Development of genu varum in achondroplasia

RELATION TO FIBULAR OVERGROWTH

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Genu varum in the achondroplastic patient has a complex and multifactorial aetiology. There is little mention in the literature of the role of fibular overgrowth. Using the ratio of fibular to tibial length as a measurement of possible fibular overgrowth, we have related it to the development of genu varum. Full-length standing anteroposterior radiographs of 53 patients with achondroplasia were analysed. There were 30 skeletally-immature and 23 skeletally-mature patients. Regression analysis was performed in order to determine if there was a causal relationship between fibular overgrowth and the various indices of alignment of the lower limb.

Analysis showed that the fibular to tibial length ratio had a significant correlation with the medial proximal tibial angle and the mechanical axial deviation in the skeletally-immature group. We conclude that there is a significant relationship between fibular overgrowth and the development of genu varum in the skeletally-immature achondroplastic patient.

The aetiology of achondroplasia is related to a mutation of the gene for fibroblast growth-factor receptor which causes inappropriate differentiation of the growth plate and a deficiency of endochondral growth.^{1,2} The condition was described by Parrott³ in 1878 and is the most common form of dwarfism, characterised by disproportionately short limbs which are rhizomelic in nature. Genu varum and ankle varus are common associated deformities.⁴

The possible causes of genu varum are deficient endochondral ossification, irregular development of the growth-plate cartilage, laxity of the lateral collateral ligament⁵ and a differential growth rate between the tibia and fibula. It has also been suggested, based on histological evidence, that fibular overgrowth is the cause.⁶ Others have proposed a combination of overgrowth of the fibula and laxity of the lateral collateral ligament in juveniles, and fibular overgrowth alone in adolescents.⁷ It has also been stated that there is no relationship between overgrowth of the fibula and the development of genu varum in achondroplasia.⁸ We have, therefore, attempted to ascertain whether a long fibula is genuinely associated with the development of genu varum and if so, how it might affect the various indices which may be used for measuring alignment of the lower limbs. In addition, we

have also considered the relationship of overgrowth to skeletal maturity and gender.

Patients and Methods

Between 1996 and 2004, 53 achondroplastic patients who had mild to severe varus deformity were treated in our hospital (Korea University, Guro Hospital) for deformities of the lower limb. There were 29 females and 24 males with a mean age of 18.2 years (1 to 48). The clinical diagnosis was supported by radiological findings in all patients.⁹ The patients were divided into two groups depending on whether they had reached skeletal maturity. They were diagnosed as being skeletally immature if the epiphyses were seen to be still open on radiographs of the lower limb. On this basis, there were 30 skeletally-immature and 23 skeletally-mature patients.

All patients had full-length standing anteroposterior (AP) radiographs taken with the patellae pointing forwards using a 51-inch cassette at a tube distance of ten feet. Also, radiographs of the calcaneum and the distal tibia were obtained. For these, the foot was positioned at 90° to the tibia and the x-ray beam angled at 45° to the x-ray plate for measurement of the tibiocalcaneal angle.^{10,11}

Radiological analysis. Various indices were measured on the AP standing film and the calcaneal axial radiographs by one of the authors (HRS).

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Fig. 1

Radiograph showing the method of measuring the lengths of the tibia and the fibula (A, tibial length; B, fibular length; fibular to tibial ratio = B:A).

Table I. Details (mean (SD)) of the indices measured for the entire study group and the skeletally-mature and skeletally-immature groups

Indices*	Entire group (n = 53)	Skeletally immature (n = 30)	Skeletally mature (n = 23)	Normal values ¹¹⁻¹³
F:T ratio	1.1 (0.0472)	1.12 (0.0582)	1.01 (0.0526)	0.96 to 0.98
MPTA (°)	83.8 (5.76)	83.2 (6.86)	84.5 (3.93)	87.2 (1.5)
LDTA (°)	94.7 (16.1)	93.7 (19.9)	96 (9.37)	88.6 (3.8)
TCA (°s)	14 (9.69)	15.2 (9.83)	12.6 (9.51)	5.50 (6.94)
MADC (mm)	23.4 (14.7)	24.5 (10.6)	22.1 (19)	9.7 (6.8)
MADG (mm)	36.3 (16.2)	28 (11.6)	24.2 (19.7)	Not available
LDFA (°)	90.9 (6.5)	91.7 (6.47)	90.3 (6.43)	87.5 (2.5)

* F:T, fibular to tibial length; MPTA, medial proximal tibial angle; LDTA, lateral distal tibial angle; TCA, tibiocalcaneal angle; MADC, conventional mechanical axis deviation; MADG, ground mechanical axis deviation; LDFA, lateral distal femoral angle

These indices were the tibial and fibular length, the medial proximal tibial angle, the lateral distal tibial angle and the lateral distal femoral angle (Figs 1 and 2). The fibular to tibial length ratio was then calculated. The tibiocalcaneal angle, a combined deformity of the distal tibia and subtalar joint was also measured as the angle formed between the tibial and calcaneal mid-diaphyseal lines (Fig. 3). The mechanical axis deviation was measured by two methods. The conventional mechanical axis deviation was measured as the distance between the centre of the knee and a line drawn from the centre of the femoral head to the centre of the talus. The ground mechanical axis deviation was measured as the distance between the centre of the knee and a line drawn from the centre of the femoral head to that of the heel when in contact with

the ground on long leg-standing radiographs (Fig. 4). A mean of three readings was taken and intra-observer variation was minimal. Each measurer's (HRS, RM) values were consistently within 1° of his other measurements. All the measurements were performed using STAR PACS Pi view STAR 5.0.6.1 software (INFINITT technology, Seoul, Korea).

