J Surg Med. 2022;6(1):9-13.
DOI: 10.28982/josam.1021045

Journal of Surgery and Medicine
e-ISSN=2602-2079

Determination of bone age and evaluating the applicability of Greulich-Pyle standards among the Turkish children

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Ethics Committee Approval
The study protocol was approved by the Ethical Committee of Afyonkarahisar Health Sciences University (2020/561).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Published
2022 January 7

Abstract

Background/Aim: Bone age (BA) is important in the diagnosis and follow-up of pediatric growth disorders. Skeletal maturation can vary according to the geographical region and climate. The goal of this study is to investigate whether Greulich-Pyle (GP) method is suitable for detecting BA for Turkish children for all age groups and both genders.
Methods: In our retrospective cohort study, the roentgenograms of all pediatric patients who visited the pediatrics or pediatric endocrinology outpatient clinics and underwent left hand and wrist radiographs for suspicious trauma or BA determination were examined with reference to the GP atlas. Patients without evidence of chronic disease or growth disorders with body size and weight values between the 25th-75th percentile were included. Poor quality roentgenograms were excluded.
Results: Radiographs of 665 patients were analyzed and 310 (161 boys and 149 girls, age range 13-203 months) patients were included. The rate of concordant BA with CA was significantly higher in the children above 120 months of age and low BA was significantly higher among the children aged 120 months or below (P<0.001). The rate of concordant BA with CA was significantly higher among girls and low BA was significantly higher among boys (P=0.014). Among patients aged 120 months or below, low BA was significantly higher in the boys (P<0.001). There were no significant differences between the boys and girls aged 120 months and above (P=1.000)
Conclusion: Although widely used in the determination BA, local studies on the accuracy and reliability of the GP method are insufficient in less developed countries. The accuracy of this method in Turkish children, especially boys under the age of 10 years, is controversial, and correct standards should be developed.

Keywords: Bone age, Greulich-Pyle, Chronogical age, Wrist and hand, Skeletal maturation

How to cite: Özgül E, Yücel A, Kaya F, Koca SB , Ertekin A. Determination of bone age and evaluating applicability of Greulich-Pyle standards among the Turkish children. J Surg Med. 2022;6(1):9-13.

Introduction

Bone age (BA) determination is used in various areas, including medical, sporting, and forensic fields [1, 2]. Medical reasons often include endocrine, genetic, orthopedic, and renal disorders. It plays an important role in the diagnosis and treatment of pediatric growth disorders for pediatric endocrinologists. Adult height and growth potential can be estimated from BA radiographs in a child with a growth abnormality. The starting time and duration of the treatment in children who need hormonal therapy depends on the correct evaluation of BA [3, 4].

The most common methods used to determine BA are Greulich-Pyle (GP) and Tanner-Whitehouse2 (TW2) techniques. Studies have shown that there is no significant difference between these two methods in determining the BA [1, 3, 5-8]. The GP method is more preferred because it is less time consuming and practical [1-3]. GP, which is still the most widely used worldwide method in detecting BA, was published by Greulich and Pyle in 1959 under the title "Radiographic atlas of skeletal development of the hand and wrist".

The GP atlas contains reference radiographic images of the left wrist and hand created according to the male and female standards from birth to the age of 19 for males and 18 for females. However, the reference images in this atlas are based on 'Caucasian' children residing in the United States whose economic and educational statuses are above average, and uses the measurements compiled in the 1930s [1, 9]. Thus, the radiographic standards used in this method are based on a narrow population that is homogeneous both genetically and socio-economically. It is unclear whether these skeletal maturation standards, which use data from the first half of the twentieth century, are applicable in the existing populations that differ geographically, genetically, and socio-economically from the GP reference population. In fact, studies conducted in many countries attempted to evaluate the accuracy of the GP atlas in various populations [1-21]. Some studies found that GP atlas can be used for bone age determination in the population they have studied [2-4, 10, 15, 17, 20]. However, studies in developing countries have raised doubts about the accuracy of the GP atlas [1, 11, 12, 14, 21].

