

# Risk factors for ankle valgus in children with hereditary multiple exostoses: a retrospective cross-sectional study

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## Abstract

**Purpose:** The aim of this study was to identify risk factors for ankle valgus in children with hereditary multiple exostoses (HME).

**Methods:** We retrospectively reviewed the medical records of patients with HME who were examined at our hospital between 2010 and 2020. Patients' age and sex were recorded along with radiographic variables including mechanical axis deviation (MAD), mechanical lateral distal tibia angle (LDTA), fibula/tibia length ratio (F/T); distal fibula station according to Malhotra's classification, location of exostoses at the ankle joint and fibular neck/physis width (N/P) ratio, which were measured from radiographs. Binary logistic regression analysis was performed to identify significant independent risk factors for ankle valgus.

**Results:** There were 61 children (20 girls and 41 boys; 122 ankles) who met the inclusion criteria. The mean age was 10.4 years (SD 3.4) and mean LDTA was 83° (SD 7°). Ankle valgus was found in 64 ankles (52%). In addition to younger age, exostoses involving the lateral aspects of the distal tibial and the medial aspect of the distal fibula (odds ratio (OR) = 4.091; 95% confidence interval (CI) 1.065 to 15.712;  $p = 0.040$ ), F/T ratio < 0.96 (OR = 4.457; 95% CI 1.498 to 13.261;  $p = 0.007$ ) and N/P ratio > 1.6 (OR = 2.855; 95% CI 1.031 to 7.907;  $p = 0.043$ ) were associated with an increased risk of developing ankle valgus, while sex and MAD were unrelated to its occurrence.

**Conclusion:** Young age, exostoses involving both the distal tibia and fibula, the F/T ratio < 0.96 and fibular N/P width ratio > 1.6 seemed to be risk factors of developing ankle valgus.

**Levels of evidence:** Prognostic studies, IV

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**Keywords:** hereditary multiple exostoses; ankle valgus; risk factors

## Introduction

Hereditary multiple exostoses (HME) is an autosomal dominant inherited skeletal condition characterized by multiple cartilage-capped exostoses primarily involving the metaphyses of long bones. HME is the most common benign bone tumour and can cause a variety of clinical problems. The most frequent lower limb deformities in HME are coxa valgus, valgus deformity of the knee and ankle and limb length discrepancies. Unlike genu valgum, ankle valgus – which has a prevalence of 54% to 69% in patients with HME<sup>1,2</sup> – is asymptomatic in children. Mild valgus can be compensated by the hindfoot but the deformity usually progresses with age and can cause pain and lateral impingement. Valgus malalignment of the ankle increases pressure on the lateral portion of the tibiotalar and talofibular joints, eventually leading to degenerative arthritis.<sup>3</sup> On the other hand, good outcomes for ankle valgus have been reported with temporary distal tibial medial hemiepiphysiodesis, which can delay or prevent osteoarthritis in skeletally immature patients.<sup>4,5</sup> Thus, if ankle valgus can be detected early on, minimally invasive surgical procedures can be performed instead of supra-malleolar osteotomy to safely and effectively correct the deformity.

The aetiology of ankle valgus in children with HME is unclear and predicting its development in paediatric patients is complicated. Ankle valgus is characterized by fibula shortening and lateral tapering of the distal tibial epiphysis.<sup>6,7</sup> While the former has been proposed as the main cause of ankle valgus,<sup>8,9</sup> it has also been suggested that the deformity is due to the location of exostoses on

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the lower legs.<sup>8,10,11</sup> The purpose of the present study was to identify risk factors associated with ankle valgus in children with HME; in addition to the abovementioned factors, we hypothesized that exostoses at the proximal fibula increase the risk of developing ankle valgus.

