

Leg Alignment in Adolescence and the Effects of Activity – a Full Leg Length MRI Study

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ABSTRACT

Introduction:

Activity levels during adolescence influence bone and joint development, and intense sporting activity is associated with the development of cam morphology of the hip. The aim of this study was to explore the relationship between leg alignment and i) activity levels ii) cam morphology.

Methods:

Prospective cross-sectional cohort study of individuals from football club academies and an age-matched control population. Assessments included questionnaires, clinical examination, and full leg length MRI scans. Primary imaging outcome measures were the hip knee angle (HKA), medial proximal tibial physeal angle (MPTPhyA), and hip alpha angle.

Results:

The cohort comprised 58 elite male footballers, 34 male controls, and 34 female controls aged 11-21 years. HKA decreased with age (increased varus), with the greatest change between 13 and 16 years (HKA 1.11 degrees (SD 2.10)), with no significant change after 16 years. Skeletally mature elite male footballers had a HKA 2.28 degrees less than male controls ($p<0.001$) and 3.73 degrees less than female controls ($p<0.001$). Negative correlations existed between HKA and Physical Activity Questionnaire Score (coefficient -0.24, $p=0.029$), and between HKA and hip alpha angle (coefficient -0.75, $p = 0.003$). A positive correlation existed between HKA and MPTPhyA (coefficient 0.32, $p = 0.008$).

Conclusions:

High activity levels during adolescence are associated with the development of cam morphology and increased varus leg alignment that develops between age 13 to 16 years. The development of varus alignment may represent a physiological adaptation to load at the proximal tibial physis, as previously shown at the proximal femoral epiphysis.

INTRODUCTION

Varus or valgus leg alignment (genu varum or valgum) increases the risk of developing knee injury and osteoarthritis[1-4] and is associated with higher tensions of the ACL[5, 6], meniscal tears[7], and patellofemoral pain syndrome[8-10]. Modification of risk factors for the development of limb malalignment may enable the prevention of injury and osteoarthritis.

Changes in leg alignment during early childhood are well documented[11], but changes in limb alignment during adolescence are less well characterized as the distal femoral physis and proximal tibial physis mature[12]. The development of genu varum during late childhood has been observed in athletic cohorts[13], but is less common in general population cohorts[14]. The age at which genu varum develops is unclear with some studies stating 13-14 years of age[12, 13, 15], and others 16 years of age[10].

Leg alignment is determined by both modifiable and non-modifiable parameters, which include gender[16, 17], obesity[18], and athletic activity[12, 15]. A higher prevalence of varus leg alignment exists in retired soccer players than a general population of the same age[19], and studies have shown that athletic activity is associated with greater varus leg alignment in males[12, 15]. In skeletally mature cohorts there is also an association between varus knee alignment and cam morphology, that is thought to develop secondary to intense sporting activity during adolescence[20-23]. However, the majority of these studies are retrospective and based on clinical examination measures[10, 12, 13, 15]. It is not known what morphological characteristics are responsible for the observed changes in leg alignment, and whether these changes take place during adolescence, as seen with cam morphology of the hip.

The aim of this study were to explore the association between leg alignment and i) physical activity level and ii) cam morphology during adolescence.

METHODS

The study was approved by our institution's Inter-Divisional Research Ethics Committee (MSDIDREC- C2-2013-11).

Study design

Prospective cross sectional observational cohort study.

Population

Individuals aged 11–21 years were recruited from an existing cohort (FAIM) comprising Southampton Football Club (SFC) Academy and Oxford United Football Club (OUFC) Academy players, and local school children (controls)[23]. Participants were invited via post, email, and telephone. Four individuals declined to participate, two did not attend their arranged appointment, and thirty individuals did not respond to invitation. Participants completed a questionnaire and underwent MRI scanning of both legs.

Activity Levels

Activity was evaluated using two methods: i) SFC and OUFC Academy (elite footballer cohort) versus general population controls; ii) Physical Activity Questionnaire (PAQ) for older children (aged 9–13 years) and adolescents (aged 14–18 years)[24]. The PAQ collects information on sport and exercise undertaken during an average week and provides a summary score of physical activity levels (a score of 1 indicates low physical activity, whereas a score of 5 indicates high physical activity)[25].

