Outcomes of Hemiepiphyseal Stapling for Genu Valgum Deformities in Patients With Multiple Hereditary Exostoses: A Comparative Study of Patients With Deformities of Idiopathic Cause

Seungcheol Kang, MD, Jae Young Kim, MD, and Soo-Sung Park, MD, PhD

Background: Patients with multiple hereditary exostoses (MHE) frequently present with a genu valgum deformity. Temporary hemiepiphysiodesis, such as hemiepiphyseal stapling, is a relatively safe surgical method to correct angular deformities in skeletally immature patients, but its outcomes for genu valgum deformity in MHE patients have not been extensively reported. We investigated the outcomes of hemiepiphyseal stapling in MHE patients (MHE group) and compared those with the outcomes in patients with idiopathic deformities (idiopathic group) after adjusting for potential bias.

Methods: Data from 70 limbs with genu valgum deformity (15 MHE and 55 idiopathic), which had undergone hemiepiphyseal stapling, were retrospectively reviewed. The outcomes were focused on the achievement of satisfactory correction and the velocity of correction. The independent effects of each characteristic on each outcome were investigated using multivariate analyses. The outcomes between the groups were also compared after 1:2 matching using propensity score analysis.

Results: The mean valgus angle of the MHE group was 7.4 ± 4.1 degrees at stapling and was corrected to 1.3 ± 3.0 degrees at staple removal. The rate of satisfactory corrections was not different between the MHE and idiopathic groups (67% and 70%, respectively, $P = 0.820$). However, the correction velocity was significantly lower in the MHE group than in the idiopathic group on both multivariate analysis ($P = 0.001$) and matching comparison (4.4 vs. 7.9 degrees/y, $P < 0.001$). The duration of correction was longer in the MHE group than in the idiopathic group by approximately half a year (1.5 ± 0.6 vs. 0.9 ± 0.3 y, respectively, $P = 0.003$).

Conclusions: In MHE patients with genu valgum deformity, satisfactory correction can be achieved by hemiepiphyseal stapling and is comparable with that seen in idiopathic patients. However, the MHE group showed lower correction velocity and required a longer time by about one half year for correction compared with the idiopathic group. Temporary hemiepiphysiodesis should be considered at an earlier age for patients with MHE compared with those with idiopathic deformity.

Level of Evidence: Level III—prognostic study.

Key Words: hereditary multiple exostoses, multiple hereditary exostoses, MHE, hemiepiphysiodesis, staple, stapling, genu valgum, growth plate, physis

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There are various causes of coronal angular deformity around the knee in children.[1] Such deformities can also present in patients with multiple hereditary exostoses (MHE), mainly as a genu valgum deformity.[2] Although there are several operative options for angular deformity around the knee, current treatment most often involves guided growth with temporary hemiepiphysiodesis for skeletally immature patients because it can be performed with ease and is associated with a low complication rate compared with corrective osteotomy.[3–5] For temporary hemiepiphysiodesis, the activity of the growth plate (physis) plays an important role because residual growth of the uncompressed physis is the primary force for gradual correction.[6] Patients with MHE have inherently abnormal physes.[7] Therefore, those patients are anecdotally believed to have poor outcomes of correction compared with patients with normal physes.

Although the outcomes are somewhat inferior to those in patients with deformities of other causes, many studies have reported the effectiveness and satisfactory results of temporary hemiepiphysiodesis for ankle valgus deformity in patients with MHE.[8,9] However, there have been few studies investigating the results of valgus deformity around the knee in patients with MHE. The purpose of the present study was to investigate the outcomes of temporary hemiepiphysiodesis for genu valgum deformity in patients with MHE (MHE group) and compare the outcomes with those of patients with idiopathic cause (idiopathic group). We hypothesized that the MHE group would have satisfactory outcomes, but that the outcome would be poorer than that of the idiopathic group.

From the Department of Orthopedic Surgery, Asan Medical Center Children's Hospital, University of Ulsan College of Medicine, Seoul, South Korea.

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Reprints: Soo-Sung Park, MD, PhD, Department of Orthopedic Surgery, Asan Medical Center Children's Hospital, University of Ulsan College of Medicine, 88, Olympic-ro, 43-gil, Songpa-gu, Seoul 138-736, South Korea. E-mail: sspark@amc.seoul.kr.