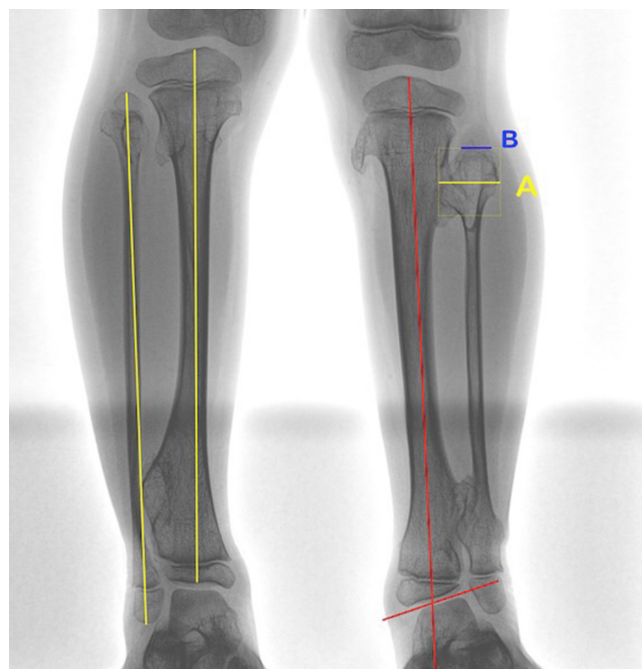
## Materials and methods

### Patients and data

This study received institutional review board approval. We retrospectively reviewed the medical records of patients with HME who were examined at our hospital between June 1, 2010 and May 31, 2020; patients more than five years old with a full-length, weight-bearing, standing anteroposterior (AP) radiograph were included in this study, while those who had undergone previous surgery of the lower limbs were excluded. Patient age and sex were recorded, a visual analogue scale was used to assess the pain level and radiographic parameters were measured twice from radiographs using UniWeb (EMB Technologies, Taipei, Taiwan) by one of the authors (YL), with two weeks between measurements to increase intraobserver reliability. Subsequently, 30 children (60 ankles), randomly selected from the 61 children, were measured by another author to assess the interobserver reliability of the measurements. The radiographic parameters included: 1) coronal mechanical axis deviation (MAD), which was evaluated according to Stevens's mechanical axis zones;<sup>12</sup> 2) mechanical lateral distal tibia angle (LDTA) assessed according to the method described by Paley<sup>13</sup> (normal range of 86° to 92°,<sup>13</sup> with an angle < 86° defined as ankle valgus); 3) fibula shortening, as determined by fibula/tibia length (F/T) ratio; 4) fibular shortening at the distal end of the fibular station according to the Malhotra classification<sup>14</sup> in patients more than ten years of age; 5) location of exostoses at the ankle joint (classified into four groups: the lateral aspect of the distal tibia, the medial aspect of the distal fibula, the lateral aspects of the distal tibia and the medial aspect of distal fibula and no involvement); and 6) fibular neck/physis width (N/P) ratio (Fig. 1), which was calculated by dividing the width of widest area of the fibular neck by the width of physeal plate in order to evaluate the effect of exostoses at the proximal fibula. For patients who underwent surgery for ankle valgus subsequently, their chief complaints before surgery and surgical procedures were collected and recorded.

### Statistical analysis

All statistical analyses were performed using SPSS v22.0 software (SPSS Inc., Chicago, Illinois). A p-value < 0.05 was considered statistically significant. The intra- and interobserver reliability of repeated radiographic mea-



**Fig. 1** The lateral distal tibial angle is measured as the angle between the long axis of the tibia and the articular surface of the tibial plafond (red line); the tibial length is measured from the plateau to the plafond, the fibula length is measured from the apex of the fibular head to the distal tip of the lateral malleolus (yellow line). The fibula/tibia length ratio is calculated by dividing the fibula length by the tibia length. We use a rectangle to enclose all exostoses around the proximal fibula and measure the length of the rectangular transverse axis. The fibular neck/physis width ratio = A/B.

