Received: 12 October 2023 | Accepted: 14 December 2023
DOI: 10.1002/ksa.12043

Knee Surgery, Sports Traumatology, Arthroscopy WILEY

The phenotypic diversity of anteromedial osteoarthritis before and after treatment with medial unicompartmental knee arthroplasty: A radiographic analysis of 1000 knees

Tarik Bayoumi[1,2] | **Gaby V. ten Noever de Brauw**[1,2] | **Lindsey V. Ruderman**[1] | **Jelle P. van der List**[2] | **Gino M. M. J. Kerkhoffs**[2,3] | **Andrew D. Pearle**[1] | **Hendrik A. Zuiderbaan**[4]

[1]Hospital for Special Surgery, Sports Medicine Institute, Weill Medical College of Cornell University, New York, New York, USA

[2]Department of Orthopaedic Surgery, Amsterdam UMC Location University of Amsterdam, Amsterdam, The Netherlands

[3]Amsterdam Movement Sciences, Sports, Amsterdam, The Netherlands

[4]Department of Orthopaedic Surgery, Medical Clinic Velsen, Velsen-Noord, The Netherlands

Correspondence
Tarik Bayoumi, Hospital for Special Surgery, Sports Medicine Institute, 535 East 70th St, New York, NY 10021, USA.
Email: tbayoumi.md@gmail.com

Funding information
None

Abstract

Purpose: This study aimed to assess phenotypic variation in the coronal plane of knees with anteromedial osteoarthritis using the functional knee phenotype classification, before and after treatment with medial unicompartmental knee arthroplasty (UKA).

Methods: The study comprised 1000 knees of 835 patients (45% females, 55% males, 90% Caucasian) who underwent medial UKA for anteromedial osteoarthritis. Pre and postoperative alignment was evaluated through the hip-knee-ankle angle (HKA), femoral mechanical angle (FMA), and tibial mechanical angle (TMA). Knees were classified according to the functional knee phenotype system which combines limb phenotype (HKA), and femoral and tibial knee phenotypes (FMA and TMA, respectively). Restoration of prearthritic coronal alignment following medial UKA was evaluated by phenotype.

Results: Preoperatively, 76 distinct and 25 relevant (prevalence ≥1%) functional knee phenotypes were identified, of which $VAR_{HKA}6°VAR_{FMA}3°NEU_{TMA}0°$ was the most common (9.4% of knees). The most prevalent limb phenotype, $VAR_{HKA}6°$, comprised 15 distinct knee phenotypes (FMA and TMA combinations). Postoperatively, 58 distinct and 17 relevant functional knee phenotypes were observed, of which $VAR_{HKA}3°NEU_{FMA}0°NEU_{TMA}0°$ had the highest prevalence at 18.3%. Knees with combined tibial and femoral deformities were associated with a lower probability of restoration of prearthritic coronal alignment following medial UKA, compared to knees without extra-articular deformity, or knees with an isolated tibial or femoral deformity.

Conclusion: Phenotype analysis using the functional knee phenotype system demonstrated a wide diversity of coronal alignment phenotypes among knees with anteromedial osteoarthritis in a predominantly Caucasian population. Following medial UKA, a reduction from 25 preoperative to 17 postoperative relevant phenotypes was observed. Consideration of

Abbreviations: FMA, femoral mechanical angle; HKA, hip-knee-ankle angle; MCL, medial collateral ligament; TMA, tibial mechanical angle; UKA, unicompartmental knee arthroplasty.

phenotypic variation can be of importance when aiming to restore prearthritic coronal alignment during medial UKA.

Level of Evidence: Level III, retrospective cohort study.

KEYWORDS

coronal alignment, knee phenotypes, prearthritic alignment, robotic-assisted surgery, unicompartmental knee arthroplasty

INTRODUCTION

Medial unicompartmental knee arthroplasty (UKA) is an effective surgical treatment for isolated anteromedial osteoarthritis (OA) of the knee [1]. However, the optimal alignment targets for UKA remain undefined, and there continues to be uncertainty about patient selection criteria [2–4]. In order to optimise alignment strategies and improve patient selection, a better understanding of the phenotypic variability of medial OA-affected knees would be of interest.

Recent studies have observed a broad variation in coronal alignment and joint line orientation in healthy and osteoarthritic knees [5–8]. These findings have underlined the shortcomings of the traditional classification of neutral, varus or valgus alignment, which disregards the phenotypes of femoral and tibial alignment that can exist within these three categories. Several novel classification systems, including the functional knee phenotype classification [7], have been put forth to comprehensively describe the relation between the mechanical axis (i.e., limb phenotype) and femoral and tibial joint line orientation (i.e., knee phenotype) of the individual knee [7, 9, 10]. However, most of these studies included both lateral and medial compartment OA-affected knees, or healthy knees, and focused on guidelines and implications for total knee arthroplasty [7, 9–12].

Although knees affected by medial compartment OA typically exhibit an anteromedial wear pattern and a varus mechanical axis, the specific coronal plane phenotypes within this group and their change during medial UKA remain largely undefined. Furthermore, it is currently unknown whether the type of phenotype affects the ability to restore prearthritic coronal alignment during medial UKA, which has been shown to have clinical implications [13, 14].

The objective of this study was to describe the variability in coronal plane phenotypes of knees with isolated anteromedial OA, before and after treatment with medial UKA, using the functional knee phenotype classification [7]. Based on the current literature [7, 8, 12], and the concept of an individualised alignment strategy for medial UKA [15], we hypothesised a large pre and postoperative diversity of coronal plane phenotypes.

METHODS

Study design

A single surgeon's arthroplasty registry (ADP) was retrospectively reviewed. A total of 1000 consecutive knees of 835 patients, who underwent robotic-arm assisted medial UKA between January 2012 and July 2022 for anteromedial OA, were randomly selected.

Patients were eligible for study inclusion if they had advanced anteromedial OA (Kellgren-Lawrence [KL] grade 3-4 on anteroposterior [AP] weight-bearing views) [16], an unaffected and asymptomatic lateral compartment (KL grade ≤2), underwent robotic-arm assisted primary medial UKA, and had complete radiographic records (pre and postoperative long-leg radiographs). Patients with a history of prior joint arthroplasty, or femoral or tibial fractures on the operative side were excluded from the study. Characteristics of the included patients are presented in Table 1.

TABLE 1 Demographics ($n = 1000$).

Variable	Mean ± SD, or *n* (%)
Age (years)	63.4 ± 9.2
Sex (female)	451 (45.1)
Race	
Caucasian	899 (89.9)
Black or African American	27 (2.7)
Asian	16 (1.6)
Other	26 (2.6)
Unknown	32 (3.2)
Laterality OA (left)	508 (50.8)
Bilateral knee OA	330 (33.0)
KL grade medial compartment	
KL grade 3	388 (38.8)
KL grade 4	612 (61.2)

Note: Demographics are presented as mean ± standard deviation (SD), or in numbers with the frequency in parentheses.

Abbreviations: KL, Kellgren-Lawrence grade; OA, osteoarthritis.

The surgical indication for medial UKA was symptomatic isolated anteromedial OA, with a varus deformity correctable to <10°, and fixed flexion deformity of <10°. Patients with significant clinical or radiographic signs of lateral compartment OA, degeneration of the lateral patellar facet, anterior cruciate ligament deficiency with clinical instability, previous medial collateral ligament (MCL) surgery, or signs of inflammatory arthritis were not deemed candidates for medial UKA.

Surgical technique

A cemented fixed-bearing medial only implant (Restoris MCK System, Mako Surgical Corp. [Stryker]) was used in all cases. A robotic-arm assisted system (Mako Surgical Corp. [Stryker]) was used for implant planning and osseous resection. The detailed surgical technique has previously been described [17]. The alignment goal was to recreate prearthritic coronal alignment (i.e., mechanical axis) by restoration of MCL tension throughout the range of motion, aiming for a 1–2 mm medial gap under valgus stress, with the implants and polyethylene insert in place. This individualised alignment technique was restricted by neutral alignment, meaning that a neutral mechanical axis was pursued in knees with estimated native valgus alignment, based on MCL tension. Given the retrospective design of this study, phenotypes were not considered during the surgery.