METHODS

Patient Selection

This study was approved by the institutional review board of our institute. Data on patients who fulfilled the following inclusion criteria were retrieved: (1) a valgus angular deformity around the knee on coronal plane; (2) treated by hemiepiphyseal stapling on either distal femur or proximal tibia from July 2004 to February 2013 (ie, the limbs undergoing stapling on both sites were excluded); (3) without any other cause for deformity such as trauma, or any kind of skeletal dysplasias/syndrome except MHE; and (4) age 16 years or younger (boys) or 13.5 years or younger (girls) at stapling. A total of 73 limbs fulfilled the criteria. Among them, 3 limbs with staple migration were excluded because such a complication can affect the appropriateness of correction and may interfere with the purpose of the present study. Finally, 70 limbs from 44 patients (15 from 11 patients with MHE and 55 from 33 patients with idiopathic origin) were retrospectively reviewed for analysis.

Operative Technique and Follow-up

We mainly followed the operative technique as previously described[10] using Blount staples (Zimmer, Warsaw, IN). The staples were removed principally when the following conditions were confirmed or achieved during follow-up: the mechanical axis passing through the center of the knee, symmetricity of both legs, or patient/parent satisfaction of the correction. Careful attention was paid during the procedure to prevent damage of the underlying periosteum on insertion or removal of staples. At postoperative week 2, patients were assessed at the clinic with simple radiographs of the operated knee to determine the success of the surgery in terms of the position of the staples and the presence of short-term complications. Thereafter, patients were regularly followed every 3 to 6 months until staple removal.

Investigated Variables

Standing anteroposterior roentgenograms with the patella facing forward and including both full-length lower extremities (teleradiograms) were taken preoperatively and at every postoperative follow-up visit. Among them, teleradiographs taken just before stapling and just before staple removal (usually within 7 d before each surgery) were selected for radiographic evaluation. The measured radiographic parameters included mechanical axis deviation (MAD) (Fig. 1),[11,12] mechanical lateral distal femoral angle (mLDFA), and medial proximal tibial angle (MPTA).[13] The mLDFA is the lateral angle between the connection of the midpoints of the hip and knee and the distal femoral joint line. The MPTA is the medial angle between a line connecting the midpoint of the knee and ankle and the proximal tibial joint line. Stapling was performed at the site of the main angular deformity, assuming a normal value of 88 degrees for mLDFA and 87 degrees for MPTA.

We converted the measured mLDFA and MPTA to the valgus angle (the deviation angle from its normal value) for analyses. For example, patients who had a main deformity on the femur with an mLDFA of 81 degrees were regarded as having a valgus angle of 7 degrees (88 − 81 degrees), and patients who had a main deformity on the tibia with an MPTA of 94 degrees were also regarded as having a valgus angle of 7 degrees (94 − 87 degrees). If an overcorrection happened (varus knee), a negative value was assigned.

The following variables were also investigated: sex; laterality (unilaterally performed vs. bilaterally performed); affected side (left vs. right); site (distal femur vs. proximal tibia); age, body weight, height, and body mass index at stapling; height change during correction (stapling to staple removal); duration of correction (the duration from stapling to staple removal); and correction velocity. With the height at staple removal, stature percentile was determined according to national growth charts.[14] The correction velocity (degrees/y) was defined as the amount of angular correction divided by the time that lapsed from staple insertion to staple removal. The correctional outcomes were divided as "overcorrected" if the final MAD passed through zone 1 or under, "completely resolved" if the MAD through zone 0, "partially resolved" if the MAD improved >1 grade of zone but did not reach zone 0, and "unresolved" if the MAD did not improve or improved but within the same zone. To assess the achievement of correction, both "overcorrected" and "completely resolved" were regarded as "satisfactory," whereas both "partially resolved" and "unresolved" were regarded as "unsatisfactory."

