.3	21.2	.833	2.93	110.3	63.5	.990	0.68	2826.6	38.6	-.280	0.27	1220.2	15.4	.100
K3R	V	2.66				1.18				1.49				0.09				0.02			
	M	3.70	38.8	45.9	.984	1.06	10.2	17.7	.956	2.67	79.0	45.2	.986	0.40	315.4	14.4	.416	0.46	2748.0	20.0	-.449
	B	4.59	72.2	77.8	.966	1.47	24.6	19.3	.930	3.13	109.7	62.5	.975	0.58	495.3	20.3	.490	1.19	7536.5	50.0	-.473
	R	5.19	95.0	98.2	.966	1.18	3.09	21.3	.935	4.04	170.1	96.7	.979	0.81	738.3	29.8	.463	0.75	4569.5	31.3	-.461
K5R	V	3.11				1.40				1.72				0.15				0.01			
	M	3.19	3.16	17.8	.988	1.07	23.6	20.1	.916	2.14	24.9	21.4	.984	0.46	234.5	21.4	-.543	0.29	7137.6	15.3	.781
	B	4.88	56.8	81.0	.929	1.67	19.7	16.0	.940	3.22	87.5	66.6	.940	0.80	475.6	35.7	-.619	1.45	38855.2	70.7	.826
	R	4.70	51.2	73.2	.944	1.04	25.6	26.7	.968	3.69	114.9	91.0	.957	0.96	590.4	44.3	-.612	0.49	13063.3	24.6	.788
K7L	V	2.11				1.03				1.22				0.02				0.06			
	M	2.60	22.7	46.5	.898	0.82	20.6	18.8	.580	1.83	49.8	34.4	.981	0.26	1028.0	14.5	.874	0.51	697.3	29.8	-.948
	B	3.12	47.7	54.7	.877	1.03	5.52	13.6	.468	2.11	72.7	44.1	.926	0.39	1558.4	18.0	.781	0.91	1337.3	49.0	-.957
	R	3.75	77.1	71.4	.891	0.90	13.0	23.7	.456	2.86	134.9	63.4	.939	0.58	2370.0	25.6	.809	0.66	925.3	36.1	-.955
K8L	V	2.99				1.37				1.62				-0.005				0.12			
	M	2.99	2.43	54.1	.973	0.88	35.3	40.8	.966	2.11	29.8	30.8	.965	0.37	719.7	24.7	.637	0.33	164.4	17.7	-.784
	B	3.86	29.0	63.7	.935	1.35	3.22	29.8	.942	2.51	54.0	44.0	.927	0.52	1012.6	29.1	.694	1.07	734.9	49.5	-.922
	R	4.08	36.6	64.9	.949	0.93	31.4	41.9	.957	3.15	93.6	66.2	.941	0.70	1348.9	37.7	.682	0.52	312.0	26.0	-.861

Subj: subject; Md: model; V: *in vivo* (measured); M: Modified model; B: Bedo model; R: Rajagopal model; Peak: maximum or minimum value during the cycle in BW; Inf: inferior; Post: posterior; Med: medial; RPE: relative peak error in % of the measured; RMS= root mean square error in % of the N/BW; R^2 = Pearson correlation coefficients.

3.2 ESTUDO 2

Tibiofemoral contact forces during gait in knee osteoarthritis patients: descriptive and predictive analysis

Abstract

Knee osteoarthritis (OA) affects functional capacity, and gait is one of the most important daily activities. Knee contact force (KCF) during this task can be estimated using musculoskeletal (MSK) models. This study aims to describe and analyze the KCF in total and in medial and lateral compartments between knee OA patients and controls, as well as to identify which features predict KCF. This cross-sectional study included 14 severe knee OA patients (OA group) and 14 controls (CTRL). Five gait cycles were analyzed using an MSK model that allows for evaluating of vertical KCF in total and distribution in the medial and lateral compartments. Comparisons between the groups were performed for discrete and time-series data. Predictive analyses were performed using a generalized linear model to predict the KCF peaks, using the joint kinematics, moments, and muscle forces as features. Predictive capacity was evaluated using R^2 adjusted and the mean absolute error (MAE). The predictive results showed that the knee extensor moment was the most important feature for predicting the first total KCF peak, with an error of around MAE=0.17 N/BW. Both the first and second peaks in the medial compartment were predicted by hip abduction moments, with errors of around 0.20 and 0.24 N/BW, respectively. The group comparison showed a reduced first peak in the medial compartment in the OA group. Additionally, higher values during the valley were identified between the peaks for the total KCF in the OA group compared to the CTRL group. Considering the most important features and the group comparisons, the OA patients reduced the knee load in the medial compartment using a gait strategy known as medial thrust. Consequently, they avoided compressive force in this region, which is usually the most affected in knee OA. Additionally, although no differences were identified for the total vertical force peaks, the sustained load between the peaks could be related to higher cartilage degeneration and pain. In the present study, the predictive models were used to improve the interpretation of the differences in knee OA patients, but in the future, the prediction capacity could be explored to predict the KCF using simpler features, such as joint angles during the tasks.

Keywords: OpenSim; musculoskeletal models; knee load; machine learning; prediction.

Introduction

Gait is a complex task that involves interactions between joint torques, motion, and the external forces applied to the body (Khera e Kumar, 2020). During the stance phase of gait, the tibiofemoral joint receives a considerable load compared to other functional tasks, with the medial compartment experiencing the highest loading between the knee regions (Zhao *et al.*, 2007; Winby *et al.*, 2009; Trepczynski *et al.*, 2014; Gupta *et al.*, 2022). Non-invasive methods using musculoskeletal (MSK) models can predict joint contact forces (Seth *et al.*, 2018). The available current models can analyze knee contact forces (KCF) and divide the tibiofemoral forces between the medial and lateral compartments (Lerner *et al.*, 2015; Bedo *et al.*, 2020).

The prevalence of knee osteoarthritis (OA) is increasing worldwide. In the United States, knee OA affects 12% of those above 60 years old and has a significant economic impact on health systems, with a cost of approximately USD 140,300 per patient over their lifetime (Lawrence *et al.*, 2008; Losina *et al.*, 2015; Gupta *et al.*, 2022). OA is a multifactorial chronic disease, and changes in biomechanics are likely to play a significant role in the pathogenesis of OA (Van Rossom *et al.*, 2023). The intensity and load distribution in the knee joint during life are related to the joint cartilage degeneration (Eckstein *et al.*, 2002; Wong e Carter, 2003).

The tibiofemoral medial compartment is the region most affected by knee OA and is related to higher load in this compartment during various functional tasks (Meireles *et al.*, 2017). Knee OA patients frequently exhibit higher KCF, joint stiffness, and reduced muscle strength, which affects their daily activities (Van Rossom *et al.*, 2023). Some studies using MSK models with knee OA patients during gait have shown that these patients are not able to reduce tibiofemoral force, but the medial compartment force is higher in OA patients compared to non-injured individuals (Kumar *et al.*, 2013; Meireles *et al.*, 2016; Van Rossom *et al.*, 2023).

MSK simulations depend on the geometry of the muscle model and often use generic models that undergo a simple and limited scaling and optimization process. However, many biomechanical features are produced by MSK simulations, and statistical comparisons between groups often ignore the relationship between the variables (Zhu *et al.*, 2016; Lu *et al.*, 2021). To reduce the time and computational demands of processing KCF, identifying kinematic or moment features that predict KCF should be investigated. Machine learning algorithms can be a powerful tool to identify relevant features, predict outcomes, and classify samples (Malhotra *et al.*, 2021). One such algorithm is the generalized linear model (GLM), which is a supervised machine learning method capable of predicting categorical and continual results (James *et al.*, 2021).

Based on previous findings on KCF during gait in OA patients, a more detailed exploration of force distribution between the medial and lateral compartments is warranted. Identifying relevant features related to these differences could provide insights for treatment using gait retraining and muscle strengthening. This study aims describe and analyze the KCF and the relevant features during gait between OA patients and healthy controls. The primary research goal is to predict the total vertical forces in the tibiofemoral joint and in the medial compartment based on the relevant KCF features. The hypothesis is that the joint moments should be the relevant features to predict the KCF peaks. The total peak may be predicted with lower errors compared to the medial compartment forces. The secondary objective is to compare and to describe KCF and muscle forces differences during gait between OA patients and controls. The total KCF should be similar between the groups, and the distribution between the medial and lateral compartment should be lower in the medial compartment for the OA group. As for the muscle forces, the knee extensors should present lower forces compared the OA group with controls.

Methods

Sample

This cross-sectional study analyzed fourteen individuals with severe

(Kellgren Lawrence grade 4), unilateral knee OA (Kellgren e Lawrence, 1957). For the control (CTRL) group, fourteen asymptomatic individuals of similar age were analyzed. Participants with a body mass index (BMI) higher than 35 kg/m² and a waist circumference higher than 102 cm for males and 88 cm for females were excluded. In the OA group, participants who had undergone any joint replacement for the lower limbs or had other degenerative conditions affecting joints other than the involved knee were also excluded, as well as those with conditions that could affect the gait, such as neurologic conditions. In the CTRL group, participants had to be asymptomatic for the lower limbs and without any recent history of injury in the lower limbs or history of severe lower limb injuries or surgery.

The OA group was evaluated for the knee symptoms using the KOOS questionnaire, which includes five domains: pain, other symptoms, activities of daily living (ADLs), sports and recreation, and quality of life (Roos e Lohmander, 2003). The study was approved by the university and hospital ethics committees. All participants provided written consent, and the research was conducted by the principles of good clinical practice and the declaration of Helsinki. The study is referenced in the clinical trials website: CT02589197.

Protocol

Before data collection, the questionnaires were applied, and a 5-minute warm-up was performed on a cycle ergometer. The data collection was performed with 10 infrared cameras (2 Vantage V5 and 8 Vero 2.2, Vicon, Oxford Metric, acquisition frequency of 200 Hz) and four force plates (model 9286B, Kistler; model FP4060, Bertec, 1000 Hz) embedded in the floor, in the middle distance of the ten meters walkway. Participants were outfitted with 45 retroreflective skin markers, following the University of Ottawa Motion Analysis Model (UOMAM) marker set (Mantovani e Lamontagne, 2017).

First, a static kinematic capture was performed with participants in a similar anatomical position, but with shoulder abduction of around 30 degrees. The participants were instructed to walk at a self-selected pace. Five valid cycles were on force plates were acquired.

Data processing

Using the Nexus 2.11 (Oxford Metrics, Oxford, UK) software, the marker trajectories were labelled, and the gaps filled. The force plate data was filtered with a 4th order (zero lag) Butterworth filter with a cut-off frequency of 10 Hz. For the kinematic data a Woltring filter with a mean standard error of 15 mm was applied. After, the data was cropped in function of the stance phase, the cycle was defined from the foot strike and the foot off using the vertical force signal from the force plate with a threshold of 10 N. The cycle was normalized to 101 points from the foot strike. The kinematic and kinetic data were exported in OpenSim formats.

The MSK modeling and process were performed in the open-source OpenSim 3.3 software (Stanford University) (Delp *et al.*, 2007a). A generic model by Bedo *et al.* (2020) combined with updated muscle-tendon parameters published by Uhlrich *et al.* (2022) was used (Pelegrinelli et al., 2023, Manuscript 1 thesis). The model included 80 lower-limb Hill-type muscle-tendon units with 37 degrees of freedom and 17 ideal torque actuators driving the upper body (Zajac, 1989; Millard *et al.*, 2013). The knee in the model has flexion rotations. The anteroposterior and superior-inferior translations are described in function of the knee flexion, and the mediolateral translation is locked (Lerner *et al.*, 2015). Also, the model allowed for estimation of the medial and lateral compartment of vertical tibiofemoral contact force for tasks with high hip and knee flexion (Lerner *et al.*, 2015; Bedo *et al.*, 2020).

The generic model was scaled for each participant using the skin markers' position to scale the body segments dimensions. The Batch OpenSim Processing Scripts (BOPS) Matlab toolbox was used to perform the inverse kinematics, inverse dynamics, static optimization, and joint reaction analyses (Bedo *et al.*, 2021). Static optimization was employed to calculate the muscle activation and forces, which minimized the sum of squared muscle activation (Hicks *et al.*, 2015). The joint reaction analysis computed the resultant forces and moments in each joint, considering the internal and external loads applied to the model during the movement. For the tibiofemoral forces, the vertical forces were considered, and the total vertical forces were computed as the sum of the lateral and medial compartment forces (Bedo *et al.*, 2020) (Pelegrinelli et al., 2023, Manuscript 1 thesis).

