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Relationships between *in vivo* dynamic knee joint loading, static alignment and tibial subchondral bone microarchitecture in end-stage knee osteoarthritis

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SUMMARY

Objective: To study, in end-stage knee osteoarthritis (OA) patients, relationships between indices of *in vivo* dynamic knee joint loads obtained pre-operatively using gait analysis, static knee alignment, and the subchondral trabecular bone (STB) microarchitecture of their excised tibial plateau quantified with 3D micro-CT.

Design: Twenty-five knee OA patients scheduled for total knee arthroplasty underwent pre-operative gait analysis. Mechanical axis deviation (MAD) was determined radiographically. Following surgery, excised tibial plateaus were micro-CT-scanned and STB microarchitecture analysed in four subregions (anteromedial, posteromedial, anterolateral, posterolateral). Regional differences in STB microarchitecture and relationships between joint loading and microarchitecture were examined.

Results: STB microarchitecture differed among subregions ($P < 0.001$), anteromedially exhibiting highest bone volume fraction (BV/TV) and lowest structure model index (SMI). Anteromedial BV/TV and SMI correlated strongest with the peak external rotation moment (ERM; $r = -0.74$, $r = 0.67$, $P < 0.01$), despite ERM being the lowest (by factor of 10) of the moments considered, with majority of ERM measures below accuracy thresholds; medial-to-lateral BV/TV ratios correlated with ERM, MAD, knee adduction moment (KAM) and internal rotation moment (|r|-range: 0.54–0.74). When controlling for walking speed, KAM and MAD, the ERM explained additional 11–30% of the variations in anteromedial BV/TV and medial-to-lateral BV/TV ratio ($R^2 = 0.59$, $R^2 = 0.69$, $P < 0.01$).

Conclusions: This preliminary study suggests significant associations between tibial plateau STB microarchitecture and knee joint loading indices in end-stage knee OA patients. Particularly, anteromedial BV/TV correlates strongest with ERM, whereas medial-to-lateral BV/TV ratio correlates strongest with indicators of medial-to-lateral joint loading (MAD, KAM) and rotational moments. However, associations with ERM should be interpreted with caution.

Introduction

Knee osteoarthritis (OA) is a debilitating disease affecting all tissues within the joint, including bone. The subchondral bone is a mechanical shock absorber, protecting the overlying articular cartilage from excessive joint loads[1]. The compromised integrity of subchondral bone plays an important role in the onset and progression of the disease[1,2]. In prospective studies, abnormal joint biomechanics that is common with knee OA[3,4], has been associated

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with rate of radiographic disease progression[5,6], while in cross-sectional studies, it has been linked with variations to joint structures (e.g., presence of cartilage defects[7], bone marrow lesions[8], variations in subchondral bone area[7,9] and cartilage thickness[10]).

Abnormal *in vivo* joint loads, indicated by frontal plane loading indices, such as knee adduction moment (KAM) measured during gait and static knee alignment from radiographs, have been associated with local variations in proximal tibia bone mineral density (BMD) and mineral content (BMC), measured by dual X-ray absorptiometry (DXA)[11–13]. DXA, however, is a two-dimensional technique which has limited spatial resolution and cannot differentiate between cortical and trabecular bone, or among different subregions within the same condyle. Furthermore, it cannot quantify bone microarchitecture, which has been shown to vary within the OA proximal tibia[14–16].

To understand the degeneration of subchondral bone in OA, it is necessary to study its microarchitecture. However, previous studies examining subchondral bone microarchitecture in humans were restricted to thin histological slices or excised bone cores[14,15]. Nowadays, X-ray micro-computed tomography (micro-CT) allows three-dimensional (3D) structural characterisation of entire bone segments including the tibial plateau, non-destructively and at high resolution[16–18]. Moreover, to the best of our knowledge, those studies exploring the bone microarchitecture, did not examine gait or *in vivo* joint biomechanics data from the same patients, to investigate possible relationships between these measures. Thus, the associations between knee joint biomechanics (including the full 3D knee moments, which differ from normal in OA[3,4]) and tibial subchondral trabecular bone (STB) microarchitecture in OA, in the same patient, remain to be investigated. Through a better understanding of how joint loading is related to local variations in subchondral bone micro-architecture in knee OA, it may be possible to better describe the role of both factors in the disease.