Statistical Analysis

Associations between correction velocity and subject variables were analyzed by a linear regression model. The effect of each variable on the achievement of correction, which was classified as "satisfactory" and "unsatisfactory," was analyzed by binary logistic regression analysis. For both regression models, multivariate analysis was performed to eliminate confounders among the variables.[15] In those multivariate models, the duration of correction, amount of correction, and valgus angle at staple removal were excluded because of their theoretical interferences with the outcomes. Body mass index was also excluded from multivariate models because of its interference with body weight and height.

For the selection of a case-matched control group, we used propensity score analysis. The propensity score is the conditional probability of being selected given the covariates; thus, it can be used to balance the confounding factors in the 2 groups and therefore reduce bias.[16] Among the 55 idiopathic patients, 30 were selected for the matched-idiopathic group (1:2 ratio, nearest neighbor approach). The propensity score was calculated for each patient based on logistic regression analysis. Patient characteristics of sex; affected side; laterality; site; and age, body weight, height, and deviated angle at stapling were used for matching. These characteristics were selected based on a discussion between 2 experienced and board-certified orthopaedic surgeons. All statistical

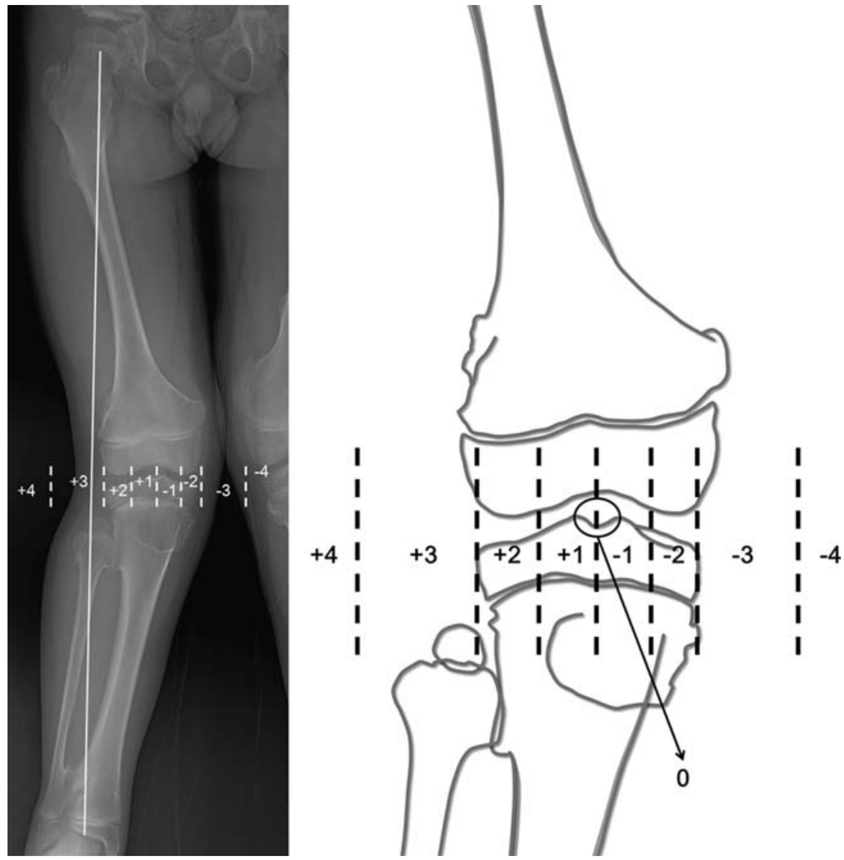

FIGURE 1. Mechanical axis deviation is defined as the distance from the midpoint of the tibial plateau to a line connecting the midpoints of the hip and ankle joint. The percentage of deviation to one half of the width of the tibial plateau was measured and divided into zones, as previously described with modifications.[11,12] Zone 1 was assigned to percentages of 0 to 50, zone 2 of 51 to 100, zone 3 of 101 to 200, and zone 4 of >200. Positive values represent the presence of valgus. In our current study, zone 0 was additionally assigned if the mechanical axis passed between the tibial spines.

analyses, except propensity score analysis, were conducted with SPSS for Windows statistical package (version 21; IBM Co., Armonk, NY), and significance was accepted for P-values of <0.05. Propensity score analysis was performed with R statistical software (Foundation for Statistical Computing, Vienna, Austria. version 3.1.0; http://cran.r-project.org/).

