

BONE MATURATION AND HEIGHT PREDICTION: HISTORICAL REVIEW OF THE CALCULATION METHODS

ABSTRACT

We conducted a historical review of the calculation methods of bone age and adult height prediction. The importance of knowing bone maturation and its importance in pediatrics and endocrinology are highlighted in this paper. The authors provides a new numerical method to calculate bone age through the carpal, metacarpal and carpalmetacarpal index, as well as to predict the child's adult height. Both transversal and longitudinal studies have been developed in the Spanish and Swiss population. This methodology can be applied to any population group to study, so it can be used in clinical methods instead of Greulich and Pyle, and Tanner Whitehouse. In this sense, you can create own standards for Latin American children. The software and publications prior to this work can be downloaded free at: www.comz.org, link-banner: Bone Maturation.

Keywords: Bone age and adult height prediction Ebrí; Spanish longitudinal casuistry; Andrea Prader; historical review bone maturation.

1. INTRODUCTION

The purpose of this paper is not to found the Ebrí methods for calculating bone age and predicted adult height, nor to present new findings, which are already accepted by the scientific community and published. This paper aims to basically make a chronological and historical review of the main existing methods of calculating bone age, including our own. In this original work, you can have an orderly historical overview of the main existing methods.

We hereby recall that the authors have developed over forty years a research work on Bone Maturation in different children's series studies: Spanish and Swiss. Studies have been conducted in anatomical regions of the Tarsus, carpal and metacarpophalangeal, having

X-rays of his left hand and right foot. The index obtained for calculating bone age in these areas are: IC (Carpal index), IMF (metacarpal phalanx index), ICMF (carpal metacarpal phalanx index), IT (Tarsus index). These index are the result of the sum of the maximum diameters of the bones of each region studied, measured in **milimeters**.

Although there are morphological methods for calculating bone age (Greulich and Pyle) we believe our methods are more accurate. The Tanner numerical method is designed for the Anglosaxon child, and therefore not adequate to apply to the Latin child. This is why we create these new methods based on Spanish child. Basically we make a historical review of bone age calculation methods, based on regions of the hand and the tarsus, including our own review.

The equations for both bone age calculation and adult height prediction are presented in previous publications. They can be used manually or using a software program. All this information can be checked at and downloaded from the website of the College of Physicians of Zaragoza (Spain): www.comz.org.es, link-banner: Bone Maturation.

2. MATERIALS AND METHODS

We reviewed the various children's series studied by us over 40 years. We performed a radiological study of left hand and right foot to a series of these children. The first casuistry studied by us (cross) was conducted in 1974 in the region of the tarsus, in 540 children (243 boys, 297 girls) from birth to 16 years of age and 96 fetuses (57 males and 39 females) [1-9]. The second cross-sectional study was from the Provincial Maternity Hospital of Zaragoza, in 1974: 17 men, 41 women, from birth to four years of age, also in the tarsus [10]. The third cross series study was on children from Zaragoza (Spain). 5225 children (2862 males, 2323 females) in 1977, this time focusing on the region of the carpal [11-15]. 17 years later, in 1993, and from these series, we conducted a second study on 836 of those children once they were already adults, retrieving their height and weight, in order to create multi-regression equations to predict adult height [16]. The fourth children's series, a length series this time, was of Swiss **child**, 1991, 36 children from 10 to 19 years of age. The study was carried out at the carpal and metacarpal regions. In this study, we compare our methods with those of Tanner and Greulich-Pyle [17-21]. Greulich-Pyle, Tanner-Whitehouse and Ebrí: In Table 1, the differences in **ages bone** by the three methods are given. The fifth series, longitudinal, conducted in 2008, was of Aragon **child** (Spanish): 160 children (73 males, 87 females) from birth to 20 years of age, with annual radiological analysis. The study was conducted in the carpal and metacarpal-phalangeal regions. As a result of this study we developed a software that allows quick and safe **diagnose** of bone age and adult height prediction of children. To do this, we insert in the software program the measurements in mm, the maximum diameter of the carpal bones and metacarpophalangeal 1st, 3rd and 5th fingers of the left hand, and the size of the child and parents [22-26]. The measurements are made with digital mouse. The software can be downloaded free from the above mentioned website.

