Neutral alignment resulting from tibial vara and opposite femoral valgus is the main morphologic pattern in healthy middle-aged patients: an exploration of a 3D-CT database

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Abstract

Purpose Given the goal of achieving optimal correction and alignment after knee arthroplasty or high tibial osteotomy, literature focusing on the inter-individual variability of the native knee, tibia and femur with regards to the coronal or sagit-tal alignment is lacking. The aim of this study was to analyse normal angular values in the healthy middle-aged population and determine differences of angular values according to inter-individual features. The first hypothesis was that common morphological patterns may be identified in the healthy middle-aged non-osteoarthritic population. The second hypothesis was that high inter-individual variability exists with regards to gender, ethnicity and alignment phenotype.

Methods A CT scan-based modelling and analysis system was used to examine the lower limb of 758 normal healthy patients (390 men, 368 women; mean age 58.5 ± 16.4 years) with available data concerning angular values and retrieved from the SOMA database. The hip–knee–ankle angle (HKA), lateral distal femoral angle (LDFA), medial proximal tibial angle (MPTA), posterior distal femoral angle (PDFA), posterior proximal tibial angle (PPTA) and non weight-bearing joint line convergence angle (nwJLCA) were then measured for each patient. Results were analysed for the entire cohort and based on gender, ethnicity and phenotype.

Results The mean HKA was 179.4° ± 2.6°, LDFA: 85.8° ± 2.0°, MPTA: 85.6° ± 2.4°, PDFA: 85.2° ± 1.5°, PPTA: 83.8° ± 2.9° and nwJLCA: 1.09° ± 0.9°. Gender was associated with higher LDFA and lower HKA for men. Ethnicity was associated with greater proximal tibial vara and distal femoral valgus for Asian patients. Patients with an overall global varus alignment had more tibia vara and less femoral valgus than patients with an overall valgus alignment.

Conclusion Even if significant differences were found based on subgroup analysis (gender, ethnicity or phenotype), this study demonstrated that neutral alignment is the main morphological pattern in the healthy middle-aged population. This neutrality is the result from tibia vara compensated by an ipsilateral femoral valgus.

Level of clinical evidence III, retrospective cohort study.

Keywords Knee · Native · Alignment · HKA · MPTA · LDFA · PPTA · JLCA · CT · HTO concepts · Phenotypes

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Abbreviations

HKA	Hip–knee–ankle angle
LDFA	Lateral distal femoral angle
MPTA	Medial proximal tibial angle
PPTA	Posterior proximal tibial angle
PDFA	Posterior distal femoral angle
nwJLCA	Non weight-bearing joint line convergence angle
CT	Computed tomography

Introduction

Achieving optimal correction when performing an high tibial osteotomy remains a timely unanswered question. Several studies have demonstrated the accuracy of correction in relation to preoperative planning is a determining factor for a successful outcome following high tibial osteotomy (HTO) [3, 4, 6, 17]. To date, there remains ambiguity with regard to the variability of native knee alignment. One recent systematic review indicated that the variability of the anatomy is oversimplified despite a wide discrepancy of all coronal anatomical angles in non-osteoarthritic and osteoarthritic knees [7, 21]. A majority of the studies found within the literature involve small samples or analysed the alignment on standing long-leg radiographs [2, 5, 20, 29]. There is still a lack of data with regards to 3D-reconstructed CT-images of alignment of the native knee.

Hirschmann et al. [8–10] recently described functional knee native phenotypes according to hip–knee–ankle angle, femoral mechanical angle and tibial mechanical angle examined on 3D-reconstructed CT scans to better understand patient's individual anatomy.

Despite this novel approach based on anatomic variations of each subject, there is still limited information available on non-osteoarthritic patients, including anatomic values on coronal and sagittal planes according to gender, ethnicity and phenotype analysis. To answer this question, further investigation is required based on analysis of CT-scans to precisely evaluate usual angular values and variability according to demographics characteristics.

This study aims to provide normal angular values in the healthy middle-aged population. A large number of phenotypes have recently been described [8–10, 21]; however, this study chose to analyse angular values according to only three commonly known phenotypes that are used in current clinical practice; varus, valgus or neutral alignment. Analysis of CT-scans of a large cohort allows better extrapolation of the results in the population. Another intention was to determine the inter-individual variations of knee angular values according to patient demographic characteristics with an emphasis placed on gender, ethnicity and phenotype. The values of inter-individual variations is scarce within the literature and ideally these values should be better understood as one value could be considered normal for one patient but could be pathological for another. The first hypothesis was that common morphological patterns may be identified in the healthy middle-aged non-osteoarthritic population. The second hypothesis was that high inter-individual variability exists according to gender, ethnicity and alignment phenotype.

Materials and methods

A CT scan-based modelling and analysis system was used for this study (SOMA, Stryker, Mahwah, New Jersey) [25]; this database has been developed to assess demographic variations. The SOMA database consists of over 25,000 bone models obtained from over 3600 patients worldwide. All scans were obtained per local legal and regulatory requirements which included ethics board approval and informed patient consent, where appropriate. CT scans were acquired exclusively for medical indications such as polytrauma (20%), CT angiography (70%) and other reasons (i.e. total joint replacement) (10%). More than 3500 normal healthy individuals without osteoarthritis were retrieved from the SOMA database, from which 758 patients (390 males and 368 females, mean age 58 ± 16 years, mean BMI 25.0 ± 4.4 kg/m^2) had reliable and complete data imaging sets that were selected and included (Table 1). Using this system, the pelvis, bilateral femora, bilateral tibia and patella were examined. Subjects with bone or joint abnormalities, substantial osteoarthritis or evidence of previous surgery were excluded before CT scan selection through radiographic inspection.

