Acta Med. Okayama, 2017
Vol. 71, No. 2, pp. 119-126

Acta Medica Okayama
http://escholarship.lib.okayama-u.ac.jp/amo/

Original Article

Scoliosis in Patients with Severe Cerebral Palsy: Three Different Courses in Adolescents

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Patients with cerebral palsy (CP) frequently present with scoliosis; however, the pattern of curve progression is difficult to predict. We aimed to clarify the natural course of the progression of scoliosis and to identify scoliosis predictors. This was a retrospective, single-center, observational study. Total of 92 CP patients from Asahikawasou Ryouiku Iryou Center in Okayama, Japan were retrospectively analyzed. Cobb angle, presence of hip dislocation and pelvic obliquity, and Gross Motor Function Classification System (GMFCS) were investigated. Severe CP was defined as GMFCS level IV or V. The mean observation period was 10.7 years. Thirty-four severe CP patients presented with scoliosis and were divided into 3 groups based on their clinical courses: severe, moderate and mild. The mean Cobb angles at the final follow-up were 129°, 53°, and 13° in the severe, moderate, and mild groups, respectively. The average progressions from 18 to 25 years were 2.7°/year, 0.7°/year, and 0.1°/year in the severe, moderate, and mild curve groups, respectively. We observed the natural course of scoliosis and identified 3 courses based on the Cobb angle at 15 and 18 years of age. This method of classification may help clinicians predict the patients' disease progression.

Key words: severe cerebral palsy, scoliosis, natural course, Cobb angle, progression

Patients with cerebral palsy (CP) frequently present with scoliosis [1,2]. However, it has been difficult to define the incidence of scoliosis in patients with CP because the previous attempts have employed populations with widely disparate ages and CP severity, and thus yielded widely different incidences [3-6]. This is particularly important in light of a study showing that severity of CP is an independent risk factor for severe scoliosis [7]. Moreover, how scoliosis progresses remains unknown, even though understanding the natural course is very important for patient management. If a curve with a high risk of progression could be identified at an early stage, the patient could receive therapy before the appearance of severe symptoms and deformity. Nonetheless, there is currently no clear consensus on the risk factors for progression at an early stage.

Puberty is a turning point in adolescent idiopathic scoliosis (AIS) [8]. Puberty starts at 11 and 13 years of age and peak height velocity is reached at 13 and 15 years of age in girls and boys, respectively [9]. The natural course of the spinal curve in AIS can be judged from the first 2 years of puberty [10-12]. We hypothesized that the progression of the spinal curve in CP patients can be predicted in puberty as well. The aim of the present study was to clarify the natural course of the progression of scoliosis and to identify the predictive factors for the progression of scoliosis in severe CP.

Received July 28, 2016; accepted October 26, 2016.
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Conflict of Interest Disclosures: No potential conflict of interest relevant to this article was reported.

Materials and Methods

Study design. This was a retrospective, single-center, observational study of adolescent CP patients from Asahikawasou Ryouiku Iryou Center in Okayama, Japan, and was approved by the ethics committee at that institution.

Study participants. Patients who had been diagnosed as having CP and admitted to our hospital between April 2014 and June 2014 were included in the present study. Some of these patients had been hospitalized multiple times throughout a period of 10 years or more. At our institution, whole spinal radiography is performed at least once a year in patients with scoliosis aged 2-30 years. Patients who had undergone spinal surgery and those in whom congenital scoliosis was diagnosed were excluded. Also, subjects were excluded if consent was withheld from parents or caregivers. A lack of specific denial from the parent left the decision up to the facility director.

Assessments. Initially, we investigated the patients' age and the presence of scoliosis, dislocation of the hip, and pelvic obliquity in a cross-sectional manner by using the information between April 2014 and June 2014. Then, the data from patients with scoliosis were retrospectively collected and analyzed. We investigated patients' clinical course and measured the current Cobb angle in each scoliosis patient. Finally, severe CP patients aged 10-30 years were further examined. We focused on the puberty period to examine whether it is possible to predict curve progression before skeletal maturity. Patients were in the supine position during the radiography examination. Scoliosis was defined as a Cobb angle $\geq 10°$. CP severity was evaluated by the Gross Motor Function Classification System (GMFCS) [13] (Table 1). Severe CP was defined as GMFCS level IV or V. Hip dislocation was defined as a migration percentage [14] of $\geq 100\%$, which means that the medial edge of the femoral head does not make contact with the lateral border of the acetabulum.