Although it is widely used in the determination of BA, local studies on the accuracy and reliability of the GP method are insufficient. To date, only a few studies were performed in Turkey regarding detecting BA with only the GP method [3, 10, 11]. Only one of these studies was conducted in all age groups and both genders and consisted of 228 patients [3]. In most of these studies, children over the age of 7 or 10 years were included. Büken et al. [10] examined girls and boys only over 11 years of age, and Koç et al. [11] examined only male patients over 7 years of age. Our study is the first one evaluating the accuracy and reliability of the use of the GP method only in the determination of BA in all age groups (13-203 months) with the highest number of patients (310 patients) in the Turkish population for both genders.

This study aimed to investigate whether the GP atlas is suitable for detecting BA for Turkish children for all age groups and both genders.

Materials and methods

The roentgenograms of all pediatric patients who visited the pediatrics or pediatric endocrinology outpatient clinics and underwent left hand and wrist radiographs for suspicious trauma or BA determination between 01.01.2020-01.12.2020 were examined retrospectively.

The patients meeting all the following criteria were included in the study: 1) No chronic disease or long-term drug use. 2) No clinical evidence of growth disorders, with values of body size and weight between the 25th and 75th percentiles for a normal age-related population. 3) Normal findings on the radiograph (without bone (including fractures) or soft tissue abnormalities).

Poor quality roentgenograms (poor sharpness or positioning and incomplete radiographs or images with artifacts) were excluded. Images with fractures, patients with known congenital anomalies, arthritis or any obvious disease of the hand and wrist that could affect skeletal maturation or interfere with BA determination were excluded. Patients whose body size and weight values were not measured were also excluded.

Digital wrist and hand images were taken from the Picture Archiving and Communication System. Posteroanterior (PA) or anteroposterior (AP) views including the distal ulna, radius, metacarpals, carpals, and phalanges were used. The BA within 2 SD of the normative data in the GP atlas were accepted as normal. The BA above or below 2 SD were considered abnormal.

The images were examined by three radiologists with 25 years, 15 years and 10 years of experience and BA was evaluated according to the GP atlas (9). The radiologists were blinded to the chronological age (CA) of each patient. Three radiologists made joint decisions for BA.

The radiographs of 665 patients were analyzed and a total of 310 patients who met the criteria were included in the study.

The study protocol was approved by the Ethics Committee of Afyonkarahisar Health Sciences University (2020/561).

Statistical analysis

All analyses were performed on SPSS v21 (SPSS Inc., Chicago, IL, USA). Histogram and Q-Q plots were used to determine whether the variables are normally distributed. Data were given as mean (standard deviation) (minimum - maximum) for continuous variables and as frequency (percentage) for categorical variables. Normally distributed variables were analyzed with the independent samples t test. Categorical variables were analyzed with the Chi-square test. Bonferroni correction method was used for pairwise comparisons. $P<0.05$ was considered statistically significant.

Results

We included 310 children (161 boys and 149 girls) in our study, with a mean age of 107.80 (49.48) months (range 13-203). The mean ages of the males and females were 111.41 (52.98) months (range 13-203) and 103.91 (45.26) months (range 14-196), respectively ($P=0.180$). The ages of 188 (60.65%) children were ≤120 months and that of 122 (39.35%) children were >120 months.

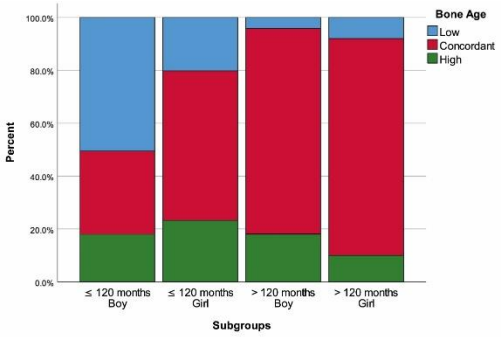
We divided the children into four subgroups according to age and gender. We had 89 (28.71%) boys and 99 (31.94%) girls aged ≤120 months, 72 (23.23%) boys and 50 (16.13%) girls aged >120 months. The mean BA was 106.80 (53.93) months (range 12- 210). BAs were lower than CA in 72 (23.23%) children, concordant with CA in 181 (58.39%) children and higher than CA in 57 (18.39%) children (Table 1, Figure 1).