The hip–knee–ankle angle (HKA), medial proximal tibial angle (MPTA), lateral distal femoral angle (LDFA), global posterior proximal tibial angle (PPTA), posterior distal femoral angle (PDFA) and the non weight-bearing joint line convergence angle (nwJLCA) were calculated for each knee. These measurements were then profiled to each bone on the database by the automated software, resulting in reproducible and consistent parameters for each subject and associated margin of error of less than 2 mm and less than 1° [1, 26].

Following a previously described method [15], HKA, MPTA, LDFA, PPTA, PDFA were determined. The HKA angle was defined by the lines connecting the centre of the femoral head, the knee and the ankle, respectively. The distal femoral axis was then created from the most distal points on the medial femoral condyle and lateral femoral condyle. The LDFA was determined by the angle between the distal femoral axis and the mechanical axis in the coronal plane, the distal femoral axis was created from the most distal points on the medial femoral condyle and lateral femoral condyle. The proximal tibial plane was created by fitting 35 points

Table 1 Demographic and anatomic parameters evaluated in the global series (left and right anatomic measurements are pooled together)

Demographic parameters	Mean ± SD	Range (min–max)
Age (year)	58.5 ± 16.4	11–92
Height (kg)	166.4 ± 8.7	140–189
Weight (cm)	69.6 ± 14.9	39–110
BMI (kg m^{-2})	25.0 ± 4.4	16–42
Anatomic parameters	Mean ± SD	Range (min–max)
HKA (°)	179.4 ± 2.6	170.8–189.8
LDFA (°)	85.8 ± 2.0	80.1–92.5
MPTA (°)	85.6 ± 2.4	77.5–98.4
PDFA (°)	85.2 ± 1.5	80.4–88.9
PPTA (°)	83.8 ± 2.9	75.3–95.5
nwJLCA (°)	1.09 ± 0.9	0–6.9

BMI body mass index, *HKA* hip–knee–ankle angle, *LDFA* lateral distal femoral angle, *MPTA* medial proximal tibial angle, *PDFA* posterior distal femoral angle, *PPTA* posterior plateau tibial angle, *nwJLCA* non weight-bearing joint line convergence angle

on the medial and lateral tibial compartments. The intersection of the proximal tibial plane and the tibial axis between the tibial knee centre and the tibial ankle centre was then determined as the MPTA in the coronal plane and as the PPTA in the sagittal plane. The posterior angle between the sagittal femoral axis connecting the anterior and posterior points of the femoral condyles and the femoral mechanical axis in the sagittal plane was defined as the PDFA. Finally, the angle connecting the distal femoral axis and the proximal tibial plane in the coronal plane was defined as the nwJLCA (Fig. 1). A correlation was analysed between BMI and age with regards to angular values. Mean differences (Δ) for each angular value between gender (men and women), ethnicity (Caucasian and Asian) and phenotypes (neutral, varus or valgus alignment) were analysed. Knees were considered as having constitutional varus if the HKA angle was less than 177°; they were considered neutral if the HKA angle was between 177° and 183° or as having constitutional valgus if the HKA angle was more than 183°. Three phenotypes were then determined.

To perform this study, an anonymized database was explored following local ethical committee approval (Aix-Marseille University) of the research protocol.

Statistical analysis

Means and standard deviations (SDs) were determined for each of the measurements made for the population. Normal (Gaussian) distributions were determined. Univariate analysis was performed using *t* tests to estimate difference between groups. Multiple linear regression models were developed to establish the determinants for each of the variables. For each model, variables with a *p* value less than 0.1 were kept in the final model.

Sample size was calculated based on the estimated MPTA measurement (MPTA = 87° ± 3° [32]) for a required level of statistical significance of $\alpha = 0.05$, and a power of $1 - \beta = 0.9$; 48 lower limb pairs would be required in each group or subgroups to detect > 2° differences. A trained statistician (MO) performed statistical analysis using SPSS software (Version 22; SPSS Inc, Chicago, IL, USA). All calculations were based on two-tailed tests.

Results

A mean HKA of 179.4° ± 2.6°, a mean LDFA of 85.8° ± 2.0°, a mean MPTA of 85.6° ± 2.4°, a mean PDFA of 75.2° ± 1.5°, a mean PPTA of 83.8° ± 2.9° and a mean nwJLCA of 1.09° ± 0.9° was observed for all the populations (Table 1 and Fig. 2).

A significant but weak correlation was found between BMI and age with regard to the HKA ($R^2 = -0.002$, $R^2 = 0.03$, respectively), LDFA ($R^2 = -0.002$, $R^2 = 0.002$ respectively), MPTA ($R^2 = 0.001$, $R^2 = 0.004$ respectively), PDFA ($R^2 = 0.002$, $R^2 = 0.01$, respectively) and PPTA ($R^2 = -0.003$, $R^2 = 0.001$, respectively) (Table 2).