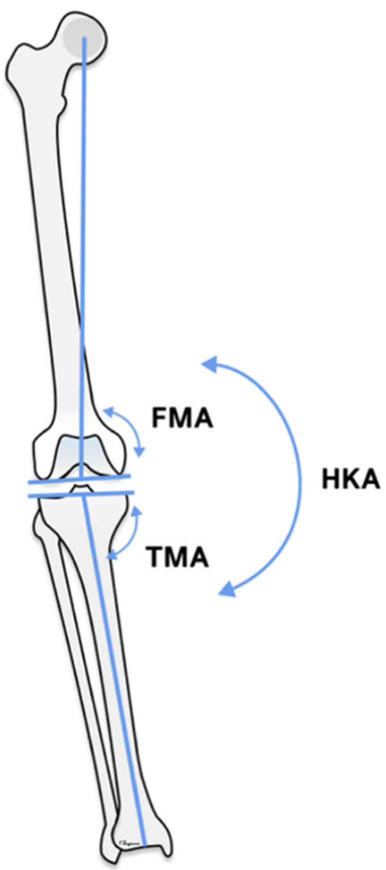

FIGURE 1 Schematic representation of measurement of the hip-knee-ankle angle (HKA), femoral mechanical angle (FMA), and tibial mechanical angle (TMA).

TABLE 2 Functional knee phenotype classification.

Parameter	Direction	Type	Range
HKA	VAR_{HKA}	$VAR_{HKA}18°$	16.5 to 19.5°
Limb phenotype		$VAR_{HKA}15°$	13.5 to 16.5°
		$VAR_{HKA}12°$	10.5 to 13.5°
		$VAR_{HKA}9°$	7.5 to 10.5°
		$VAR_{HKA}6°$	4.5 to 7.5°
		$VAR_{HKA}3°$	1.5 to 4.5°
	NEU_{HKA}	$NEU_{HKA}0°$	−1.5 to 1.5°
	VAL_{HKA}	$VAL_{HKA}3°$	−1.5 to −4.5°
FMA	VAR_{FMA}	$VAR_{FMA}12°$	79.5 to 82.5°
Femoral phenotype		$VAR_{FMA}9°$	82.5 to 85.5°
		$VAR_{FMA}6°$	85.5 to 88.5°
		$VAR_{FMA}3°$	88.5 to 91.5°
	NEU_{FMA}	$NEU_{FMA}0°$	91.5 to 94.5°
	VAL_{FMA}	$VAL_{FMA}3°$	94.5 to 97.5°
		$VAL_{FMA}6°$	97.5 to 100.5°
TMA	VAR_{TMA}	$VAR_{TMA}9°$	76.5 to 79.5°
Tibial phenotype		$VAR_{TMA}6°$	79.5 to 82.5°
		$VAR_{TMA}3°$	82.5 to 85.5°
	NEU_{TMA}	$NEU_{TMA}0°$	85.5 to 88.5°
	VAL_{TMA}	$VAL_{TMA}3°$	88.5 to 91.5°
	VAL_{TMA}	$VAL_{TMA}6°$	91.5 to 94.5°

Note: The functional knee phenotype classification [7] consists of a combination of three parameters, including the hip-knee-ankle angle (HKA), the femoral mechanical angle (FMA), and the tibial mechanical angle (TMA). The definition and corresponding range in degrees is given for each parameter.
Abbreviations: NEU, neutral; VAL, valgus; VAR, varus.

Radiographic evaluation

Routine weight-bearing long-leg AP radiographs were used for assessment of coronal alignment. Radiographs were obtained preoperatively and 6 weeks postoperatively. According to a standardised protocol, patients were instructed to stand with their feet together as close as possible while having their knees in full extension, their patellae aligned with the X-ray beam, and their bodyweight evenly distributed over both limbs.

The hip-knee-ankle angle (HKA) was defined as the angle between the mechanical axes of the femur and tibia (Figure 1). The lateral femoral angle (LDFA) was measured as the lateral angle between the mechanical femoral axis and joint line of the distal femur. The femoral mechanical angle (FMA; Figure 1) was derived from the LDFA (FMA = 180°-mLDFA). The tibial mechanical angle (TMA) was defined as the medial angle of the mechanical tibial axis and proximal tibial joint line (Figure 1). Measurements were taken by one observer (GVB) and independently repeated by a second observer (LVR) on a random sample (n = 100). Angles were measured to the tenth of a degree. Inter-observer reliability was analysed through interclass correlation coefficients (ICC), using a two-way mixed-model with absolute agreement. ICC among observers was 0.97 (95% confidence interval [CI] 0.96–0.98) for HKA, 0.89 (95% CI, 0.82–0.93) for FMA, and 0.90 (95% CI, 0.85–0.93) for TMA.

Functional knee phenotype classification

Knees were classified according to the functional knee phenotype system, introduced by Hirschmann et al. [7]. The system integrates three coronal alignment parameters, including limb phenotype (HKA) and femoral and tibial knee phenotype (FMA and TMA, respectively) into a "functional knee phenotype." Each phenotype covers a range of ±1.5° from the baseline value for that specific parameter, derived from previously reported means of healthy individuals (HKA: 0°; FMA: 93°; TMA: 87°) [7]. The classification first describes the direction of alignment (i.e., neutral, varus, or valgus), with the respective parameter subsequently indicated in subscript (i.e., HKA, FMA, TMA). The mean deviation from the phenotype-specific baseline value is indicated in increments of 3° (e.g., $VAR_{HKA}3°$, $VAR_{HKA}6°$ etc.). For example, the functional knee phenotype of a patient with a neutral HKA, neutral FMA, and neutral TMA would be $NEU_{HKA}0°NEU_{FMA}0°NEU_{TMA}0°$. Table 2 displays the definition and range of each phenotype.

Restoration of prearthritic coronal alignment

Prearthritic (i.e., native) coronal alignment was estimated using the arithmetic hip-knee-ankle angle (aHKA) [15, 18]. Restoration of prearthritic coronal alignment following medial UKA was classified according to a previously reported system [13] as prearthritically aligned (Group 1, Figure 2a), overcorrection from the