Imaging Protocol

Leg length and femoral morphology were assessed using a 3 Tesla Philips Achieva platform and torso coil (Philips Healthcare). Stacked T1 weighted Turbo Spin Echo (TSE) coronal pelvis was used to image whole leg length: Turbo factor 5, Number of Sampling Excitations (NSA 2),

FOV 490mm x 351 mm x 278mm, 10% overlap of FOV for stacking T1, 5 stacks along the coronal lower limb plane, voxel size 1.44 x 1.44 x 8mm reconstructed acquisition spatial resolution 1.8 x 2.6 x 8, no SENSE, reconstruction matrix 336mm x252mm, Repetition Time (TR) 1008ms, Echo Time (TE) 7.6ms, number of slices 31, slice gap 1mm, half scan 70%. Leg length sequences were acquired with participants supine with patellae perpendicular to the table and feet shoulder width apart. Weight bearing was simulated using a platform beneath the feet with 50% of the weight of a participant applied perpendicular to the axis of the lower limbs using rope and pulleys. The field of view was aligned on the centre of the femoral head and talus in the sagittal plane and images of the pelvis to mid femur, femur to mid tibia, and mid tibia to sole of the foot were stitched together to produce a single image that includes both lower limbs.

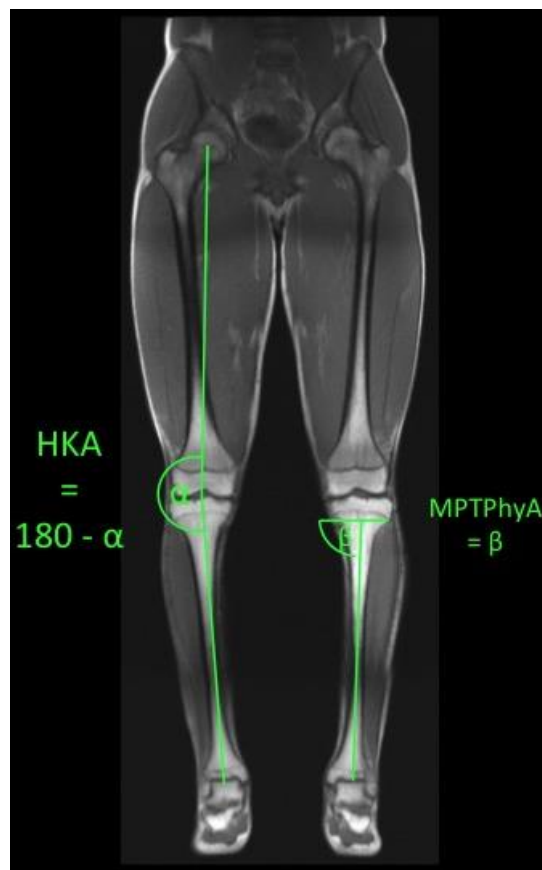
Three-dimensional (3D) water selective fluid (WATSf): 3D WATSf sequence was used to image femoral head morphology. The coronal axis (12 o'clock position) was positioned parallel to the axis of the proximal femur diaphysis[23]. Sequence variant = 3D Gradient/Fast Field Echo with binomial pulse (1:3:3:1); Repetition time (TR) = 13.65ms; Echo time (TE) = 6.9ms; excitation Flip angle = 30 degrees; bandwidth = 145Hz/pixel; interpolated voxel size 0.29mm x 0.29mm x 0.4mm; averages= 2; acquired in true sagittal orientation. 3D multiplanar reconstructions were performed using OsiriX Software (V.6.0.2, Pixmeo).

Imaging Outcome Measures

The primary outcome measure in this study was the Hip Knee Angle (HKA). The HKA is defined as the angle formed by the intercept of the femoral mechanical axis and the tibial mechanical axis[26-29]. The HKA is expressed as a deviation from 180° with a negative value

for varus alignment and a positive value for valgus alignment[30] (Figure 1). HKA was treated as a continuous variable. Medial tibial physeal morphology was quantified using the Medial Proximal Tibial Physis Angle (MPTPhyA) (Figure 5-3). MPTPhyA is defined as the medial intercept between the anatomical axis of tibia and the physeal line of the proximal tibia[30]. (Figure 1)

Figure 0- Full leg length weight bearing MRI of a 16 year old male showing Hip-Knee-Angle (HKA) and Medial Proximal Tibial Physis Angle (MPTPhyA) measures.



Cam morphology was quantified using the alpha angle for cartilage on radial slices at 11 o'clock, 12 o'clock, 1 o'clock, 2 o'clock, and 3 o'clock. Alpha angle was calculated by drawing a line from the centre of a best-fit circle surrounding the femoral head to the midpoint of a line transecting the narrowest portion of the femoral neck. A further line was then drawn from the centre of the best-fit circle to where the contour of the femoral head first exits this circle. The alpha angle is the angle between these two lines. Cartilage alpha angle was selected because in skeletally immature hips the ossified regions of the femoral head do not reflect the overall hip shape. The mean alpha angle from 11 o'clock to 3 o'clock was taken as the primary measure of cam morphology in this study.