The univariate analysis did not find any significant difference between men and women knee angular values ($p > 0.05$) except for HKA and LDFA ($\Delta = 1.25° \pm 0.18°$, $\Delta = 1.15 \pm 0.14$, respectively, $p < 0.001$). Tibial anatomy was found to be similar between men and women, whereas femoral anatomy on coronal plane was significantly influenced by gender with a higher LDFA for men. Those differences were transposed to global alignment difference with higher HKA for women (Table 3).

Caucasian subjects had less tibia vara and reduced femoral valgus than the Asian population which affected the overall global alignment: HKA ($\Delta = 0.53° \pm 0.19°$;

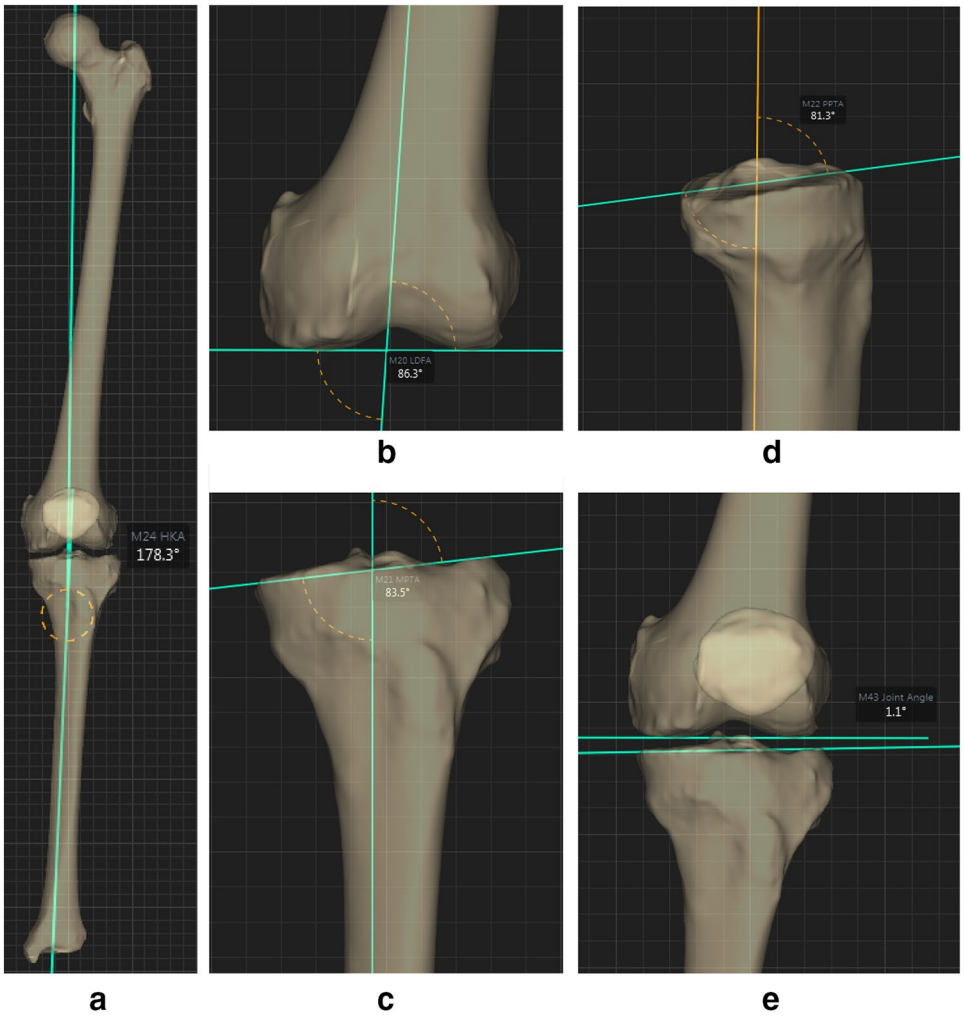


Fig. 1 Illustrations of the anatomical measurements. **a** HKA hip–knee–ankle angle; **b** LDFA lateral distal femoral angle; **c** MPTA medial proximal tibial angle; **d** PPTA posterior plateau tibial angle; **e** nwJLCA non-weight-bearing joint line convergence angle

$p < 0.01$), LDFA ($\Delta = 0.63° \pm 0.15°$; $p < 0.01$), MPTA ($\Delta = 1.51° \pm 0.17°$; $p < 0.01$). PPTA ($\Delta = 1.90° \pm 0.20°$; $p < 0.01$) and PDFA ($\Delta = 0.28° \pm 0.11°$; $p < 0.01$) were also different between ethnicities, whilst no variation was found for nwJLCA ($\Delta = 0.06° \pm 0.07°$; $p = 0.39$) (Table 4).