The following variables were extracted for the time series and discrete results (peaks, valley and integrals): vertical, mediolateral and anteroposterior ground reaction forces (N/BW); hip sagittal and frontal range of motion in degrees (deg); knee in sagittal plane (deg); hip and knee flexor internal moments normalized by body weight and height (Nm/BW*height) (Moisio *et al.*, 2003); hip internal abduction moment (Nm/BW*height); muscle forces (N/BW) of the vasti medialis, lateralis and intermedius, rectus femoris, biceps femoris long and short head, semimembranosus, semitendinosus, medial and lateral gastrocnemius, gluteus medius and hip abductor muscles; tibiofemoral vertical forces in total, in medial and lateral compartment in N/BW. A full description of the peaks extracted is presented in the supplementary material.

Prediction analysis

The stepwise generalized linear model was used to predict the outcomes considered in this analysis: first and second vertical peaks of the medial compartment and in total for tibiofemoral forces. The GLM was applied with a linear model with a Poisson distribution, a canonical link function, and a criterium for feature selection, namely, the minimum Akaike (aic) information criterion (James *et al.*, 2021). All variables presented in the supplementary material were included as predictor variables (features) in the model. The models were tested at different features complexity level, starting with only kinematic data (IK step), adding kinematic plus moment (ID step), and finally including muscle forces (SO step).

The data for both conditions were initially divided into a training set (70%) and test set (30%). The division was random selected by participants, so all the cycles for each participant were considered. Thus, ten OA patients and ten controls were included in the training set, and the remaining eight individuals were used for the test set. Initially, the analyzes were performed on the full sample, which included both the OA and control group. To test the relevance of the selected features in OA patients, the same model was tested only with OA group data for training and test. After the models were determined, a prediction Matlab function was employed in the test dataset, and the prediction performance was analyzed.

Statistical analysis

The comparisons for the anthropometric and discrete data were tested about the normality distribution. After the Mann-Whitney test was used, the results are presented in median (Md) and the interquartile range (25; 75%). The effect size (*r*) was calculated and classified as small (0.1-0.3), medium (0.3-0.5) or large effect (higher than 0.5) (Cohen, 1988). The time-series comparisons were performed using the Statistical nonparametric mapping (SnPM) for independent samples (Pataky, 2010). The predictive models are tested in function of R^2 adjusted, mean absolute error (MAE), and the error in percentual to the measured peak (James *et al.*, 2021). The 5% significance level was employed for all analysis and performed in Matlab and SPSS 26.

Results

The sample characteristics and the gait speed comparisons are presented in table 1, with no differences between the groups. The KOOS results for the OA group are also presented. In table 2, the GRF joint kinematics and moments are presented. The vertical GRF showed a lower second peak in the OA group compared to controls, and the valley was higher in the OA group. The medial second peak force was higher in CTRL group, for the anteroposterior no differences from the peaks were identified. For the time series comparison, the AP force was lower in the OA group between 37-78% of the cycle (P<0.001) (Figure 1).

The discrete data for the hip in sagittal and frontal plane comparison did not show differences between the groups. In time series comparison the hip in sagittal plane was reduced for the OA group between 46-84% of cycle (P=0.005) (Figure 1). For the frontal plane the difference was between 0-13% of cycle (P=0.015), lower in OA group. For the knee, the extension and the range of motion was reduced in OA group. During the cycle the reduced extension was identified between 41-84% of the stance cycle (P<0.001). About the moments the flexor peak was higher in CTRL group. In the time series analysis of the moments the hip extensor (P=0.002) and abductor (P=0.024) were higher in CTRL group. Also, the knee flexor moment was reduced in OA group at the beginning of the cycle (P=0.006) and between 49-76% of cycle (P=0.003).

Table 1. Sample information and KOOS results.

	OA Med (25; 75%)	**CTRL** Med (25; 75%)
Sex (Females/Males)	6/8	7/7
Age (years)	63.7 (55.2; 68.1)	63 (60; 64)
Body mass (kg)	80.2 (70.4; 85.3)	73.6 (61.0; 77.7)
Height (m)	1.67 (1.61; 1.77)	1.69 (1.65; 1.73)
Gait speed (m/s)	1.27 (1.02; 1.35)	1.24 (1.15; 1.40)
KOOS		
Pain (%)	55.5 (46.5; 67.3)	
Symptoms (%)	50 (36.6; 58)	
ADL (%)	68.4 (55.9; 82.7)	
Sports and Rec (%)	30 (23.7; 35)	
QOL (%)	21.9 (17.2; 40.6)	

Med: median; Knee injury and Osteoarthritis Outcome Score; ADL: activities of daily living; Rec: recreation; QOL: quality of life.

Table 2. GRF, joint kinematic and moments.

		OA Med (25; 75%)	**CTRL** Med (25; 75%)	*P* (*r*)
Vertical GRF	1st peak (N/BW)	1.09 (0.97; 1.14)	1.08 (1.06; 1.20)	.312 (.191)
	2nd peak (N/BW)	**1.04 (0.99; 1.12)**	**1.10 (1.07; 1.16)**	**.019 (.442)**
	Valley (N/BW)	**0.78 (0.72; 0.89)**	**0.74 (0.69; 0.77)**	**.035 (.399)**
	Integral (AU)	78.9 (76.8; 81.1)	80.4 (79.3; 81.2)	.089 (.321)
AP GRF	Negative peak (N/BW)	- 0.19 (-0.14; -0.21)	- 0.19 (-0.18; -0.22)	.581 (.104)
	Positive peak (N/BW)	0.21 (0.15; 0.23)	0.22 (0.18; 0.23)	.383 (.164)
ML GRF	1st medial peak (N/BW)	-0.05 (-0.04; -0.06)	-0.06 (-0.05; -0.08)	.098 (.312)
	2nd medial peak (N/BW)	**-0.04 (-0.03; -0.05)**	**-0.06 (-0.04; -0.07)**	**.022 (.434)**
Hip sagital kinematics	Flexion peak (deg)	39.5 (30.4; 47.4)	34.7 (31.6; 40.7)	.383 (.164)
	Extension peak (deg)	-6.8 (1.4; -15.6)	-14.7 (-10.3; -16.0)	.081 (.329)
	ROM (deg)	46.4 (45.0; 48.5)	49.5 (46.7; 51.7)	.081 (.329)
Hip frontal kinematics	Adduction peak (deg)	6.6 (5.3; 8.8)	7.1 (5.2; 7.9)	.927 (.017)
	Abduction peak (deg)	-5.3 (-3.4; -7.5)	-5.2 (-3.5; -9.5)	.890 (.026)
	ROM (deg)	12.1 (10.4; 13.0)	11.7 (10.7; 15.4)	.818 (.043)
Knee sagital kinematics	Flexion peak (deg)	23.9 (19.6; 29.7)	24.0 (19.5; 26.9)	.679 (.078)
	Extension peak (deg)	**14.0 (8.6; 24.1)**	**6.8 (2.7; 10.5)**	**.001 (.625)**
	ROM (deg)	**31.7 (28.5; 34.2)**	**38.3 (36.1; 41.1)**	**.001 (.651)**
Hip flexor moment	Flexor peak (Nm/BW*h)	0.10 (0.06; 0.13)	0.13 (0.10; 0.15)	.098 (.312)
	Extensor peak (Nm/BW*h)	-0.12 (-0.10; -0.16)	-0.14 (-0.10; -0.16)	.646 (.086)
Hip adductor moment	1st abductor peak (Nm/BW*h)	-0.14 (-0.12; -0.17)	-0.16 (-0.14; -0.17)	.251 (.217)
	2nd abductor peak (Nm/BW*h)	-0.13 (-0.10; -0.16)	-0.13 (-0.12; -0.15)	.713 (.069)
Knee flexor moment	Flexor peak (Nm/BW*h)	**0.01 (-0.00; 0.03)**	**0.03 (0.01; 0.06)**	**.029 (.412)**
	Extensor peak (Nm/BW*h)	-0.10 (-0.09; -0.13)	-0.11 (-0.08; -0.12)	.963 (.008)

GRF: ground reaction force; AP: anteroposterior; ML: mediolateral; Valley: minimum value between the two peaks; N/BW: Newton/body weight; AU: arbitrary units; med: median; ROM: range of motion; Nm/BW*h: Newton.metro/body weight*height.

The muscle force results during the gait are presented in table 3 and figure 2. Between the knee extensor muscles only the rectus femoris showed differences between the groups. The first peak and the integral were higher in the OA group. The rectus femoris presented higher force during 41-74% of the cycle in the OA group (*P*=0.008). Only the biceps femoral short head showed difference with higher peak in CTRL group. In time series analysis the semimembranosus (0-5%; *P*=0.003) and semitendinosus (0-3%; *P*=0.005) were higher in CTRL group at the beginning of the cycle. The lateral gastrocnemius presented a lower peak and lower values during 61-72% (*P*=0.007) of the cycle in OA group. The first peak and integral for the abductor muscles were higher in CTRL group. The difference was identified in the time series close to the first peak between 2-23% (*P*=0.001) of the cycle. The gluteus medius also, the first peak and integral were lower in OA group, with difference in time series between 0-29% of the cycle (*P*<0.001).

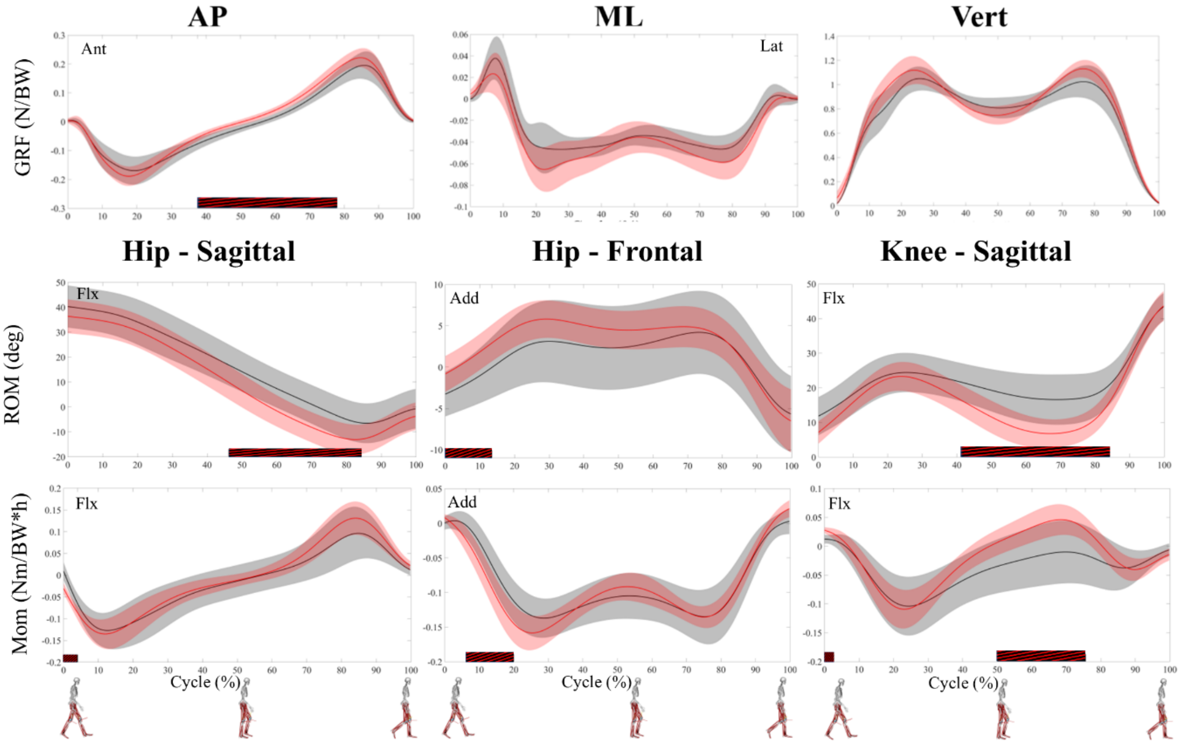

Figure 1. GRF, joint kinematic and kinetic time-series comparisons.
The black line is reference to the OA group and the red for the CTRL group, the rectangle indicates the cycle phase where the significant differences occurred. ROM: range of motion; Mom internal moment; Nm/BW*h: Newton.metre/body weight*height.

Table 3. Discrete results for muscle force during the gait.