Statistical Analysis

Statistical calculations were performed using STATA V.14.1 (College Station, Texas, USA). Distribution of values was examined using histograms and kernel density plots. Inverse probability weighting with regression adjustment modelling[31] was adopted to assess variables that predict leg alignment to account for selection bias. Multivariate linear regression modeling was used to evaluate the relationship between variables. Variables included in the multivariate analysis were cohort, age, gender and activity level. Interactions were evaluated with linear regression of each combination of variables that are associated with HKA. None reached statistical significance; hence no interaction terms were included in the multivariate models. Statistical significance was set at $p < 0.05$.

Reproducibility was studied for each of the imaging outcome measures adopted in this study; HKA, MPTPhyA, and alpha angle. Measurements were repeated by the principal investigator a minimum of 1 month after the initial measurements (intra-observer reproducibility), and also by a clinical research fellow with experience of musculoskeletal imaging research (inter-

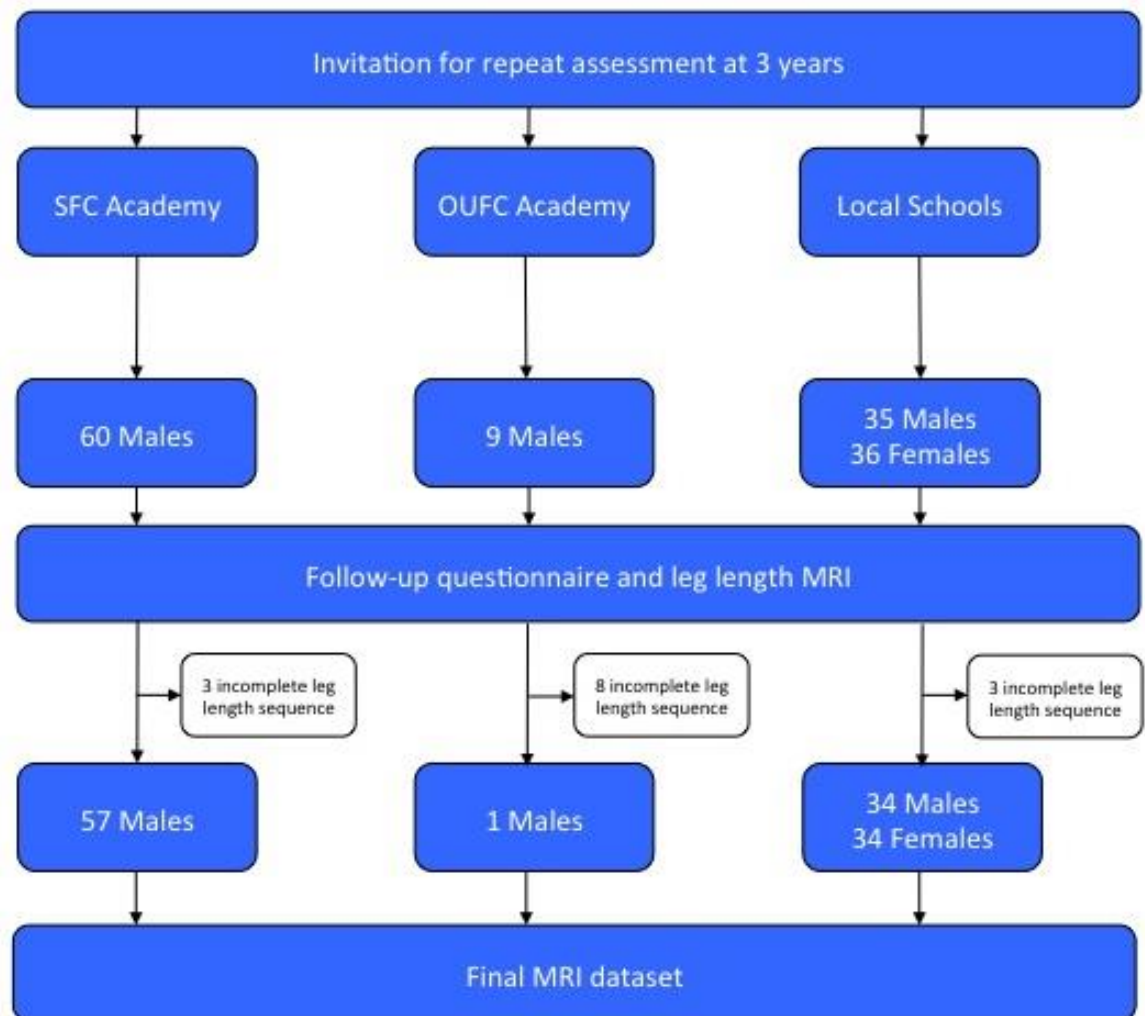
observer reproducibility). Ten imaging sets were selected at random from the cohort for reproducibility measures. Reproducibility was assessed using intra-class and inter-class correlations (ICC), the smallest detectable difference (SDD), and the Root Mean Square of the Coefficient of Variance (RMSCoV). SDD was calculated as the standard deviation of the mean difference between readings multiplied by 1.96 and RMSCoV was calculated as the root mean square of the change divided by the mean, multiplied by 100[32].