3. RESULTS

From the index outlined in the Introduction: IC, IMF, ICMF and IT, were obtained IVOS (ossification assessment indexes) [22,23,26]. In these publications

we tested the validity of these methods. It showed how our bone assessment index are closely correlated with chronological age, allowing the use of regression equations to calculate the bone age and to predict the adult height. These rates are the result of a sum of measures in mm, made from the maximum distances of the ossification core of the carpal, metacarpophalangeal and tarsus [26]. It is also possible to predict adult height from multi regression equations, by entering the size of the child, parents and ossification index in the software program. Bone age by Ebrí method, we consider suitable for the study of Latin American children (see Table 1).

4. DISCUSSION

Both growth and bone maturation are biological phenomena through which living beings increase their mass progressively acquiring a morphological and functional maturation. Bone maturation manifests as endochondral ossification core and epiphyseal fusion, disappearing conjunction cartilage. The evaluation of the individual's growth and determining periods of intense growth occurring during ripening, provide important clinical information for interdisciplinary diagnosis, especially for pediatric endocrinologist, in order to control a child's normal growth. It is of interest to calculate bone age not only for the pediatrician and endocrinologist, but in sports medicine, in order to avoid negative influences of intensive training on the growth and maturity of young athletes. It is also of interest in Forensics, when they analyse human remains badly damaged, **presumably** belonging to children or young individuals. This has been credited by authors like Ebrí Torné [5]; Peña et al. [27]; Eiben et al. [28]; Osterback et al. [29]; Brooks-Gunn et al. [30]; Theintz et al. [31]; Espina de Ferreira et al. [32]. Bone age also provides a basis for predicting namely height and to follow the evolution of the child after a treatment in this regard. It is also of interest to the parents themselves, who want to know the future height of their children [33-34].

Chronological age is routinely used to assess the level of development and maturation of the patient. It is not always a reliable indicator, and in such **doubt** cases, the **ray** of the left hand is indicated for bone age. This is, for some authors, the best parameter of overall development of growth [35]. Bone age expresses the maturation process of the human being, and this process is particularly reflected in the evolutionary dynamics of the small bones of the hand. Therefore, and in the opinion of most authors cited, it is recommended that each country has its own anthropometric standards. This is necessary for the validation of other methods of estimating bone age

Table 1. Comparison of Greulich-Pyle, Tanner Whitehouse and Ebrí bone age calculation methods. Differences between them

A-Greulich and Pyle:	
1-	Morphological, qualitative, and approximate method for bone age calculation.
2-	We cannot discard the subject approach of the explorer in regards to an accurate diagnosis. In order to minimize this problem, the serial observations of a single patient have to be done by the same observer.
3-	Frequent asynchronies in early ages, which hinder an accurate diagnosis of the bone age.
4-	Created for American child, with early maturation. As a result, it can yield gaps of false advancement of bone age in Latin child.
5-	It uses chronological age as the measurement unit, but not all children are equal.
6-	Greulich & Pyle atlas only offers the average value, but not the normal margin expressed in percentages or standard deviations, within which a radiography cannot be considered as pathological.
B-Tanner-Whitehouse:	
1-	British numerical method, created for Anglosaxon child.
2-	Technically difficult. It requires the observer a great experience.
3-	It assigns values to the ossifying bones in the late stages of the carpal with a doubtful interpretation, due to large punctuation breaks by overlapping cores and to a non-strict universality of some of the index described, implying differences of up to two years (Andersen 1971).
4-	Gaps for Latin child, generally providing false advancements of the bone age.
C-Ebrí:	
1-	Numerical method, suitable for Latinamerican child. For these children it does not require to correct gaps in bone age in regards to the two methods.
2-	Relativizes the appearance of asynchronies, as it provides an average value of all the bones and its maximum lengths.
3-	Software method that enables a direct and fast calculation of the bone age and adult height prediction.

and the search for alternative techniques that increase accuracy in calculating bone age, creating new standards, especially in length series.