Statistical analysis. The results are given as the mean ± SD. Simple linear regression analysis of the fibular to tibial length ratio and the other indices was performed to determine any causal relationship. Bonferroni adjustment was applied in interpreting the p-values obtained to reflect multiple testing. We considered that the adjustment would provide us with a more specific and sensitive interpretation of our results. Correlation analysis was also done to find a sta-

Fig. 2

Anteroposterior standing long-leg radiograph showing the method of calculating the orientation angles (LDFA, lateral distal femoral angle; MPTA, medial proximal tibial angle; LDTA, lateral distal tibial angle).

tistical relationship between the fibular to tibial length ratio and the difference between the conventional mechanical axis deviation and the ground mechanical axis deviation, as well as between the tibiofemoral angle and the conventional mechanical axis deviation and ground mechanical axis deviation. The normal values of the fibula to tibial length and other indices were reported in previous studies (Table I).¹¹⁻¹³

A p-value of < 0.05 was considered to be significant.

Results

All the limbs showed a varus deformity at the knee and ankle. The mean conventional mechanical axis deviation and ground mechanical axis deviation was 23.4 ± 14.7 mm and 36.3 ± 16.2 mm, respectively. The significant difference ($p = 0.035$) between these values occurred because heel varus was taken into account when measuring the ground mechanical axis deviation. The mean fibular to tibial length ratio was 1.12 ± 0.0582 in the skeletally-immature and

1.01 ± 0.0526 in the skeletally-mature groups, which showed that tibial growth caught up with fibular growth as maturity was reached (Table I).

The fibular to tibial length ratio correlated well with the medial proximal tibial angle for the entire group and in the skeletally-immature combined male and female group. Our data showed a significant relationship to the development of the medial proximal tibial angle in the entire group ($p = 0.003$), in the skeletally-immature entire group ($p = 0.006$), and in the skeletally-mature female group ($p = 0.022$).

The fibular to tibial length ratio significantly affected the conventional mechanical axis deviation ($p = 0.031$) and the ground mechanical axis deviation ($p = 0.032$) in the skeletally-immature group. There was a significant effect of the tibiofemoral angle over the conventional mechanical axis deviation in the skeletally-immature female group ($p = 0.046$) and in the skeletally-mature entire group ($p = 0.035$). The tibiofemoral angle also significantly affected the ground mechanical axis deviation in the skeletally-mature entire group ($p = 0.015$; Table II).

Discussion

Bowing of the legs is the most common deformity in achondroplasia. It is first noticed at the standing age in 40% of all achondroplastic children and progresses rapidly at the age of three to four years, and again at six to seven years.¹⁴ The final progression of this deformity takes place during the pubertal growth spurt. Ponseti⁶ suggested that deformity of the lower limbs in achondroplasia was due to a failure of enchondral ossification leading to undergrowth of the tibia and relative overgrowth of the fibula. Stanley et al⁷ stated that in children aged between two and six years, varus deformity was associated with overgrowth of the proximal fibula and laxity of the lateral collateral ligament. The distal tibial varus which occurs in children between eight and 11 years of age appears to be associated with progressive overgrowth of the distal fibula, which leads to limitation of eversion of the hindfoot. This causes increased pressure on the medial side of the distal tibial physis and distal tibia vara. Ain et al⁸ stated that although fibular overgrowth was present in patients with achondroplasia, the length of the fibula was not related to the alignment of the lower limb. His study was conducted on skeletally-immature patients only and the method of seeking a correlation took account only of fibular growth. By contrast, our study had different study groups and correlated the fibular to tibial length ratio with various other indices. In particular, we have used the ground mechanical axis deviation as a valuable guideline for the alignment of the lower limb and this takes into account additional deformity below the level of the ankle.

The conventional method of measuring the mechanical axis deviation neglects hindfoot varus or valgus and may give an erroneous estimate of abnormal axial forces and the long-term risk of degenerative arthritis at the knee. Including the foot in the radiological measurement of limb alignment may increase the validity of surgical planning for

Fig. 3

Radiograph of the calcaneal axial view used for measurement of the tibio-calcaneal angle (XY, the line representing the long axis of the distal tibia; UV, the line representing the long axis of the calcaneum; The tibio-calcaneal angle (TCA) is the angle between XY and UV).