Table 1: Summary of variables

	Value n(%)
Gender	
Boy	161 (51.94%)
Girl	149 (48.06%)
Age (months)	107.80 (49.48) (13 - 203)
≤ 120	188 (60.65%)
> 120	122 (39.35%)
Subgroups	
≤ 120 months Boy	89 (28.71%)
≤ 120 months Girl	99 (31.94%)
> 120 months Boy	72 (23.23%)
> 120 months Girl	50 (16.13%)
Bone age (months)	106.80 (53.93) (12 - 210)
Low	72 (23.23%)
Concordant	181 (58.39%)
High	57 (18.39%)

Data are given as mean (standard deviation) (minimum - maximum) for continuous variables and as frequency (percentage) for categorical variables

Figure 1: Bone age estimates with regards to the subgroups



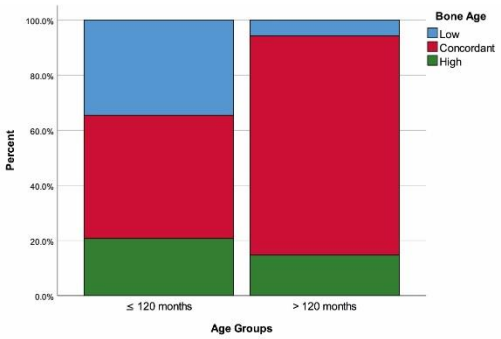
The concordant BA percentage was significantly higher among the children aged 120 months (79.51%) than among those aged ≤120 months (44.68%). Low BA percentage was significantly higher among children aged ≤120 months (34.57%) than in the children aged >120 months (5.74%) (P<0.001). High BA percentages were similar (Table 2, Figure 2).

Table 2: Bone age estimates with regards to the age groups

	Age groups		
	≤ 120 months (n=188)	> 120 months (n=122)	*P*-value
Bone age			
Low	65 (34.57%)	7 (5.74%)	<0.001
Concordant	84 (44.68%)	97 (79.51%)	
High	39 (20.74%)	18 (14.75%)	

Data are given as frequency (percentage)

Figure 2: Bone age estimates with regards to the age groups



The rate of concordant BA with CA was significantly higher among girls (65.10%) than among boys (52.17%). Low BA percentages were significantly higher among the boys (29.81%) than among the girls (16.11%) (P=0.014). High BA percentages were similar (Table 3, Figure 3-6).

Table 3: Bone age estimates with regards to gender

	Gender		
	Boy (n=161)	Girl (n=149)	*P*-value
Bone age			
Low	48 (29.81%)	24 (16.11%)	0.014
Concordant	84 (52.17%)	97 (65.10%)	
High	29 (18.01%)	28 (18.79%)	

Data are given as frequency (percentage)