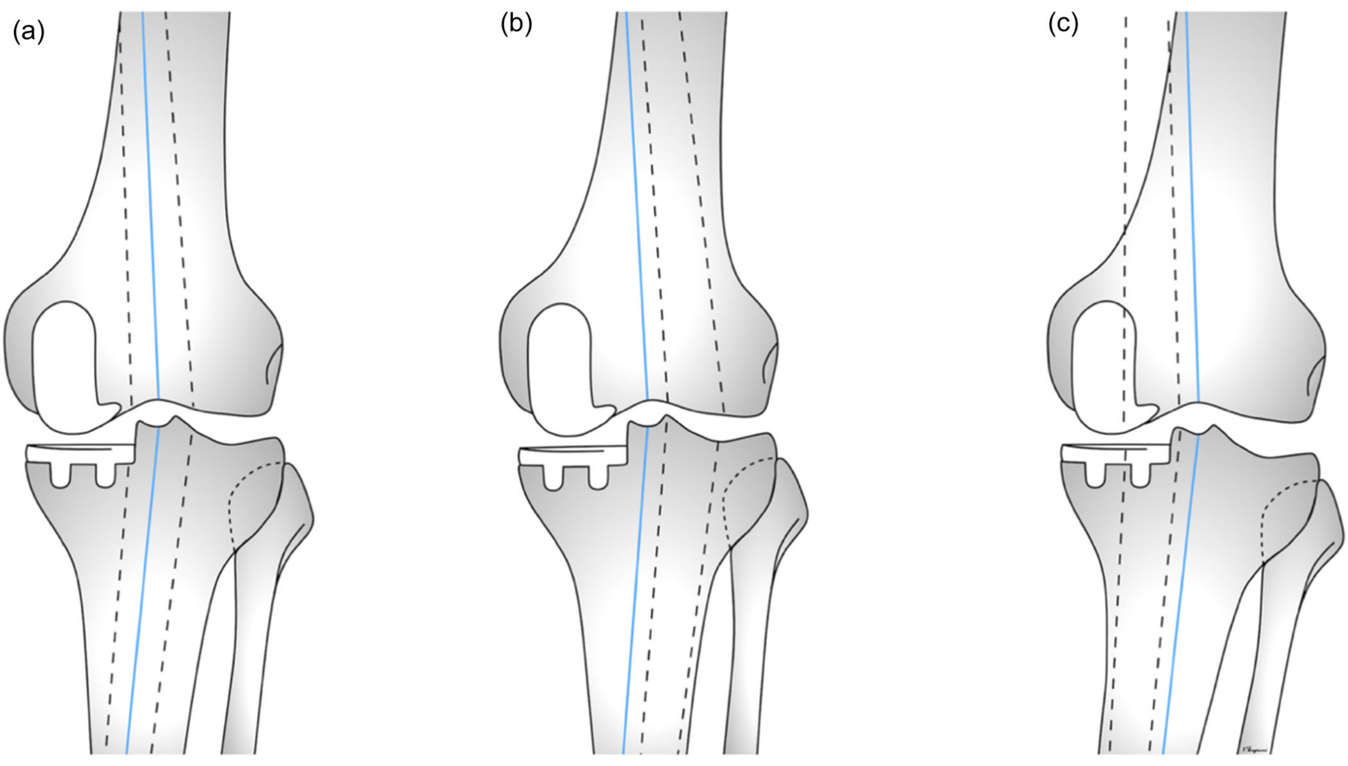

FIGURE 2 Classification of prearthritic alignment restoration following medial unicompartmental knee arthroplasty [13]. The continuous blue line indicates the postoperative mechanical axis (i.e., hip-knee-ankle angle [HKA]). The margins of ±2.0° of estimated prearthritic alignment (i.e., arithmetic hip-knee-ankle angle [aHKA]) are indicated by the dashed lines. (a) Prearthritically aligned knee (Group 1), defined by a postoperative HKA within ±2. 0° of its aHKA. (b) Non-prearthritically aligned knee with overcorrection from its prearthritic alignment (Group 2), defined by a postoperative HKA of >2. 0° smaller than its aHKA. (c) Non-prearthritically aligned knee with under correction of its prearthritic alignment (Group 3), defined by a postoperative HKA of >2.0° larger than its aHKA (Group 3). Image reproduced from original work with permission of Bayoumi et al. [13].

prearthritic coronal alignment (Group 2, Figure 2b), or under correction from the prearthritic coronal alignment (Group 3, Figure 2c). One-hundred fifty-nine knees (15.9%) with an estimated prearthritic coronal alignment in valgus (aHKA ≤−1°) were excluded from this specific analysis, as those knees were typically neutralised during medial UKA and no attempt was made to restore prearthritic coronal alignment.

Statistical analysis

Prevalence of pre and postoperative phenotypes were calculated and presented in numbers and frequencies for the total sample and by sex. The Shapiro-Wilk test was used to test continuous variables for a normal distribution. Independent *t*-tests or Mann-Whitney U tests were conducted to compare parametric and nonparametric continuous data between sexes, respectively. Correlations were analysed using Pearson's correlation coefficient for parametric data and Spearman's rank correlation coefficient for nonparametric data. Discrete variables were compared using Chi-square test or Fisher's exact test when appropriate. Post hoc power analysis was performed using G*Power 3.1 [19], yielding high power (0.99) for the observed differences in prevalence of deformity location between males and females, and proportions of knees with restored prearthritic coronal alignment between subgroups with extra-articular deformities. The level of significance was set at 0.05 for all tests. All analyses were performed in R version 4.1.2. (R Foundation for Statistical Computing).

Ethical aspects

Institutional Review Board approval from the Institutional Review Board of the Hospital for Special Surgery (#2022-1401) was obtained prior to the start of the study. Given the retrospective nature of this study, patient consent was not applicable.

RESULTS

Functional knee phenotypes

Preoperatively, 76 functional knee phenotypes were identified. Fifty-one phenotypes had a prevalence of <1%. Hence, the 25 phenotypes with a prevalence of ≥1% were considered relevant. The most common preoperative functional phenotype was $VAR_{HKA}6°$ $VAR_{FMA}3°NEU_{TMA}0°$ (9.4%; Table 3). Independent of

TABLE 3 The five most common pre and postoperative functional knee phenotypes.

Rank	Functional knee phenotype	Total $n = 1000$	Male $n = 549$	Female $n = 451$
	Preoperatively	n (%)		
1	$VAR_{HKA}6°$ $VAR_{FMA}3°$ $NEU_{TMA}0°$	94 (9.4)	51 (9.3)	43 (9.5)
2	$VAR_{HKA}6°$ $NEU_{FMA}0°$ $NEU_{TMA}0°$	93 (9.3)	54 (9.8)	39 (8.6)
3	$VAR_{HKA}3°$ $NEU_{FMA}0°$ $NEU_{TMA}0°$	91 (9.1)	49 (8.9)	42 (9.3)
4	$VAR_{HKA}9°$ $NEU_{FMA}0°$ $VAR_{TMA}3°$	74 (7.4)	49 (8.9)	25 (5.5)
5	$VAR_{HKA}6°$ $NEU_{FMA}0°$ $VAR_{TMA}3°$	64 (6.4)	42 (7.7)	22 (4.9)
	p value[a]			0.324
Total		416 (41.6)	245 (44.6)	171 (37.9)
	Following medial UKA			
1	$VAR_{HKA}3°$ $NEU_{FMA}0°$ $NEU_{TMA}0°$	183 (18.3)	97 (17.7)	86 (19.1)
2	$NEU_{HKA}0°$ $NEU_{FMA}0°$ $NEU_{TMA}0°$	98 (9.8)	60 (10.9)	38 (8.4)
3	$NEU_{HKA}0°$ $VAL_{FMA}3°$ $NEU_{TMA}0°$	69 (6.9)	37 (6.7)	32 (7.1)
4	$VAR_{HKA}3°$ $NEU_{FMA}0°$ $VAR_{TMA}3°$	68 (6.8)	42 (7.7)	26 (5.8)
5	$NEU_{HKA}0°$ $NEU_{FMA}0°$ $VAL_{TMA}3°$	58 (5.8)	24 (4.4)	34 (7.5)
	p value[a]			0.114
Total		705 (47.6)	260 (47.4)	216 (47.9)

Note: Top five most common functional phenotypes of knees with advanced isolated anteromedial osteoarthritis, prior to and following medial unicompartmental knee arthroplasty (UKA) are presented in numbers with the frequency in parentheses. The prevalence of each functional knee phenotype is given for the total cohort and by sex.

Abbreviations: FMA, femoral mechanical angle; HKA, hip-knee-ankle angle; NEU, neutral; TMA, tibial mechanical angle; VAL, valgus; VAR, varus.

[a]Comparison of prevalence of functional knee phenotypes by sex.

TABLE 4 Distribution of preoperative femoral and tibial phenotypes.

	FMA							
	$VAR_{FMA}12°$	$VAR_{FMA}9°$	$VAR_{FMA}6°$	$VAR_{FMA}3°$	$NEU_{FMA}0°$	$VAL_{FMA}3°$	$VAL_{FMA}6°$	Total
TMA								
$VAR_{TMA}6°$	—	—	2 (0.2)	15 (1.5)	32 (3.2)	10 (1.0)	—	59 (5.9)
$VAR_{TMA}3°$	—	1 (0.1)	23 (2.3)	135 (13.5)	167 (16.7)	30 (3.0)	—	356 (35.6)
$NEU_{TMA}0°$	—	1 (0.1)	21 (2.1)	187 (18.7)	220 (22.0)	35 (3.5)	2 (0.2)	466 (46.6)
$VAL_{TMA}3°$	1 (0.1)	2 (0.2)	8 (0.8)	46 (4.6)	46 (4.6)	7 (0.7)	—	110 (11.0)
$VAL_{TMA}6°$	—	—	1 (0.1)	3 (3.0)	4 (0.6)	1 (0.1)	—	9 (0.9)
Total	1 (0.1)	4 (0.4)	55 (5.5)	386 (38.6)	469 (46.9)	83 (8.3)	2 (0.2)	1000 (100)

Note: The distribution of combinations of femoral and tibial phenotypes (i.e., knee phenotype) of knees with advanced anteromedial osteoarthritis is presented in numbers with the frequencies in parentheses. The heatmap represents the prevalence of each combination (green indicates the highest and red the lowest prevalence).
Abbreviations: FMA, femoral mechanical angle; NEU, neutral; TMA, tibial mechanical angle; VAL, valgus; VAR, varus.