		OA	**CTRL**	
		Med (25; 75%)	Med (25; 75%)	*P* (*r*)
Vastus medialis	Peak (N/BW)	0.27 (0.18; 0.34)	0.29 (0.24; 0.33)	.408 (.156)
	Integral (AU)	7.08 (4.07; 13.93)	7.19 (5.82; 8.65)	.963 (.008)
Vastus lateralis	Peak (N/BW)	1.03 (0.71; 1.32)	1.14 (0.91; 1.25)	.435 (.147)
	Integral (AU)	26.2 (14.7; 51.90)	26.3 (20.7; 32.0)	.963 (.008)
Vastus intermedius	Peak (N/BW)	0.10 (0.07; 0.13)	0.11 (0.09; 0.12)	.435 (.147)
	Integral (AU)	2.80 (1.65; 5.51)	2.85 (2.28; 3.45)	.963 (.008)
Rectus femoris	1st peak (N/BW)	**0.47 (0.28; 0.66)**	**0.16 (0.06; 0.28)**	**.008 (.503)**
	2nd peak(N/BW)	0.88 (0.71; 0.97)	0.83 (0.68; 1.03)	.846 (.036)
	Integral (AU)	**34.6 (25.0; 48.7)**	**22.5 (19.2; 28.3)**	**.039 (.390)**
Biceps (long head)	Peak (N/BW)	0.09 (0.08; 0.14)	0.11 (0.09; 0.15)	.168 (.260)
	Integral (AU)	1.68 (1.19; 2.88)	2.16 (1.68; 2.54)	.312 (.191)
Biceps (short head)	Peak (N/BW)	**0.04 (0.01; 0.06)**	**0.06 (0.05; 0.07)**	**.022 (.434)**
	Integral (AU)	**1.59 (0.31; 2.09)**	**2.08 (1.52; 2.69)**	**.022 (.434)**
Semimembranosus	Peak (N/BW)	0.13 (0.08; 0.20)	0.25 (0.15; 0.27)	.054 (.364)
	Integral (AU)	2.18 (1.67; 3.92)	3.80 (2.52; 5.39)	.098 (.312)
Semitendinosus	Peak (N/BW)	0.03 (0.02; 0.04)	0.04 (0.03; 0.05)	.215 (.234)
	Integral (AU)	0.62 (0.34; 0.77)	0.72 (0.63; 0.97)	.098 (.312
Medial gastrocnemius	Peak (N/BW)	1.18 (0.88; 1.31)	1.29 (1.03; 1.48)	.089 (.321)
	Integral (AU)	40.1 (29.0; 47.6)	44.0 (33.6; 52.4)	.408 (.156)
Lateral gastrocnemius	Peak (N/BW)	**0.32 (0.23; 0.37)**	**0.38 (0.31; 0.43)**	**.022 (.434)**
	Integral (AU)	11.2 (7.8; 13.6)	13.1 (10.1; 15.3)	.168 (.260)
Abductor muscles	1st peak (N/BW)	**2.10 (1.80; 2.31)**	**2.60 (2.13; 2.66)**	**.010 (.486)**
	2nd peak(N/BW)	1.52 (1.06; 1.76)	1.69 (1.53; 2.12)	.098 (.031)
	Integral (AU)	**116.9 (95.0; 142.8)**	**144.5 (129.2; 157.12)**	**.024 (.425)**
Gluteus medius	1st peak (N/BW)	**1.18 (1.06; 1.28)**	**1.52 (1.32; 1.65)**	**.004 (.547)**
	2nd peak(N/BW)	1.00 (0.64; 1.05)	1.07 (0.95; 1.21)	.073 (.338)
	Integral (AU)	**71.2 (53.9; 84.8)**	**89.5 (75.0; 94.6)**	**.024 (.425)**

N/BW: Newton/body weight; AU: arbitrary units. Med: median; Abductor muscles: sum of superior fiber of the gluteus maximus, gluteus medius and minimum, piriformis, sartorius and tensor fasciae latae.

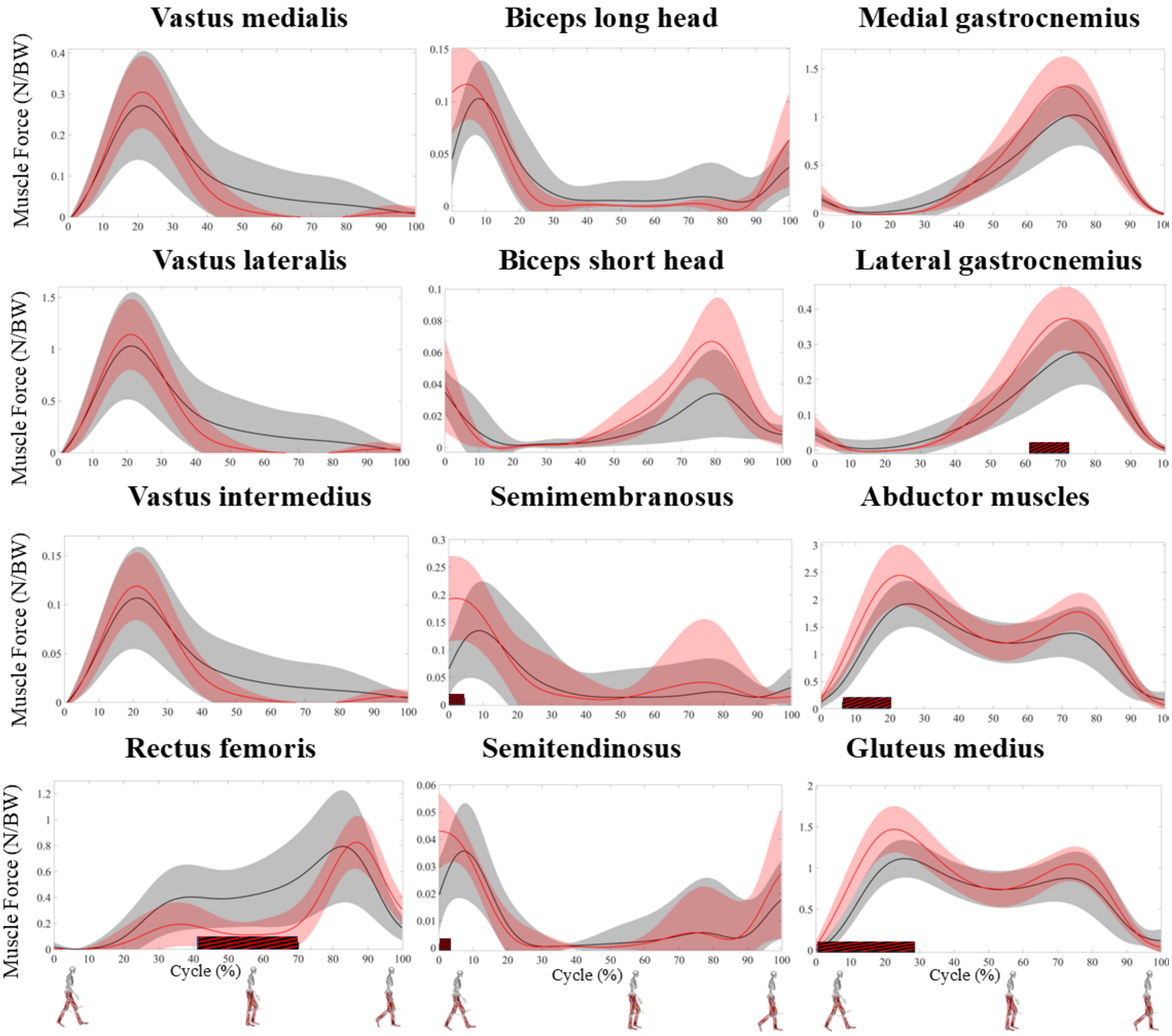

Figure 2. Muscle force during the stance phase.
The black line is reference to the OA group and the red for the CTRL group, the rectangle indicates the cycle phase where the significant differences occurred. N/BW: Newton/body weight; Abductor muscles: sum of superior fiber of the gluteus maximus, gluteus medius and minimum, piriformis, sartorius and tensor fasciae latae.

The KCF results are presented in table 4 and figure 3. For the discrete results the differences were only for the valley results. The valley in medial compartment and for total were higher in OA group, showing a sustained load between the groups in OA group. In time series for the medial compartment, a difference was found between 8-22% of the cycle (P=0.006), close to the first peak with lower values for the OA group. For the lateral compartment the CTRL group presented higher force close to the end of cycle (5-100%; *P*=0.008). For the total vertical force, the time series difference corroborates the valley results and the OA group presented higher forces between the two peaks (38-54%; *P*=0.001). The ratio between lateral/medial compartment was similar between the groups.

Table 4. Discrete results for the vertical KCF.

		OA Med (25; 75%)	**CTRL** Med (25; 75%)	*P* (*r*)
Medial compartment	1st peak (N/BW)	2.26 (1.84; 2.55)	2.43 (2.05; 2.62)	.270 (.208)
	2nd peak (N/BW)	2.54 (2.01; 2.86)	2.41 (2.23; 2.68)	.927 (.017)
	Valley (N/BW)	**1.63 (1.23; 1.90)**	**1.30 (1.20; 1.45)**	**.043 (.382)**
	Integral (AU)	153.3 (132.4; 200.7)	159.0 (152.2; 170.0)	.783 (.052)
Lateral compartment	1st peak (N/BW)	0.52 (0.38; 0.95)	0.46 (0.38; 0.59)	.491 (.130)
	2nd peak (N/BW)	0.74 (0.23; 1.09)	0.79 (0.57; 0.98)	.713 (.069)
	Integral (AU)	41.4 (11.6; 73.1)	38.9 (29.2; 44.1)	.679 (.078)
Total	1st peak (N/BW)	2.64 (2.19; 3.07)	2.73 (2.24; 2.92)	.783 (.052)
	2nd peak (N/BW)	3.26 (2.80; 3.60)	3.16 (2.78; 3.48)	.783 (.052)
	Valley (N/BW)	**1.85 (1.59; 2.44)**	**1.37 (1.30; 1.60)**	**.001 (.651)**
	Integral (AU)	204.0 (186.7; 226.4)	197.4 (191.7; 205.7)	.408 (156)
Lateral/medial ratio	1st peak (%)	21.4 (17.1; 57.9)	19.2 (15.0; 24.7)	.251 (.217)
	2nd peak (%)	31.0 (9.06; 55.8)	32.0 (24.8; 39.8)	.890 (.026)

N/BW: Newton/body weight; AU: arbitrary units; Med: median; Valley: minimum value between the two peaks.

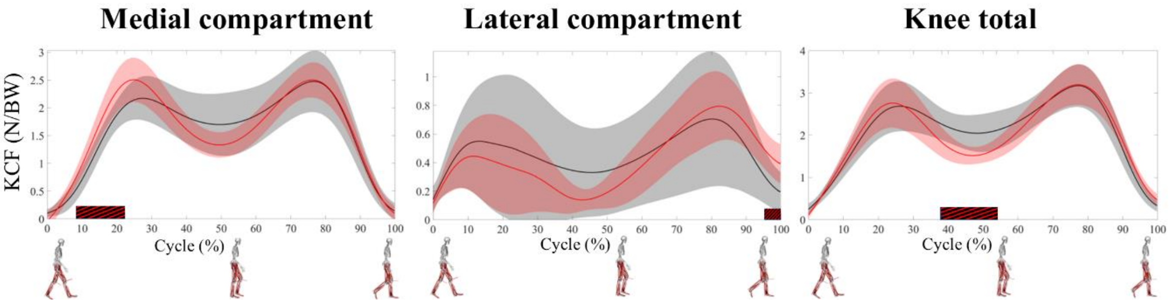

Figure 3. Vertical KCF comparisons during the cycle.
The black line is reference to the OA group and the red for the CTRL group, the rectangle indicates the cycle phase where the significant differences occurred. N/BW: Newton/body weight.

The predictive results for the KCF peaks in total and for the medial compartment are presented in table 5, and the correlations between the selected features and outcomes in each model are presented in figure 4. For the first peak, it was possible to predict the outcome using only the knee flexion peak angle. Including the knee extension moment or the vastus medialis increases the accuracy of the predictions. The correlation is negative for the knee moment and positive for the vastus medialis and knee flexion angles (Figure 4 A; B; C). For all three models, the correlations and prediction accuracy were similar when only OA data was used for training and testing. With regards to the second peak, the predictive model was effective only using muscle force and the knee extension angle. The model trained with full sample included the gastrocnemius lateralis, while the model with only OA data included the gastrocnemius medialis. The figure shows that the muscle force has a higher correlation influence on the models compared to the knee angle (Figure 4 D;E).

About the medial compartment, the hip abduction peaks moments are considered in the models. For the first peak, in the full sample, the first hip abduction peak moment was included in the model with a prediction error of about 8% and a negative correlation (Figure 4 - F). For the same peak, using only OA data for training and testing, the model needs to include the hip abductors muscles' force, with higher prediction errors (16%) and a positive correlation (Figure 4 - G). Concerning the second peak, the hip abduction moment (2nd peak) was included in the model for the full sample and only with OA data. The correlation was negative (Figure 4 - H), with a prediction error of about 11% and 15% for the full sample and OA set, respectively.