In this work we have considered of general interest to make a brief historical overview including Greulich-Pyle and Tanner methods. Our contribution developed in the regions of the hand and foot, is included in this study. We will also make a brief comment on the methods of adult height prediction based on bone age.

Interest in bone maturation dates from the late nineteenth century, in the pre-Roentgen period, when Sappey in 1874 [36], Hartman in 1877 [37] and Cruvelhier in 1983 [38] researched on the body for transverse serial sections procedures studying the ossification core. Since the advent of the Roentgen period in 1895, researches are carried out using radiography. In this sense, Pryor in 1907 [39] and 1923 [40] propose three postulates: a) the result of the appearance of the core is a hereditary character; b) the rate of appearance of ossification centers is faster in females; and c) the ossification is bilaterally symmetrical. At the same time, anatomists and radiologists agree that the number of ossification points that gradually appear on radiographies may be an index of biological development.

The breakthrough in the study of osteogenesis is performed by Todd in 1937 [41] when he undertakes the description of each of the cores of the hand and wrist from its appearance to its adult state. It used for this purpose a series of radiographies of healthy children of Cleveland (EE. UU). This author observes that there are some radiographic images that are always in the evolution of a single core. Todd describes these as universal images for that core, then draws and standardizes, calling them determinants of maturity. Greulich and Pyle and his disciples called them indicators of maturity and state in their atlas in 1959 [42].

To overcome the difficulties described in the Greulich and Pyle method, especially the asynchronies, we created numerical methods. These methods offer the advantage of morphological greater accuracy, therefore reducing much of the subjectivity of the observer when using the atlas. The atlas used as a measurement unit of chronological age presupposes that bone maturation has its own pace, accelerating at certain ages such as puberty, not being like this throughout the years of maturation. Andersen, 1971 [43]. Tanner et al. in 1959 [44], published a variant of the great contribution of the Atlas of Cleveland, hand and wrist. The TW method was modified since its release in 1959, with the publication of three versions,

which have tried to improve accuracy [45]. This year, Tanner, Whitehouse and Hely, again undertake the description of maturation indices for the hand and wrist. Remove 2nd and 4th fingers, pisiform and sesamoid, and describe the maturational development of 20 bones: the carpus 7 and 13 epiphysis of the short bones of the hand and the radius and ulna. Its major innovation is to introduce numerical methods, something that the analysis of an X-ray should be core by core. The observer of the radiography searches in the method of Greulich and Pyle for the state of maturation that most closely matches the model description, but once the maturation index is determined it will give a numerical value, and the x-ray analysis will be expressed by the succession of twenty numerical values, whose sum defines the maturational level of the individual. The scale runs from 1 to 1000 points, then drawing bone maturation curves that resemble the size. Tables based on the British population transform these numerical methods in bone age. In 1962, they published their first complete system, known by the acronym TWI. They established that ossification begins in the lunate at the time of 13% of the overall maturity, and the fusion of the distal epiphysis of the thumb, is verified at 88% of maturity [46]. This method was criticized by Andersen, 1971 [43], since in the last stages of carpal there are big score jumps. Therefore a stadium difference may cause difficulties to recognize it due to overlapping core and non-strict universality of some of the index described. As a result, it can assume two years differences. Moreover, the carpal bones, lacking cartilage growth, make Tanner et al. in 1972 [47] change some aspects of their TWI method and publish their TWII method.