Table II. Outcome of regression analysis (p-value) for comparisons between groups and also by gender

Comparison*	Entire group			Skeletally-immature entire group			Skeletally-mature entire group		
	(n = 53)	Male [†]	Female [†]	(n = 30)	Male [†]	Female [†]	(n = 23)	Male [†]	Female [†]
Gender									
FT ratio: MPTA	0.003 [‡]	0.100	0.022 [‡]	0.006 [‡]	0.100	0.040 [‡]	0.183	1.000	0.022 [‡]
FT ratio: LDTA	0.611	1.000	1.000	0.577	1.000	0.642 [‡]	0.462	1.000	1.000
FT ratio: LDFA	0.091	0.356	0.570	0.053	0.468	0.018 [‡]	0.782	1.000	1.000
FT ratio: TCA	0.651	0.100	1.000	0.530	0.152	1.000	0.808	1.000	1.000
FT ratio: MADC	0.226	0.540	1.000	0.031 [‡]	0.148	0.154	0.939	1.000	1.000
FT ratio: MADG	0.223	0.408	1.000	0.032 [‡]	0.092	0.136	0.941	1.000	1.000
FT ratio: MADG-MADC	0.256	0.292	1.000	0.211	0.710	0.454	0.995	0.390	0.862
TCA:MADC	0.410	0.506	0.964	0.079	0.318	0.046 [‡]	0.035 [‡]	1.000	0.030 [‡]
TCA:MADG	0.268	0.432	0.682	0.117	0.270	0.054	0.015 [‡]	0.998	0.012 [‡]
TCA:MADG-MADC	0.123	1.000	0.378	0.970	1.000	1.000	<0.001 [‡]	1.000	0.004 [‡]

* F:T, fibular to tibial length; MPTA, medial proximal tibial angle; LDTA, lateral distal tibial angle; LDFA, lateral distal femoral angle; TCA, tibio-calcaneal angle; MADC, conventional mechanical axis deviation; MADG, ground mechanical axis deviation

[†] p-value after the Bonferroni adjustment method

[‡] p-value < 0.05

correction of malalignment as proposed by Guichet et al.¹⁵ Thus the ground mechanical axis deviation was considered to be more relevant than the conventional mechanical axis deviation since it took into consideration the varus heel.¹¹

In our study we observed that the fibular to tibial length ratio was significantly related to the alignment indices of the lower limb and had a causal relationship with them. However, this causal relationship was only seen until skeletal maturity. After this, the fibular to tibial length ratio had

Fig. 4

Radiograph showing the calculation of the conventional mechanical axis deviation (MADC) and the ground mechanical axis deviation (MADG). The MADC is the distance of the conventional mechanical axis from the centre of the knee and the MADG is the distance between the centre of the knee and a line drawn from the femoral head to the centre of the heel when in contact with the ground (TCA, tibio-calcaneal angle).

no relationship to the limb-length alignment indices. This suggests that the fibular growth rate exceeds the tibial growth rate in achondroplastic patients during their formative years, but that the difference is minimised as age advances towards skeletal maturity. Thus, fibular to tibial length ratio bears no causal relationship to lower-limb alignment indices in the skeletally-mature group.

The persistence of deformity after skeletal maturity led us to conclude that the upper tibial metaphyseal deformation which had already taken place in childhood did not completely correct with the accelerated tibial growth which occurred closer to skeletal maturity. Another important finding was that the tibio-calcaneal angle also showed a significant relationship to the conventional mechanical axis deviation and the ground mechanical axis deviation in our study. This suggests that fibular overgrowth does have a role to play in the development of genu varum in patients with achondroplasia. Also, heel varus plays a significant part in changing the loading axis of the lower limb as shown by the relationship of the tibio-calcaneal angle to the ground mechanical axis deviation. This confirms the importance of considering the ground mechanical axis deviation as a better index of measurement of overall limb alignment than the conventional mechanical axis deviation. A limitation of our

study was that the effect of tibial torsion on limb alignment was not considered. Rotational deformity of the tibia often complicates varus deformity and has a significant effect on axial malalignment.^{16,17} In future, we plan to investigate the relationship between rotational and axial malalignment using CT in achondroplastic patients.

Despite the presence of the varus knee in achondroplasia, degenerative arthritis occurs rarely. However, recurrent knee and ankle pain affects 70% of children between the age of four and ten years with combined varus deformity at the knee and hindfoot.¹⁴ The longer fibula may be the site of a painful calcaneal impingement bursitis when there is severe varus deformity of the distal tibia and a compensatory valgus position at the ankle.¹⁸ Kopits¹⁹ reported that the incidence of axial malalignment of the lower limb was 35.5% in 150 achondroplastic patients and that 26 (17.3%) required osteotomy for symptomatic malalignment.

We therefore recommend early epiphysiodesis or partial excisional osteotomy of the proximal fibula to minimise the progression of the genu varum deformity in severe cases and monofocal or bifocal osteotomy before skeletal maturity at the proximal tibia and/or distal tibia when there is symptomatic malalignment.

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