Five hundred and sixty-three patients (74.3%) had a neutral alignment, one hundred and twenty-nine (17.0%) varus alignment and sixty-six (8.7%) patients had valgus alignment. Significant differences were observed for all angular parameters according to alignment phenotype except for nwJLCA, mean differences were not significantly different between varus and valgus phenotypes (Table 5). Global varus alignment were associated with higher tibia vara and lower femoral valgus (Δ MPTA $= 5.1° \pm 0.3°$; Δ LDFA $= 3.4° \pm 0.3°$; $p < 0.001$), whereas global valgus alignment resulted from higher femoral valgus and reduced tibia vara (Δ MPTA $= 5.1° \pm 0.3°$; Δ LDFA $= 3.4° \pm 0.3°$; $p < 0.001$) (Table 5). For all three alignments, mean values for tibia were varus and valgus for femur. For neutral alignment, MPTA was $85.8° \pm 2.1°$ and LDFA $85.7° \pm 1.8°$; for varus alignment MPTA was $83.3° \pm 2.1°$ and LDFA $87.4° \pm 1.9°$; for valgus alignment MPTA was $88.4° \pm 2.0°$ and LDFA $84.0° \pm 1.8°$.

The mean anatomical values for the three phenotypes according to gender were also collected (Table 6).

The multivariate analysis found significant differences between femoral and tibial angular values according to gender, ethnicity or phenotype. BMI was only associated with HKA. With regard to angular values the AD varies according to age except for HKA and nwJLCA (Table 7).

Discussion

The pertinent findings of this present study demonstrate global neutral lower-limb alignment of the middle-aged population resulted from tibia vara (4°) and ipsilateral femoral valgus (4°). Significant inter-individual variations were observed; women were found to have a higher femoral valgus, with regards to ethnicity, Caucasian patients were

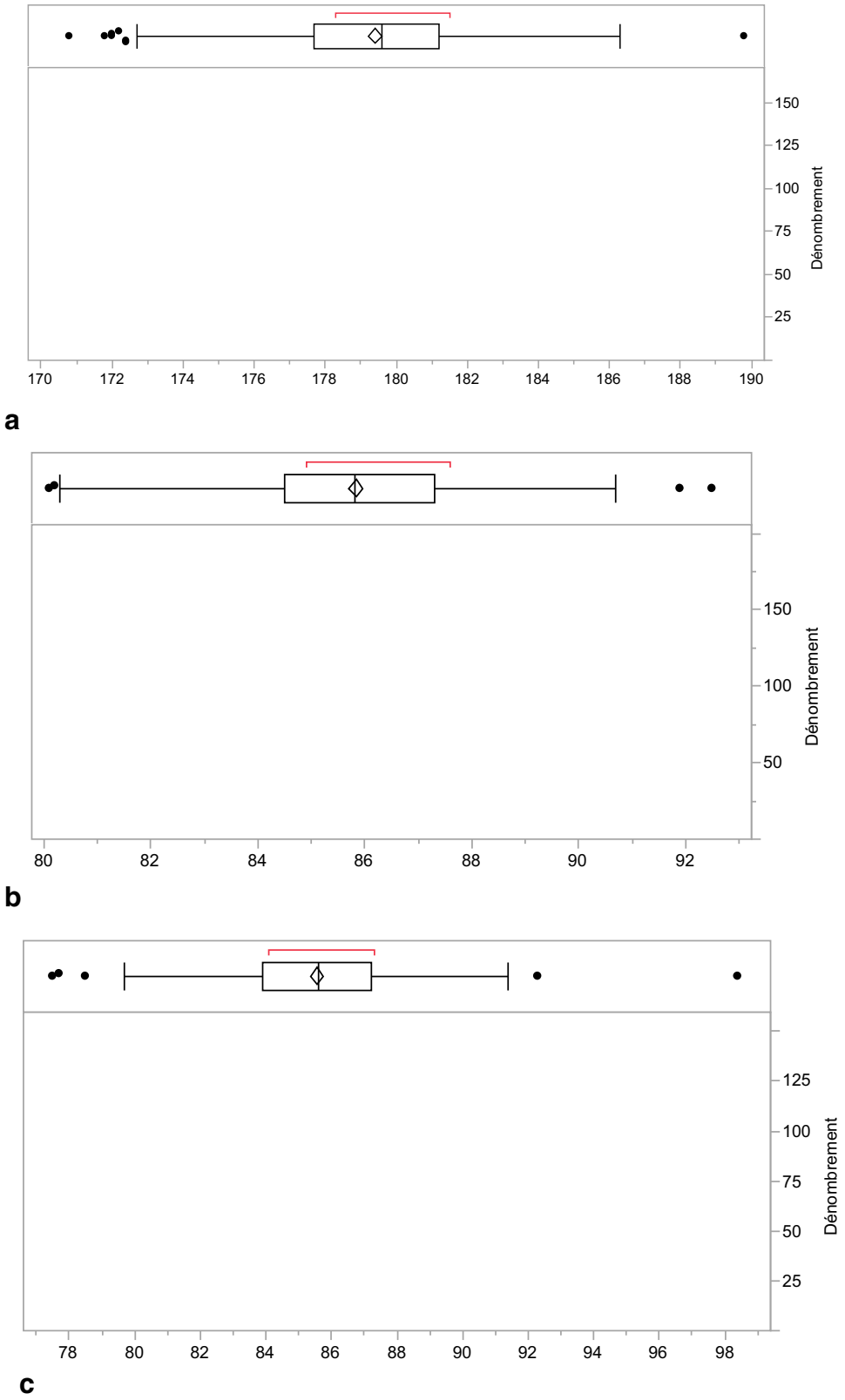
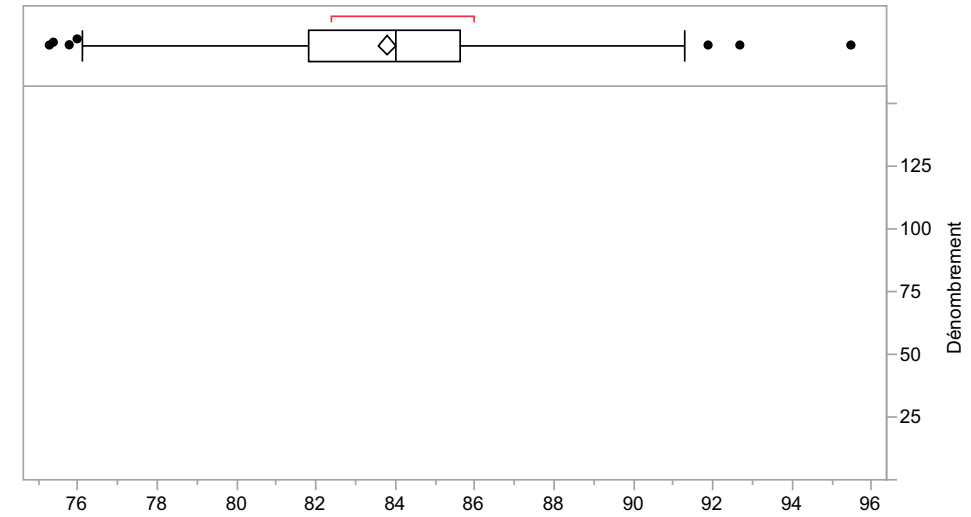