20 bones are analyzed in the method. Scales are verified separately for the seven core carpal and the remaining thirteen cores of short and long bone (ossification centers of the 2nd and 4th fingers, and sesamoid pisiform are eliminated). This scale is known as RUS (Radius, ulna, short bones). Different scales for both genders are also used, because although all cores mature earlier in women than in men, not all have the same precocity. It also suppresses the last stage in the core of radius, ulna, large, pyramidal, lunate, scaphoid, and trapezoid. The difference between the score of the carpal and RUS increases with age, 13 in case of boys and 11 in case of girls, when the 97th percentile of the score Carpal has reached maturity, which does not happen in the case of RUS. The TW2 RUS scale has greater biological use since its reliability is higher than TW2 Carpal or even that of 20 TW2 bones. It is better correlated with pubertal changes and has a greater

predictive value of adult height. Therefore it is integrated in its method of predicting adult height. Possibly the differences between the scores RUS and carpal bone may reflect hormonal differences, says Wenzel et al, 1982 [48].

The numerical cotation of each study, can produce similar curves to the curve size and the one obtained by Acheson, applying their original scale sigmoid curves to hip and pelvis. This will be assigned to a radiography problem of chronological age corresponding to percentile or, if preferred to give the results in terms of bone age. Applying the TW method, they have pointed out differences in the bone maturation pattern of the population of the population studied. Kumi Ashizawa, [49] and Haavikko K et al. [50], comparing the Tanner-Whitehouse method applied to Japanese children, found out that in boys the skeletal age of 6/7 years matches chronological age. After 7 years skeletal age is advanced over chronological age, and so gradually until 16 years of age. From that age on, the differences are reduced. In girls, the bone age seems to coincide with chronological age for ages below 6 years. From that age on, the skeletal age remains ahead of chronological age until 15 years of age, when they match again, and then it declines. We therefore conclude that the method of Tanner must be modified in order to be applied to different populations.

In 1975 Martí Henneberg and Vilardell [35], studied carpal bone maturation of a mixed population of normal children in Mundet Barcelona, with the TWI method. They translate the results on the curves of the French length study, noting that there is a delay in the maturation of Spanish children in regards to the French. In 1971 Andersen [43] finds an average of 5.9 months relative to the Greulich and Pyle atlas. Fray, in 1971 [51], compared the Greulich & Pyle and Tanner methods in a sample of Hong Kong children, and found that TW bone age / chronological age ratio exceeds bone relation GP / chronological age. In 1975 Ferrández Longás [33] summarizes the comparison between GP and TW2 atlas, concluding that the systematic error in GP is lower than TW2. It is fast and consumes little time. The data found by GP can be used to analyze the pathological growth, since the values obtained in the same population differ less from a Gaussian distribution curve obtained by TW. It is ideal for routine practice. Likewise, GP is suitable for growth problems with differences between EC and EO. It allows interpolation between two bone ages, which cannot be done with the TW2 method. However, replicability of individual readings is better with Tanner, making it suitable for length studies that have been done by the same researcher. It is quantitatively more accurate. It also is ideal for cases in which chronological age is like bone age.

With numerical methods we assess the rate of maturation from qualitative and subjective to an objective and quantitative assessment that provide numerical series, also opening the door to research and mathematical analysis. The latest revision of the Tanner method was conducted in 2001, using a sample of US origin to standardize the RUS and Carpal systems, and was called TW3 [52]. The method is based on assigning scores to 20 specific ossification cores of the hand, wrist and distal epiphysis of the radius and ulna. These scores are awarded according to a scale of development from the letter A to the letter H, or I, depending on ossification core studied. The practitioner has to allocate a certain level or stage of development when the ossification core meets the described criteria.

The TW3 system is divided into two systems. The first evaluates the distal epiphysis of the radius and ulna; metacarpals: 1, 3 and 5; proximal phalanges: 1, 3, 5; middle phalanges: 3 and 5; and the distal phalanges: 1, 3 and 5. The second evaluates the following bones: big, hamate, pyramidal, lunate, scaphoid, trapezium and trapezoid. After assigning scores to each ossification core, these are summed to obtain a rate of skeletal maturation, one for each system, which is subsequently transformed into bone age according to specific conversion tables, which are divided by sex and system. The TW2 method differs from TW3 especially in the type of sample, since in the latest version of Tanner, American and European individuals are included, while in the TW2 only Europeans are included, as in the TW1. For TW3 American population, the reference bone maturation method could be Ahmed ML et al. [53]. Lopez P, et al. published in 2007 [54] made by the method of TW3 and conducted on school children from the Venezuelan ethnic groups Wayúu and Creole "Municipio Maracaibo" (Zulia State), Morón A, et al. [55].