RESULTS

Participant demographics

140 individuals (280 legs) (mean age 185 months, SD 32 months) completed leg length MRI scans. Leg length MRI sequence outcomes were incomplete in 14 individuals (28 legs) due to movement artefact. The cohort with completed scans comprised 58 elite male footballers (mean age 178 months (SD 29 months)), 34 male controls (mean age 185 months (SD 32 months)), and 34 female controls (mean age 197 months (SD 35 months)). (Figure 2) (Table 1)

Figure 2 - Recruitment flowchart for study.



Change in Leg Alignment with Age

HKA

HKA decreased with age in all participants up to 16 years, after which no significant change was observed. . Mean leg alignment values for each age group were valgus up to 14 years of age (1.10 degrees (SD 1.98)) and became varus from 15 years (-0.40 degrees(SD 2.28)). (Table 1) (Figure 3) Individuals with an open physis had valgus leg alignment and individuals with a closed physis had varus leg alignment. Adjusting for activity level and gender,

individuals with a closed physis had a HKA 1.37 degrees less than individuals with an open physis ($p<0.001$). (Table 2)

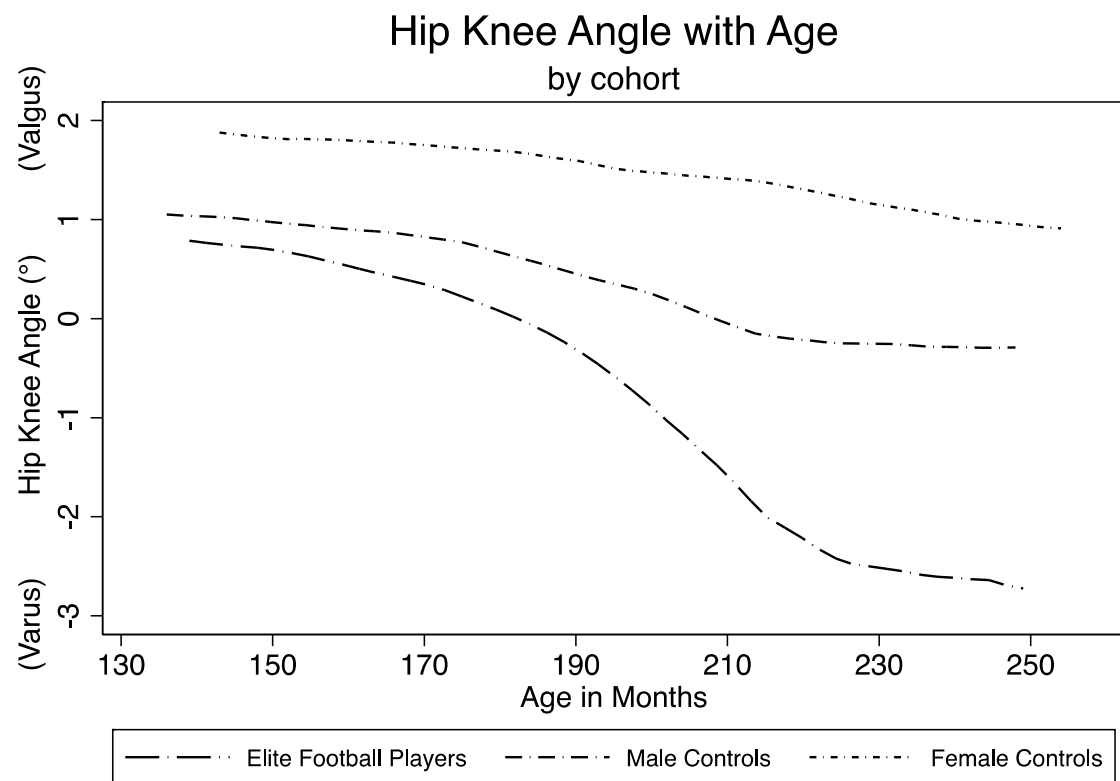
Table 1 - Hip Knee Angle, and Medial Proximal Tibial Physeal Angle, and hip alpha angle by Cohort and Age Group.