Fig. 2 Distribution of the anatomical measurements. **a** nwHKA non-weight-bearing hip–knee–ankle angle; **b** LDFA lateral distal femoral angle; **c** MPTA medial proximal tibial angle**; d** PPTA posterior plateau tibial angle; **e** PDFA posterior distal femoral angle

observed to have less tibia vara and femoral valgus and finally bone alignment phenotype, differences for most of the lower limb angular values were observed.

The mean HKA was neutral (179.4° ± 2.6°), similar to previously published studies [2, 8, 29]. The overall range of HKA values varied from 170.8° to 189.8° similar to the

Fig. 2 (continued)



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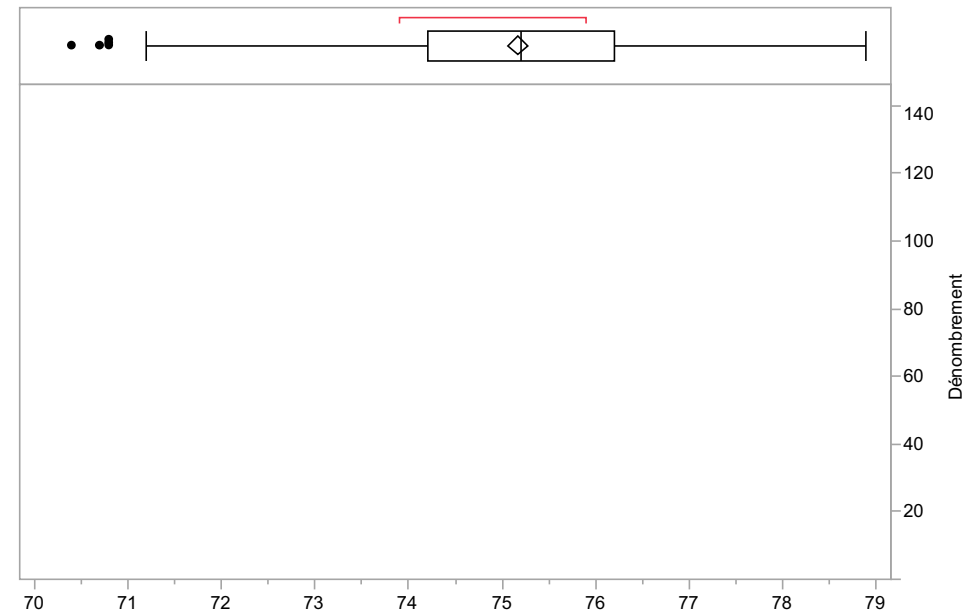

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Table 2 Univariate analysis regarding asymmetry influencing factors; all *p* values calculated using analysis of variance testing (ANOVA)

Factors for MD	HKA	LDFA	MPTA	PDFA	PPTA	nwJLCA
Gender	n.s	n.s	n.s	n.s	n.s	n.s
Age	$p=0.001$ $R^2=0.01$	$p<0.001$ $R^2=0.004$	$p=0.0003$ $R^2=0.006$	$p=0.0005$ $R^2=0.005$	$p<0.0001$ $R^2=-0.003$	n.s
BMI	$p=0.0002$ $R^2=-0.01$	$p=0.004$ $R^2=0.01$	$p=0.03$ $R^2=0.01$	$p<0.0001$ $R^2=-0.01$	$p=0.003$ $R^2=0.009$	n.s
Ethnicity	n.s	n.s	n.s	n.s	n.s	n.s
Neutral alignment	n.s	n.s	n.s	n.s	n.s	n.s