Statistical analysis. The Shapiro-Wilk test was used to determine whether the data were normally distributed. The chi-square test and Kruskal-Wallis test were used to compare patient groups. All *p*-values were 2 sided, and *p*-values of 0.05 or less were considered statistically significant. All statistical analyses were performed using EZR software (Saitama Medical Center, Jichi Medical University, Saitama, Japan). We used imputation-based procedures for analyzing data sets with missing values. When we had a missing value, the average of the values immediately before and after was used.

Results

Ninety-six CP patients were admitted to the hospital during the investigation period. Four patients were excluded for the following reasons: surgery, 1 case; congenital scoliosis, 1 case; and no radiography examination, 2 cases. As a result, 92 patients were finally enrolled in this study. The mean patient age and mean observation period were 25.3 ± 14.5 years and 8.5 ± 6.6 years, respectively. Among the 92 patients, 1 (1%), 10 (11%), 8 (9%), 23 (25%), and 50 (54%) were classified

Table 1 Gross Motor Function Classification System (GMFCS)

GMFCS Level 1	Children walk indoors and climb stairs without limitation. Children perform gross motor skills including running and jumping, but speed, balance and coordination are impaired.
GMFCS Level 2	Children walk indoors and outdoors and climb stairs holding onto a railing but experience limitations walking on uneven surfaces and inclines and walking in crowds or confined spaces.
GMFCS Level 3	Children walk indoors or outdoors on a level surface with an assistive mobility device. Children may climb stairs holding onto a railing. Children may propel a wheelchair manually or are transported when traveling for long distances or outdoors on uneven terrain.
GMFCS Level 4	Children may continue to walk for short distances with a walker or rely more on wheeled mobility at home and school and in the community.
GMFCS Level 5	Physical impairment restricts voluntary control of movement and the ability to maintain antigravity head and trunk postures. All areas of motor function are limited. Children have no means of independent mobility and are transported.

We defined severe cerebral palsy as GMFCS level Ⅳ or Ⅴ.

as GMFCS level I, II, III, IV, and V, respectively. The presence of scoliosis, dislocation of the hip, and pelvic obliquity were identified in 46 (50%), 21 (23%), and 26 (28%) patients, respectively. The mean Cobb angle was 55.1 ± 33.3° (Table 2).

After evaluating the presence of scoliosis, the severity of CP, and the average Cobb angle, all patients were divided into the following age groups and further analyzed (Table 3). The prevalences of scoliosis in the CP groups aged 0-9 years, 10-19 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years, and 60-69 years were 22.2% (2/9), 44.4% (12/27), 71.4% (20/28), 53.3% (8/15), 0% (0/3), 38% (3/8), and 50% (1/2), respectively. The rates of severe CP in the groups aged 0-9 years, 10-19 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years, and 60-69 years were 66.7% (6/9), 74.1% (20/27), 82.1% (23/28), 75.0% (12/15), 100% (3/3), 100% (8/8), and 50% (1/2) respectively. The mean Cobb angles were 40.5 ± 18°, 44.3 ± 35°, 61.0 ± 44°, 52.0 ± 34°, 0°, 84.3 ± 30°, and 30° in the groups aged 0-9 years, 10-19 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years, and 60-69 years, respectively (Fig. 1). There were no patients with scoliosis in the 40-49 years age group, and there was only 1 patient with scoliosis in the 60-69 years group. The severity of CP and the Cobb angle by age are shown in Fig. 2. The course of the Cobb angle in 46 scoliosis cases from 2 to 30 years is shown in Fig. 3. Thirty-four patients with severe CP (GMFCS IV or V) and scoliosis

Table 2 Cross-sectional study results

		Average ± SD	Min	Max
Age (years)		25.3 ± 14.5	5	69
period (years)		8.5 ± 6.6	0	29
Cobb angle		55.1 ± 33.3°	0	150
Male / Female		53/49	n	%
Scoliosis (≧10°)			46	50%
Dislocation of hip			21	23%
Pelvic obliquity			26	28%
GMFCS	Ⅰ		1	1%
	Ⅱ		10	11%
	Ⅲ		8	9%
	Ⅳ		23	25%
	Ⅴ		50	54%

Characteristic data of all participants are shown in the table.
GMFCS: Gross Motor Function Classification System.