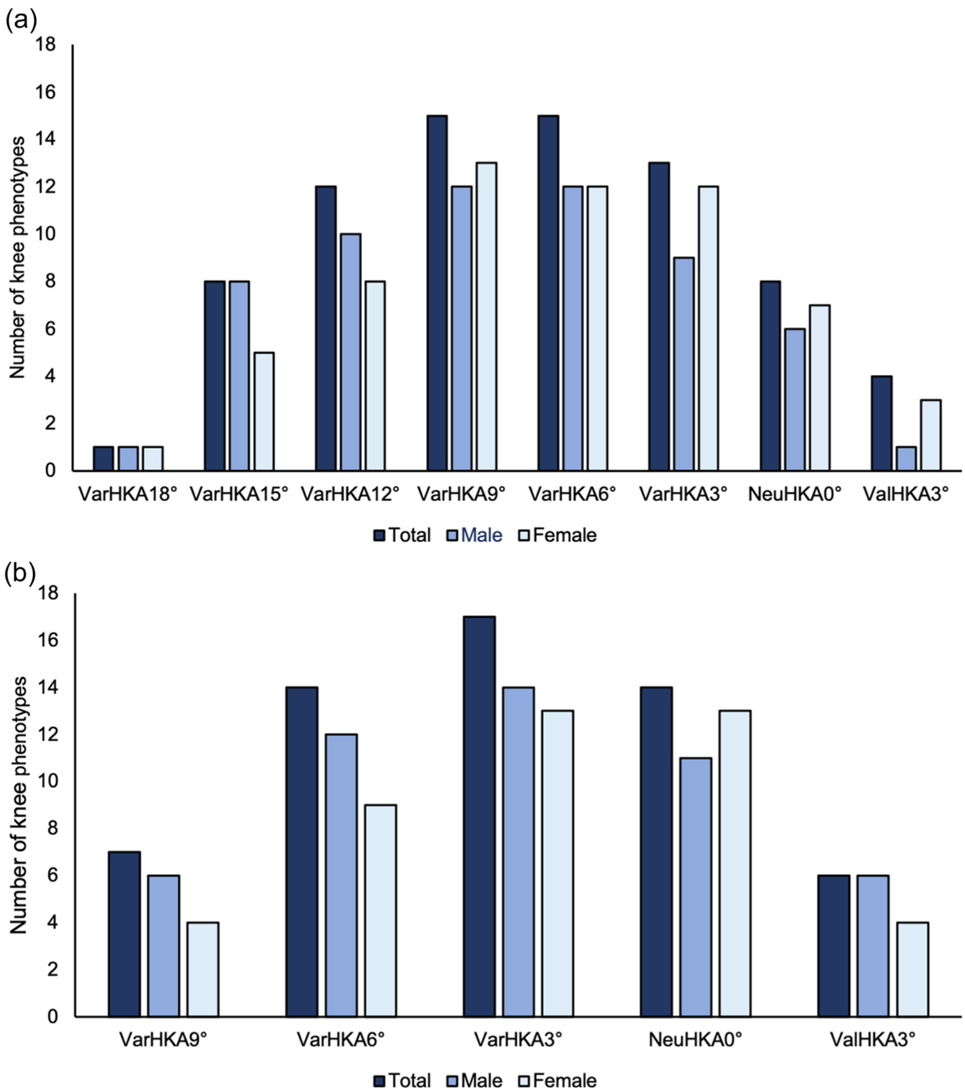

FIGURE 3 Distribution of knee phenotypes (i.e., combination of femoral and tibial phenotype) in relation to the observed limb phenotypes of knees with advanced isolated medial compartment osteoarthritis. (a) Preoperative distribution. (b) Distribution following medial unicompartmental knee arthroplasty.

HKA, the most prevalent preoperative combination of femoral and tibial phenotypes (i.e., knee phenotype) was $NEU_{FMA}0°NEU_{TMA}0°$ (Table 4). Following medial UKA, a total of 58 functional knee phenotypes were identified. Forty-one postoperative phenotypes had a prevalence of <1%. Hence, 17 postoperative phenotypes were considered relevant. The most prevalent postoperative functional knee phenotype was VAR_{HKA} $3°NEU_{FMA}0°NEU_{TMA}0°$ (18.3%).

The five most frequently observed pre and postoperative functional knee phenotypes are presented in Table 3. An overview of all observed functional knee phenotypes is available online as Supporting Information in Appendix Table A1. Sex-based analysis demonstrated differences in mean values of pre and postoperative coronal alignment parameters between males and females (Appendix Table A2), however, there was no sex-related variation in distribution of the five most common functional knee phenotypes (Table 3).

Distribution of limb phenotypes

Preoperatively, limb phenotypes $VAR_{HKA}6°$ (33.8%) and $VAR_{HKA}9°$ (27.5%) were most frequently observed and included 15 distinct knee phenotypes each (Figure 3a). Postoperatively, limb phenotypes $VAR_{HKA}3°$ (47.1%), and $NEU_{HKA}0°$ (31.4%), were most common and these included 14 and 17 knee phenotypes, respectively (Figure 3b). Figure 3 demonstrates a similar distribution between sexes of pre and postoperative knee phenotypes, in relation to the observed limb phenotypes.

Location of the extra-articular deformity

Among knees with limb phenotype $VAR_{HKA}3°$, nearly half (48.4%) had no extra-articular deformity (Table 5). Limb phenotypes $VAR_{HKA}6°$ and $VAR_{HKA}9°$ were observed more frequently in combination with isolated tibial or femoral deformities, while more severe varus limb phenotypes more often exhibited a combined tibial and femoral deformity. Similar patterns were observed when analysed by age, without overall differences between age groups ($p = 0.970$; Appendix Table A3). Females more frequently had an isolated femoral deformity ($p = 0.3$; Table 6).

Restoration of prearthritic coronal alignment

Rates of prearthritically aligned knees following medial UKA were comparable among the five most common preoperative functional knee phenotypes (Appendix Table A4). Significant variations were observed in rates of prearthritically aligned knees when analysed by location of the preoperative deformity (Table 7). Post hoc pairwise comparison demonstrated a smaller overall proportion of prearthritically aligned knees among knees with a combined deformity compared to knees without extra-articular deformity ($p = 0.002$), isolated tibial deformity ($p < 0.001$), or isolated femoral deformity ($p = 0.01$). The magnitude of restoration of prearthritic coronal alignment was weakly correlated with preoperative TMA (correlation coefficient, 0.30,

TABLE 5 Distribution of location of the deformity in varus limb phenotypes.

		Total ($n = 952$)	**$VAR_{HKA}3°$ ($n = 188$)**	**$VAR_{HKA}6°$ ($n = 338$)**	**$VAR_{HKA}9°$ ($n = 275$)**	**$VAR_{HKA}12°$ ($n = 125$)**	**$VAR_{HKA}15°$ ($n = 26$)**
Location of deformity	Definition	*n* (%)					
No extra-art. deformity	NEU_{FMA} - NEU_{TMA}	**213 (22.3)**	**91 (48.4)**	**93 (27.5)**	**29 (10.5)**	**—**	**—**
Tibial deformity	NEU_{FMA} -VAR_{TMA}	199 (20.9)	16 (8.5)	65 (19.2)	88 (32.0)	26 (20.8)	4 (15.4)
	NEU_{FMA} -VAL_{TMA}	30 (3.1)	19 (10.1)	11 (3.3)	—	—	—
	Total	**229 (24.0)**	**35 (18.6)**	**76 (22.5)**	**88 (32.0)**	**26 (20.8)**	**4 (15.4)**
Femoral deformity	VAR_{FMA} - NEU_{TMA}	206 (21.6)	11 (5.9)	99 (29.3)	72 (26.2)	22 (17.6)	2 (7.7)
	VAL_{FMA} - NEU_{TMA}	27 (2.8)	17 (9.0)	9 (2.7)	1 (0.4)	—	—
	Total	**233 (24.4)**	**28 (14.9)**	**108 (32.0)**	**73 (26.5)**	**22 (17.6)**	**2 (7.7)**
Combined deformity	VAR_{FMA} -VAR_{TMA}	174 (8.2)	—	19 (5.6)	64 (23.3)	71 (56.8)	20 (76.9)
	VAR_{FMA} - VAL_{TMA}	58 (6.1)	19 (10.1)	23 (6.8)	12 (4.4)	4 (3.2)	—
	VAL_{FMA} - VAL_{TMA}	5 (0.5)	5 (2.7)	—	—	—	—
	VAL_{FMA} - VAR_{TMA}	40 (4.2)	10 (5.3)	19 (5.6)	9 (3.3)	2 (1.6)	—
	Total	**277 (29.0)**	**34 (18.1)**	**61 (18.0)**	**85 (30.9)**	**77 (61.6)**	**20 (76.9)**

Note: Distribution of location of the deformity in varus limb phenotypes is presented in numbers with the frequencies in parentheses.