Table 5. Comparison between prediction models for the total and medial compartment KCF peak

Sample	**Features included**	**Features selected**	**Regression model**	**R² Adj**	**MAE (N/BW)**	**Pred Error (%)**
			TOTAL			
			1st peak			
Full	Kin	x5: knee flexion peak	Exp (0.2871) + x5*(0.0302)	0.565	0.253	9.19
OA	Kin	x5: knee flexion peak	Exp (0.1596) + x5*(0.0346)	0.747	0.306	10.20
Full	Kin+mom	x12: knee ext mom	Exp (0.3562) + x12*(-5.788)	0.792	0.177	6.36
OA	Kin+mom	x12: knee ext mom	Exp (0.3186) + x12*(-5.8552)	0.922	0.214	7.09
Full	Kin+mom+muscl	x13: vastus medialis	Exp (0.4958) + x13*(1.763)	0.847	0.138	5.28
OA	Kin+mom+muscl	x14: vastus lateralis	Exp (0.5547) + x14*(0.4047)	0.860	0.139	4.57
			2nd peak			
Full	Kin+mom+muscl	x23: lateral gastrocnemius	Exp (0.7642) + x23*(1.1333)	0.649	0.468	13.70
OA	--	--	No model was successful	--	--	--
			MEDIAL COMPARTMENT			
			1st peak			
Full	Kin+mom	x9: hip abdu mom1st peak	Exp (0.0560) + x9*(-5.0259)	0.622	0.206	8.14
OA	Kin+mom+muscl	x24: hip abdu musc 1st peak	Exp (0.0761) + x24*(0.3427)	0.615	0.426	15.95
			2nd peak			
Full	Kin+mom	x10: hip abdu mom 2nd peak	Exp (0.3396) + x10*(-4.1226)	0.581	0.242	8.79
OA	Kin+mom	x10: hip abdu mom 2nd peak	Exp (0.2897) + x10*(-4.2103)	0.710	0.369	12.19

Full: full sample for test and training set; OA: only OA group for training and test set; kin: kinematics; mom: moments: muscl: muscle forces; Exp: exponential; R² Adj: R² adjusted; MAE: Mean Absolute Error; N/BW: Newton/body weight; Pred: prediction.

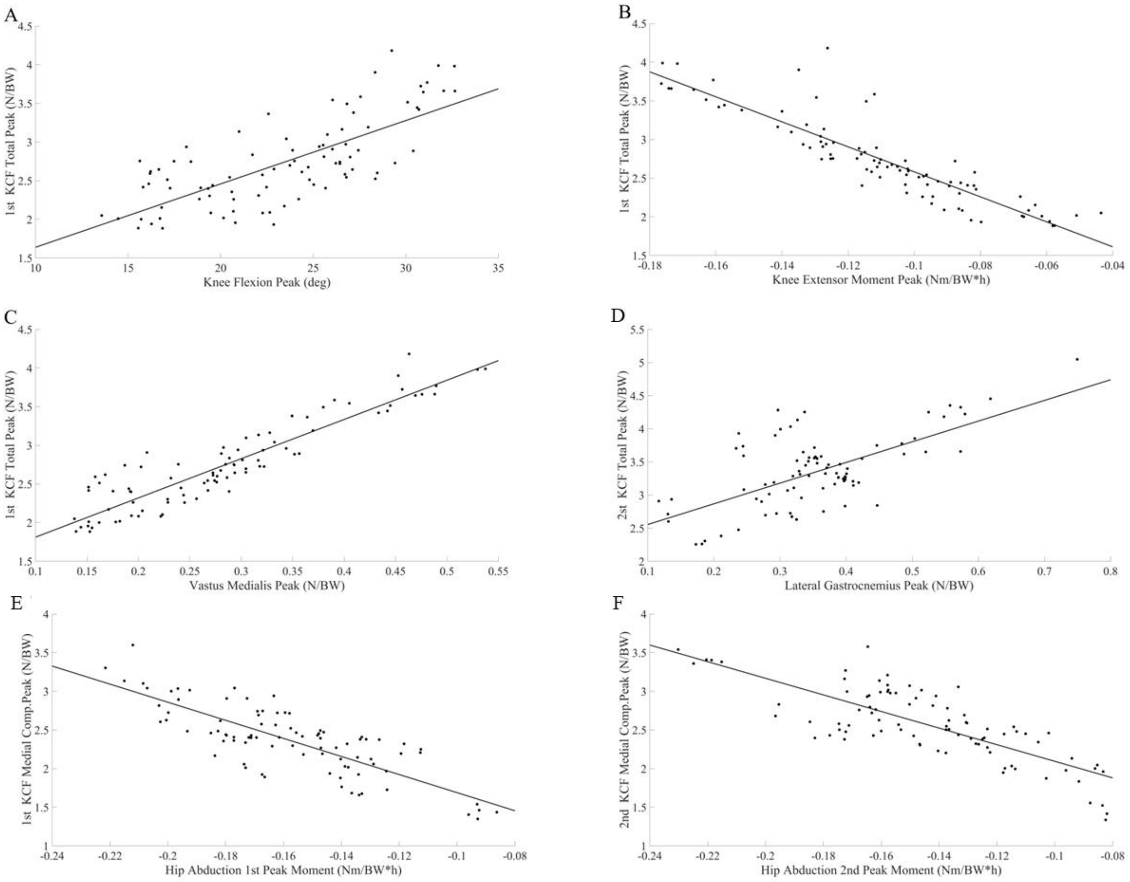

Figure 4. Correlation plots with the full sample for the features included in the models.

A, B and C are referent to the three models for the 1st total KCF peak; D is referent for the 2nd total KCF peak; E the feature selected for the 1st medial compartment peak, and F for the 2nd medial compartment.

Discussion

The general aims of this study were describe and analyze the KCF and relevant features during gait between patients with OA and healthy controls. The primary hypothesis was confirmed, showing that joint moments were the most relevant features for the first peak in total KCF and the two medial compartment peaks. The total KCF peak was better predicted than the medial compartment for the first peak. The secondary hypothesis found that the total KCF peaks were similar between the groups, but the OA group had a higher valley. Additionally, the first medial compartment peak force was lower in the OA group compared to controls. Regarding the muscle forces, the vastus presented similar forces between the groups, but the rectus femoris had a higher force in the OA group during gait. In general, the results highlighted the importance of knee flexor and extensor moments, and hip abduction moments for knee force distribution between the medial and lateral compartments.

The internal knee extension moment was the most relevant features for the first peak of total vertical KCF, and reducing the knee moment may decrease the first peak of KCF. This moment is related to quadriceps contraction to counterbalance knee flexion during the loading response phase (Schipplein e Andriacchi, 1991; Creaby, 2015). In the comparative analysis performed in the present study, the first peak of total KCF was not different between the groups. Also, no differences were detected for the knee extensor muscle, the knee flexion angle peak and for the knee extension moment. Meireles *et al.* (2016) found higher first KCF peak only in patients with established knee OA. In the present study, the knee extensor muscle activation was similar between the groups, possibly related to the KCF attenuation for the first peak (Mikesky *et al.*, 2006).

The valley of the total vertical force was higher in OA group compared to controls. In this instance, the knee ROM was different between the groups, with limited extension for the OA group. Additionally, the rectus femoris still activated between the peaks. These findings indicated a higher sustained load in the knee. Although the peaks are similar, the sustained load could be related to cartilage damage and pain. The knee stiffness is related to reduced knee excursion, altered hip-knee coordination, and higher co-contraction caused by pain, instability and limited strength (Schmitt e Rudolph, 2008; Gustafson *et al.*, 2019; Wang *et al.*, 2021; Pelegrinelli *et al.*, 2022).

Regarding the medial compartment KCF results, the model selected hip abduction moments to predict both first and second peaks. The hip moment and motion in frontal plane are involved in medial and lateral compartment force distribution (Lewinson *et al.*, 2014; Rynne *et al.*, 2022). The comparative results showed a lower hip abduction moment and reduced abductor muscle activation in the OA group compared to controls, which corroborates with the lower medial compartment in the same instance during the gait. The medial thrust is considered an effective gait strategy to reduce the medial knee load, and this knee region is the most affected in knee OA (Bowd *et al.*, 2019; Bokaeian *et al.*, 2021; Gerbrands *et al.*, 2023).

No difference was identified for the second medial compartment peaks. The predictive analysis showed that the hip abduction moment was the most relevant feature, and no differences were found for hip moment and motion in this instance. The same peak was similar between early and established knee OA compared to controls during gait (Meireles *et al.*, 2016; Meireles *et al.*, 2017). The second peak is more related to the propulsion for the balance phase and knee flexors muscles, with a higher contribution from the gastrocnemius muscles (Uhlrich *et al.*, 2022). In the present study, the gastrocnemius showed higher activation in control groups with a greater knee flexor moment. However, knee extension was reduced in the OA group in the same instance, resulting in similar knee contact force was similar between the groups. These results were similar to those found by Uhlrich *et al.* (2022), where gastrocnemius avoidance reduced the second peak of the total KCF. In this present study, considering that the patients were in end stage of knee OA, this may reflect a pain avoidance strategy. Possibly, considering the vertical GRF magnitude, the same level of gastrocnemius activation would cause a higher KCF second peak.

The sample size was limited, increasing the sample could improve the power and capacity of the regression models to predict KCF peaks. The MSK modelling employed in this study had some limitations, such as the scaling process, which was performed only using skin markers position. This could be improved with a more specific scaling process using MRI (Saxby *et al.*, 2020; Killen *et al.*, 2021). Furthermore, the static optimization process was used for muscle activation and joint force calculations, which is considered adequate for estimating joint contact forces, but is limited investigating muscle forces (Knarr e Higginson, 2015).

In the present study, predictive models were used with the aim of identifying the relevant features to predicting KCF results, to improve understanding about of how tibiofemoral forces are affected in knee OA. Although, in the literature different regression machine learning models have been employed to predict the knee forces, peaks and time-series (Giarmatzis e Zacharaki, 2020; Burton *et al.*, 2021). Future studies should test different predictive model with the goal of improving predictive capacity. Additionally, different injured populations and varying level of OA should be explored.

In conclusion, the proposed regression model, using GLM, was able to predict the first peak of total KCF and the two peaks for the medial compartment using either the knee flexion or the hip abduction moments. The first peak of total

KCF, which is related the load absorption during the stance phase, had the small errors in prediction compared to the other peaks. In group comparisons, this peak was lower in OA group. In general, the joint moments selected for the models showed some difference between the groups and were related to the differences in KCF. Although no differences were identified between the groups for the total vertical KCF peaks, the valley was higher in the OA group, indicating a more sustained load in the injured knee compared to controls. The muscle forces showed small differences between the groups, but the OA showed reduced force for the hip abductors, which is related to the reduced first medial compartment peak. This indicates a strategy to reduce the vertical force in the medial compartment during the gait instance of the load absorption.

Conflict of interest statement

The authors declare no conflict of interests.

Acknowledge

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Supplementary material

Supplementary table. Variables included for the predictive analysis.

		Variable
Joint kinematics	Hip	Max flexion
		Max extension
		Adduction peak
		Abduction peak
	knee	Flexion peak
		Extension peak
GRF	AP	Posterior peak
		Anterior peak
	ML	1st medial peak
		2st medial peak
	Vertical	1st peak
		2st peak
Joint moments	Hip	Max extensor
		Max flexor
		1st adduction peak
		2st adduction peak
	Knee	Max extensor
		Max flexor
Muscle forces	Vastus medialis	Max
	Vastus lateralis	Max
	Vastu intermedius	Max
	Rectus femoris	1st peak
		2st peak
	Biceps (longhead)	Max
	Biceps (short head)	Max
	Semimembranosus	Max
	Semitendinosus	Max
	Medial gastrocnemius	Max
	Lateral gastrocnemius	Max
	Abductor muscles	1st peak
		2st peak
	Gluteus medius	1st peak
		2st peak

Abductor muscles: sum of superior fiber of the gluteus maximus, gluteus medius and minimum, piriformis, sartorius and tensor fasciae latae. Max: maximum value.

3.3 ESTUDO 3

Tibiofemoral contact forces and muscle demands in knee osteoarthritis patients during the stand-to-sit and sit-to-stand tasks

Abstract

This study compared muscle and knee contact force (KCF) differences in patients with knee osteoarthritis (OA) and controls (CTRL group) during sit-to-stand and stand-to-sit tasks. Twelve patients with severe unilateral knee OA and eleven controls were analyzed. A musculoskeletal model was used to analyze vertical tibiofemoral forces (total, and medial and lateral compartments). Joint moments, muscle forces and KCF were compared between the groups and the affected and non-affected sides. For the stand-to-sit task, vastus medialis, vastus lateralis, and vastus intermedius showed reduced force compared to CTRL. For vastus lateralis, the OA group showed approximately 20% lower peak force. In both tasks, the OA group exhibited lower tibiofemoral forces in total and in the medial compartment, compared with CTRL. When comparing affected vs non-affected sides, the OA group showed a 40% reduction in peak force in the medial compartment on the affected side for stand-to-sit. For sit-to-stand, the same reduction in peak force was 22%. Stand-to-sit showed greater differences compared to sit-to-stand in total and in the medial compartment. The lateral compartment force was unchanged for both tasks. The medial compartment often has more joint damage in knee OA patients, and the results suggest a movement strategy to reduce the medial load. The study found that OA patients exhibited reduced force in the vastus muscles during stand-to-sit, indicating a deficit in their ability to recruit these muscles eccentrically. Lastly, the contralateral knee experienced increased load during both tasks, which could relate to secondary development of OA in that knee.