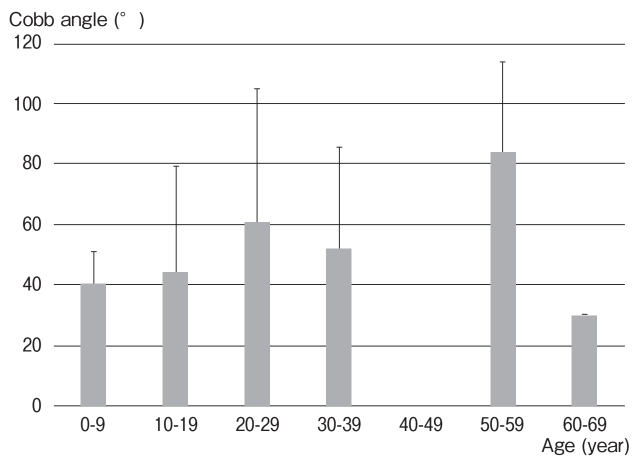

Fig. 1 Average Cobb angle among the age groups (n = 46).

Table 3 Demographic characteristics of all subjects according to Gross Motor Function

Age	GMFCS Ⅰ	Ⅱ	Ⅲ	Ⅳ	Ⅴ	Total
0–9	0/0	0/2	0/1	0/1	2/5	2/9
10–19	0/1	0/5	1/1	3/7	8/13	12/27
20–29	0/0	0/0	0/5	5/5	15/18	20/28
30–39	0/0	1/3	0/0	3/4	4/8	8/15
40–49	0/0	0/0	0/0	0/1	0/2	0/3
50–59	0/0	0/0	0/0	1/4	2/4	3/8
60–69	0/0	0/0	1/1	0/1	0/0	1/2
Total	0/1	1/10	2/8	12/23	31/50	46/92

Classification System (GMFCS) and age groups.
Number of indexes patients with scoliosis/all patients. GMFCS: Gross Motor Function Classification System.

were further investigated regarding their scoliosis progression during puberty.

Fig. 4 shows data from these patients ranging from the 10- to 30-year age period. The mean observation period was 10.7 years. The participants were divided into 3 groups: severe-, moderate- and mild-curve groups. The severe-curve group included patients with a Cobb angle ≥ 50° at 15 years. The moderate-curve group included patients with a Cobb angle < 50° at 15 years and ≥ 20° at 18 years. The mild-curve group included patients with a Cobb angle < 20° at 18 years (Fig. 5). The mean Cobb angles at the final follow up were 129 ± 9.5°, 53 ± 15°, and 13 ± 11° in the severe-, moderate-, and mild-curve groups, respectively. A significant difference in the mean Cobb angle among the 3 groups was found at 11 years (Kruskal-Wallis test, $p < 0.05$). Significant differences in the Cobb angle between the mild vs. moderate, mild vs. severe, and moderate vs. severe groups were seen at 15 years (Table 4). The prevalences of hip dislocation in the severe, moderate and mild groups were 38.5% (5/13), 33. 3% (4/12), and 12.5% (1/9), and the prevalences of pelvic obliquity were 61.5% (8/13), 66.7% (8/12), and 22.2% (2/9), respectively (Table 5). No significant difference in the incidence of hip dislocation ($p = 0.41$, Fisher's exact Test) or pelvic obliquity ($p = 0.119$, Fisher's exact Test) was observed among the 3 groups.

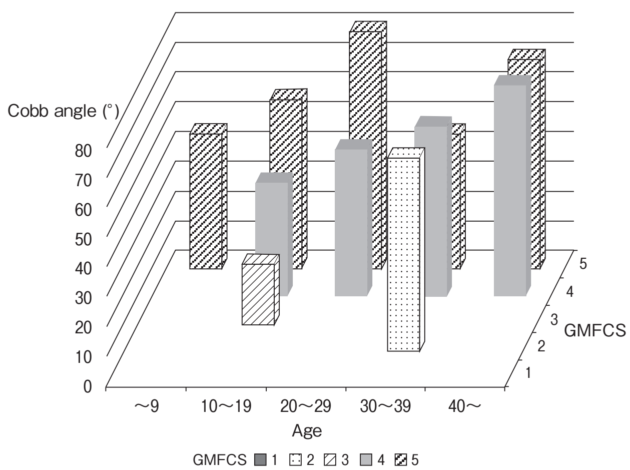

Fig. 2 The severity of CP and the Cobb angle by age.