surements was evaluated based on intraclass correlation coefficient (ICC) (two-way random model with absolute agreement) for continuous variables and weighted kappa for ordinal variables. Interpretation of ICC was as follows: < 0.50, poor; between 0.50 and 0.75, fair; between 0.75 and 0.90, good; > 0.90, excellent. Kappa values > 0.8 indicate excellent agreement; values between 0.41 to 0.60 indicate substantial agreement; and values < 0.40 represent moderate agreement. The parametric Kolmogorov–Smirnov test was used to verify the normal distribution of the data. Continuous variables including age, F/T, N/P ratios and LDTA (take the average of two measurements' results) are presented as mean and SD. Pearson's chi-squared test was used to compare variables between patients with and those without ankle valgus. Binary logistic regression analysis was used to identify significant independent risk factors for ankle valgus. All significant variables ( $p < 0.05$ ) and those with a trend toward significance ( $p < 0.10$ ) were entered into the regression model using the forward conditional method. Multicollinearity analysis was performed prior to regression analysis to identify collinear variables.

## Results

### Demographic and clinical characteristics of the study population

There were 61 children (122 ankles) who met the inclusion criteria for the study, including 20 girls and 41 boys. The mean age was 10.4 years (SD 3.4; 5.0 to 17.9), and the mean LDTA was 83° (SD 7°; 53° to 93°). The intra- and interobserver reliability for repeated measurements of the variables were good to excellent (Table 1). In all, 52% (64 of 122) of all ankles have a valgus deformity, 28 were left ankle and 36 were right. We found no significant difference in sex ( $p = 0.449$ ) or side ( $p = 0.147$ ) with regard to the occurrence of ankle valgus deformity. In 35 ankles there were no exostoses; in the others, exostoses involved the lateral aspect of the distal tibia ( $n = 42$ ), the medial aspect of distal fibular ( $n = 16$ ) or both ( $n = 29$ ). This last group of patients had a significantly smaller LDTA than the others (Table 2), while no significant difference in LDTA was observed between patients with exostoses at the lateral aspect of the distal tibia vs the medial aspect of distal fibula ( $p = 0.899$ ).

We measured coronal MAD in the lower limbs from AP radiographs; 44 limbs had a normal mechanical axis,

and there were 69 with genu valgum and nine with genu varus. Lower limb malalignment (i.e. MAD) was weakly associated with the occurrence of ankle valgus ( $r = 0.219$ ;  $p = 0.011$ ; Kendall's tau-b test).

The mean F/T ratio was 0.97 (SD 0.03; 0.88 to 1.1) and was significantly correlated with the development of ankle valgus ( $r = 0.33$ ;  $p < 0.001$ ). In five of the 122 limbs, there were no exostoses at the proximal fibula. The mean N/P ratio was 1.7 (SD 0.5) and showed a weak correlation with the occurrence of ankle valgus ( $r = 0.229$ ;  $p = 0.013$ ). There was a significant negative linear correlation between N/P and F/T ratios ( $r = -0.526$ ;  $p < 0.001$ ).

### Analysis of risk factors for ankle valgus in paediatric HME patients

In the binary logistic regression model, age (odds ratio (OR) = 1.371; 95% confidence interval (CI) 1.173 to 1.602;  $p = 0.000$ ), F/T ratio  $< 0.96$  (OR = 4.457; 95% CI 1.498 to 13.261;  $p = 0.007$ ), exostoses involving the lateral aspects of the distal tibia and the medial aspect of distal fibula (OR = 4.091; 95% CI 1.065 to 15.712;  $p = 0.040$ ) and N/P ratio  $> 1.6$  (OR = 2.855; 95% CI 1.031 to 7.907;  $p = 0.043$ ) were significantly associated with more severe ankle valgus. In contrast, lower limb malalignment was unrelated to the development of ankle valgus (Table 3).

Malhotra's classification was used to evaluate the fibular station in patients more than ten years old (31 patients, 62 limbs). There was a significant negative association between distal fibular station and LDTA ( $r = -0.702$ ;  $p < 0.001$ ; Spearman's rho). Malhotra grade III was associated with a significantly smaller LDTA than other grades (Fig. 2).