Figure 3. Bone age estimates with regards to gender

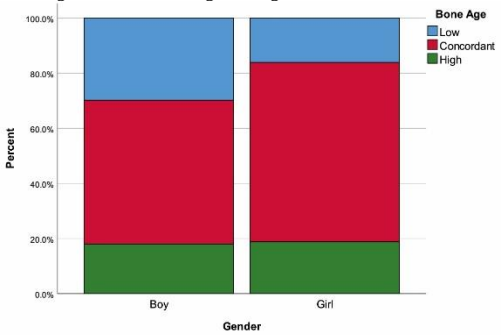


Figure 4. Boxplot of the age with regard to gender

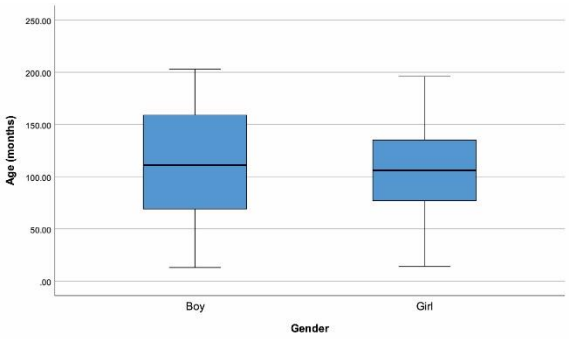


Figure 5: Left wrist and hand radiographs of a 147-month-old and female patient. With reference to the Greulich-Pyle atlas, the bone age is consistent with chronological age.

Figure 6: Radiograph of left wrist and hand is given. Based on Greulich-Pyle atlas, the bone age is lower than the chronological age in the 77-month-old male patient.

Among patients aged ≤120 months, we found significant differences between the subgroups with regards to BA estimates (P<0.001). Concordant BA percentage was significantly higher in girls (56.57%) than in boys (31.46%). Low BA percentage was significantly higher in boys (50.56%) than in girls (20.20%) (P<0.001). High BA percentages were similar between the boys and girls. There were no significant differences between boys and girls aged >120 months with regards to BA estimates (P=1.000) (Table 4).

Among the boys, concordant BA percentage was significantly higher in those aged >120 months (77.78%) than those aged ≤120 months (31.46%). Low BA percentages were significantly higher among those aged ≤120 months (50.56%)

than in those aged >120 months (4.17%) (P<0.001). High BA percentages were similar between boys aged ≤120 months and those aged >120 months (Table 4).

Among the girls, concordant BA percentages were significantly higher in those aged >120 months (82.00%) than in those aged ≤120 months (56.57%) (P=0.036). Low and high BA percentages were similar between girls aged ≤120 months and those aged >120 months (Table 4).

Table 4: Bone age estimates with regards to subgroups

	Subgroups				
	≤ 120 months Boy (n=89)	≤ 120 months Girl (n=99)	> 120 months Boy (n=72)	> 120 months Girl (n=50)	*P*-value
Bone age					
Low	45 (50.56%) [a]	20 (20.20%) [b]	3 (4.17%) [c]	4 (8.00%) [bc]	<0.001
Concordant	28 (31.46%) [a]	56 (56.57%) [b]	56 (77.78%) [c]	41 (82.00%) [c]	
High	16 (17.98%) [a]	23 (23.23%) [a]	13 (18.06%) [a]	5 (10.00%) [a]	

Data are given as frequency (percentage). Same letters denote the lack of statistically significant difference between subgroups.

Discussion

Identifying the BA and comparing it with the CA is very important, especially for pediatric endocrinologists, to understand whether patients are growing properly, to make treatment decisions if necessary and to monitor treatment outcomes. Today, BA is often determined from the left wrist and hand radiographs with reference to the GP atlas. However, skeletal maturation may vary depending on the geographical region, and socioeconomic and ethnic group differences [2]. Our study was conducted to determine whether the GP atlas is adequate for Turkish children born after the 2000s.

The GP atlas is based on research conducted by T. Wingate Todd on radiographs of the left wrist and hand. The method involves direct comparison with standard same-sex radiographs by analyzing features such as ossification centers, bone numbers and contours, and examination of growth plates. Standards are classified by sex and give median skeletal maturity for CA [3, 9].

In TW2, which is the other method used much more rarely in the determination of BA, a bone-specific approach is taken, and a separate grading is assigned for each bone of the hand and wrist with the average or median grading used as BA [3]. GP atlas is more preferred in the determination of the BA because it can be applied more easily in daily practice and does not cause time loss.