Age (years)	Individuals (Legs)	Hip Knee Angle Mean(\pm SD)	Medial Proximal Tibial Physeal Angle Mean(\pm SD)	Alpha Angle Mean(\pm SD)
All Individuals				
11-12	24 (48)	1.19 (\pm 1.75)	92.56 (\pm 2.87)	55.57 (\pm 7.90)
13-14	41 (82)	1.11 (\pm 2.10)	93.19 (\pm 2.90)	62.10 (\pm 8.56)
15-16	24 (48)	-0.30 (\pm 2.63)	92.01 (\pm 3.49)	61.89 (\pm 8.94)
17-18	20 (40)	-0.29 (\pm 2.02)	91.73 (\pm 3.79)	62.09 (\pm 13.07)
Over 18	17 (34)	-0.54 (\pm 2.01)	90.74 (\pm 3.15)	60.47 (\pm 8.46)
Average	126 (252)	0.38 (\pm 2.25)	92.27 (\pm 3.32)	60.60 (\pm 9.62)
Male Footballers				
11-12	12 (24)	0.86 (\pm 1.54)	90.92 (\pm 2.13)	57.61 (\pm 9.58)
13-14	23 (46)	0.97 (\pm 2.40)	92.91 (\pm 2.73)	65.18 (\pm 8.91)
15-16	12 (24)	-1.54 (\pm 2.70)	90.41 (\pm 2.58)	64.08 (\pm 10.79)
17-18	5 (10)	-2.49 (\pm 1.39)	89.19 (\pm 3.37)	72.73 (\pm 9.76)
Over 18	6 (12)	-2.79 (\pm 0.58)	88.57 (\pm 2.84)	62.69 (\pm 12.11)
Average	58 (116)	-0.40 (\pm 2.59)	91.11 (\pm 3.15)	63.78 (\pm 10.49)
Male Controls				
11-12	6 (12)	0.43 (\pm 1.78)	92.85 (\pm 1.94)	53.85 (\pm 6.02)
13-14	11 (22)	1.53 (\pm 1.44)	92.72 (\pm 2.25)	58.05 (\pm 7.08)
15-16	7 (14)	-0.10 (\pm 1.46)	93.07 (\pm 2.80)	60.80 (\pm 7.07)
17-18	7 (14)	-0.56 (\pm 1.29)	92.28 (\pm 3.27)	67.99 (\pm 11.72)
Over 18	3 (6)	0.20 (\pm 0.76)	92.93 (\pm 1.82)	60.49 (\pm 2.95)
Average	34 (68)	0.45 (\pm 1.62)	92.77 (\pm 2.41)	60.14 (\pm 8.95)
Female Controls				
11-12	6 (12)	2.60 (\pm 1.37)	95.57 (\pm 2.47)	53.21 (\pm 4.49)
13-14	7 (14)	0.89 (\pm 1.92)	94.85 (\pm 3.85)	58.39 (\pm 5.02)
15-16	5 (10)	2.42 (\pm 1.38)	95.90 (\pm 3.85)	58.16 (\pm 4.17)
17-18	8 (16)	1.31 (\pm 1.39)	93.71 (\pm 3.52)	50.29 (\pm 3.39)
Over 18	8 (16)	0.85 (\pm 1.49)	91.64 (\pm 2.86)	58.79 (\pm 6.35)
Average	34 (68)	1.51 (\pm 1.65)	94.20 (\pm 3.60)	55.63 (\pm 5.91)

Table 2 - Predictors of change in Hip Knee Angle. *Age and cohort as covariables. **Age, gender and activity level as covariables. *Physcal maturity, gender, and activity levels as covariables**