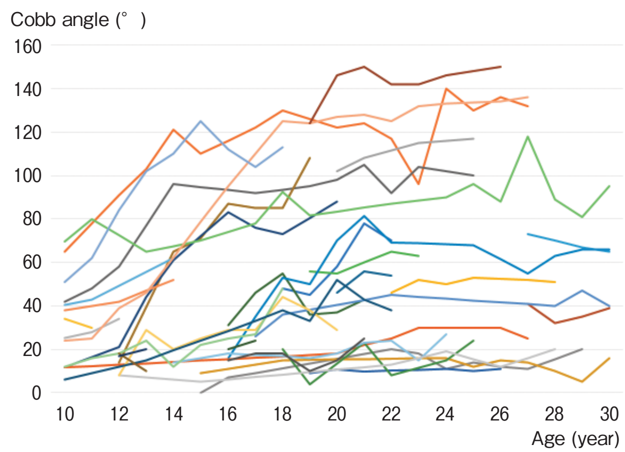

Fig. 4 The course of progression of scoliosis with severe cerebral palsy (GMFCS IV or V) from 10 to 30 years of age (n = 30). GMFCS, Gross Motor Function Classification System.

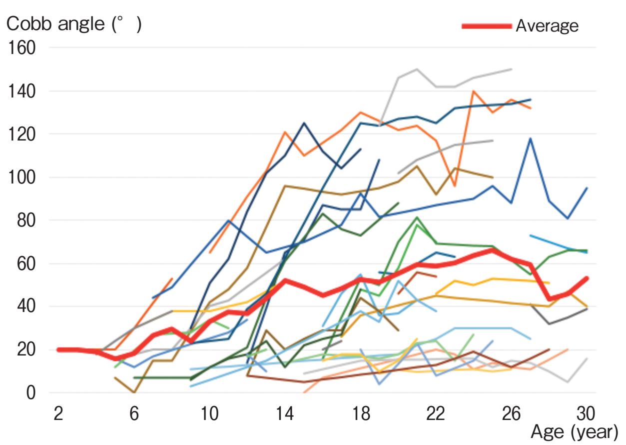

Fig. 3 The course of progression of scoliosis between 2 and 30 years of age.

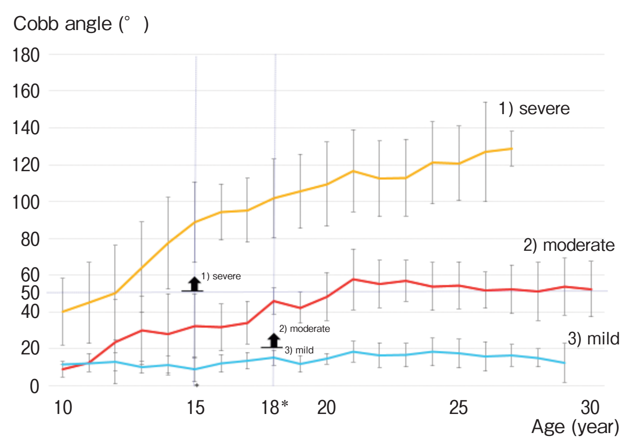

Fig. 5 The different courses of progression of scoliosis between the 3 groups.
*$p < 0.01$ by Kruskal-Wallis test.

Table 4 *P*-value of comparison of Cobb angle among 3 groups at each age

	Age	10	11	12	13	14	15	16	17	18
three groups	$p=$	0.06000	0.04000	0.02400	0.00470	0.00420	0.00140	0.00033	0.00021	0.00013
mild vs moderate	$p=$	–	–	–	–	–	0.0480	0.0065	0.0035	0.0064
mild vs severe	$p=$	–	–	0.0420	0.0270	0.0270	0.0076	0.0035	0.0035	0.0017
moderate vs severe	$p=$	–	–	–	–	0.0170	0.0180	0.0035	0.0017	0.0064

The Kruskal-Wallis test was used for analysis among the 3 groups. *P* value adjustment by the Bonferroni method was used for tests between 2 groups.

