

Difference between bone age at the hand and elbow at the onset of puberty

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Abstract

In the pubertal period, bone age advances rapidly in conjunction with growth spurts. Precise bone-age assessments in this period are important, but results from the hand and elbow can be different. We aimed to compare the bone age between the hand and elbow around puberty onset and to elucidate the chronological age confirming puberty onset according to elbow-based bone age.

A total of 211 peripubertal subjects (127 boys and 84 girls) who underwent hand and elbow radiographs within 2 months was enrolled. Two radiologists and a pediatric orthopedic surgeon assessed bone age. Hand bone age was graded using the Greulich–Pyle (GP) method, and elbow bone age was determined using the Sauvegrain method. The correlation of 2 methods was evaluated by Demining regression analysis, and the mean absolute difference (MAD) with chronological age was compared between prepubertal and pubertal subjects. Receiver-operating characteristic curve analysis was performed to determine the chronological age confirming puberty onset.

There was a statistically significant difference in bone age revealed by the GP and Sauvegrain methods in the pubertal group. In the pubertal group, the MAD was 1.26 ± 0.90 years with the GP method and 0.61 ± 0.47 years with the Sauvegrain method in boys (P < .001), while in girls, the MAD was 0.84 ± 0.60 years and 0.53 ± 0.36 years with the same 2 methods (P = .033). The chronological age for confirming puberty onset using the elbow was 12.2 years in boys and 10.3 years in girls.

The bone ages of hand and elbow were different at puberty, and the elbow was a more reliable location for bone-age assessment at puberty. Puberty onset according to elbow occurred slightly earlier than expected.

Abbreviations: AP = anteroposterior, CI = confidence interval, GP = Greulich–Pyle, ICC = intra-class correlation coefficient, MAD = mean absolute difference, PHV = peak height velocity, ROC = receiver-operating characteristic.

Keywords: bone age, chronological age, elbow, hand, puberty

1. Introduction

Bone age is an important indicator of developmental status and sexual maturity and is a predictor of adult height in adolescents.^[1-3] In the pubertal period, bone age advances rapidly through growth spurts. Prior research suggests that puberty starts at a bone age of 13 years and ends at 15 years in

boys and starts at 11 years and ends at 13 years in girls.^[4] It is well-known, however, that chronological age is not identical to bone age.^[5] Determining bone age and the beginning of puberty is important for pediatric clinicians seeking to make height predictions or decisions regarding hormone therapy. In the surgical field, it is especially important to be able to estimate

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disease progression in pediatric patients with limb-length discrepancies or idiopathic scoliosis as these influence the timing and method of surgery.

The most commonly used method for assessing bone age is the Greulich and Pyle (GP) method, which is an atlas comparison technique based on a radiograph of the left hand.^[6] However, this method has limitations during puberty because morphological changes of hand and wrist bones vary and are not prominent during this period. In addition, the bone ages of 14.5 years in boys and 11.5 and 12.5 years in girls are not represented in the atlas. For these reasons, the Sauvegrain method, which is a scoring system based on anteroposterior (AP) and lateral elbow radiographs, was introduced for assessing bone age during puberty because significant morphological changes in elbow ossification centers allow regular 6-month interval scaling for bone age.^[7] In addition, this method is well correlated with peak height velocity (PHV), which is defined as the period of fastest growth during puberty and is a valuable marker for assessing the phase of puberty and predicting remaining growth.^[8] Some authors have reported the usefulness of the Sauvegrain method in determining timing of epiphysiodesis for limb-length discrepancies and spinal arthrodesis for idiopathic scoliosis.

To our knowledge, however, the among-patient difference between bone ages of the hand and elbow has not been largely addressed. The purpose of this study was to compare the difference between bone ages of hand and elbow around the pubertal period according to chronological age. With this approach, we attempted to verify the usefulness of measuring elbow bone age at puberty. Furthermore, we aimed to determine the chronological age of puberty onset using the elbow-based bone age in both boys and girls.

2. Materials and methods

2.1. Study population

The institutional review board of our institution approved this retrospective study and waived the need for written informed consent. From March 2004 to February 2020, pre-pubertal and pubertal subjects (girls aged 7–14 years and boys aged 9–16 years) with hand AP and elbow AP and lateral radiographs collaged within a 2-month interval were enrolled. Individuals with a clinical history of growth disorders such as precocious or delayed puberty and radiographic evidence of fracture or deformity were excluded. We aimed to image the left hand and left elbow but, if only the right side was available, right-side radiographs were included.