		Legs	Mean HKA (±SD)	Univariate regression			Multivariate regression 1*			Multivariate regression 2**			Multivariate regression 3***		
				Coefficient	95% CI	P value	Coefficient	95% CI	P value	Coefficient	95% CI	P value	Coefficient	95% CI	P value
Age at baseline	Months (continuous)	252					-0.031	-0.04 to -0.03	<0.001	-0.03	-1.94 to -1.23	<0.001			
Physis	Open	136	0.82 (±2.09)	-0.88	-1.43 to -0.34	0.002							-	-	-
	Closed	116	-0.07 (±2.32)	-	-	-							-1.37	-1.95 to -0.78	<0.001
Gender	Male	186	-0.03 (±2.31)	-2.05 to 1.02	-1.91 to -1.17	<0.001				-1.48	-2.05 to -0.90	<0.001	-1.68	-2.44 to -0.91	<0.001
	Female	68	1.51 (±1.65)	-	-	-				-	-	-	-	-	-
BMI		252	-	-0.04	-0.07 to -0.01	0.036									
Dominant leg	Dominant	139	0.58 (±2.10)	0.44	-1.00 to 0.12	0.127									
	Non Dominant	115	0.14 (±2.42)	-	-	-									
Cohort	Footballers	118	-0.31 (±2.59)	-	-	-	-	-	-	-					
	Male controls	68	0.45 (±1.62)	0.76	0.16 to 1.36	0.013	1.04	0.48 to 1.61	<0.001						
	Female controls	68	1.51 (±1.65)	1.81	1.21 to 2.42	<0.001	2.22	1.61 to 2.84	<0.001						
PAQ	Linear	252								-0.74	-0.97 to -0.52	<0.001	-0.76	-1.12 to -0.40	<0.001

Figure 3 - Hip Knee Angle (HKA) with age for elite footballers, male controls, and female controls.
Polynomial regression fit with 95% CI.



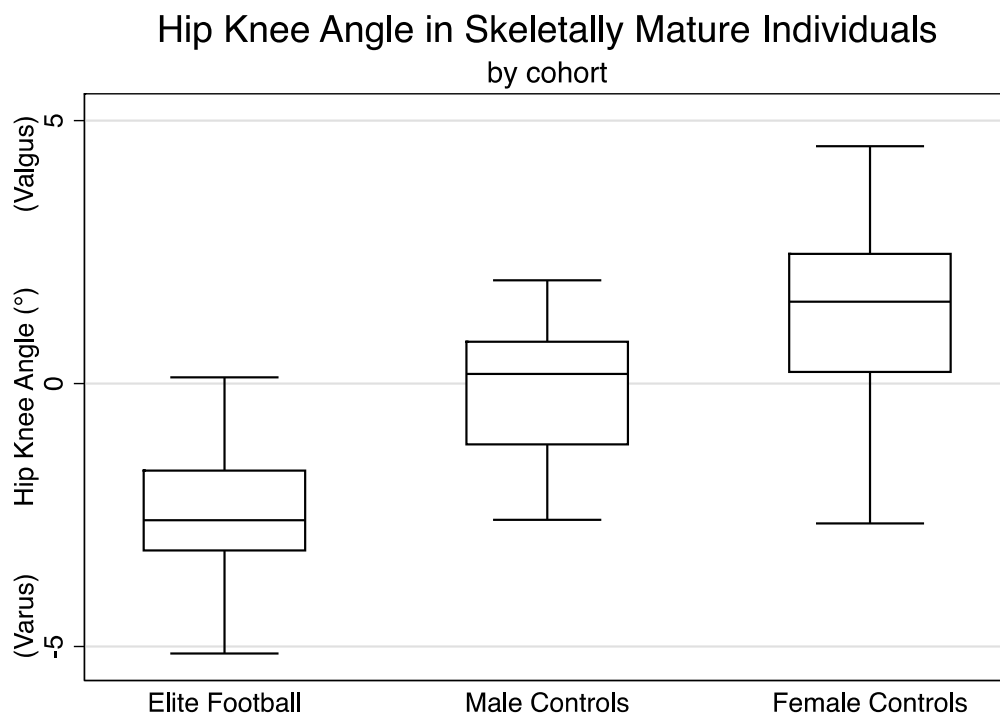
Male controls had a decrease in HKA with age, changing from valgus to varus alignment after 14 years of age. Female controls also showed a general decrease in HKA with age, but remained in valgus alignment throughout all age groups. (Table 1)

Factors Associated With Leg Alignment

Elite level football players had significantly more varus leg alignment than controls. Adjusting for age, elite male footballers had a HKA 0.87 degrees less than male controls

($p < 0.001$) and 2.22 degrees less than female controls ($p < 0.001$) (Table 2). In skeletally mature individuals mean HKA for elite male footballers was -2.38 degrees (SD 2.01, range -6.85 to 3.44), for male controls was -0.97 degrees (SD 1.23, range -2.59 to 1.96), and for female controls was 1.35 degrees (SD 1.68, range -2.66 to 4.51). Elite male footballers had a HKA 2.28 degrees less than male controls ($p < 0.001$) and 3.73 degrees less than female controls ($p < 0.001$). (Figure 4)

Figure 4 - Hip Knee Angle in Skeletally Mature Individuals by Cohort. Box and whisker plot.