Table 5 Demographic characteristics of all subjects regarding dislocation of hip and pelvic obliquity

		Scoliosis (≧10°)				No scoliosis	Total
GMFCS		Ⅰ, Ⅱ, Ⅲ	Ⅳ or Ⅴ				
			severe	moderate	mild		
Dislocation of hip	(+)	6	5	4	1	5	21
	(−)	6	8	8	8	41	71
Total		12	13	12	9	46	92
		Scoliosis (≧10°)				No scoliosis	Total
GMFCS		Ⅰ, Ⅱ, Ⅲ	Ⅳ or Ⅴ				
			severe	moderate	mild		
Pelvic obliquity	(+)	7	8	8	2	1	26
	(−)	5	5	4	7	45	66
Total		12	13	12	9	46	92

The prevalences of hip dislocation were 38.5% (5/13), 33.3% (4/12), and 12.5% (1/9) in the mild group, moderate group, and severe group, respectively. The prevalences of pelvic obliquity were 61.5% (8/13), 66.7% (8/12), and 22.2% (2/9). No significant difference in the incidence of hip dislocation and pelvic obliquity was observed among the 3 groups.

Discussion

Although the cumulative incidence of severe scoliosis has been reported [7], it is unclear how and when the spinal curve progresses rapidly. Insufficient understanding of the clinical course of scoliosis in CP patients is a serious problem for its treatment, because conservative therapy in CP patients cannot prevent curve progression [15-18], and the curve progresses even after skeletal maturity [19]. Therefore, untreated cases often present with severe scoliosis. Severe scoliosis can lead to problems when sitting, pressure sores [20], respiratory problems [21], secondary hip dislocation [22], and wind swept deformity [23,24]. These symptoms complicate the quality of life of patients [25], and make it difficult for their caregivers to care for them.

Careful management of AIS is required particularly during the first 2 years of puberty, from 11 to 13 years of age in girls and from 13 to 15 years of age in boys. Patients showing progression of 1°/month (12°/year) during that period are likely to require surgery [8]. We thus consider the period from 11 to 15 years of age as an important one and define the time of skeletal maturity as 18 years of age. We therefore focused on the full puberty period from 11 to 18 years of age. Regarding bone maturation, the mean bone age of boys with CP was the same as that of healthy boys, but a high prevalence of both delayed and advanced skeletal maturity was noted in boys with CP [26]. Individual variations result from malnutrition, health condition, and endocrine abnormalities. In order to observe curve progression after skeletal maturity, the previous study evaluated patients up to 30 years of age.

By observing the course of the spinal curve, it was clear that patients with a Cobb angle of 50° before 15 years of age would progress to severe scoliosis at the final follow-up. On the other hand, it seemed that patients with a Cobb angle < 50° at 15 years of age followed 2 different courses: in one course, the spinal curve advanced to 40-60°, and in the other course, it settled to under 20° at the final follow up. We adopted 20° as the threshold separating the mild and moderate group based on previous articles noting a 20° angle as moderate or severe, or the criterion for starting treatment with a brace [27, 28]. Therefore, we suggested that CP patients with scoliosis could be divided into severe-, moderate-, and mild-curve groups based on the natural course over time. The mean Cobb angle at the final follow up was 129 ± 9.5° in the severe group, 53 ± 15° in the moderate group, and 13 ± 11° in the mild group. It has been reported that scoliosis in CP patients progresses at a constant speed even after a growth spurt. A previous paper showed that curve progression of 1.4°/year in curves greater than 50° and 0.8°/year in curves less than 50° occurred after completion of growth [16]. In the present study, the mean final Cobb angle in the moderate group reached approximately 50° at completion of growth. Based on the previous paper, it was difficult to divide patients into either group. Relying only on the 50° Cobb angle to predict progression after skeletal maturity may lead to an inaccurate prediction of the scoliosis progression. Therefore, in order to predict the course of the curve after a growth spurt, it was reasonable to divide the patients into 3 groups rather than divide them into 2 groups using a 50° Cobb angle as a cutoff. Based on our classification, the progression of scoliosis at around 15 years of age was considered important from a clinical point of view. Furthermore, in cases with a Cobb angle < 20° at the end of puberty, frequent observation is unnecessary because progression may be minimal. The average progression of the curve after skeletal maturity was 3.0°/year in the severe-curve group, 0.5°/year in the moderate-curve group, and 0.1°/year in the mild-curve group.