RESULTS

Outcomes of Hemiepiphyseal Stapling

The clinicoradiological characteristics of patients and the outcomes of hemiepiphyseal stapling for the MHE and idiopathic groups are shown in Table 1. For MHE group patients, the mean valgus angle was 7.4 ± 4.1 degrees at stapling and was corrected to 1.3 ± 3.0 degrees at staple removal. No patients showed zone ≥ 2 deformities at staple removal. For comparisons between the MHE and idiopathic groups, although the duration of correction and correction velocity differed, there were no differences in MAD passing zone at stapling and at staple removal. In addition, subgroup comparison according to the anatomic sites was performed, and the correction velocity of proximal tibia was significantly different. There was also no difference in height between groups, but the MHE group showed shorter stature percentile when age and sex matched to the idiopathic group (Fig. 2).

Correction Velocity

The results of multivariate analysis of correction velocity using a linear regression model are shown in Table 2. The underlying cause of genu valgum (MHE vs. idiopathic) significantly affected the correction velocity: the MHE group showed slower correction velocity than the idiopathic group.

Achievement of Correction

The results of multivariate analysis of achievement of correction using binary logistic regression model are shown in Table 3. Contrary to correction velocity, the underlying cause of genu valgum (MHE vs. idiopathic) did not affect the outcome ($P = 0.521$).

Matching Analysis

Comparisons between the MHE group and the matched idiopathic group are shown in Table 4. There

TABLE 1. Clinicoradiological Characteristics and the Outcomes of Hemiepiphyseal Stapling in the MHE and Idiopathic Study Groups

	Total (n = 70)	Idiopathic Group (n = 55)	MHE Group (n = 15)	P
Clinicoradiological characteristics				
Sex [n (%)]				0.137
Male	43 (61.4)	31 (56.4)	12 (80.0)	
Female	27 (38.6)	24 (43.6)	3 (20.0)	
Laterality				0.010*
Bilaterally	51 (72.9)	44 (80.0)	7 (46.7)	
Unilaterally	19 (27.1)	11 (20.0)	8 (53.3)	
Affected side				0.967
Right	37 (52.9)	29 (52.7)	8 (53.3)	
Left	33 (47.1)	26 (47.3)	7 (46.7)	
Site				0.042*
Distal femur	31 (44.3)	28 (50.9)	3 (20.0)	
Proximal tibia	39 (55.7)	27 (49.1)	12 (80.0)	
Age at stapling	12.4 ± 1.9	12.2 ± 1.9	13.2 ± 1.6	0.056
Body weight at stapling	50.0 ± 14.0	51.0 ± 14.3	46.1 ± 12.3	0.226
Height at stapling	152.0 ± 10.7	152.2 ± 11.0	151.2 ± 9.6	0.733
Height at staple removal	158.6 ± 10.4	158.4 ± 10.7	159.2 ± 9.7	0.791
Height change during correction	6.6 ± 2.9	6.2 ± 2.8	8.1 ± 2.8	0.024*
Stature percentile at staple removal (%)†				0.027*
< 10th	12.9	9.1	26.7	
10-25th	14.3	9.1	33.3	
25-50th	11.4	10.9	13.3	
50-75th	30.0	32.7	20.0	
75-90th	10.0	10.9	6.7	
≥ 90th	21.4	27.3	0	
BMI at stapling	21.3 ± 4.2	21.7 ± 4.3	19.9 ± 3.8	0.161
Outcomes of hemiepiphyseal stapling				
Valgus angle at stapling	6.8 ± 3.7	6.6 ± 3.6	7.4 ± 4.1	0.455
Valgus angle at staple removal	−0.0 ± 3.3	–0.4 ± 3.3	1.3 ± 3.0	0.074
Mechanical axis deviation at stapling [n (%)]				0.881
Zone 1	21 (30.0)	17 (30.9)	4 (26.7)	
Zone 2	38 (54.3)	29 (52.7)	9 (60.0)	
Zone 3	11 (15.7)	9 (16.4)	2 (13.3)	
Mechanical axis deviation at staple removal [n (%)]				0.247
Zone −1 or under	15 (21.4)	13 (23.6)	2 (13.3)	
Zone 0	41 (58.6)	33 (60.0)	8 (53.3)	
Zone 1	12 (17.1)	7 (12.7)	5 (33.3)	
Zone 2 or over	2 (2.9)	2 (3.6)	0	
Amount of correction	6.8 ± 3.7	7.0 ± 3.9	6.1 ± 2.8	0.408
Duration of correction (y)	1.1 ± 0.6	1.0 ± 0.6	1.5 ± 0.6	0.009*
Correction velocity (deg./y)	7.0 ± 3.5	7.7 ± 3.5	4.4 ± 2.0	< 0.001*
Correction velocity for site (deg./y)‡				
Distal femur (n = 31)	7.7 ± 3.4	7.9 ± 3.5	6.6 ± 1.6	0.558
Proximal tibia (n = 39)	6.4 ± 3.6	7.5 ± 3.6	3.8 ± 1.8	< 0.001*