Males had significantly more varus leg alignment than females. Adjusting for age and activity level, males had a HKA 1.48 degrees less than females ($p < 0.001$) (Table 2). Adjusting for age and activity levels, skeletally mature males had a HKA 2.05 degrees less than females ($p < 0.001$).

Individuals with high activity levels (PAQ score) had significantly more varus leg alignment than individuals with low activity levels. Adjusting for age and gender in a multivariate linear regression model there was a significant negative association between PAQ score and HKA (coefficient -0.24, $p=0.029$). Adjusting for gender in skeletally mature individuals there was a significant negative linear relationship between PAQ score and HKA (coefficient -0.54, $p=0.028$).

Significant association was seen between BMI and HKA in univariate but not multivariate regression analysis. There was no significant association between leg dominance and HKA. (Table 2)

Mechanism of Varus Knee Morphology Formation

Mean Medial Proximal Tibial Physis Angle (MPTPhyA) was 92.27 degrees (SD 3.32 degrees) (Table 1). In this study individuals with a lower MPTPhyA had more varus leg alignment. A positive linear relationship existed between MPTPhyA and HKA (coefficient 0.32, $p = 0.008$). Elite level football players had significantly lower MPTPhyA values than controls. Adjusting for age, elite male footballers had MPTPhyA 1.85 degrees lower than male controls ($p<0.001$) and 3.51 degrees lower than female controls ($p<0.001$). Individuals with high activity levels (PAQ score) had a significantly lower MPTPhyA than individuals with low activity levels. There was a negative linear relationship between PAQ score and MPTPhyA (coefficient -0.05, $p=0.025$).

Cam hip morphology and Leg Alignment

In this study individuals with a high alpha angle had more varus leg alignment. A negative linear relationship existed between average alpha angle and HKA (coefficient -0.75, $p = 0.003$).

Reproducibility

HKA: Intra observer ICC was 0.99 (95% CI: 0.97 – 0.1.00), SDD was 0.83, and RMSCoV was 30.22%. Inter-observer ICC was 0.95 (95% CI: 0.91 – 0.99), SDD was 1.60, and RMSCoV was 57.61%.

MPTPhyA: Intra observer ICC was 0.92 (95% CI: 0.85- 0.99), SDD was 1.99, and RMSCoV was 1.10%. Inter-observer ICC was 0.91 (95% CI: 0.83 – 0.99), SDD was 2.16, and RMSCoV was 1.21%.

Alpha Angle: Intra observer ICC was 0.99 (95% CI:0.98 – 1.00), SDD was 3.39 degrees, and RMSCoV was 3.00%. Inter-observer ICC was 0.91 (95% CI:0.87 – 0.95), SDD was 4.22 degrees, and RMSCoV was 4.61%.

DISCUSSION

The aim of this study was to investigate the development of leg alignment with age and to characterise the risk factors for varus leg alignment. Identifying individuals at risk of varus alignment may allow the development of preventative strategies. This study demonstrates that males undertaking intense exercise between the ages of 11 and 16 years are at greatest risk of developing varus leg alignment, which may be secondary to changes at the medial proximal tibial physis.

Change in Leg Alignment with Age

Studies have demonstrated that leg alignment progresses from varus alignment in the infant to valgus alignment in early childhood then back towards neutral alignment prior to adolescence[11, 14, 36]. However, changes in leg alignment during adolescence have not been well characterised due to a lack of imaging studies.

Our results demonstrate that leg alignment continues to move from valgus towards varus during adolescence. In this study a decrease in HKA was present in all individuals from 11 years of age until skeletal maturity. The greatest change towards varus alignment occurred between the ages of 14 and 15 years, with no significant decrease in HKA occurring after 16 years.

These findings agree with previous reports, and the change from valgus to varus alignment in males at 14-15 years corresponds to clinical examination findings from previous studies[10, 12]. However, our results would suggest that leg alignment stops evolving after 16 years of age. This disagrees with the clinical findings of Thijs et al[12] who suggested the intermalleolar distance increased up until 18 years of age. Clinical assessment of leg alignment is likely to be more susceptible to measurement error than imaging outcomes and may also be influenced by soft tissue in addition to bone morphology. In addition, the cohort used by Thijs et al consisted of entirely caucasian males, none of whom practiced football. The comparative diversity in ethnicity, gender, and sports practice in the cohort may limit generalisability to other cohorts.