2.2. Bone-age assessment

To blind the assessments, all radiographs were stored in a file from which the patient characteristics except sex were deleted. Three experts (W.Y.J., a pediatric orthopedic surgeon with 12 years of experience; K.S.A., a musculoskeletal radiologist with 16 years of experience; and S.O., a pediatric radiologist with 7 years of experience) assessed bone age without knowledge of the subject's chronological age. The hand bone age was determined using the GP method by K.S.A and S.O., and the elbow bone age was determined with the Sauvegrain method by W.Y.J. and K.S.A. The Sauvegrain method is based on a 27-point scoring system and takes into account the following 4 anatomical structures of the elbow: the lateral condyle (1–9 points), the trochlea (1–5 points), the

olecranon apophysis (1–7 points), and the proximal radial epiphysis (1–6 points).^[9] A score of 0 points was applied for each part in which the secondary ossification center was not visible, slightly broadening the age range regardless of chronological age. After bone-age assessment, subjects with Sauvegrain scores less than 8 points were additionally excluded because the method is only able to accurately assess those with a total score greater than or equal to 8 points. More than two-thirds of all cases were interpreted independently to evaluate inter-observer agreements, and the rest were interpreted in consensus. Chronological age was calculated as the study date of the elbow radiographs minus the birth date and was expressed in years to the nearest hundredth.

2.3. Statistical analysis

The inter-observer reliability was calculated using the intra-class correlation coefficient (ICC) with a 95% confidence interval (CI). The inter-observer agreement was categorized as follows according to value of ICC: 0 to 0.20, poor; 0.21 to 0.40, fair; 0.41 to 0.60, moderate; 0.61 to 0.80, substantial; and 0.81 to 1.00, excellent.

Deming regression analysis was performed to estimate the difference in bone ages from the 2 methods.^[10] For subgroup analysis, boys were divided at the age of 13 years into prepubertal (<13 years) and pubertal (≥13 years) subpopulations, while girls were divided at the age of 11 years into pre-pubertal (<11 years) and pubertal (≥11 years) subpopulations. The mean absolute difference (MAD) between bone age and chronological age was calculated, and paired *t* test was used to compare the MAD between the 2 methods in the pre-pubertal and pubertal groups. We also compared the proportion of cases with MAD within 6 months between the 2 methods using McNemar test. In each subgroup, Deming regression analysis was performed.

Receiver-operating characteristic (ROC) curve analysis was conducted to determine the cutoff chronological age suggesting the beginning of puberty. According to a previous report, a score of 3 points for the olecranon apophysis, which is a stage involving double ossification centers of olecranon apophysis, is considered to suggest the beginning of puberty.^[11] The cutoff value for puberty was set to more than 3 points for the olecranon apophysis (i.e., the puberty group had an olecranon apophysis score \geq 3 points and the pre-puberty group had an olecranon apophysis score <3 points). The optimal cutoff value was determined by Youden index. All statistical analyses were conducted using SAS software version 9.4 (SAS Institute Inc., Cary, NC), and a *P* value less than .05 was considered to indicate statistical significance.

3. Results

3.1. Subject demographics and inter-observer agreements

After exclusion of 9 subjects with total Sauvegrain score less than 8 points, a total of 211 subjects was enrolled, including 127 boys $(12.80 \pm 1.63 \text{ years})$ and 84 girls $(10.52 \pm 1.32 \text{ years})$. Among 211 pairs of elbow and hand, 33 elbows and 17 hands were right sided. A total of 185 pairs (87.7%) of hand and elbow radiographs was collected on the same day. The mean absolute interval between hand and elbow examinations was 0.86 ± 6.93 days.

Inter-observer agreement was excellent for both the GP (ICC: 92.78, 95% CI: 90.25–94.68) and Sauvegrain (ICC: 98.62, 95%

Table 1	
Inter-observer reliability of the GP and Sauvegrain	n methods.

	ICC (%)	(95% CI)
GP bone age	92.8	(90.3-94.7)
Sauvegrain bone age	98.6	(98.1-99.0)
Lateral condyle	98.9	(98.5-99.2)
Trochlea	95.3	(93.6-96.5)
Olecranon apophysis	97.4	(96.4-98.0)
Proximal radial epiphysis	93.9	(91.8-95.5)

CI = confidence interval, GP = Greulich-Pyle, ICC = intra-class correlation coefficient.

CI: 98.13–98.98) methods, but the ICC was higher with use of the Sauvegrain method. Considering body parts, the lateral condyle showed the highest ICC, followed by the olecranon apophysis, trochlea, and proximal radial epiphysis, with all values being higher than those achieved with the GP method. The ICC between observers in each method is reported in Table 1.