The goal was to determine the influence of the racial factor of these children from different ethnic groups in bone maturation, and to see if there were differences. The sample included 160 hand and wrist radiographies of healthy individuals of both genders, aged between 7 and 14 years. Children met the anthropometric parameters of normal height and weight, between 10th and 90th percentiles of the "Fundacredesa Foundation", which conducted a comprehensive study between 1981 and 1987 [56] on the Venezuelan boy, whose main goal was to establish their identity from the biological, social and cultural points of view. They saw that there were no statistically significant differences in bone maturation between the two ethnic groups. However, they

observed a tendency for a higher RUS bone age in Wayuu, and for a higher Carpal bone age in the Creoles, children and girls alike. Nevertheless, no differences in bone maturation between both genders were found.

When checking the relationship between chronological age and estimated bone age, both variables were significantly correlated. There is also a positive correlation between estimated bone age and chronological age. They concluded that the TW3 method is reliable for estimating the age of a person in one's region.

In 1988, Ebrí Torne [5] provides a new own numerical method for bone age calculation, called carpal index and IVO-carpal. This is a sum of maximum Carpal core diameters from a Spanish cross casuistry of 5225 children of both genders, and he adapts it to a simple software program. In 1993, he publishes his method in French [57]. In 1989 [14] he publishes tables and graphs of the chronology of carpal ossification points, and the maximum diameters of the carpal ossification core. He analyzes hamate, radial epiphysis, and in some children pyramidal bones, as well, in the first year of life. These index, statistically significant, represented a new contribution to the numerical methodology, providing a new methodology for future studies on all populations, in order to create own standards, without having to rely on a foreign methodical like Tanner, for that. In 1992, Ebrí, presented at the XVIII International Congress of Pediatrics Alape, held in Seville, the carpal index (CI) and metacarpalphalanx index (MIF) to calculate bone age [15], in Swiss length population from the Kinderspital of Zurich. In 1993, the same author publishes the IVO (evaluative ossification index) Carpal, applied to Swiss population, and also presents the percentile index [17]. In 1994, Ebrí Torné publishes new equations for calculating bone age in the carpal, for children from birth to two and four years [13]. In the same year, he published a statistical (variance analysis) and descriptive carpal bone age study on Swiss child, using the Tanner and Ebrí methods, making a comparative study between them. Each one follows its own methodology, but both methods are concordant for the child's bone age [18]. In 1996, Ebrí Torné published the IVO (evaluative ossification index)-Metacarpalphalanx, applied to Swiss children, and compared these children with Tanner II RUS. The author finds that when applying Ebrí-Metacarpalphalanx method on the Swiss child there is less discrepancy between bone age and chronological age, with significantly statistical differences [19]. In 1997, the same author, performed a comparative study between bone ages: Rus Tanner, Tanner Carpal, Carpal Ebrí, metacarpofalángico Greulich

and Pyle Ebrí and Greulich and Pyle, on these same Swiss children. He found evidence that there are statistically significant differences ($p < 0.1$ to 0.01) between the bone ages. In women, minor discordance is between Greulich-Pyle, and Ebrí-MIF, Ebrí-Carpal. In males, they are between Greulich-Pyle and Ebrí-Carpal [20]. In 2012 and 2013, Ebrí Torné and Ebrí Verde [22-23,25] applied the carpal, metacarpal phalanx and carpal metacarpal phalanx index to a length series of Spanish children (Andrea Prader Foundation), with ages ranging from birth to 20 years. They used the "Statistix" Statistical software for the statistical work. Regarding Ebrí bone ages, Greulich and Pyle overestimate 6 months in females and 3, 7 months in males, whereas Tanner does it up to 4, 7 months in females and 5 months in males. When the bone age is obtained with our ossifying index, it is not necessary to do any correction. We have to know the differences in regards to Ebrí bone ages when the bone age is calculated by TW2 and Greulich-Pyle. Thus they obtained predictive equations for bone age and adult height for a length series of Spanish child. They provided a software program that allows a fast calculation of both predictions.