Abbreviations: FMA, femoral mechanical angle; HKA, hip-knee-ankle angle; NEU, neutral; TMA, tibial mechanical angle; VAL, valgus; VAR, varus.

TABLE 6 Distribution of the location of the deformity in varus limb phenotypes by sex.

Location of deformity	Definition	Total Male	Total Female	*p* value	$VAR_{HKA}3°$ Male	$VAR_{HKA}3°$ Female	*p* value	$VAR_{HKA}6°$ Male	$VAR_{HKA}6°$ Female	*p* value
No extra-art. deformity	NEU_{FMA} - NEU_{TMA}	**112 (21.2)**	**101 (23.9)**	0.319	**49 (58.3)**	**42 (40.0)**	0.01*	**54 (29.3)**	**39 (25.3)**	0.409
Tibial deformity	NEU_{FMA} - VAR_{TMA}	130 (24.6)	69 (16.3)		7 (8.3)	9 (8.7)		43 (23.4)	22 (14.3)	
	NEU_{FMA} - VAL_{TMA}	9 (1.7)	21 (5.0)		6 (7.1)	13 (12.5)		3 (1.6)	8 (5.2)	
	Total	**139 (26.3)**	**90 (21.3)**	0.073	**13 (15.5)**	**22 (21.2)**	0.320	**46 (25.0)**	**30 (19.5)**	0.226
Femoral deformity	VAR_{FMA} - NEU_{TMA}	108 (20.4)	98 (23.2)		3 (3.6)	8 (7.7)		53 (28.8)	46 (29.9)	
	VAL_{FMA} - NEU_{TMA}	7 (1.3)	20 (4.7)		3 (3.6)	14 (13.5)		4 (2.2)	5 (3.2)	
	Total	**115 (21.7)**	**118 (27.9)**	0.03*	**6 (7.1)**	**22 (21.2)**	0.01*	**57 (31.0)**	**51 (33.1)**	0.674
Combined deformity	VAR_{FMA} - VAR_{TMA}	113 (21.4)	61 (14.4)		—	—		9 (4.9)	10 (6.5)	
	VAR_{FMA} - VAL_{TMA}	24 (4.5)	34 (8.0)		9 (10.7)	10 (9.6)		7 (3.8)	16 (10.4)	
	VAL_{FMA} - VAL_{TMA}	2 (0.4)	3 (0.7)		2 (2.4)	3 (2.9)		—	—	
	VAL_{FMA} - VAR_{TMA}	24 (4.5)	16 (3.8)		5 (6.0)	5 (4.8)		11 (6.0)	8 (5.2)	
	Total	**163 (30.8)**	**114 (27.0)**	0.192	**16 (19.0)**	**18 (17.3)**	0.758	**27 (14.7)**	**34 (22.1)**	0.070

Location deformity	Definition	$VAR_{HKA}9°$ Male	$VAR_{HKA}9°$ Female	*p* value	$VAR_{HKA}12°$ Male	$VAR_{HKA}12°$ Female	*p* value	$VAR_{HKA}15°$ Male	$VAR_{HKA}15°$ Female	*p* value
No extra-art. deformity	NEU_{FMA} - NEU_{TMA}	**9 (5.6)**	**20 (17.7)**	0.001*	**—**	**—**	*n/a*	**—**	**—**	*n/a*
Tibial deformity	NEU_{FMA} - VAR_{TMA}	61 (37.7)	27 (23.9)		16 (19.3)	10 (23.8)		3 (18.8)	1 (10.0)	
	NEU_{FMA} - VAL_{TMA}	—	—		—	—		—	—	
	Total	**61 (37.7)**	**27 (23.9)**	0.02*	**16 (19.3)**	**10 (23.8)**	0.555	**3 (18.8)**	**1 (10.0)**	0.667
Femoral deformity	VAR_{FMA} - NEU_{TMA}	38 (23.5)	32 (30.1)		12 (14.5)	10 (23.8)		2 (12.5)	—	
	VAL_{FMA} - NEU_{TMA}	—	1 (0.9)		—	—		—	—	
	Total	**38 (23.5)**	**33 (31.0)**	0.164	**12 (14.5)**	**10 (23.8)**	0.194	**2 (12.5)**	—	*n/a*
Combined deformity	VAR_{FMA} - VAR_{TMA}	42 (25.9)	22 (19.5)		51 (61.4)	20 (47.6)		11 (68.8)	9 (90.0)	
	VAR_{FMA} - VAL_{TMA}	6 (3.7)	6 (5.3)		2 (2.4)	2 (4.8)		—	—	
	VAL_{FMA} - VAL_{TMA}	—	—		—	—		—	—	
	VAL_{FMA} - VAR_{TMA}	6 (3.7)	3 (2.7)		2 (2.4)	—		—	—	
	Total	**54 (33.3)**	**31 (27.4)**	0.297	**55 (63.3)**	**22 (52.4)**	0.131	**11 (68.8)**	**9 (90.0)**	0.211

Note: Distribution of the location of the deformity in varus limb phenotypes by sex is presented in numbers with the frequencies in parentheses.

Abbreviations: FMA, femoral mechanical angle; HKA, hip-knee-ankle angle; n/a, not applicable; NEU, neutral; TMA, tibial mechanical angle; VAL, valgus; VAR, varus.

*Indicates statistical significance.

$p < 0.001$; Figure 4), and FMA (correlation coefficient, 0.26, $p < 0.001$; Figure 5).

DISCUSSION

The most important findings of this study were that phenotype analysis of 1000 knees with isolated anteromedial OA demonstrated a high diversity of functional knee phenotypes in a predominantly Caucasian study population. Preoperatively, 25 relevant functional knee phenotypes were identified. Following treatment with medial UKA, a reduction in diversity was observed, including 17 relevant postoperative functional knee phenotypes. Knees with combined tibial and femoral deformities were overall less frequently restored to their prearthritic coronal alignment following medial UKA.

Up until recently, there was a lack of literature evaluating the diversity of coronal phenotypes in knees with anteromedial OA [8]. The current study demonstrated a wide variation of functional knee phenotypes among knees with this type of OA, identifying 76 distinct

TABLE 7 Probability of restoring prearthritic coronal alignment following medial unicompartmental knee arthroplasty based on location of the deformity.