R^2 correlation coefficient, *MD* mean difference, *BMI* body mass index, *HKA* hip–knee–ankle angle, LDFA lateral distal femoral angle, *MPTA* medial proximal tibial angle, *PDFA* posterior distal femoral angle, *PPTA* posterior plateau tibial angle, *nwJLCA* non-weight-bearing joint line convergence angle, *n.s* not significant, *MD* means differences

Table 3 Univariate analysis estimating means angular values between men and women

Anatomic parameters	Men ($n=390$)		Women ($n=368$)		p value
	Mean ± SD	Range (min–max)	Mean ± SD	Range (min–max)	
HKA (°)	178.8 ± 2.5	170.8–189.8	180 ± 2.5	171.8–186.3	< 0.001
LDFA (°)	86.4 ± 1.8	81.2–92.5	85.2 ± 2.0	80.1–90.3	< 0.001
MPTA (°)	85.5 ± 2.4	79.9–98.4	85.6 ± 2.5	77.5–91.4	n.s
PDFA (°)	85.1 ± 1.4	80.4–88.6	85.3 ± 1.6	80.8–88.9	n.s
PPTA (°)	83.6 ± 3.1	75.3–95.5	84 ± 2.7	80.3–91.3	n.s
nwJLCA (°)	1.1 ± 0.8	0–5.2	1.1 ± 1.0	0–6.9	n.s

HKA hip–knee–ankle angle, *LDFA* lateral distal femoral angle, *MPTA* medial proximal tibial angle, *PDFA* posterior distal femoral angle, *PPTA* posterior plateau tibial angle, *nwJLCA* non-weight-bearing joint line convergence angle, *n.s* not significant

Table 4 Univariate analysis estimating means angular values between Caucasian and Asian patients

Anatomic parameters	Caucasian ($n=442$)		Asian ($n=316$)		p value
	Mean ± SD	Range (min–max)	Mean ± SD	Range (min–max)	
HKA (°)	179.6 ± 2.5	170.8–186.1	179.1 ± 2.7	171.8–189.8	< 0.01
LDFA (°)	86.1 ± 1.9	80.1–90.3	85.5 ± 2.1	80.2–92.5	< 0.01
MPTA (°)	86.2 ± 2.2	77.7–92.3	84.7 ± 2.5	77.5–98.4	< 0.01
PDFA (°)	85.3 ± 1.5	80.8–88.9	85.0 ± 1.5	83.9–88.5	< 0.05
PPTA (°)	84.6 ± 2.5	77.0–92.7	82.7 ± 3.1	75.3–95.5	< 0.01
nwJLCA (°)	1.12 ± 0.99	0–6.9	1.06 ± 0.77	0–4.1	n.s

HKA hip–knee–ankle angle, *LDFA* lateral distal femoral angle, *MPTA* medial proximal tibial angle, *PDFA* posterior distal femoral angle, *PPTA* posterior plateau tibial angle, *nwJLCA* non-weight-bearing joint line convergence angle, *n.s* not significant

Table 5 Means difference between the three morphotypes: varus, neutral and valgus

Anatomical parameters	Means differences (Δ varus vs valgus)	95% Confidence interval	p value	Means differences (Δ neutral vs valgus)	95% Confidence interval	p value	Means differences (Δ varus vs neutral)	95% Confidence interval	p value
HKA (°)	8.5	8.0–8.9	< 0.001	4.1	3.7–4.4	< 0.001	4.4	4.2–4.7	< 0.001
LDFA (°)	3.4	2.8–3.9	< 0.001	1.7	1.3–2.2	< 0.001	1.7	1.3–2.0	< 0.001
MPTA (°)	5.1	4.5–5.7	< 0.001	2.6	2.1–3.1	< 0.001	2.5	2.1–2.9	< 0.001
PDFA (°)	1.5	1.0–1.9	< 0.001	0.8	0.4–1.2	< 0.001	0.7	0.4–1.0	< 0.001
PPTA (°)	2.5	1.7–3.4	< 0.001	1.3	0.6–2.0	< 0.001	1.2	0.6–1.7	< 0.001
nwJLCA (°)	0.12	0.14–0.39	n.s	0.47	0.24–0.70	< 0.001	0.34	0.14–0.39	< 0.001

HKA hip–knee–ankle angle, *LDFA* lateral distal femoral angle, *MPTA* medial proximal tibial angle, *PDFA* posterior distal femoral angle, *PPTA* posterior plateau tibial angle, *nwJLCA* non-weight-bearing joint line convergence angle, *Δ* mean absolute difference

results of Hirschmann et al. who demonstrated values of 172.6° to 187.1° [8]. Therefore, the variability of the anatomy can be considered to be wide in all the three groups of our knee phenotypes. Hirschman et al. proposed limb phenotypes that cover a smaller range of values and found 18 to 43 functional knee phenotypes based on HKA, tibial mechanical angle and femoral mechanical angle [8–10].

This classification was not used in the present study even if it shall provide several important advantages concerning the high variability of the native coronal alignment and its clinical applications. Indeed, due to the lack of sagittal angular parameters and comparative analysis for all angular knee parameters between phenotypes in the literature, patients were separated into three phenotypes (varus, neutral and valgus) based solely on the HKA angle.