Surgery was performed on 11 ankles (seven patients, 17%), including tension band plate hemiepiphysiodesis in ten and supramalleolar osteotomy in one ankle. Ankle val-

**Table 1** Intra and interobserver repeatability for the variables

Variables	Intraobserver reliability (95%CI)	Interobserver reliability (95%CI)	Measure
MAD	0.986 (0.966 to 1.006)	0.953 (0.916 to 0.989)	QWK
LDTA	0.965 (0.949 to 0.976)	0.810 (0.736 to 0.865)	ICC
F/T ratio	0.905 (0.865 to 0.933)	0.808 (0.698 to 0.881)	ICC
Malhotra's grade	0.970 (0.936 to 1.005)	0.885 (0.822 to 0.948)	QWK
N/P ratio	0.932 (0.903 to 0.952)	0.825 (0.674 to 0.902)	ICC

CI, confidence interval; MAD, mechanical axis deviation; QWK, Quadratic weighted kappa; LDTA, lateral distal tibia angle; ICC, intraclass correlation coefficient; F/T, fibula/tibia length; N/P ratio, fibular neck/physis width

**Table 2** Lateral distal tibial angle (LDTA) at different sites involved in exostoses of the ankle joint

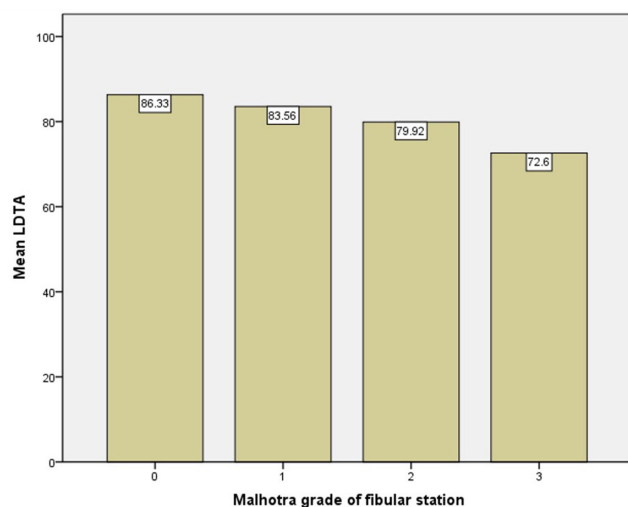
Location of exostoses	Number of ankles	LDTA	Comparison between involved sites	p-value
No exostosis (A)	35	86°	B	0.028
			C	0.072
			D	0.000
			A	0.028
Lateral aspect of distal tibia only (B)	42	83°	C	0.899
			D	0.004
			A	0.072
			B	0.899
Medial aspect of distal fibula only (C)	16	83°	D	0.032
			A	0.000
			B	0.004
			C	0.032
Both distal tibia and fibula (D)	29	79°	A	0.000
			B	0.004
			C	0.032
			A	0.000

Post hoc tests were used to compare the LDTA between different sites involved in exostoses of the ankle joint. A p-value  $< 0.05$  was considered statistically significant.

**Table 3** Risk factors associated with ankle valgus in hereditary multiple exostoses

Predictor	Ankle valgus		p-value	Exp(B)	Exp (B) 95% CI	
	No	Yes			Lower	Upper
Age			0.000	1.371	1.173	1.602
F/T ratio			0.007	4.457	1.498	13.261
$\geq 0.96$	49	32				
$< 0.96$	9	32				
N/P ratio			0.043	2.855	1.031	7.907
$\leq 1.6$	38	24				
$> 1.6$	20	40				
Location of exostoses						
A	24	11	0.111			
B/C	27	31	0.441			
D	7	22	0.040	4.091	1.065	15.712
MAD						
Zone (-1, -2)	7	2	0.950			
Zone (0, 1)	41	39	0.959			
Zone (2, 3)	10	23	0.908			

CI, confidence interval; F/T, fibula/tibia length; N/P, fibular neck/physis width; A, no exostoses; B, lateral aspect of distal tibia only; C, medial aspect of distal fibula only; D, both distal tibia and fibula; MAD, mechanical axis deviation; Exp(B), exponentiation of the B coefficient



**Fig. 2** There was a significant negative association between Malhotra grade and lateral distal tibial angle (LDTA). Patients with Malhotra grade III have the smallest LDTA.

gus was diagnosed by doctors from a full-length standing AP radiograph during consultation for exostoses around the ankle joint, except in one patient whose ankle deformity was noted by his parents. No patient complained of pain or limited range of movement of the ankle before the surgery.