Keywords: OpenSim; musculoskeletal models; osteoarthritis; functional task; joint reaction forces.

Introduction

Knee osteoarthritis (OA) damages the bones, cartilage, and synovial membrane. The progressive degeneration of the joint decreases its ability to absorb and dissipate the tibiofemoral forces while maintaining stability during weight-bearing tasks (Øiestad *et al.*, 2015; Petrella *et al.*, 2021). The sit-to-stand and stand-to-sit tasks are performed multiple times each day, averaging around 60 times daily (Dall e Kerr, 2010) and are among the most commonly affected daily activities in knee OA patients (Gandek *et al.*, 2019). A limitation in performing these tasks has a large functional impact on the person's quality of life (Guralnik *et al.*, 1995; Savelberg *et al.*, 2007).

Among daily tasks, sitting down and standing up are considered more demanding activities with higher joint loading than walking or going upstairs (Su *et al.*, 1998; Kutzner *et al.*, 2010; Taylor *et al.*, 2017). Sitting down and standing up are bilateral tasks, and asymmetries are often present in cases of disease or injury. In patients with knee OA, the transfer of load increases on the contralateral side according to the disease progression (Christiansen e Stevens-Lapsley, 2010; Duffell *et al.*, 2013). In severe knee OA patients, the load transfer can reach up to 87% for the non-affected (Duffell *et al.*, 2013).

The unequal load distribution between the medial and lateral tibiofemoral compartments is a critical biomechanical factor for developing knee OA (Goulston *et al.*, 2016; Zhang e Liu, 2022). It is relevant to investigate the tibiofemoral forces during functional tasks, such as sitting down and standing up. To evaluate the joint forces with noninvasive methods, some musculoskeletal (MSK) models have been published to evaluate the knee contact forces and the distribution between the medial and lateral compartments, including for tasks with high knee and hip flexion (Lerner *et al.*, 2015; Bedo *et al.*, 2020).

Strength deficits often present in knee OA patients and have a considerable impact on the ability to perform sitting down and standing up tasks (Savelberg *et al.*, 2007; Bohannon, 2009; Lamontagne *et al.*, 2012). Caruthers *et al.* (2020) used simulations to investigate the effects of muscle weakness on performing sit-to-stand tasks and found that quadriceps weakness had the greatest impact compared to other muscles. Conservative treatment for knee OA is often targeted at increasing quadriceps strength in patients who have difficulty performing sitting down and standing up tasks (Lange *et al.*, 2008; Caruthers *et al.*, 2016).

Given the biomechanical differences found in the literature among patients with knee OA for sitting down and standing up, it is important to investigate the impact of joint loading during the execution of both tasks. This study aimed to compare knee contact and muscle forces during the sit-to-stand and stand-to-sit tasks. The following hypotheses were formulated: the OA group will exhibit a reduced vertical force in the affected knee; the medial compartment should be the most affected in terms of vertical forces during both tasks; and the knee extensor muscles are expected to be more relevant in detecting differences between the groups.

Methods

Sample

This cross-sectional study analyzed twelve individuals with severe (Kellgren Lawrence grade 4), unilateral knee OA (Kellgren e Lawrence, 1957). For the control (CTRL) group, eleven asymptomatic individuals of similar age were analyzed. Participants with a body mass index (BMI) higher than 35 kg/m² and a waist circumference higher than 102 cm for males and 88 cm for females were excluded. In the OA group, participants who had undergone joint replacement for the lower limbs or had other degenerative conditions affecting their joints besides the involved knee were also excluded, as well as those with conditions that could affect the execution of functional tasks, such as neurological conditions. In the CTRL group, participants had to be asymptomatic for the lower limbs with no recent history of injury in the lower limbs or history of severe lower limb injuries or surgery.

The OA group was evaluated for knee symptoms using the KOOS questionnaire, which includes five domains: pain, other symptoms, activities of daily living (ADLs), sports and recreation, and quality of life (Roos e Lohmander, 2003). The study was approved by the university and hospital ethics committees. All participants provided written consent, and the research was conducted by the principles of good clinical practice and the declaration of Helsinki. The study is referenced in the clinical trials website: NCT02589197.

Protocol

Before data collection, participants performed a 5-minute warm-up on a cycle ergometer. The data was collected with 10 infrared cameras (2 Vantage V5 and 8 Vero 2.2, Vicon, Oxford Metric, acquisition frequency of 200 Hz) and two force plates (model FP4060, Bertec, 1000 Hz) embedded in the floor. Participants were outfitted with 45 retroreflective skin markers, following the University of Ottawa Motion Analysis Model (UOMAM) marker set (Mantovani e Lamontagne, 2017). First, a static kinematic capture was performed with participants in the anatomical position but with shoulder abduction of around 30 degrees. The tasks were performed with feet parallel and hip-width apart, with one foot on each force plate and arms stretched out anteriorly. The tasks were performed using a height-adjustable bench, which was set to the height of the participant's tibial tuberosity. The test sequence began with sit-to-stand. The patient started in a seated position and was instructed to stretch out their arms anteriorly. After the command was given, the patient moved to a standing position. They then returned to the sitting down position with ten seconds of rest before repeating the test. Next, the stand-to-sit task was performed with the same instructions. Five trials were performed for each task at a self-selected speed (Turcot *et al.*, 2012; Petrella *et al.*, 2021)

Data processing

First, using the Nexus 2.11 (Oxford Metrics, Oxford, UK) software, the marker trajectories were labelled, and any gaps were filled. The kinematic data was filtered using a Woltring filter with a mean standard error of 15 mm. The force plate data was filtered using a 4th order (zero lag) Butterworth filter with a cut-off frequency of 10 Hz. The sit-to-stand cycle was cropped with the start being defined by the first anterior displacement of the shoulder markers, and the end by maximum hip extension (Savelberg *et al.*, 2007). The start of the stand-to-sit task was defined as the initiation of hip flexion, and the end as the moment where hip extension stabilized (Roy *et al.*, 2006). Both cycles were normalized to 101 points from each task's start to end.

The MSK modeling and processing were performed in the open-source OpenSim 3.3 software (Stanford University) (Delp *et al.*, 2007a). A generic model by Bedo *et al.* (2020) combined with updated muscle-tendon parameters published by Uhlrich *et al.* (2022) was used (Pelegrinelli et al., 2023, Manuscript 1 thesis). The model included 80 lower-limb Hill-type muscle-tendon units with 37 degrees of freedom and 17 ideal torque actuators driving the upper body (Zajac, 1989; Millard *et al.*, 2013). The knee in the model has flexion rotations. The anteroposterior and superior-inferior translations are described as functions of knee flexion, and the mediolateral translation is locked (Lerner *et al.*, 2015). Also, the model allowed for estimation of vertical tibiofemoral contact force in the medial and lateral compartment for tasks with high hip and knee flexion (Lerner *et al.*, 2015; Bedo *et al.*, 2020).

The generic model was scaled for each participant using the skin markers' position to scale the body segments dimensions. The Batch OpenSim Processing Scripts (BOPS) Matlab toolbox was used to perform the inverse kinematics, inverse dynamics, static optimization, and joint reaction analyses (Bedo *et al.*, 2021). Static optimization was employed to calculate the muscle activation and forces, which minimized the sum of squared muscle activation (Hicks *et al.*, 2015). The joint reaction analysis computed the resultant forces and moments in each joint, considering the internal and external loads applied to the model during the movement. For the tibiofemoral forces, the vertical forces were considered, and the total vertical forces were computed as the sum of the lateral and medial compartment forces (Bedo *et al.*, 2020) (Pelegrinelli et al., 2023, Manuscript 1 thesis).

The following variables were extracted for the time series and discrete results (peaks and integrals): knee and hip sagittal range of motion (ROM) in degrees (deg); hip and knee extensor moments normalized by body weight (BW) and height (Nm/BW*height) (Moisio *et al.*, 2003); muscle forces for quadriceps (vasti and rectus femoris) and hamstring (biceps femoris long and short head, semimembranosus and semitendinosus) muscles in N/BW; tibiofemoral vertical forces in total, in medial and lateral compartment in N/BW. The knee contact forces were presented for both limbs, defined as the involved limb for the affected side in the OA group or the dominant limb for the CTRL group and the non-affected limb. The dominant limb was defined by asking the participant for their preferred foot for kicking a ball (Chapman *et al.*, 1987).

Statistical analysis

The anthropometric and discrete data were tested for normality. Subsequently, the Mann-Whitney test was used for group comparisons and the Wilcoxon test for the side-to-side comparison. The results are presented as the median (Md) and the interquartile range (25; 75%). The effect size (*r*) was calculated and classified as small (0.1-0.3), medium (0.3-0.5) or large effect (higher than 0.5)

(Cohen, 1988). The time-series comparisons were performed using Statistical nonparametric mapping (SnPM) for independent samples or the paired test for side-to-side comparisons (Pataky, 2010). The 5% significance level was employed for all analysis and performed in Matlab and SPSS 26.

Results

Group demographics and KOOS results are presented in Table 1. No group differences were identified for sex, age, or BMI. The joint kinematics and moments are presented in Table 2 (peaks/ ROM) and Figure 1. The hip ROM was higher in the CTRL group for both sit-to-stand and stand-to-sit tasks (Table 2), but this difference was close to the start or ending position when the OA group had limited hip extension (Figure 1). The hip extensor moment showed differences only for the sit-to-stand task, and this difference was between 86-98% of the cycle. The OA group started the stand-to-sit and ended the sit-to-stand task with more knee flexion (15 to 20 deg) than the CTRL group (Figure 1). The peak knee extensor moment was lower in the OA group for both tasks.

Table 1. Sample information and KOOS results.

	OA Med (25; 75%)	**CTRL** Med (25; 75%)
Sex (Females/Males)	8/5	5/6
Age (years)	66 (59.5; 69.1)	63 (60; 65)
Body mass (kg)	76.4 (67.4; 83.2)	73.6 (60.7; 85.0)
Height (m)	1.67 (1.60; 1.75)	1.68 (1.56; 1.74)
KOOS		
Pain (%)	63.9 (52.8; 69.4)	
Symptoms (%)	50 (46.4; 60.7)	
ADL (%)	70.6 (61.8; 82.4)	
Sports and Rec (%)	30 (25; 35)	
QOL (%)	31.3 (18.8; 50.0)	

Med: median; Knee injury and Osteoarthritis Outcome Score; ADL: activities of daily living; Rec: recreation; QOL: quality of life.

Table 2. Between-group comparison for the discrete joint kinematics and moments in the sagittal plane.

	OA Med (25; 75%)	**CTRL** Med (25; 75%)	*P* (r)
Sit-to-stand			
Hip flexion peak (°)	85.7 (77.0; 90.9)	89.3 (85.9; 91.1)	.218 (.256)
Hip ROM (°)	**76.3 (67.1; 80.5)**	**87.5 (77.9; 90.2)**	**.006 (.577)**
Hip ext mom peak (Nm/BW*h)	-0.145 (-0.133; -0.161)	-0.144 (-0.134; -0.196)	.622 (102)
Knee flexion peak (°)	90.1 (84.0; 94.5)	86.5 (84.4; 98.6)	.853 (.038)
Knee ROM (°)	76.7 (72.1; 80.4)	83.4 (76.4; 91.1)	.074 (.372)
Kneee ext mom peak (Nm/BW*h)	**-0.070 (-0.050; -0.088)**	**-0.134 (-0.078; -0.170)**	**.031 (.449)**
Stand-to-sit			
Hip flexion peak (°)	89.2 (80.5; 93.8)	91.6 (88.0; 96.9)	.242 (.243)
Hip ROM (°)	**75.6 (70.7; 82.8)**	**88.1 (79.0; 95.7)**	**.010 (.539)**
Hip ext mom peak (Nm/BW*h)	-0.148 (-0.128; -0.156)	-0.166 (-0.131; -0.197)	.157 (.295)
Knee flexion peak (°)	87.7 (82.2; 93.4)	85.2 (83.7; 96.5)	.853 (.038)
Knee ROM (°)	73.9 (69.2; 78.5)	78.8 (73.7; 89.8)	.065 (.385)
Kneee ext mom peak (Nm/BW*h)	**-0.055 (-0.047; -0.072)**	**-0.109 (-0.066; -0.143)**	**.010 (.539)**

Med: median; ROM: range of motion; Mom: moment; ext: extensor; Nm/BW*h: Newton.metre/body weight*height.