In this present study the distal femur was approximately in 4° valgus (85.8° ± 2.0°) and the proximal tibia in 4° varus (85.6° ± 2.4°) in contrast to other studies where mean femoral valgus was between 2° and 7° [2, 5, 9, 14] and mean tibial varus between 2° and 3° [5, 27, 31].

Previous studies found MPTA values for men and women similar to this study, thus Nakano et al. showed a MPTA

Table 6 Measurement parameters for all morphotypes and for both genders separately

Parameter	All ($n=758$)			Men ($n=390$)			Women ($n=368$)		
	Varus (HKA < 177°)	Neutral (HKA ± 180°)	Valgus (HKA > 183°)	Varus (HKA < 177°)	Neutral (HKA ± 180°)	Valgus (HKA > 183°)	Varus (HKA < 177°)	Neutral (HKA ± 180°)	Valgus (HKA > 183°)
HKA (°)	175.4 ± 1.3	179.8 ± 1.5	183.9 ± 1.1	175.4 ± 1.2	179.5 ± 1.5	183.9 ± 1.5	175.2 ± 1.4	180.1 ± 1.4	183.9 ± 0.9
LDFA (°)	87.4 ± 1.9	85.7 ± 1.8	84.0 ± 1.8	87.6 ± 1.6	86.1 ± 1.7	85.1 ± 1.5	86.8 ± 2.3	85.3 ± 1.8	83.5 ± 1.7
MPTA (°)	83.3 ± 2.1	85.8 ± 2.1	88.4 ± 2.0	83.6 ± 1.9	85.8 ± 2.0	89.4 ± 2.6	82.7 ± 2.3	85.7 ± 2.2	87.9 ± 1.5
PDFA (°)	84.5 ± 1.6	85.2 ± 1.4	86.0 ± 1.5	84.8 ± 1.4	85.1 ± 1.4	85.7 ± 1.6	84.0 ± 1.9	85.3 ± 1.5	86.2 ± 1.5
PPTA (°)	82.7 ± 3.0	83.9 ± 2.8	85.2 ± 2.9	82.9 ± 3.1	83.6 ± 3.0	86.1 ± 3.8	82.2 ± 2.7	84.1 ± 2.6	84.9 ± 2.5
nwJLCA (°)	1.3 ± 1.1	1.0 ± 0.8	1.5 ± 1.2	1.2 ± 1.0	1.0 ± 0.7	1.5 ± 1.2	1.5 ± 1.4	1.0 ± 0.8	1.4 ± 1.3

HKA hip–knee–ankle angle, *LDFA* lateral distal femoral angle, *MPTA* medial proximal tibial angle, *PDFA* posterior distal femoral angle, *PPTA* posterior plateau tibial angle, *nwJLCA* non-weight-bearing joint line convergence angle

Table 7 Multivariate analysis regarding variation of means differences for factors influencing angular values

Confounding factors for MD	HKA	LDFA	MPTA	PDFA	PPTA	nwJLCA
Gender	$p<0.001$	$p<0.001$	$p<0.05$	n.s	n.s	n.s
Age	n.s	$p=0.01$	$p<0.001$	$p<0.001$	$p<0.05$	n.s
BMI	$p<0.05$	n.s	n.s	n.s	n.s	n.s
Ethnicity	$p<0.05$	$p<0.001$	$p<0.01$	$p<0.001$	$p<0.001$	n.s
Alignment	$p<0.001$	$p<0.001$	$p<0.001$	$p<0.001$	$p<0.001$	$p<0.001$

All p values calculated using multiple analysis of variance testing (MANOVA), *BMI* body mass index, *HKA* hip–knee–ankle angle, *LDFA* lateral distal femoral angle, *MPTA* medial proximal tibial angle, *PDFA* posterior distal femoral angle, *PPTA posterior* plateau tibial angle, *nwJLCA* non-weight-bearing joint line convergence angle, *ns* not significant, *MD* means differences

at 85.6° ± 2.2° for male and 85.1° ± 2.4° for female, Tang et al. found the tibia to be a little more varus for women (84.6° ± 2.5°) than for men (85.1° ± 2.3°) [22, 30] and Bellemans et al. found the opposite results with more varus in the tibia for men (86.5° ± 2.2°) in comparison to women (87.6° ± 1.8°) [2]. Similar to the results of this study, two other authors reported higher valgus in the femur for women than for men [5, 14].

Few studies have evaluated the influence of ethnicity on lower limb angular values. Hovinga et al. found a difference between healthy young Caucasian and Japanese young adults, with a higher varus alignment for Japanese patients [11]. Another study has published similar results with higher varus for the Australian Caucasian populations in comparison to the Japanese population [28]. Knee shape differences in three-dimensional analysis among Caucasian, African and Asian populations were also identified with regards to the size of the distal femur and proximal tibia but not for angular values [19]. There is also noted variation within the range of motion and this differs amongst ethnic groups and subsequently authors have advocated that implants designs for total knee arthroplasty must incorporate these characteristics [18]. If all parameters of our study were significantly different between ethnicity except for JLCA, mean differences (Δ) were weak. Alignment was more varus for Asian population similar to previous studies but only MPTA and PPTA differences were more than 1° for Caucasian subjects. This significant but minor anatomic differences should be clarified to specify whether this might play a role in total knee arthroplasty or osteotomy.