## Discussion

Ankle valgus deformity is a coronal plane deformity observed in approximately half of patients in HME.<sup>1,2,15</sup> This corresponds to our results, in which 52% of ankles (64/122) had valgus deformity. The deformity was asymptomatic and showed insidious progression in most cases, with corrective surgery performed on only 17% (11/64) of the ankles. Although all patients were pain free in this series, degenerative joint disease may occur secondary to ankle malalignment with increasing age. In a study of the natural history of 38 adult patients (mean age, 42 years) with HME, 19% showed degeneration of the ankle joint by radiography, with more severe valgus deformity in patients with osteoarthritis; based on these findings, the authors speculated that mild valgus deformity can eventually lead to degenerative changes with aging, and suggested prophylactic surgery to correct ankle alignment.<sup>16</sup>

The risk factors of ankle valgus in HME are not well known. Fibular shortening was found to be associated with ankle valgus. One study demonstrated that Malhotra grade was significantly correlated with the occurrence of ankle valgus in male patients;<sup>11</sup> and another reported that the fibula grew more slowly than the tibia, resulting in fibular shortening and ankle valgus, which was the only factor associated with the progression of valgus deformity.<sup>9</sup>

These results support the theory that imbalance growth rates of the tibia and fibula exert a tethering effect on the interosseous membrane and ligaments between the two parallel long bones.<sup>15</sup> In patients with HME, the tibia is concave toward the relatively short fibula, leading to valgus deformity of the ankle.

In agreement with the above findings, we found that a short fibula length was significantly correlated with the occurrence of ankle valgus. The normal F/T ratio is reported to be 1.00;<sup>15</sup> the mean ratio in our patients was lower at 0.97 (SD 0.03), reflecting the shortness of the fibula compared with the tibia. As the distal fibular physis is located 2 mm to 3 mm distal to the talar dome until the age of around eight years in normal children,<sup>7</sup> Malhotra grade was only evaluated in patients older than ten years in this study. The tethering effect of the shorter fibula on the tibia was demonstrated by the significant association between Malhotra grade and LDTA, with the greatest degree of ankle deformity corresponding to Malhotra grade III.

By broadening the scope of observation when evaluating ankle deformity, it was demonstrated that lesions in both proximal and distal tibiofibular joints had a significant impact on ankle valgus and fibular shortening.<sup>10</sup> Similarly, our data confirmed our initial assumption that patients with larger exostoses at the proximal fibula had more severe ankle valgus; the rate of proximal fibula involvement of 96% in our study was comparable with the previously reported rate of 97%.<sup>15</sup> By evaluating the width of the widest area of the fibular neck, we determined that the N/P ratio was negatively correlated with F/T ratio. A possible explanation for this result is that the narrow fibular growth plate is more vulnerable to growth impairment than the tibia; thus, the size of exostoses would be inversely correlated with fibula growth rate. For exostoses at the proximal fibula, a N/P ratio > 1.6 was significantly associated with the occurrence of ankle valgus, indicating that a higher N/P ratio is a risk factor for ankle deformity in HME.

The prevalence of distal tibia exostoses involvement in the literature varies from 64% to 92%, and varies from 57% to 85% of the distal end of the fibula.<sup>15,17</sup> Exostoses are frequently present in the lateral aspect of the distal tibia and the medial aspect of the distal fibula. In agreement with previous work,<sup>11</sup> we found that patients with exostoses involving both the lateral aspect of the distal tibia and the medial aspect of the distal fibula had more severe valgus deformity. Metaphysis exostoses caused the disturbance of the adjacent growth plate, resulting in another tethering effect on the lateral physis of the distal tibia.