3.2. Difference between GP bone age and Sauvegrain bone age

Deming regression analysis revealed the existence of a statistically significant difference in results between the GP and Sauvegrain methods (slope: 0.794, 95% CI: 0.733–0.855), as the 95% CI of slope did not include 1 (Fig. 1). In subgroup analysis, there was no statistically significant difference in the results between the 2 methods concerning pre-puberty age (slope: 0.955, 95% CI: 0.845–1.065; intercept 0.856, 95% CI: -0.413 to 2.126) (Fig. 2A), where the 95% CI of slope included 1 and the 95% CI of the intercept included 0. However, in the pubertal age group, there was a significant difference in the results attained between the 2 methods (slope: 0.646, 95% CI: 0.567–0.724) (Fig. 2B), indicating that an overall difference was apparent in the pubertal age group.

3.3. The MADs of the GP and Sauvegrain methods in prepubertal and pubertal groups

The MAD of chronological age between the 2 methods by sex and age group (pre-puberty and puberty) was compared. In boys who had experienced puberty, the GP method revealed an MAD of 1.26 ± 0.90 years, while the Sauvegrain method revealed a MAD of 0.61 ± 0.47 years (P < .001). Meanwhile, in girls who had experienced puberty, the MAD values were 0.84 ± 0.60 years with the GP method and 0.53 ± 0.36 years with the Sauvegrain method (P = .033). Conversely, the variation in MAD was not significant between boys and girls who had not yet experienced puberty (P = .476 and P = .997, retrospectively). The MADs of the GP and Sauvegrain methods in the pre-pubertal and pubertal groups are shown in Table 2.

In comparison of the proportion of cases with MAD within 6 months between the 2 methods by sex and puberty, there was a significant difference between outcomes of the GP and Sauvegrain methods in boys who had experienced puberty (19.2% and 53.9%, respectively; P < .001). This proportion was also higher with use of the Sauvegrain method (52.9%) in comparison with the GP method (38.2%) in girls who had experienced puberty (P = .223). However, for those who had not yet experienced puberty, the difference was not significant for either sex. A comparison of the proportion of cases with MAD within 6 months between the 2 methods by sex and puberty is presented in Table 3.

3.4. Chronological age of puberty onset based on elbow bone age

The estimated optimal chronological age for puberty onset obtained by analyzing ROC curves based on the olecranon apophysis status was 12.2 years in boys (sensitivity: 98.9%, specificity: 91.7%, area under the curve: 0.99, 95% CI: 0.98–1.0)







Figure 2. Deming regression analysis for the comparison of GP and Sauvegrain bone-age results according to age group: pre-puberty (A) and puberty (B). GP = Greulich–Pyle.

and 10.3 years in girls (sensitivity: 88.1%, specificity: 92.0%, area under the curve: 0.95, 95% CI: 0.918–0.997). ROC curves for puberty prediction according to status of the olecranon apophysis in boys and girls are shown in Figure 3.

4. Discussion

In this study, the bone ages of the hand and elbow were different at puberty, and elbow was a more reliable location for bone-age assessment at puberty in both boys and girls. Elbow-based puberty onset occurred at 12.2 years in boys and 10.3 years in girls, which were slightly earlier than the expected chronological ages in the normal population.

In assessing bone age, the GP method, which is the most commonly used approach, uses left-hand radiographs. However, there are limitations in applying this method during puberty due to variations in the morphological changes of the hand bones during this period and the propensity for a non-linear scale

Table 2

Comparison of mean absolute differences with chronological age between the GP and Sauvegrain methods by sex and puberty.

	MAD, mean (SD)		
	GP bone age	Sauvegrain bone age	P value
Total (n=211)	1.00 (0.72)	0.82 (0.62)	.002
Pre-puberty (n = 125)	0.93 (0.63)	0.98 (0.68)	.471
Puberty (n $=$ 86)	1.09 (0.82)	0.58 (0.43)	<.001
Boys (n=127)	1.07 (0.76)	0.85 (0.66)	.009
Pre-puberty (n=75)	0.94 (0.62)	1.02 (0.72)	.399
Puberty (n = 52)	1.26 (0.90)	0.61 (0.47)	<.001
Girls $(n = 84)$	0.88 (0.63)	0.76 (0.55)	.093
Pre-puberty (n=50)	0.91 (0.66)	0.91 (0.61)	.996
Puberty $(n = 34)$	0.84 (0.60)	0.53 (0.36)	.012

Table 3

Comparison of the proportion of cases with MAD w	vithin 6 months
between the GP and Sauvegrain methods by sex a	ind puberty.