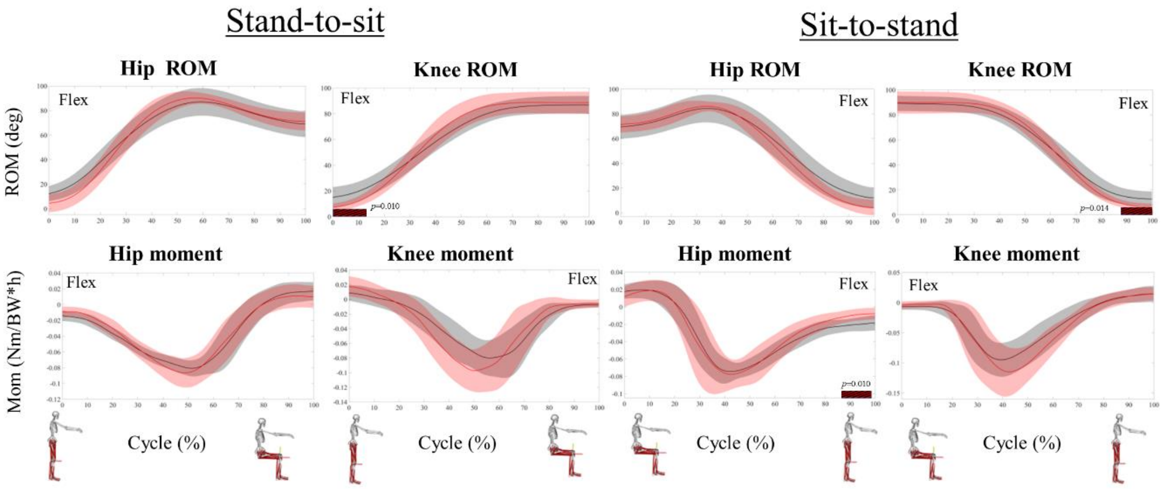

Figure 1. Between-group comparison for the time-varying kinematics and moments for the hip and knee in the sagittal plane.

The black line is reference to the OA group and the red for the CTRL group, the rectangle indicates the cycle phase where the significant differences occurred. ROM: range of motion; Mom: internal moment; Nm/BW*h: Newton.metre/body weight*height.

Table 3 and figure 2 present the muscle force results. The peak forces showed a difference only for the stand-to-sit task and for the vastus intermedius and vastus lateralis, with lower peaks for the OA group. For the time-series comparison, the three vasti showed reduced force for the OA group between 40-51% of the movement for the stand-to-sit task. The discrete data did not show differences between the groups during the sit-to-stand task. For the time-series comparison, the rectus femoris showed a reduced force at the end of the movement for the OA group, between 90-100%. Also, the long head of the biceps femoris forces were lower at the end of the movement for the OA group.

Table 3. Between-group comparison of peak muscle forces (N/BW).

	OA Med (25; 75%)	CTRL Med (25; 75%)	*P* (*r*)	OA Med (25; 75%)	CTRL Med (25; 75%)	*P* (*r*)
		Stand-to-sit			**Sit-to-stand**	
Vastus lateralis	0.52 (0.43; 0.58)	0.67 (0.50; 0.74)	.065 (.384)	0.63 (0.58; 0.66)	0.71 (0.61; 0.86)	.157 (.295)
Vastus medialis	**2.09 (1.76; 2.28)**	**2.59 (2.06; 2.93)**	**.049 (.410)**	2.41 (2.26; 2.59)	2.57 (2.34; 3.16)	.124 (.320)
Vastus intermedius	**0.17 (0.15; 0.19)**	**0.22 (0.18; 0.25)**	**.006 (.577)**	0.20 (0.18; 0.22)	0.21 (0.20; 0.29)	.065 (.384)
Rectus femoris	0.29 (0.16; 0.35)	0.18 (0.12; 0.35)	.580 (.115)	0.35 (0.27; 0.37)	0.32 (0.16; 0.37)	.667 (.089)
Quadriceps	3.02 (2.67; 3.28)	3.68 (3.12; 4.22)	.124 (.320)	3.61 (3.41; 3.70)	3.76 (3.37; 4.60)	.157 (.295)
Femoral bíceps	0.24 (0.21; 0.33)	0.33 (0.25; 0.47)	.196 (.269)	0.34 (0.30; 0.58)	0.37 (0.31; 0.46)	.902 (.025)
Semimembranosus	0.44 (0.31; 0.58)	0.60 (0.35; 0.75)	.124 (.320)	0.48 (0.40; 0.63)	0.41 (0.33; 0.77)	.667 (.089)
Semitendinosus	0.07 (0.06; 0.08)	0.07 (0.05; 0.10)	.758 (.064)	0.05 (0.04; 0.07)	0.03 (0.02; 0.07)	.667 (.089)
Hamstrings	0.79 (0.56; 0.91)	0.95 (0.59; 1.22)	.242 (.243)	0.89 (0.74; 1.06)	0.84 (0.65; 1.11)	.667 (.089)
Knee flexors	0.81 (0.58; 0.92)	1.10 (0.74; 1.23)	.110 (.333)	0.92 (0.79; 1.06)	0.84 (0.68; 1.13)	.806 (.051)

Med: median; Quadriceps: vasti and rectus femoris summed; Hamstrings: the sum of femoral biceps, semimembranosus, and semitendinosus; knee flexors: sum of the hamstrings and gastrocnemius medialis and lateralis.

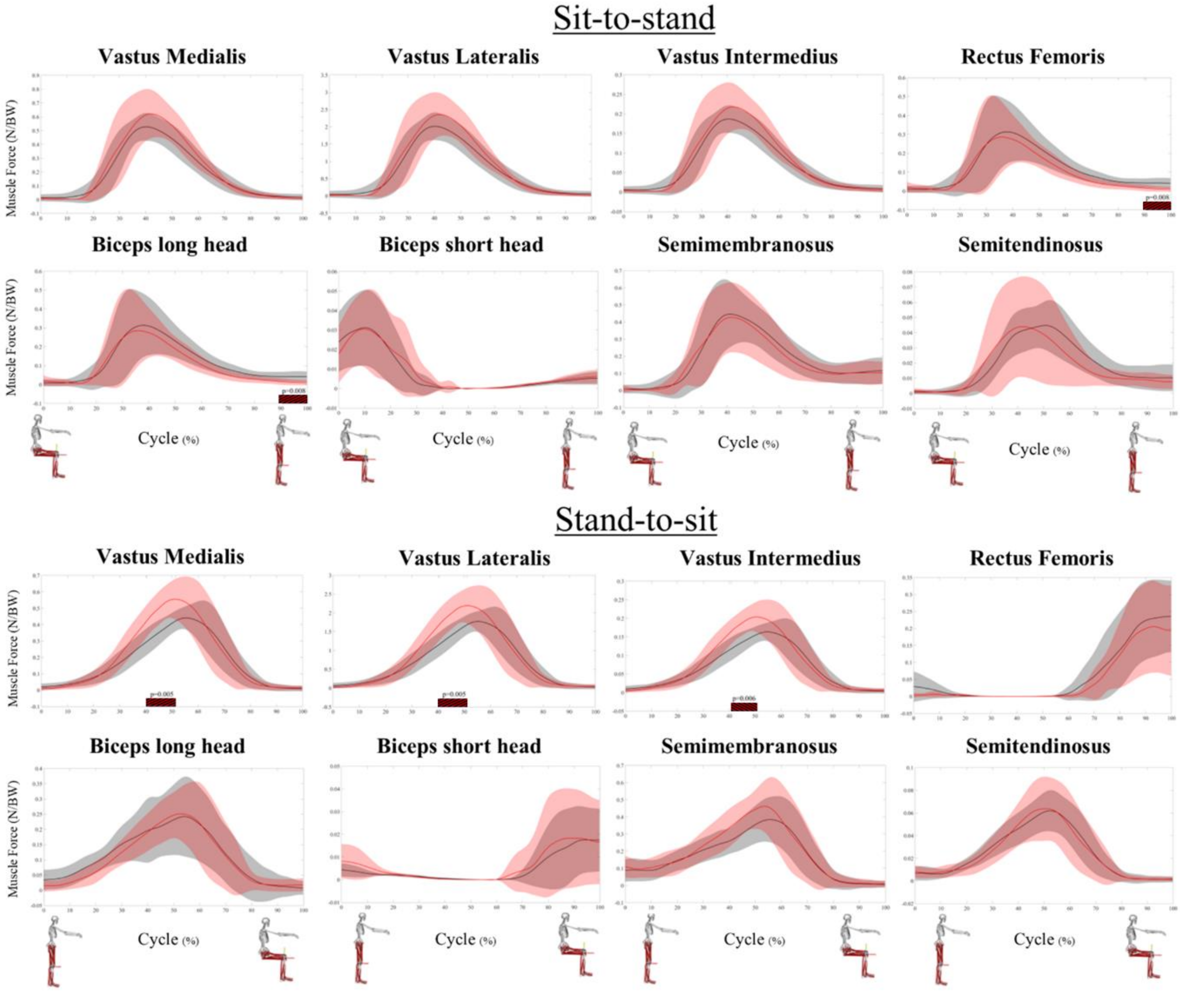

Figure 2. Between-group, statistical non-parametric mapping comparison of time-varying muscle forces.

The black line (mean) and shaded area (standard deviation) represent the OA group and the red line and shaded area represent the CTRL group, the rectangle indicates the phase of the movement where the differences occurred. N/BW: Newton/body weight.

The knee contact force comparisons between OA and CTRL groups are presented in table 4. For the sit-to-stand task, the peak force in the medial compartment was lower in the OA group than in the CTRL. The affected/non-affected ratio showed a reduced ratio for the OA group (0.78 N/BW), indicating a reduced force on the affected side. For the control group, the ratio was close to 1, indicating little difference between the sides. For the same task, the total vertical force showed a smaller side-to-side ratio for the OA group, but to a lesser extent (0.84 N/BW) compared to the medial compartment result. For the lateral compartment, no differences were identified between the groups. No differences were identified for the time series comparison (Figure 3).

The stand-to-sit task showed differences only for the medial compartment and total. The medial compartment peak force was lower in the OA group compared to the CTRL group. The involved/noninvolved side ratio was lower for the OA group. The ratio indicates 40% lower force on the involved side, lower than the difference for the sit-to-stand task. For the total vertical force, the peak was 0.65 N/BW lower in the OA group. Also, the involved/noninvolved ratio was smaller in the OA group. The time series comparisons are presented in figure 3, with no differences between the groups.

Table 4. Between-group, discrete comparison of medial, lateral, and total knee contact forces.

		OA Med (25; 75%)	**CTRL** Med (25; 75%)	*P* (*r*)
		Sit-to-stand		
Medial compartment	Peak (N/BW)	**1.22 (0.94; 1.46)**	**1.50 (1.24; 1.71)**	**.036 (.436)**
	Integral (AU)	64.1 (52.7; 73.7)	73.9 (60.7; 82.8)	.140 (.307)
	Inv/noninv ratio (N/BW)	**0.78 (0.70; 0.90)**	**0.95 (0.84; 1.23)**	**.016 (.500)**
Lateral compartment	Peak (N/BW)	2.56 (2.43; 2.74)	2.53 (2.38; 3.02)	.667 (.089)
	Integral (AU)	86.7 (75.4; 102.3)	89.0 (76.62; 97.2)	.854 (.038)
	Inv/noninv ratio (N/BW)	0.90 (0.83; 0.98)	0.98 (0.03;1.05)	.667 (.089)
Vertical total	Peak (N/BW)	3.71 (3.63; 4.00)	4.10 (3.55; 4.80)	.157 (.295)
	Integral (AU)	154.1 (137.0; 160.3)	155.4 (140.4; 176.5)	.498 (.141)
	Inv/noninv ratio (N/BW)	**0.84 (0.81; 0.98)**	**1.01 (0.96; 1.08)**	**.010 (.539)**
Medio/lateral ratio	Peak (N/BW)	1.98 (1.76; 2.76)	1.75 (1.64; 2.07)	.157 (.295)
		Stand-to-sit		
Medial compartment	Peak (N/BW)	**0.94 (0.62; 1.09)**	**1.17 (0.86; 1.37)**	**.097 (.346)**
	Integral (AU)	Integral (AU)	54.3 (42.4; 65.2)	.424 (.166)
	Inv/noninv ratio (N/BW)	**0.60 (0.35; 0.74)**	**0.90 (0.56; 0.94)**	**.016 (.500)**
Lateral compartment	Peak (N/BW)	1.89 (1.90; 2.15)	2.05 (1.80; 2.53)	.065 (.384)
	Integral (AU)	67.6 (61.8; 77.4)	70.5 (61.5; 88.2)	.580 (.115)
	Inv/noninv ratio (N/BW)	0.76 (0.66; 0.83)	0.85 (0.74; 1.00)	.085 (.359)
Vertical total	Peak (N/BW)	**2.76 (2.54; 3.27)**	**3.41 (2.65; 3.76)**	**.036 (.436)**
	Integral (AU)	125.5 (101.5; 150.2)	124.8 (117.6; 141.1)	.424 (.166)
	Inv/noninv ratio (N/BW)	**0.75 (0.52; 0.80)**	**0.94 (0.67; 0.99)**	**.023 (.474)**
Medio/lateral ratio	Peak (N/BW)	1.50 (1.36; 1.85)	1.53 (1.45; 1.50)	.951 (.012)

N/BW: Newton/body weight; AU: arbitrary units; Med: median; inv: involved; noninv: noninvolved (contralateral for OA group; non dominant for CTRL group).