Jabalameli et al. found similar JLCA (1° ± 1.6°) with no differences between gender [14] similar to those findings by Hsu et al. (0.4° ± 1.6°) [12]. However, there is some disagreement in the literature, higher JLCA values were observed by Cooke et al. (1.69° ± 1.34°) and lower values for Bellemans et al. (0.51° ± 1.05°) [2, 5].

This variation could be explained by two reasons: the measurement methods employed and weight bearing conditions. To date, no study has evaluated the JLCA with a high degree of accuracy. The proximal tibial plane was defined to measure JLCA which includes not only the coronal plane but also the sagittal plane. The CT scans in this current study were performed under non-weight bearing conditions; however, this can compromise interpretation of the results, Yazdanpanh et al. observed that the JLCA varies with weight-bearing conditions [34]. Many authors found that BMI and JLCA are associated with higher discrepancy between preoperative alignment planning and postoperative alignment after high tibial osteotomy [16, 17, 24, 33]. The results of the present study showed significant differences for JLCA to be only associated with mechanical alignment.

BMI was only associated with HKA differences and not for other angular values; it has been shown that higher BMI was associated with an increased failure rate after total knee arthroplasty, the same study showed that patients with BMI < 23 kg m^{-2} had an higher failure rate [23]. These results suggest that target's alignment for HKA after knee arthroplasty may vary slightly depending on the BMI.

Finally, neutral alignment was a significant predictor to emphasize the specificity of each angular value, and this is probably the most important reason of them all. The mean AD between neutral versus varus and neutral versus valgus alignment was similar with highest values for MPTA and LDFA. Differences of mean AD between varus and valgus were significant for all anatomical parameters except for JLCA. These observed results may have a major impact on knee osteotomy which is performed mostly according to the measurement of the HKA. Phenotype alignment based on HKA without considering LDFA and MPTA may lead to unexpected discrepancy of the correction angle or inappropriate correction with poor clinical results.

Mean values of varus on tibial side and valgus on femoral side were 4°; these values are higher than those in previously published studies [2, 5, 27, 31]. This point is important to consider because an overcorrection can lead to unphysiological loading. Thus, when planning high tibial or distal femur osteotomy, the surgeon needs to take into account that the normal physiological value of femoral and tibial bone morphology is 4° of valgus and 4° of varus, respectively.

This study has limitations. Considering the retrospective nature of the database evaluation, it was not possible to evaluate information regarding patient's social behaviour such as sport and activity level. Concerning patient selection, only asymptomatic knees without bony abnormalities were included; however, this population does not represent patients requiring operative knee treatment. The use of the SOMA database allows assessment of demographic variations with an underlying aim to develop orthopaedic implants for both osteoarthritic and non-osteoarthritic knees. However, there are limitations; the patient's medical history is unknown and only patients that have attended hospital were included in the database, both of which could lead to selection bias. However, the reported values are clinically accepted and represent a large demographic group, which inherently allows the current study to perform secondary analyses with statistical power.

The accuracy of the CT scan-based modelling and analysis system supported the intrinsic value of the study. Arbitrary landmarks for angular measurements were defined and set. This then allowed the automated software to replicate these landmarks on subsequent scans of individual subjects giving rise to reproducible and accurate angular measurements. Most previous published series relied on long leg radiographs; however, this study used 3D-reconstructed CT scans to investigate variability among gender, age, ethnicity and knee phenotype. The data accrued and analysed from this study confirm that there is a correlation between these parameters and the knee's angular values. However, the measurements were limited to the Caucasian and Asian population only and data focusing on other ethnicities needs to be explored.

The clinical relevance to define normal angular values in non-osteoarthritic knees in cases of osteotomy is critical. Substantial correction of the tibial or femoral metaphysis could result in very abnormal bony anatomy (for example; 10° owHTO for a MPTA of 83° tibia will produce a 93° MPTA which would represent an uncommon bony morphology in our series (< 0.5%). With regard to total knee replacement, alignment strategies such as anatomical alignment or kinematic alignment were often based on Hungerford and Krakow definitions of tibial and femoral frontal angular values [13]. Those strategies fit with physiological native and healthy patients' knees.

Conclusion

Even if significant differences were found based on subgroup analysis (gender, ethnicity or phenotype), this study demonstrated that neutral alignment is the main morphological pattern in the healthy middle-aged population. This neutrality is the result from tibia vara compensated by an ipsilateral femoral valgus.

Author contributions MO, KK and SP: designed the protocol and performed statistical analysis; SL and FA: collected the Data; GM: wrote the initial draft and perform edition the different version of the manuscript; MO, KK and SP: corrected the different versions of the draft. All the authors approved the submitted version.

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Compliance with ethical standards

Conflict of interest GM, CJ, AS have nothing to disclose. MO and KK are educational consultant for Stryker, Arthrex and Newclip. FA and SL are paid employee of Stryker. SP is educational consultant and receive royalties from Zimmer Biomet.

Ethical approval The local ethics committee approved our study protocol prior to investigation (number: 2019-015333-13).

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