Leg alignment is believed to be primarily determined by growth at the distal femoral physis and proximal tibial physis mature[12]. In this study individuals with an open physis had valgus leg alignment and individuals with a closed physis had varus leg alignment. This furthers the argument that leg alignment changes take place in the immature skeleton, and agrees with previous reports that moving from valgus to varus alignment continues until the completion of skeletal growth[36].

Risk Factors for Varus Leg Alignment

Our results demonstrate that activity level and gender play a significant role in the development of varus leg alignment. In skeletally mature individuals elite male footballers had a HKA 2.28 degrees less than male controls and 3.73 degrees less than female controls. Higher PAQ scores were also significantly associated with more varus leg alignment.

While athletes have been shown to have more varus HKA values in adult cohorts[16, 30], the effects of high activity on the HKA in adolescents was previously unknown. The degree of varus alignment in skeletally mature elite level footballers in this study compares favourably with elite football players from previous adult cohorts where HKA was -2.7 to -3.2 degrees[30]. Skeletally mature control males in this study also had a comparable mean HKA compared to controls from previous cohorts where HKA was -0.9 degrees[30]. Although the differences in HKA between cohorts and age groups appear small they remain greater than the intra-observer and inter-observer smallest detectable difference, which were 0.83 degrees and 1.60 degrees respectively. Moreover, these small values are likely to be clinically significant, as a leg alignment deviation of only 3 degrees from neutral is considered pathological[16, 37].

Males had significantly more varus leg alignment than females. Although males on average had higher PAQ scores, this was controlled for in the regression models. This finding is in agreement with reports from other cohorts where males showed greater clinical and imaging measures of varus alignment[16, 17, 30]. However, female controls in this study showed a mean valgus leg alignment, whereas a mean varus alignment has previously been reported in female control cohorts[30]. Females reach skeletal maturation earlier than males, as such significant changes in leg alignment prior to 11 years may be taking place that this study has not accounted for. Further research with a greater age range comparing male and female elite athlete cohorts is required to fully elucidate the role of gender in the development of leg alignment.

It has been previously suggested that the kicking movement might be partly responsible for the difference in HKA between elite football players and controls[10, 13, 15]. However, in our study there was no significant difference between the dominant and non-dominant legs of elite footballers or controls, which is in agreement with the findings of Colyn et al[30].

Association between Femoral Morphology and Leg Alignment

In this study individuals with a high alpha angle had more varus leg alignment. Cam morphology is thought to develop around 11-14 years of age[23], when individuals are developing varus leg alignment. Possible explanations are that loading forces applied to the proximal femoral physis and proximal tibial physis cause morphology adaptation at both sites. However, it is also possible that changes at one physis affect loading at other physes. An association between cam morphology and abnormal leg alignment has

previously been identified in adult cohorts, where individuals with tibia vara were more likely to have cam morphology[20, 21]. Further study is required to elucidate the extent of the relationship between activity levels and morphological changes at the physis and epiphysis.

Mechanism of Varus Leg Alignment Development

Varus leg alignment was associated with lower MPTPhyA values in this study. The mechanism of development of varus leg alignment is not well understood, however a low medial proximal tibial angle has been associated with varus leg alignment in previous adult imaging studies[30]. The aetiology of genu varum is likely multifactorial but biomechanical overloading of the proximal medial tibial physis is a possible pathomechanism[33-35]. Besier et al[38] measured external loading of the knee joint during running and cutting manoeuvres. They reported that varus and valgus loads placed on the joint increased dramatically during cutting tasks compared with normal running. Cook et al[34] showed that mechanical overload of the physis leads to a progressive deformity. Varus alignment is likely to represent a potentially modifiable physiological adaptation to load. Indeed, it has been suggested that developmental genu varum may be beneficial for balance and stability during youth[39] and may therefore offer an advantage in adolescent elite footballers.

Limitations

The main limitation of this study is the possible selection bias, with x number from the FAIM cohort not participating. The study design allows exploration of association but not casuation. Furthermore, it is not possible to comment on the change in leg alignment

within individuals over time based on the findings from this study. Further limitations apply to the measurement methodology of full leg length MRI scans, the use of which has not previously been validated. However, our measurement methodology showed high reproducibility. Moreover, there is no agreed diagnostic threshold for varus leg alignment.

Conclusion

The development of varus leg alignment is greatest age 13 to 16 years. There is no significant change in leg alignment after 16 years of age or after skeletal maturity. Physical activity during adolescence is strongly associated with the development of varus leg alignment in males. A lower MPTPhyA value is likely to represent physiological adaptation to load and be the mechanism by which varus leg alignment develops.

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