Although the hand has preferably been the region most frequently chosen by the authors for the study of ossification, it has not yet been universally accepted. Thus in 1943, Lipford and Sontag proposed other skeletal areas other than the hand and wrist [58]. In 1955 Pyle and Hoerr referred to the knee [59]. In 1979 Sempé valued over 3,000 elbows and developed distribution curves values, demonstrating that pubertal phenomena correlates very closely to the bone maturation level of this anatomical region, enabling to foresee when puberty will take place [60]. The method of cervical vertebrae: CVMS (cervical vertebral maturation stages) on the lateral radiography for evaluation of cephalometric bone age, is now used as a tool to evaluate maturation growing patients [61]. In 1977 the Torne Ebrí called tarsal Index (IT) is published. It is a numerical method for calculating bone age in children from birth to the age of 16, and is the subject of his doctoral thesis. This index increased over the child's development and significantly correlated with chronological age. This is why standards of cross Spanish population were created [1]. The same author, in the X Congress of the Spanish Anatomical Society, found the bones calcaneus, talus, cuboid, and the third wedge, in children until the first year of life. He defends his statement that: "It is useful for the pediatrician to create an atlas of the foot in the first year of life" [2].

In 1979, in a numerical study of ossification done in the same region, Ebrí Torne also found differences

between the right and left tarsus by 3.3%, although for greater uniformity of the study, it valued statistically the right side [3].

In the same year, in a study of core sequences developed in the tarsus of children of both genders, the evidence is that up to seven years of age typical core sequences are comparable between boys and girls. Then they are not, depending the specific dynamics of each core. This dynamism follows the biological need required to better meet the needs of architectural support of the individual [3]. In the same year, the author presents the so-called IVO tarsal, a numerical method to calculate bone age, developed from a Spanish cross-sectional study of 540 children [4]. In 1990 this method is published in English [7]. In that year, he performed a radiographic length study over a year and half in the Provincial Maternity in Zaragoza. The ages of these children range from birth to four years. He compared the core sequences of normal children with stunted children and the premature baby twins, showing that stunted children had a more advanced core chronology, while premature and twins were more delayed than other children [10]. In 1988 he published the first atlas of the hand and foot radiographies selected from a Spanish population of 5225 children (hand) and 540 (foot), three years before the group Hernandez et al. [6] published its Atlas. In 1991, Hernandez M et al. [62] published a variant of the Atlas, based on a lateral radiography of left foot and ankle. The latest review of the Tanner method was conducted in 2001, using a sample of US origin to standardize the RUS and Carpal system. This review was called TW3 [53].

In 1992 Ebrí Torné applied the so-called tarsal index birth to two to four years, and provided new equations for calculating bone age [8]. In 1993 this method is published in English [9].

All these studies show differences between the bone age of the different populations studied. These differences between the values of bone maturity confirm the influence of genetic, racial and environmental factors in the development of an individual, hence the desirability of each population having its own standards. In this sense, Ebrí Torné and Ebrí Verde recommend the application of his method in any population study in order to create their own standards, and not to use foreign standards.

Recently, in the awakening of 40 years of research, the authors publish their method of measuring bone age in English [26].