*$P < 0.05$.
†According to age and sex.
‡Subgroup comparison according to the anatomic sites.
BMI indicates body mass index; MHE, multiple hereditary exostoses.

was no significant difference in the rate of achievement of correction between the 2 groups: about 67% of the MHE group and 70% of the idiopathic group achieved satisfactory correction. However, the MHE group showed significantly lower correction velocity and longer duration of correction compared with the idiopathic group. These differences primarily seem to originate from the cases of proximal tibia.

DISCUSSION

Temporary hemiepiphysiodesis is regarded as a relatively safe surgical method to correct angular deformity for skeletally immature patients.[3–5] Patients with MHE are known to have a high rate of knee deformity, with nearly a third of patients developing genu valgum,[2,17] but the outcomes of temporary hemiepiphysiodesis for those patients have been rarely reported.

We evaluated the outcomes of MHE patients with genu valgum after temporary hemiepiphysiodesis and compared the outcomes to those of patients with idiopathic cause for knee deformity. The outcomes were focused on the achievement of correction (satisfactory vs. unsatisfactory) and correction velocity (mean degree of angle corrected per year). To eliminate any potential

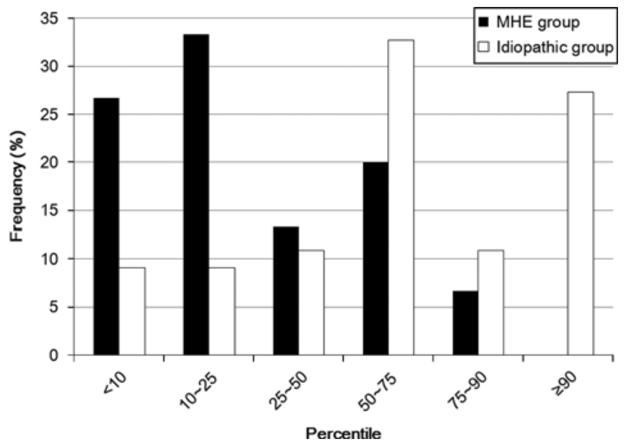

FIGURE 2. Stature percentile at staple removal of the MHE and idiopathic groups according to age and sex by national growth charts.[14] Although the mean height did not differ, the MHE group showed shorter stature when adjusted by age and sex ($P=0.027$). Stature was below the 25th percentile in 60% of patients in the MHE group. MHE indicates multiple hereditary exostoses.

bias, we further performed multivariate analysis (linear regression model and binary logistic regression model) and matching comparison using propensity score analysis. Using both statistical techniques, no significant difference in satisfactory achievement of correction was found, but there was a significant difference in the velocity of correction: the MHE group showed significantly lower correction velocity than the idiopathic group on both multivariate analysis ($B = -3.108$, $P = 0.001$) and matching comparison (4.4 vs. 7.9 degrees/y, $P < 0.001$). Although statistically indeterminable, this difference seems to originate from the cases of proximal tibia. To

TABLE 2. Multivariate Results for Correction Velocity Using Linear Regression Analysis

Characteristics	*B* (slope)	β†	*P*
Sex			
Male vs. female	−2.163	−0.299	0.005*
Side			
Right vs. left	0.060	0.008	0.930
Laterality			
Unilaterally vs. bilaterally	0.414	0.052	0.611
Site			
Distal femur vs. proximal tibia	−1.701	−0.240	0.021*
Age at stapling	−0.700	−0.383	0.012*
Body weight at stapling	−0.051	−0.201	0.184
Height at stapling	0.028	0.085	0.631
Height change during correction	0.110	0.090	0.396
Valgus angle at stapling	0.246	0.258	0.022*
Underlying disease			
Idiopathic vs. MHE	−3.108	−0.362	0.001*

*$P < 0.05$.