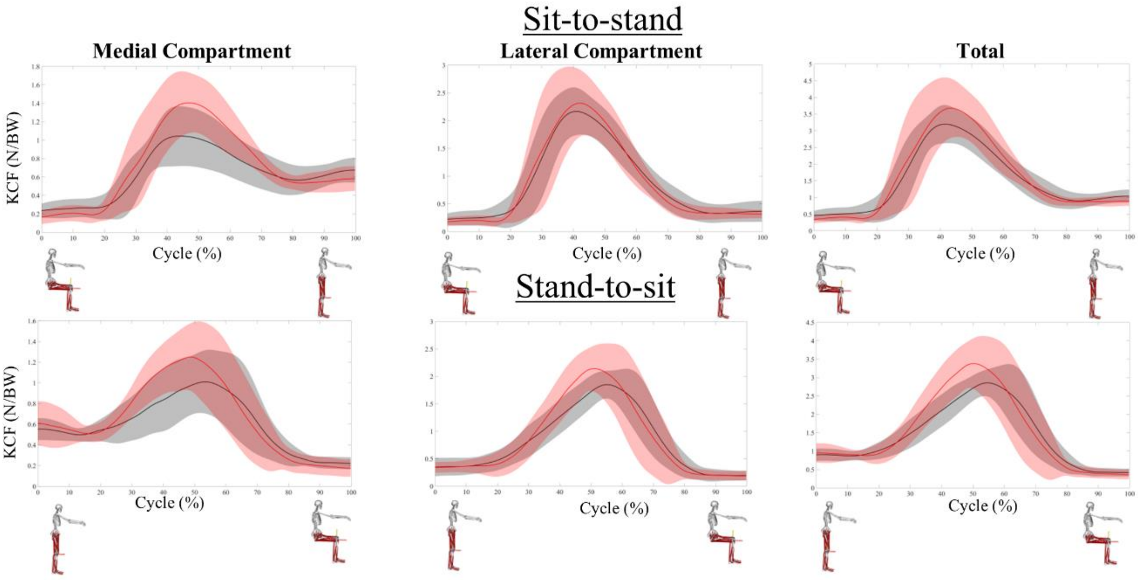

Figure 3. Between-group, statistical non-parametric mapping comparison of time-varying medial, lateral and total knee contact forces.
The black line is reference to the OA group and the red is for CTRL group. N/BW: Newton/body weight.

The comparison between the sides is presented in table 5 and figure 4. For both tasks, the CTRL group showed no differences between the dominant and non- sides. For the OA group, the total vertical force was 14% and 16% lower on the affected sides for sit-to-stand and stand-to-sit tasks, respectively. This difference occurred after and during the time of peak forces in the sit-to-stand time series comparison. In contrast, the difference was identified before and during the time of peak forces for the stand-to-sit task. The medial compartment differences between the sides were greater during the stand-to-sit task (28% lower for the affected side) than sit-to-stand (21%). In the time series comparison, the differences occurred most during the cycle for the stand-to-sit task compared to sit-to-stand. The lateral compartment force showed differences in the time-series comparison only for the sit-to-stand task. The lateral compartment peak force was lower on the affected side for both tasks, with a greater difference for the stand-to-sit (11% lower on the affected side) compared to sit-to-stand (6%).

Table 5. Side-to-side, discrete comparison for peak medial, lateral, and total knee contact forces in the OA group (N/BW).

	Involved Med (25; 75%)	**Noninvolved** Med (25; 75%)	***P (r)***	**Involved** Med (25; 75%)	**Noninvolved** Med (25; 75%)	***P (r)***
	AO group			**CTRL group**		
			Sit-to-stand			
Medial	**1.22 (0.94; 1.46)**	**1.54 (1.27; 1.88)**	**.015 (.702)**	1.50 (1.24; 1.71)	1.47 (1.41; 1.54)	1.00 (0.0)
Lateral	**2.56 (2.43; 2.74)**	**2.73 (2.56; 3.22)**	**.019 (.679)**	2.53 (2.38; 3.02)	2.66 (2.33; 3.03)	.477 (.214)
Total	**3.71 (3.63; 4.00)**	**4.30 (3.97; 4.41)**	**.006 (.792)**	4.10 (3.55; 4.80)	4.11 (3.82; 4.65)	.722 (.217)
			Stand-to-sit			
Medial	**1.09 (0.94; 1.44)**	**1.52 (1.37; 1.80)**	**.015 (.702)**	1.37 (1.17; 1.68)	1.48 (1.32; 1.54)	.424 (.241)
Lateral	**2.15 (1.89; 2.35)**	**2.42 (2.13; 2.75)**	**.023 (.656)**	2.53 (2.05; 3.09)	2.49 (2.02; 2.95)	.424 (.241)
Total	**3.27 (2.76; 3.46)**	**3.87 (3.60; 4.42)**	**.006 (.792)**	3.76 (3.41; 4.59)	3.94 (3.30; 4.43)	.929 (.026)

Medial: medial compartment; Lateral: lateral compartment; med: median.

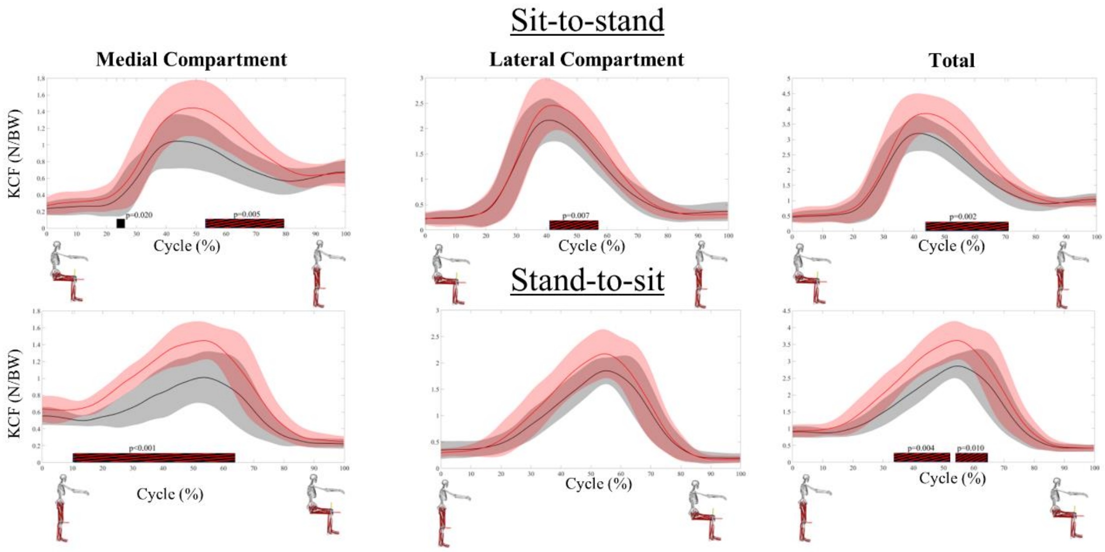

Figure 4. Side-to-side, statistical non-parametric mapping comparison of time-varying medial, lateral and total knee contact forces in the OA.

The black line is reference to the OA group and the red for the CTRL group, the rectangle indicates the cycle phase where the differences occurred. N/BW: Newton/body weight.

Discussion

This study aimed to compare the differences between knee contact and muscle forces during the sit-to-stand and stand-to-sit tasks in severe knee OA patients compared to controls. The first hypothesis, that the OA groups would show a reduction in KCF on the affected knee was confirmed, as the total vertical and medial compartment forces were lower compared to the contralateral side only for the OA group. For the controls, there were no differences between the sides. Secondly, only the medial compartment showed differences between the groups, confirming the hypothesis that the medial compartment is more affected by knee OA than the lateral compartment. For the muscle forces, the hypothesis regarding the knee extensor muscles was only confirmed for the stand-to-sit task, where the OA group presented reduced forces for the vasti muscles.

Sitting down and standing up tasks require a large knee extension moment (Yoshioka *et al.*, 2007; Bobbert *et al.*, 2016). The results of this study identified a reduced peak knee extensor moment in the OA group for both tasks, with the knee moment peak being reduced by close to 50% in the OA group compared to controls. Other studies, including a systematic review with 322 knee OA patients, reported a lower knee extensor peak during these tasks (Turcot *et al.*, 2012; Jarvis *et al.*, 2013; Sonoo *et al.*, 2019). Although the hip moment was similar between the groups, knee OA patients may increase the hip moment to reduce the knee moments during the standing up task (Petrella *et al.*, 2019).

The muscle force peaks showed differences only for the vasti muscles, and only during the stand-to-sit task, with the vasti muscle forces being reduced in the OA group compared to the CTRL group. Our results concur with an electromyographic study with knee OA patients which showed reduced vastus lateral activation during sitting down (Bouchouras *et al.*, 2020). Reduced quadriceps and increased femoral biceps activation were identified during the sitting down task in knee OA patients (Fu *et al.*, 2021). The sitting down task, compared to standing up, requires more eccentric work for the knee extensors (Davidson *et al.*, 2013), and this difference could be important in improving treatment for these patients. Often, older adults require greater knee extensor capacity to perform sitting down and standing up tasks (Hortobágyi *et al.*, 2003), so a strength deficit in knee extensors in OA patients reduces their functional capacity to perform these tasks (Caruthers *et al.*, 2020).

Differences in tibiofemoral contact forces between the groups were observed only for the peaks, with significant differences found for the medial compartment and the total force. Among the two knee compartments, only the medial compartment showed differences, which is the region most affected in knee OA patients. The distribution of contact forces between the medial and lateral compartments did not differ significantly between the groups. The ratio found in this study is similar to that reported for healthy adults (Van Rossom *et al.*, 2018). The total KCF was lower in the OA group compared to controls only during the sitting down task, which supports the differences observed in muscle forces. These findings suggest that sitting down, and the eccentric muscle contraction it involves, is a more discriminant task for knee OA patients than the standing up task, as it puts greater demand on these patients.

Only the OA group observed differences in KCF between the sides, with reduced contact forces on the affected side. No significant differences were observed in the control group, where the ratio between the sides was close to 1 for the medial compartment and the total force. In the OA group, the ratio was reduced, indicating reduced forces on the affected side, with lower ratios during the stand-to-sit compared to the sit-to-stand task. The knee contact forces on the affected side showed differences during a large portion of the movement, and consistently during the time peak forces were experienced. It is common for the contralateral side to receive more load during these tasks (Turcot *et al.*, 2012; Duffell *et al.*, 2013). The increased contact forces on the non-affected side could be a risk factor for developing OA in that knee (Thorsen *et al.*, 2021; Hummer *et al.*, 2022).

Some limitations should be taken into consideration in this study. Although differences were identified, increasing the sample size could enhance the statistical power of the results. The model used in the study is generic and employs a simple static optimization technique. While static optimization is effective for predicting joint reaction forces (Knarr e Higginson, 2015), other methods, such as computed muscle control (CMC), may be more accurate for predicting muscle forces. However, the model used in this study presented an error of approximately 15%, overestimating the total vertical force for both tasks compared to *in vivo* data. This error is considered acceptable for this type of analysis (Pelegrinelli et al., 2023, Manuscript 1 thesis).

In conclusion, vertical total knee contact forces are more affected during the sitting down task. The lateral compartment forces were unchanged in either task, with no differences between the groups. The medial compartment is often the region most affected in knee OA patients, and reducing the medial load could be a strategy for alleviating painful movements. The OA group showed higher contact forces on the contralateral side, possibly a strategy to reduce forces on the affected knee. Additionally, the OA patients exhibited reduced knee extensor force, particularly in the vastus muscles during sitting down.

Conflict of interest statement

The authors declare no conflict of interests.

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4 CONSIDERAÇÕES FINAIS

A tese teve como objetivo geral identificar as diferenças nas forças de contato tibiofemoral em pacientes com OA de joelho durante as tarefas de marcha, sentar e levantar. Inicialmente, ao aplicar os modelos disponíveis na literatura para a análise das forças de contato tibiofemoral nos compartimentos medial e lateral, foi identificado uma grande variabilidade de resultados entre os artigos quanto a magnitude da força nas tarefas a serem analisadas. Somado a isto, o modelo escolhido incialmente para análise não havia sido testado quanto ao erro na estimação da força de contato comparado a dados medidos *in vivo*. Diante desta lacuna e da publicação de um modelo com ajustes na geometria e propriedades de modelos MSK de membros inferiores, no estudo 1, um modelo adaptado foi testado quanto à capacidade de estimar as forças de contato em uma amostra com prótese instrumentada para as tarefas de sentar, levantar e marcha.