Our data showed that valgus deformity progressed with increasing age, in contrast to findings from a longitudinal study of 33 patients that found no significant relationship between age and the development of ankle valgus.<sup>9</sup> This discrepancy may be explained by differences in research design and sample characteristics. Our

cross-sectional study included paediatric and adolescent patients with a broader age range (5.0 years to 17.9 years) than the patients in the previous investigation, where most patients were less than ten years old. However, a longitudinal study design is better for analyzing the progression of ankle deformity with age. Other variables such as sex and coronal MAD had no correlation or were only weakly correlated with the occurrence of ankle valgus. Male sex has been linked to more severe clinical presentation,<sup>11,18</sup> but this was not supported by our data; however, as the physis closes later in male than in female patients, a more detailed examination of skeletally mature patients is warranted to determine whether sex influences ankle valgus risk or severity. Fibular shortening may have a tethering effect on both knee and ankle joints. Coronal angular deformity around the knee is common in patients with HME, and valgus deformity usually derives from angulation of the proximal tibia. Although it was weakly associated with the occurrence of ankle valgus, MAD was not a significant risk factor. Moreover, we found that genu valgum was unlikely to result in ankle valgus.

In general, two tethering effects might lead to valgus deformity. One of them was the shortening of the fibula, and the other was the growth disturbance of distal tibial physis. Therefore, several procedures are used for the treatment of ankle valgus including guided growth techniques with a medial malleolar transphyseal screw or tension band plate and fibular lengthening, both of which have good outcomes. The former involves inhibiting the growth of the medial physis of the distal tibia.<sup>4,5,19</sup> However, a slower correction velocity in guided growth was reported in patients with HME than in non-HME patients.<sup>5,20</sup> By investigating and quantifying the risk factors, surgeons can detect ankle valgus early and use these micro-invasive procedures for treatment.

A shortcoming of the present study was its retrospective cross-sectional design; given that valgus deformity progresses with age, a prospective longitudinal follow-up is needed to validate the risk factors identified by our analysis. Additionally, as most patients were symptomless, ankle valgus was initially diagnosed by radiography and the analyses were based on radiographic variables measured by an investigator, although there was good intra- and interobserver reliability for repeated measurements. In this study, the ICC and Kappa values of the intraobserver were higher than that of interobserver, indicating that intraobserver reliability was more consistent than interobserver reliability. It is optimal for patients to follow-up with the same doctor to achieve a maximum of reproducibility. Another potential problem was that the limb rotation might affect the measurement accuracy of coronal alignment; even though a patellar forward position full-length, weight-bearing AP radiograph may minimize the measurement errors.

## Conclusion

In patients older than five years, young age, exostoses involving both the lateral aspect of the distal tibia and the medial aspect of the distal fibula, the F/T length ratio < 0.96 and fibular N/P width ratio > 1.6 seemed to be risk factors of developing ankle valgus. For paediatric patients with these features, regular clinical examinations (e.g. every 12 months) are recommended.

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## COMPLIANCE WITH ETHICAL STANDARDS

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### ETHICAL STATEMENT

**Ethical approval:** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed Consent:** Informed consent was not required for this work.

### ICMJE CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest. This study was funded by Science and Technology commission of Shanghai, China (Grant No.19511106103).

### AUTHOR CONTRIBUTIONS

WZ: Study conception and design, Writing original draft preparation, Commented on previous versions of the manuscript/read the final manuscript.

ZW: Study conception and design, Writing original draft preparation, Commented on previous versions of the manuscript/read the final manuscript.

MC: Study conception and design, Data collection and analysis, Commented on previous versions of the manuscript.

YL: Study conception and design, Writing review and response to the reviewers, Revised the manuscript, Final approval of the version, Data collection and analysis, Commented on previous versions of the manuscript/read and approved the final manuscript.

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