†For the binary form "characteristic a vs. b," a positive β means that characteristic b is more favorable as shown by a higher correction rate than characteristic a, and negative means a lower correction velocity. For the continuous form, β is positive if the increase in characteristic is related to a higher correction velocity.

MHE indicates multiple hereditary exostoses.

TABLE 3. Multivariate Results for Achievement of Correction (Satisfactory vs. Unsatisfactory) Using Binary Logistic Regression

Characteristics	OR (95% CI)	*P*
Sex		0.159
Male	4.139 (0.574-29.854)	
Female	1 (reference)	
Side		0.544
Right	1.676 (0.316-8.889)	
Left	1 (reference)	
Laterality		0.018*
Bilaterally	7.310 (1.397-38.244)	
Unilaterally	1 (reference)	
Site		0.051
Distal femur	8.130 (0.991-66.723)	
Proximal tibia	1 (reference)	
Age at stapling	0.261 (0.090-0.757)	0.013*
Body weight at stapling	1.065 (0.954-1.190)	0.262
Height at stapling	1.057 (0.923-1.212)	0.422
Height change during correction	1.417 (1.010-1.988)	0.044*
Valgus angle at stapling	0.749 (0.555-1.010)	0.058
Underlying disease		0.521
MHE	1.921 (0.262-14.101)	
Idiopathic	1 (reference)	

*$P < 0.05$.

CI indicates confidence interval; MHE, multiple hereditary exostoses; OR, odds ratio.

our knowledge, our current study is the first to investigate the outcomes of temporary hemiepiphysiodesis and reveal a slow correction velocity in MHE patients compared with patients with knee deformity of idiopathic cause.

As most physicians anecdotally believe, we suggest that the abnormal growth capacity of physes around the knee is the main cause for slow correction velocity. We performed a literature review of studies supporting slow correction velocity in MHE patients. In MHE patients, a genetic mutation in the developing long bone results in growth disturbance of chondrocytes.[7] The exostoses are thought to influence longitudinal limb growth, with a quarter of patients having a limb length discrepancy.[2] This growth disturbance is believed to be responsible for the slow growth rate and finally associated with the short stature of MHE patients. Although MHE patients were excluded from that study, Boero et al[6] reported a slower correction velocity of patients with osteochondral dysplasia/syndrome compared with patients with idiopathic cause. They tried to exclude patients with diseases with slow growth rate,[6] but most diseases included are known to be associated with short stature or dwarfism.[18,19] It is concordant with our present study: although there was no difference in height between groups, the stature percentile according to age and sex was significantly lower in the MHE group than in the idiopathic group. In contrast, the height change during correction was even higher in the MHE group. We have no clear explanation for this result, but it could be partly explained by the late spinal contribution to height. Further studies including leg length change are needed to clarify this finding.

It could be argued by some that only the mild form of MHE can be treated with temporary hemiepiphysiodesis,

TABLE 4. Comparison of the Multiple Hereditary Exostoses Group and Matched Patients Among the Idiopathic Group