There are some studies conducted in various countries that determine BA according to the GP atlas. Mora et al. [4] analyzed BA according to the GP atlas for African American and European American children, found significant differences of BA and concluded that the GP standards are unclear for European and African American children. Groell et al. [2] evaluated BA for 47 European children and concluded that the GP atlas could be safely used for European children. Van Rijn et al. [15] examined the Dutch children's BA and found the GP method usable for BA determination. Al Shamrani et al. [17] evaluated the radiographs of 392 patients taken due to trauma in United Kingdom. They observed that there was no significant difference between BA and CA when the GP atlas was used. De Donno et al. [18] examined 300 healthy Italian children and stated that GP atlas yielded results compatible with CA. Dantas et al. [19] investigated the applicability of the GP atlas for the Brazilian population on 150 cases between the ages of 5 and 18 years. They stated that BA is often greater than CA in the female age group, nevertheless, this method is reliable in determining the BA. In a study in South Africa, Govender et al. [1] evaluated the radiographs of 102 patients aged between 0 and 21 years retrospectively. They reported that BA was significantly low in the GP method for both genders and that a novel method should be developed for their country.

There are also studies in the literature questioning the accuracy of the GP method in the Turkish population. Büken et al. [10] evaluated the left-hand wrist radiographs of 251 patients, including boys and girls older than 11 years. They stated that the method could be used by clinicians. Cantekin et al. [20] examined the BAs of 757 boys and girls over the age of 7 years according to the GP atlas. They conducted a BA examination on eastern Turkish children and stated that the average differences between BA and CA were practically insignificant. In our study, we found that BA and CAs were concordant in girls and boys over 10 years of age, and there was incompatibility in boys younger than 10 years of age.

Güngör et al. [21] examined the left-hand wrist radiographs of 535 male and female patients over 10 years of age in the Mediterranean region of Turkey. The difference between CA and BA was significant. BA was smaller in males between the ages of 10 and 15 years and greater in females between the ages of 10 and 18 years. They stated it is appropriate to use GP method in Southern Turkish children, although a revision was needed to get better results and minimize errors [21]. Unlike this study, we found BA and CA to be compatible in patients over 10 years of age in both genders in our study.

In the study of Koç et al. [11], in which 225 male patients over 7 years of age were examined, it was stated that Turkish boys may have a different skeletal maturation process than American children. Therefore, it was concluded that the GP Atlas is not fully applicable to Turkish boys to determine BA but that it can be used with some modifications. In our study, we obtained similar results and found that BA was significantly lower in boys in all age groups.

In a study designed by Aydin et al. [3] on 228 patients, including all age groups and genders in Turkish children, it was stated that the GP atlas could be used for the determination of BA in Turkish children safely. Among the studies evaluating the reliability of GP atlas in determining BA in Turkish children in the literature, Aydin et al.'s [3] study includes all age groups and both genders. Our study also includes all age groups and both genders with more patients. Although similar age groups and both genders were included, the results of Aydın et al.'s study differ from ours. While they [3] stated that the GP atlas is applicable for Turkish children, we found that BA was significantly lower in boys, especially those under 10 years of age.

This study was designed to avoid the impact of growth retardation and obesity on skeletal maturation by including children with known height and weight values between the 25th and 75th percentiles. In our study, when we compared both genders in all age groups, BA was significantly lower in males and significantly concordant in females. Among patients aged ≤120 months, BA was significantly lower in males, while it was

concordant with CA in females. Over 120 months, significantly concordant BAs and CAs were found in both genders.

Limitations

Our study has two limitations: First, due to its retrospective design, the nutritional status or medical history of the patients was known to the extent stated in the anamnesis. It is possible for some patients to have nutritional deficiency or systemic diseases not specifically mentioned in the anamnesis. However, on the other hand, it actually reflects the examined population in this respect. Second, the children participating in this study were all from the same geographic region; therefore, the differences between our results and the GP method may be partly due to the geographic location or climate differences.

Conclusion

Recent studies have shown that skeletal maturation can vary according to the geographical region and climate. The GP atlas, which is frequently used, was created based on regional and old data. The accuracy of the GP atlas in determining BA in Turkish children, especially males under the age of 10 years, is controversial and correct standards should be developed with data based on the Turkish population.

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