Location of Deformity	Definition	No. knees[a]	Prearthritically aligned Group 1 Within 2.0° of prearthritic coronal alignment *n* (%)	Non-prearthritically aligned Group 2 >2.0° overcorrected from the prearthritic coronal alignment *n* (%)	Group 3 >2.0° under corrected from the prearthritic coronal alignment *n* (%)
No extra-art. deformity	NEU_{FMA} - NEU_{TMA}	**172**	**128 (74.4)**	**5 (2.9)**	**39 (22.7)**
Tibial deformity	NEU_{FMA} - VAR_{TMA}	199	149 (74.9)	27 (13.6)	23 (11.6)
	NEU_{FMA} - VAL_{TMA}	0	—	—	—
	Total	**199**	**149 (74.9)**	**27 (13.6)**	**23 (11.6)**
Femoral deformity	VAR_{FMA} - NEU_{TMA}	209	148 (70.8)	34 (16.3)	27 (12.9)
	VAL_{FMA} - NEU_{TMA}	0	—	—	—
	Total	**209**	**148 (70.8)**	**34 (16.3)**	**27 (12.9)**
Combined deformity	VAR_{FMA} - VAR_{TMA}	176	94 (53.4)	75 (42.6)	7 (4.0)
	VAR_{FMA} - VAL_{TMA}	46	36 (78.2)	3 (6.5)	7 (15.2)
	VAL_{FMA} - VAL_{TMA}	0	—	—	—
	VAL_{FMA} - VAR_{TMA}	39	26 (66.7)	4 (10.3)	9 (23.1)
	Total	**261**	**156 (59.8)**	**82 (31.4)**	**23 (8.8)**
	p value[b]		0.001[c]		

Note: The probability of restoring prearthritic coronal alignment is given for the five most prevalent preoperative functional knee phenotypes. The distribution is presented in numbers with the frequencies in parentheses.

Abbreviations: FMA, femoral mechanical angle; HKA, hip-knee-ankle angle; NEU, neutral; TMA, tibial mechanical angle; VAL, valgus; VAR, varus.

[a]A total of 159 knees with an estimated prearthritic coronal alignment in valgus were excluded from this analysis.

[b]Comparison of overall proportions of knees restored to their prearthritic coronal alignment (within ±2.0°) by location of the deformity (total numbers in bold).

[c]Indicates statistical significance.

phenotypes in total, as opposed to 43 different phenotypes previously observed in a non-OA population [7]. The most common phenotype represented only 9.4% of all knees, and the five most prevalent phenotypes comprised 41.6% of all included knees. The range of functional knee phenotypes, as well as the variety of knee phenotypes within each limb phenotype group (Figure 3a), further underline the level of phenotypic heterogeneity that can exists among knees with anteromedial OA, even among those with a similar mechanical axis.

While the clinical relevance of this multitude of phenotypes remains to be further explored, one can argue that certain phenotypes may be less suitable for UKA treatment, or, may require a different alignment strategy in order achieve favourable outcomes. It has recently been demonstrated that restoration of prearthritic alignment during medial UKA may lead to improved outcomes [13, 14]. The current study showed similar rates of knees restored to their prearthritic coronal alignment among the most prevalent functional knee phenotypes. However, knees with combined femoral and tibial deformities were overall less frequently restored to their prearthritic coronal alignment, compared to knees without deformity, or isolated femoral or tibial deformity. This finding is consistent with the weak correlation between prearthritic alignment restoration and the magnitude of preoperative TMA and FMA, suggesting that TMA or FMA outliers alone do not necessarily influence restoration of prearthritic coronal alignment. Hence, a better understanding of phenotypic variability of anteromedial OA may aid to optimise candidate selection and alignment strategies, but further research into the correlation between phenotypes and postoperative performance is warranted to elucidate which alignment technique is best suited for which phenotype.

Consistent with the current observations, previous literature has reported a wide variability of phenotypes among healthy and OA-affected knees [7, 8, 11, 12]. To our knowledge, one other study [8] has described functional knee phenotypes of medial OA. Huan et al. [8] identified a large variation of functional knee phenotypes in a Japanese population, which appeared to be greater compared to the present study. Their five most common functional knee phenotypes represented

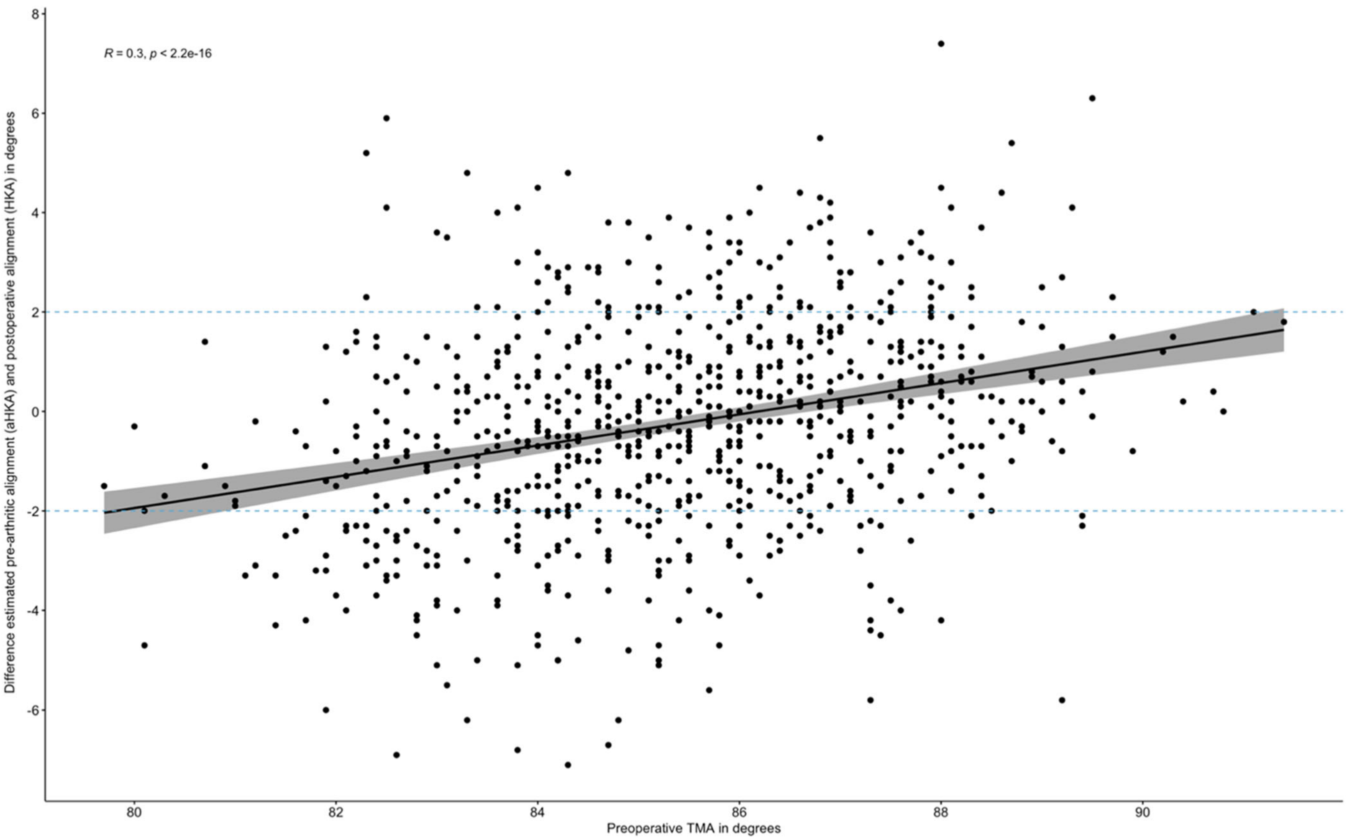

FIGURE 4 Relation between preoperative tibial mechanical angle (TMA) and the magnitude of restoration of prearthritic alignment (i.e., difference between arithmetic hip-knee-ankle angle [aHKA] and postoperative mechanical alignment [HKA]) following medial unicompartmental knee arthroplasty (correlation coefficient: 0.30, $R^2 = 0.09$; $p < 0.001$). The dashed blue lines represent the boundaries of restoration of postoperative HKA within ±2.0° of prearthritic alignment.

21.8% of all 879 knees, as opposed to 41.6% in the current study. Phenotypic differences seemed mainly characterised by more severe varus limb phenotypes (range, $NEU_{HKA}0°$ to $VAR_{HKA}24°$), and larger proportions of knees with a varus femur (56.8% vs. 44.6% in the present study), and varus tibia (76.0% vs. 41.5% in the present study), implicating a higher prevalence of extra-articular deformities in the Japanese population with anteromedial OA [8]. Additionally, the unequal sex distribution in their cohort [8], (80% females) may have further contributed to differences compared to the current study. In line with these observations, a recent systematic review reported a wide geographic variation in coronal knee phenotypes of healthy and arthritic knees [20]. These findings further emphasise the importance of considering ethnic differences in understanding knee phenotypic variation at the population level.