	MAD \leq 6 months, n (%)		
	GP bone age	Sauvegrain bone age	P value
Total (n=211)	61 (28.9)	82 (38.9)	.029
Pre-puberty (n=125)	38 (30.4)	36 (28.8)	.777
Puberty (n $=$ 86)	23 (26.7)	46 (53.5)	.001
Boys (n = 127)	32 (25.2)	50 (39.4)	.014
Pre-puberty (n=75)	22 (29.3)	22 (29.3)	>.999
Puberty (n = 52)	10 (19.2)	28 (53.9)	<.001
Girls $(n = 84)$	29 (34.5)	32 (38.1)	.631
Pre-puberty (n = 50)	16 (32.0)	14 (28.0)	.670
Puberty (n=34)	19 (38.2)	18 (52.9)	.225

GP = Greulich-Pyle, MAD = mean absolute difference.

GP=Greulich-Pyle, MAD=mean absolute difference.

interval. On the other hand, the Sauvegrain method, which employs elbow radiographs, provides data on bone age at puberty with excellent reproducibility and a regular 6-month scale.^[9] In our study, the inter-observer agreement was excellent with both the GP (ICC: 92.78) and Sauvegrain (ICC: 98.62) methods around puberty. However, the Sauvegrain method presented higher ICCs, concordant with the results of previous studies postulating the superiority of the Sauvegrain method.^[9]

For precise evaluation of bone age, a 6-month interval is usually applied, especially when deciding surgery timing for addressing lower-limb length discrepancies and idiopathic scoliosis.^[5,11-14] When we calculated the proportion of MAD within 6 months for the 2 methods, the Sauvegrain method showed a higher ratio than the GP method during puberty both in boys (P < .001) and girls (P = .223). This might be a natural consequence of the fact that the GP method cannot support

several age ranges on a 6-month scale. Although the difference was not statistically significant in girls, we posit that an insufficient sample size influenced this result. There was no significant difference between the 2 methods in either sex among those who had not yet undergone puberty. The GP method might have an advantage in the pre-puberty population considering the wider age range of this group. However, in the borderlinepubertal or pubertal period, elbow and hand radiographs should be assessed.

Another advantage of examining the elbow is its reliable correlation with timing of PHV. The olecranon apophysis is a valuable landmark during the accelerating pubertal growth phase of PHV.^[15] In patients with idiopathic scoliosis, determining the timing of PHV provides valuable information on the likelihood of progression of this condition to a magnitude requiring spinal arthrodesis.[16]



Figure 3. ROC curves for puberty prediction power of elbow bone age in boys (A) and girls (B). The optimal cutoff age was 12.2 years in boys (sensitivity: 98.9%, specificity: 91.7%, accuracy: 96.9%) and 10.3 years in girls (sensitivity: 88.1%, specificity: 92.0%, accuracy: 89.3%) by Yuden index. ROC = receiver-operating characteristic.

Bone age is closely related to the onset of puberty. The assessment of onset of puberty is important in children to support interpretation of endocrine and growth status. Many authors have reported that the age of puberty onset has shown a downward secular trend over the past few decades.^[17–20] A possible explanation for this emerging global early puberty trend is greater exposure to endocrine-disrupting chemicals, genetic traits, and changes in nutrition and body fat amount.^[21] In this context, we aimed to suggest a revised cutoff age for puberty onset according to olecranon-based bone age because the olecranon apophysis has shown good correlation with the acceleration phase of PHV.^[11] Notably, our results suggest an earlier chronological age for puberty onset in both boys and girls than what is currently accepted.

Our study has several limitations. First, the number of included subjects was relatively small; larger population studies are needed for confirmation of our results. Second, the study was a retrospective investigation with a limited cohort. We evaluated eligible patients who visited a tertiary hospital and who underwent hand and elbow radiographs within 2 months; however, most of them were emergency department visitors due to trauma, with a male sex dominance. Although pediatric trauma hand radiographs can be a source of population-specific data for bone age,^[22] a more stratified normal-population study is required to verify our results. Third, we used available right hand and elbow radiographs to maximize the sample size despite both the GP and Sauvegrain methods recommending the use of left-side images. Although some authors have reported that the difference in bone age according to side is not significant in the hands,^[23] variable side and location differences can exist at certain ages. Fourth, we grouped pre-puberty and puberty subjects based on chronological age; however, pubertal-age grouping should have been based on bone age. Because we attempted to compare the bone age of 2 sites, we hypothesized that bone age is linearly proportional to chronological age in normal subjects. Finally, we only evaluated members of the Korean population. Because bone age can show variations according to ethnic group,^[24] our results need to be validated and compared with those of other ethnic groups.

In conclusion, bone ages of the hand and elbow showed differences at puberty but not in pre-puberty. The elbow might be a more reliable location for bone-age assessment at puberty. Elbow and hand radiographs should be assessed in the pubertal period. The elbow-based puberty onset age was 12.2 years in boys and 10.3 years in girls, which were slightly earlier than previously reported chronological ages in the normal population.

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