In the present study, 13 subjects were more than 40 years old, which was a small number compared with the number of subjects under 40 years old. According to a recent report about the long-term prognosis of CP patients, the average life expectancy of a 15-year-old girl with the most severe disability is 14 years [29, 30]. This may be the reason why there were only a few patients over 40 years of age in the present study. The prevalence of scoliosis increases with age up to 30 years. The peak incidence of scoliosis was observed in the group aged 20-29 years. Similar results were found regarding the age-specific Cobb angle. Further, there was great variation in the Cobb angle among cases. According to the severity of CP by age, the population with GMFCS level V was the highest in the 20-29 age group. The prevalence of scoliosis and mean Cobb angle were highest in the 20-29 age group; this may have been due to the severity of CP. In other words, the prevalence of scoliosis appears to increase until patients reach their twenties and then reach a plateau. The deviation of the Cobb angle increased more in the 20-29 age group than in the 10-19 age group. Based on this, we considered that it was important to observe the progression of scoliosis from 10 years of age to 29 years of age. The mean Cobb angle also increased with age from 2 to 30 years.

Several studies on the progression of scoliosis in CP have been published. Previously reported risk factors of scoliosis included the severity of CP by GMFCS [7, 23], age at onset [16], magnitude of the curve [16, 19], pelvic obliquity [29], and hip dislocation [22, 31, 32]. In another report, half of the patients with GMFCS level IV or V progressed to severe scoliosis at 20 years of age [7]. Physicians have difficulty deciding whether to manage patients with GMFCS grade IV or V. Therefore, the present study was limited to subjects with GMFCS level IV or V. Saito *et al*. observed the natural course of scoliosis in 37 patients with mild and severe CP [16]. They noted that a spinal curve of more than 40° before 15 years of age and total body involvement are high risk factors; however, 6 of the patients were ambulatory and were not considered to have severe CP. This study included 73 severe CP patients defined by GMFCS level IV or V, among whom 34 (46.6%) had scoliosis defined by a Cobb angle ≥ 10°. Inan *et al*. reported that unilateral hip dislocation and pelvic obliquity do not affect the progression of scoliosis, but unilateral hip dislocation affects pelvic obliquity [33]. Porter *et al*. evaluated patients with GMFCS level V and showed that hip dislocation and pelvic obliquity are risk factors of progression [31]. In our study, no significant difference was observed among the 3 groups.

The present study has some limitations. Children with severe CP (GMFCS level IV or V) are unable to maintain a standing-sitting position. In the present study, radiography was performed with patients in the supine position, and there may have been measurement errors caused by this posture, since the Cobb angle in the sitting position is likely to be greater than that in the supine position. In fact, radiographic improvement of the Cobb angle from the previous year was found in some cases. Considering the possibility of measurement error, a Cobb angle of 20° might be suitable for a clinically meaningful diagnosis of scoliosis. Second, the exclusion of surgery cases in the present study could be considered to have introduced a selection bias. This concern may be valid when a lot of cases leading to surgery are excluded; however, we encountered only one case that we had to exclude due to surgery, so this exclusion likely did not invalidate our results. Finally, in clinical practice it may be necessary to confirm the skeletal age by radiograph examination of the elbow joint or hand [26, 34, 35]. The present study utilized the average of multiple cases for analysis.

In conclusion, the natural history of scoliosis in severe CP patients defined by GMFCS level IV or V was investigated until the age of 30 years. Three groups were formed based on the clinical courses of scoliosis in CP patients: severe-, moderate-, and mild-curve groups. The Cobb angle at 15 years of age was found to be a predictor of the progression of scoliosis after skeletal maturity and the magnitude of the curve at approximately 30 years of age. The Cobb angle at 18 years of age serves as a more useful reference to distinguish the mild course from the moderate course. The progressions of the curve after skeletal maturity in the moderate group and mild group were lower than those reported previously. Classifying patients into these 3 groups may help clinicians predict the patients' prognosis and improve their management.

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