	MHE Group (n = 15)	Idiopathic Group, Matched (n = 30)	P
Matched variables			
Sex [n (%)]			0.726
Male	12 (80.0)	22 (73.3)	
Female	3 (20.0)	8 (26.7)	
Affected side [n (%)]			1.000
Right	8 (53.3)	16 (53.3)	
Left	7 (46.7)	14 (46.7)	
Laterality [n (%)]			0.197
Bilaterally	7 (46.7)	10 (33.3)	
Unilaterally	8 (53.3)	20 (66.7)	
Site [n (%)]			0.492
Distal femur	3 (20.0)	10 (33.3)	
Proximal tibia	12 (80.0)	20 (66.7)	
Age at stapling	13.2 ± 1.6	12.7 ± 2.0	0.391
Body weight at stapling	46.1 ± 12.3	47.5 ± 15.0	0.743
Height at stapling	151.2 ± 9.6	150.7 ± 12.3	0.895
Valgus angle at stapling	7.4 ± 4.1	7.5 ± 3.7	0.957
Unmatched variables			
Achievement of correction [n (%)]			0.820†
Satisfactory	10 (66.7)	21 (70.0)	
Overcorrected	2 (13.3)	6 (20.0)	
Completely resolved	8 (53.3)	15 (50.0)	
Unsatisfactory	5 (33.3)	9 (30.0)	
Partially resolved	5 (33.3)	7 (23.3)	
Unresolved	0	2 (6.7)	
Duration of correction (y)	1.5 ± 0.6	0.9 ± 0.3	0.003*
Correction velocity (deg./y)	4.4 ± 2.0	7.9 ± 3.6	< 0.001*
Correction velocity for site (deg./y)‡			
Distal femur (n = 13)	6.6 ± 1.6	6.8 ± 3.4	0.914
Proximal tibia (n = 32)	3.8 ± 1.8	8.4 ± 3.6	< 0.001*

*$P < 0.05$.
†Comparison between "resolved" versus "unresolved" cases.
‡Subgroup comparison according to the anatomic sites.

but our present cohort included a relatively severe spectrum of the disease compared with the general population of MHE patients. The severity of phenotype is known to be associated with genotype (EXT mutation), sex, and number of lesions.[20,21] Although genotype evaluation was not routinely performed in our current study cohort, other parameters strongly indicate a severe disease spectrum. All patients in our present investigation had exostoses near to all of the physes of their lower extremities, and the mean number of exostoses around the knee was almost double the mean found in a previous study (data not shown).[21] In addition, many previous studies with large populations have reported that male sex was associated with a more severe phenotype[20]; the study population of our present study showed a male-dominant sex ratio (80%) compared with previous studies (around 50% of male sex rate).[3,15]

There are some other considerations that should be noted when interpreting the results of the present study. First, as for the achievement of correction, we used the term "satisfactory correction" for convenient statistical comparison. As described in the Methods section, "unsatisfactory correction" does not indicate a failure of hemiepiphyseal stapling: that is, the 30% rate of unsatisfactory correction should not be confused with the failure rate. The results of hemiepiphyseal stapling for both patient groups were excellent. Only 2 patients (2.9%) among our 70 study cases had unresolved correction after hemiepiphyseal stapling. Second, we used statistical methods to reduce the confounding effects of various biases, but the possibility of bias cannot be fully excluded. Although the probability of remaining bias in our propensity score analysis is reported to be low and comparable with that of a randomized-controlled trial,[22] such analysis remains subject to biases from unobserved differences.[16] The possibilities of statistical error should also be considered during interpreting the subgroup comparison of correction velocity according to the anatomic sites. Although the primary difference of correction velocity between the 2 groups seems to originate from the cases of proximal tibia, it might be violated by small sample size and uneven matching of anatomic sites. Future studies with a large cohort are surely needed. Third, the retrospective nature of this study could also limit the application of our results.

There was another noteworthy finding from our current analyses. The overcorrection rate was higher in the idiopathic group than in the MHE group. Therefore, we may have tended to undercorrect for the deformity in the MHE group to meet the similar features of the contralateral limb, whereas we may have tended to overcorrect for the deformity in the idiopathic group to compensate for the rebound phenomenon. Furthermore, the correction velocity may additionally affect the tendency of overcorrection; in other words, the faster correction velocity may result in a shorter duration of correction to staple removal resulting higher chance of overcorrection.

In conclusion, satisfactory correction could be achieved by hemiepiphyseal stapling in MHE patients with a genu valgum deformity, with outcomes comparable with those of idiopathic patients. However, MHE patients showed a lower correction velocity and additionally needed about 6 months for correction compared with idiopathic cases. Temporary hemiepiphysiodesis should be considered at an earlier age for MHE patients.

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