This study explores, in end-stage OA patients undergoing total knee arthroplasty (TKA), relationships between indices of *in vivo* dynamic knee joint loads obtained pre-operatively using 3D gait analysis (full 3D knee moments, tibiofemoral joint reaction forces), static knee alignment (mechanical axis deviation (MAD), medial proximal tibial angle) and regional proximal tibia subchondral bone microarchitecture of their excised knees quantified with 3D micro-CT. The objective was to determine which biomechanical factors described the greatest variation in subregional STB microarchitecture and distribution of the bone across the tibia plateau. We hypothesised that the frontal plane loading indices (static alignment, peak adduction moments and impulse), indicators of medial tibial compartment loading[19] and medial-to-lateral distribution of load[20], would be factors most strongly associated with the medial condyle STB microarchitecture and medial-to-lateral distribution of bone in the tibial plateau.

Methods

Participants

Twenty-five ($n = 25$) adult patients with end-stage knee OA, scheduled for TKA, were recruited from the orthopaedics departments at the Royal Adelaide Hospital, Repatriation General Hospital and Burnside War Memorial Hospital in Adelaide, Australia (Table I). In all patients indication for surgery was painful and symptomatic knee OA, and unsatisfactory response to non-invasive treatments. This criteria established our operational definition of end-stage knee OA. The radiographic (Kellgren–Lawrence) grade of the examined joints ranged from two (mild) to four (severe; Table II). Patients were excluded from this study if: they were unable to walk unaided for 10 m; had a history of inflammatory arthritis; had neurological disorders that would affect walking; had severe cardiovascular or pulmonary disease; had isolated patellofemoral knee OA; or were unable to understand English. This study received ethics approval from the Southern Adelaide Clinical and Royal Adelaide Hospital Human Research Ethics Committees. All patients provided written informed consent prior to their involvement.

Table I
Summary of physical characteristics and gait parameters of total knee arthroplasty patients ($n = 25$)

Age (years)	68 ± 7
Gender (male:females)	11:14
Affected limb (right:left)	13:12
Height (m)	1.66 ± 0.09
Body mass (kg)	91.6 ± 18.0
BMI (kg/m^2)	32.9 ± 4.4
WOMAC (total)	56 ± 13
Pain	12 ± 2
Stiffness	6 ± 1
Function	39 ± 12
Walking speed (m/s)	0.70 ± 0.25
Knee moments (Nm/kg)	
Knee flexion moment, KFM	0.35 ± 0.23
Knee extension moment, KEM	−0.11 ± 0.29
First peak adduction moment, KAM_1	−0.40 ± 0.23
Second peak adduction moment, KAM_2	−0.39 ± 0.22
Knee adduction moment impulse	27.0 ± 14.2
External rotation moment, ERM	0.022 ± 0.023
Internal rotation moment, IRM	−0.085 ± 0.079
Joint reaction force (BW)	3.02 ± 0.96
Static alignment	
Mechanical axis deviation (mm)	9.2 ± 34.8
Medial proximal tibial angle (°)	90.1 ± 2.7

Average ± standard deviation. BW, bodyweights.

Table II
Summary of knee radiographic features of all end-stage OA patients ($n = 25$)

Kellgren-Lawrence grade	Grade	Number of subjects	
	2	4	
	3	7	
	4	14	
OARSI atlas radiographic features	**Score**	**Number of subjects**	
		Medial condyle	Lateral Condyle
Osteophyte	0	2	3
	1	13	14
	2	6	8
	3	4	0
Joint space narrowing	0	3	14
	1	5	6
	2	6	3
	3	11	2
Bone sclerosis	Present	13	6
	Absent	12	19

OA: osteoarthritis; OARSI: Osteoarthritis Research Society International.
All 13 patients exhibiting medial condyle bone sclerosis had varus-aligned joints (MAD >15 mm), whereas for the six patients with lateral sclerosis, five were valgus-aligned (MAD <0 mm) and one neutrally-aligned (MAD 0–15 mm).[30]

Gait analysis

Patients underwent pre-operative gait analysis within 1 week prior to surgery. Three successful walking trials were collected with the patient walking, without footwear, at self-selected speed along a 10-m walkway. 3D kinematics and ground reaction force data were collected using 12 VICON MX-F20 cameras (Vicon Metrics, Oxford, UK) and four floor-embedded force platforms (2 × 9281B,

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