To that end, this study also examined phenotypic variation by sex. Despite differences in mean values of radiographic parameters, the distribution of functional knee phenotypes was similar between sexes. Nevertheless, the five most prevalent phenotypes covered a lower proportion of the female population (37.9% of knees) compared to the male population (44.6% of knees), suggesting a higher degree of phenotypic variation among female knees. Furthermore, there was a higher prevalence of isolated femoral deformities among females compared males. Although the present study did not assess the clinical impact of sex-related phenotype differences, it has previously been suggested that anatomical variations may contribute to divergent outcomes between males and females following medial UKA, and these may therefore be important to consider [21–26].

This study recognises several limitations. First, the study and phenotype system did not address sagittal plane alignment, which may be a major variable in the overall alignment of the individual knee. Second, radiographic evaluation was performed using weight-bearing AP radiographs, and any pre or postoperative flexion deficits may have influenced our observations. However, weight-bearing radiographs may more accurately reflect the patient's functional position compared to evaluation in supine position. Third, the study population consisted primarily of Caucasian patients and results may therefore not be generalisable to other ethnic groups.

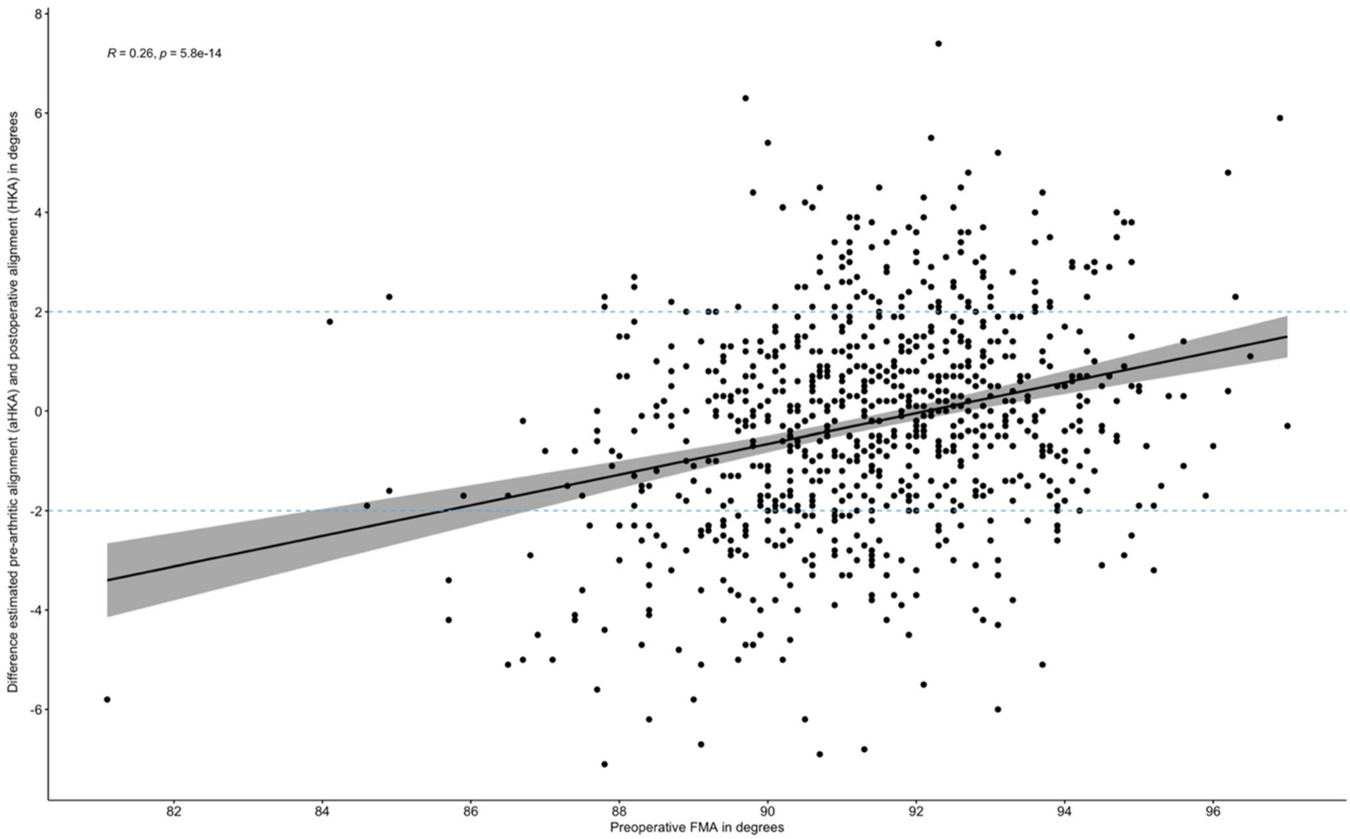

FIGURE 5 Relation between preoperative femoral mechanical angle (FMA) and the magnitude of restoration of prearthritic alignment (i.e., difference between arithmetic hip-knee-ankle angle [aHKA] and postoperative mechanical alignment [HKA]) following medial unicompartmental knee arthroplasty (correlation coefficient: 0.26, $R^2 = 0.07$; $p < 0.001$). The dashed blue lines represent the boundaries of restoration of postoperative HKA within ±2.0° of estimated prearthritic alignment.

Fourth, estimation of prearthritic coronal alignment was based on a methodology with limitations of its own [18] and may deviate from the actual predisease alignment. Fifth, associations between functional knee phenotypes and clinical outcomes were not assessed, leaving the clinical relevance of functional knee phenotypes and implications for UKA candidacy yet to be further established. Nonetheless, data of this study, which delineates the phenotypic variation among knees with a specific form of OA using a combination of coronal alignment parameters, may provide a first step towards a more personalised approach in knee arthroplasty.

CONCLUSION

Phenotype analysis using the functional knee phenotype system demonstrated a wide diversity of coronal alignment phenotypes among knees with anteromedial OA in a predominantly Caucasian population. Following treatment with medial UKA, a reduction from 25 preoperative to 17 relevant postoperative phenotypes was observed. Consideration of phenotypic variation can be of importance when aiming to restore prearthritic coronal alignment during medial UKA.

AUTHOR CONTRIBUTIONS

Tarik Bayoumi: Conceptualisation; methodology; formal analysis; investigation; data curation; writing—original draft; writing—review and editing; visualisation. **Gaby V. ten Noever de Brauw:** Data collection; methodology; investigation; writing—review and editing. **Lindsey V. Ruderman:** Data collection; methodology; investigation; writing—review and editing. **Jelle P. van der List:** Conceptualisation; methodology; investigation; writing—review and editing. **Gino M. M. J. Kerkhoffs:** Conceptualisation; methodology; investigation; writing—review and editing. **Andrew D. Pearle:** Conceptualisation; methodology; investigation; resources; writing—review and editing. **Hendrik A. Zuiderbaan:** Conceptualisation; methodology; investigation; writing—review and editing.

ACKNOWLEDGEMENTS

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST STATEMENT

Dr. Andrew D. Pearle is a consultant for Smith & Nephew and for DePuy Synthes. Dr. Hendrik A. Zuiderbaan is a consultant for Smith & Nephew. The other authors declare they have no potential conflict of interest.

ETHICS STATEMENT

Approval from the Institutional Review Board of the Hospital for Special Surgery was obtained prior to the start of the study (#2022-1401).