No primeiro estudo, foi identificado que as forças de cisalhamento anteroposterior e mediolateral são estimadas com grandes erros em relação ao medido na prótese instrumentada. Diante disso, nós não recomendamos a análise destes resultados com os três modelos avaliados. Para as forças verticais tibiofemoral total e nos compartimentos medial e lateral durante a marcha os três modelos foram similares. No entanto, para as tarefas de sentar e levantar, o modelo adaptado proposto apresentou maior correlação e menores erros de magnitude, de forma que recomendamos o emprego deste modelo em atividades que envolvem maior amplitude de flexão de joelho e quadril. Até o presente momento, estes resultados indicam ser o modelo genérico com menores erros para a análises destas atividades, mas é importante ressaltar e considerar a magnitude dos erros identificados no presente estudo para futuras análises. Os resultados do estudo 1 devem ser considerados em novas pesquisas com modelos MSK para análise das forças no joelho, de tal forma que a publicação do mesmo deve ter impacto em futuros trabalhos na área ao trazer resultados mais promissores que os modelos disponíveis no momento em que essa tese foi redigida.

A adaptação e avaliação do MSK permitiu que os estudos seguintes, aplicados sob o ponto de vista clínico, pudessem ser conduzidos. O estudo 2 foi voltado ao processo de caracterização das forças de contato tibiofemoral e a distribuição entre os compartimentos medial e lateral entre pacientes com OA grave de joelho e controles saudáveis. Diante da necessidade de compreender melhor quais variáveis mais contribuem ou correlacionam com as forças de contato total e no compartimento medial, o mais afetado na OA de joelho, um modelo preditivo também foi extensamente explorado e aplicado. Com o modelo, foi possível identificar variáveis preditoras para os picos de força no joelho e compreender melhor esta relação. Além disso, foi uma primeira contribuição de como as forças de contato podem ser preditas com variáveis relativamente mais simples de serem calculadas. Os resultados mostraram que o momento extensor do joelho e o abdutor de quadril foram os mais relevantes para predizer o primeiro pico da força de contato tibiofemoral total e para os dois picos no compartimento medial, respectivamente. Na comparação entre os grupos o vale entre os picos foi maior no grupo OA, indicando uma maior carga sustentada durante a fase de apoio da marcha. O primeiro pico da força medial foi menor no grupo OA, somado ao resultado das demais variáveis indica uma estratégia de minimizar a compressão medial reduzindo a dor durante a execução da marcha.

Entendendo a necessidade de explorar tarefas adicionais que sejam desafiadoras a pacientes com OA, o estudo 3 é um dos primeiros a comparar as forças de contato nos compartimentos, o desempenho muscular e as assimetrias entre os lados durante as tarefas de sentar e levantar. Os resultados indicaram que a força vertical total tibiofemoral foi mais afetada na tarefa de sentar em relação ao levantar. Assim como no estudo da marcha, a magnitude da força no compartimento medial foi menor no grupo OA em ambas as tarefas comparado aos controles. A natureza bilateral da tarefa permite que assimetrias entre os lados sejam identificadas, no grupo controle não foram identificadas diferenças nas forças de contato na comparação entre os lados. Entretanto, no grupo OA, todas as forças foram reduzidas no lado afetado comparado com o contralateral, principalmente em relação a força total e no compartimento medial. Também, a ativação dos vastos foi reduzida no grupo OA durante a tarefa de sentar, indicando uma limitação na contração excêntrica nos pacientes com OA de joelho avançada.

Os dois últimos estudos apontam algumas considerações para o tratamento destes pacientes, como o retreinamento da marcha estimulando a medialização do membro inferior para a linha média a fim de reduzir a compressão no compartimento medial. Também, a reduzida força muscular dos extensores de joelho em atividades em que a contração é principalmente excêntrica fornece uma indicação para o treinamento deste grupo muscular utilizando o controle excêntrico. Embora nosso estudo tenha analisado apenas pacientes em estágio final da OA de joelho, as diferenças identificadas são também relevantes para a reabilitação após a artroplastia, quando indicada, considerando que recuperação do padrão de marcha será limitado em acordo com as modificações encontradas no estágio prévio a artroplastia.

Algumas análises propostas para a tese foram limitadas por diversos fatores, mas principalmente pela limitação da amostra e do prazo de finalização da tese que foram afetados pela pandemia nos últimos anos. Durante o desenvolvimento da tese novas questões de pesquisa foram levantadas e o objetivo geral da tese foi alcançado. No entanto, os resultados e análises limitadas indicam que futuras pesquisas devem realizar as mesmas análises envolvendo pacientes em diferentes estágios da OA de joelho para compreender melhor a progressão da doença e como as atividades funcionais são afetadas. Também, um maior tamanho amostral deve aumentar o efeito dos resultados e melhorar a capacidade preditiva do modelo de regressão proposto. Ainda, são encontrados na literatura diversos modelos de aprendizagem de máquina para predição, de forma que mais modelos devem ser testados a fim de melhorar a capacidade preditiva. Melhores modelos preditivos, que utilizem variáveis mecânicas que requeiram pouca instrumentação, são promissores para viabilizar importantes estimativas de força de contato articulares em ambientes clínicos onde laboratórios de biomecânica são raramente disponíveis.

Por fim, concluímos que o modelo musculoesquelético identificado como o que melhor estimava as forças de contato foi capaz de identificar diferenças entre indivíduos saudáveis e com OA durante as tarefas de marcha, sentar e levantar. Também, os resultados indicaram um grande potencial para predizer os picos de força de contato com modelos de aprendizagem de máquina. Considerando os principais achados dos estudos aplicados da presente tese, estratégias de redução da carga no joelho afetado são empregadas para minimizar a dor, e o compartimento medial foi o mais afetado.

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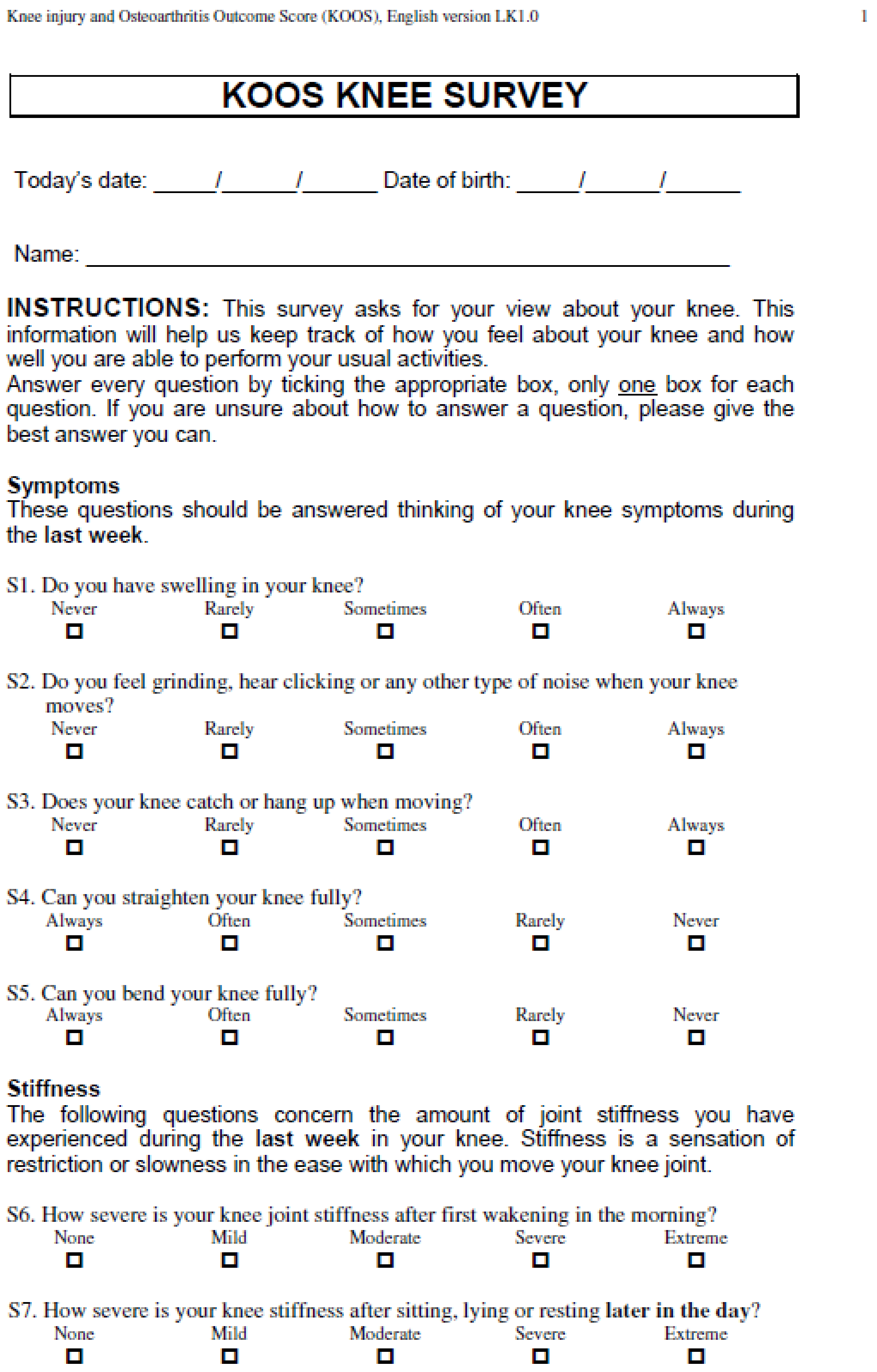
ANEXOS

Anexo 1. KOOS Questionário (versão aplicada).



Knee injury and Osteoarthritis Outcome Score (KOOS), English version LK1.0 1

KOOS KNEE SURVEY

Today's date: _____/______/______ Date of birth: _____/______/______

Name: ____

INSTRUCTIONS: This survey asks for your view about your knee. This information will help us keep track of how you feel about your knee and how well you are able to perform your usual activities.
Answer every question by ticking the appropriate box, only one box for each question. If you are unsure about how to answer a question, please give the best answer you can.

Symptoms
These questions should be answered thinking of your knee symptoms during the **last week**.

S1. Do you have swelling in your knee?

Never	Rarely	Sometimes	Often	Always
☐	☐	☐	☐	☐

S2. Do you feel grinding, hear clicking or any other type of noise when your knee moves?

Never	Rarely	Sometimes	Often	Always
☐	☐	☐	☐	☐

S3. Does your knee catch or hang up when moving?

Never	Rarely	Sometimes	Often	Always
☐	☐	☐	☐	☐

S4. Can you straighten your knee fully?

Always	Often	Sometimes	Rarely	Never
☐	☐	☐	☐	☐

S5. Can you bend your knee fully?

Always	Often	Sometimes	Rarely	Never
☐	☐	☐	☐	☐

Stiffness
The following questions concern the amount of joint stiffness you have experienced during the **last week** in your knee. Stiffness is a sensation of restriction or slowness in the ease with which you move your knee joint.

S6. How severe is your knee joint stiffness after first wakening in the morning?

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

S7. How severe is your knee stiffness after sitting, lying or resting **later in the day**?

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Pain

P1. How often do you experience knee pain?

Never	Monthly	Weekly	Daily	Always
☐	☐	☐	☐	☐

What amount of knee pain have you experienced the **last week** during the following activities?

P2. Twisting/pivoting on your knee

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P3. Straightening knee fully

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P4. Bending knee fully

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P5. Walking on flat surface

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P6. Going up or down stairs

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P7. At night while in bed

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P8. Sitting or lying

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P9. Standing upright

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Function, daily living

The following questions concern your physical function. By this we mean your ability to move around and to look after yourself. For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A1. Descending stairs

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A2. Ascending stairs

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A3. Rising from sitting

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A4. Standing

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A5. Bending to floor/pick up an object

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A6. Walking on flat surface

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A7. Getting in/out of car

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A8. Going shopping

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A9. Putting on socks/stockings

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A10. Rising from bed

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A11. Taking off socks/stockings

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A12. Lying in bed (turning over, maintaining knee position)

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A13. Getting in/out of bath

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A14. Sitting

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A15. Getting on/off toilet

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A16. Heavy domestic duties (moving heavy boxes, scrubbing floors, etc)

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A17. Light domestic duties (cooking, dusting, etc)

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Function, sports and recreational activities

The following questions concern your physical function when being active on a higher level. The questions should be answered thinking of what degree of difficulty you have experienced during the **last week** due to your knee.

SP1. Squatting

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP2. Running

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP3. Jumping

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP4. Twisting/pivoting on your injured knee

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP5. Kneeling

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Quality of Life

Q1. How often are you aware of your knee problem?

Never	Monthly	Weekly	Daily	Constantly
☐	☐	☐	☐	☐

Q2. Have you modified your life style to avoid potentially damaging activities to your knee?

Not at all	Mildly	Moderately	Severely	Totally
☐	☐	☐	☐	☐

Q3. How much are you troubled with lack of confidence in your knee?

Not at all	Mildly	Moderately	Severely	Extremely
☐	☐	☐	☐	☐

Q4. In general, how much difficulty do you have with your knee?

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Thank you very much for completing all the questions in this questionnaire.

Anexo 2. Modelos de marcadores utilizados no estudo 2 e 3 (UOMAM Model).