ORCID

Tarik Bayoumi https://orcid.org/0000-0002-4723-8572
Gaby V. ten Noever de Brauw https://orcid.org/0009-0000-3913-3458
Lindsey V. Ruderman https://orcid.org/0000-0002-7012-9243
Jelle P. van der List https://orcid.org/0000-0002-7940-5152
Gino M. M. J. Kerkhoffs https://orcid.org/0000-0001-5916-7049
Andrew D. Pearle https://orcid.org/0000-0001-8809-5347
Hendrik A. Zuiderbaan https://orcid.org/0000-0001-9544-7048

REFERENCES

1. Wilson, H.A., Middleton, R., Abram, S.G.F., Smith, S., Alvand, A., Jackson, W.F. et al. (2019) Patient relevant outcomes of unicompartmental versus total knee replacement: systematic review and meta-analysis. *BMJ*, 364, l352.
2. Kleeblad, L.J., van der List, J.P., Pearle, A.D., Fragomen, A.T. & Rozbruch, S.R. (2018) Predicting the feasibility of correcting mechanical axis in large varus deformities with unicompartmental knee arthroplasty. *The Journal of Arthroplasty*, 33, 372–378.
3. Mittal, A., Meshram, P., Kim, W.H. & Kim, T.K. (2020) Unicompartmental knee arthroplasty, an enigma, and the ten enigmas of medial UKA. *Journal of Orthopaedics and Traumatology*, 21, 15.
4. Petterson, S.C., Blood, T.D. & Plancher, K.D. (2020) Role of alignment in successful clinical outcomes following medial unicompartmental knee arthroplasty: current concepts. *Journal of ISAKOS*, 5, 224–228.
5. Bellemans, J., Colyn, W., Vandenneucker, H. & Victor, J. (2012) The Chitranjan Ranawat award: is neutral mechanical alignment normal for all patients? The concept of constitutional varus. *Clinical Orthopaedics & Related Research*, 470, 45–53.
6. Hess, S., Moser, L.B., Amsler, F., Behrend, H. & Hirschmann, M.T. (2019) Highly variable coronal tibial and femoral alignment in osteoarthritic knees: a systematic review. *Knee Surgery, Sports Traumatology, Arthroscopy*, 27, 1368–1377.
7. Hirschmann, M.T., Moser, L.B., Amsler, F., Behrend, H., Leclerq, V. & Hess, S. (2019) Functional knee phenotypes: a novel classification for phenotyping the coronal lower limb alignment based on the native alignment in young non-osteoarthritic patients. *Knee Surgery, Sports Traumatology, Arthroscopy*, 27, 1394–1402.
8. Huan, W., Mochizuki, T., Tanifuji, O. & Kawashima, H. (2022) Variability of functional knee phenotype for coronal alignment in advanced varus knee osteoarthritis in the Japanese population. *Knee Surgery, Sports Traumatology, Arthroscopy*, 31, 1451–1461.
9. MacDessi, S.J., Griffiths-Jones, W., Harris, I.A., Bellemans, J. & Chen, D.B. (2021) Coronal plane alignment of the knee (CPAK) classification: a new system for describing knee phenotypes. *The Bone & Joint Journal*, 103-b(2), 329–337.
10. Mullaji, A., Shah, R., Bhoskar, R., Singh, A., Haidermota, M. & Thakur, H. (2022) Seven phenotypes of varus osteoarthritic knees can be identified in the coronal plane. *Knee Surgery, Sports Traumatology, Arthroscopy*, 30, 2793–2805.
11. Hess, S., Moser, L.B., Robertson, E.L., Behrend, H., Amsler, F., Iordache, E. et al. (2022) Osteoarthritic and non-osteoarthritic patients show comparable coronal knee joint line orientations in a cross-sectional study based on 3D reconstructed CT images. *Knee Surgery, Sports Traumatology, Arthroscopy*, 30, 407–418.
12. Huber, S., Mitterer, J.A., Vallant, S.M., Simon, S., Hanak-Hammerl, F., Schwarz, G.M. et al. (2023) Gender-specific distribution of knee morphology according to CPAK and functional phenotype classification: analysis of 8739 osteoarthritic knees prior to total knee arthroplasty using artificial intelligence. *Knee Surgery, Sports Traumatology, Arthroscopy*, 31, 4220–4230. Available from: https://doi.org/10.1007/s00167-023-07459-z
13. Bayoumi, T., Burger, J.A., Ruderman, L.V., van der List, J.P., Zuiderbaan, H.A., Kerkhoffs, G.M.M.J. et al. (2023) Restoration or relative overcorrection of pre-arthritic coronal alignment leads to improved results following medial unicompartmental knee arthroplasty. *Knee Surgery, Sports Traumatology, Arthroscopy*, 31, 3981–3991. Available from: https://doi.org/10.1007/s00167-023-07441-9
14. Plancher, K.D., Brite, J.E., Briggs, K.K. & Petterson, S.C. (2022) Pre-arthritic/kinematic alignment in fixed-bearing medial unicompartmental knee arthroplasty results in return to activity at mean 10-year follow-up. *Journal of Bone and Joint Surgery*, 104, 1081–1089.
15. Bayoumi, T., Burger, J.A., Zuiderbaan, H.A., Ruderman, L.V., Nguyen, J.T. & Pearle, A.D. (2023) Robotic-assisted medial unicompartmental knee arthroplasty restores estimated pre-arthritic coronal limb alignment: a retrospective cohort study. *The Knee*, 41, 180–189.
16. Kellgren, J.H. & Lawrence, J.S. (1957) Radiological assessment of osteo-arthrosis. *Annals of the Rheumatic Diseases*, 16, 494–502.
17. Pearle, A.D., O'Loughlin, P.F. & Kendoff, D.O. (2010) Robot-assisted unicompartmental knee arthroplasty. *The Journal of Arthroplasty*, 25, 230–237.
18. Griffiths-Jones, W., Chen, D.B., Harris, I.A., Bellemans, J. & MacDessi, S.J. (2021) Arithmetic hip-knee-ankle angle (aHKA): an algorithm for estimating constitutional lower limb alignment in the arthritic patient population. *Bone & Joint Open*, 2, 351–358.
19. Faul, F., Erdfelder, E., Lang, A.G. & Buchner, A. (2007) G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, 39, 175–191.
20. Pagan, C.A., Karasavvidis, T., Lebrun, D.G., Jang, S.J., MacDessi, S.J. & Vigdorchik, J.M. (2023) Geographic variation in knee phenotypes based on the coronal plane alignment of the knee classification: a systematic review. *The Journal of Arthroplasty*, 38, 1892–1899. Available from: https://doi.org/10.1016/j.arth.2023.03.047
21. Australian Orthopedic Association National Joint Replacement Registry (2021). *Hip, knee & shoulder arthroplasty: 2021 annual report. Adelaide*. Report number: AOA 1-432.
22. Bayoumi, T., Kleeblad, L.J., Borus, T.A., Coon, T.M., Dounchis, J., Nguyen, J.T. et al. (2023) Ten-year survivorship and patient satisfaction following robotic-arm-assisted medial unicompartmental

knee arthroplasty: a prospective multicenter study. *Journal of Bone and Joint Surgery*, 105, 933–942.
23. Kleeblad, L.J., Borus, T.A., Coon, T.M., Dounchis, J., Nguyen, J.T. & Pearle, A.D. (2018) Midterm survivorship and patient satisfaction of robotic-arm-assisted medial unicompartmental knee arthroplasty: a multicenter study. *The Journal of Arthroplasty*, 33, 1719–1726.
24. National Joint Registry. (2021) *18th Annual Report. National joint registry for England, Wales, Northern Ireland and the Isle of Man*.
25. van der List, J.P., Chawla, H., Zuiderbaan, H.A. & Pearle, A.D. (2016) The role of preoperative patient characteristics on outcomes of unicompartmental knee arthroplasty: a meta-analysis critique. *The Journal of Arthroplasty*, 31, 2617–2627.
26. Zambianchi, F., Daffara, V., Franceschi, G., Banchelli, F., Marcovigi, A. & Catani, F. (2021) Robotic arm-assisted unicompartmental knee arthroplasty: high survivorship and good patient-related outcomes at a minimum five years of follow-up. *Knee Surgery, Sports Traumatology, Arthroscopy*, 29, 3316–3322.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Bayoumi, T., ten Noever de Brauw, G.V., Ruderman, L.V., van der List, J.P., Kerkhoffs, G.M.M.J., Pearle, A.D. et al. (2024) The phenotypic diversity of anteromedial osteoarthritis before and after treatment with medial unicompartmental knee arthroplasty: a radiographic analysis of 1000 knees. *Knee Surgery, Sports Traumatology, Arthroscopy*, 1–13. https://doi.org/10.1002/ksa.12043