Many years ago, prediction children height was based on methods that did not account on bone age. Currently the most widely used methods are those based on it. The first clinical application of bone age in predicting height was made by Gill and Abbot in 1942 [63], to predict the elongation of the femur and tibia. In 1979 Sobradillo postulated that in order to consider a prediction method correct it must have a reasonable accuracy over a wide range of ages. In addition the prediction error should be small. This proves true not only in cases of normal growth, but also in different pathologies [34]. Of all the methods of predicting adult height, one of the most widely used is that of Bayley and Pinneau, based on the Greulich and Pyle atlas [64]. In 1975 Tanner et al. [53] also described a method based on different regression equations, calculating adult height based on the current height, chronological age, bone age, according to the TW2-RUS quantitative method, constants and medium height parents. The latest version of Tanner height prediction is the quantitative method TW3. This system can be used from 4 years of age, but may overestimate the final height, being valid in calculations of excessive height and constitutional delay of puberty, but not being applicable to endocrinopathys: defects hGH, hypothyroidism and Turner syndrome. In 1975, Roche -Wainer and Thissen, describe a method using the correlation coefficients between adult height and the following parameters: Length (rather than standing height), weight, bone age as the Greulich and Pyle atlas for hand and wrist, and parental height [65].

Ferrández Longás et al. [34] in 1975, said that the method of Bayley and Pinneau is the method with a minor error in cases of endocrinopathys, while the three methods are of similar value and valid in normal cases. The precision of the three methods increases with age, approximately up to 10 years. In terms of bone age related to chronological age, the TW2-RUS and Roche methods are more accurate. When the advancement or delay of bone maturation is greater, the Bayley-Pinneau method leads to less error [34]. In 1979 Ebrí Torné, Swiss normal child, made forecasts predicting adult height. He introduced its predictive methodically carving in bone ages Ebrí-carpal and metacarpalphalanx. He compared these forecasts with those obtained by Tanner II Rus and Carpal through their own bone ages; and Bayley-Pinneau from Greulich-Pyle bone age. He found that the absolute errors in Ebrí's prediction were lower than those obtained by Bayley-Pinneau, without significant differences. Regarding Tanner's predictions, Ebrí absolute errors were minor and statistically significant between 10 and 14 years of age [21].

In 2005 Ferrández Longás et al. [66] published a method for predicting adult height of Spanish children length series: "Andrea Prader Center" (CAP). It is based on multi-regression equations and Greulich - Pyle and TW2 bone age. Ebrí Torné and Ebrí Verde apply to this same length casuistry, bone ages by bone index: carpal, metacarpalphalanx and carpalmetacarpalphalanx, for the purpose of obtaining adult height prediction equations [22-23]. After applying the methodology of adult height prediction to all Ebrí bone ages in order to compare and declare the reliability of all forecasts from a common base, no significant differences were found, thus proving its validity.

Ebrí Torne had already reached the same conclusion in several works on Swiss length series: that it is better to use own equations developed in each country through their own biological somatometric variables [19]. These same authors made a comparative study of these adult height predictions obtained through mentioned bone ages with predictions of adult height obtained with bone age of Greulich-Pyle, and Tanner-W2 methods, without obtaining significant differences [20].

5. CONCLUSIONS

- 1- The carpal and meta-carpal-phalange bones are the anatomic areas more admitted for bone age calculation, although the tarsus is also admitted.
- 2- The advantage of using this method of bone age calculation, with its four index: IVO-IC, IVO.IMF, IVO-ICMF for the hand, and IVO-IT for the tarsus region. It provides a more accurate diagnosis for bone age calculation in Latin child, so we can dispense with the Tanner method, more appropriate for Anglosaxon child, thus eliminating the asynchronies and the interpretation subjectivity of the Greulich and Pyle method.
- 3- Applying the Ebrí method it is not necessary to correct bone age gaps in Latinamerican child, as opposed to the other methods.
- 4- With the Ebrí method we can directly obtain the adult height prediction of the child.
- 5- The Ebrí methodical base for obtaining the bone age can be applied to any population group in order to create new research standards.
- 6- From the Ebrí method, and for research purposes, we can obtain new casuistry from different populations.

You can download the software program for free at www.comz.org, link-banner: Bone maturation.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Ebrí Torne B. Contribution to the study of ossification of Tarsus. Study of bone age from birth to 16 years, following numerical methodology based on an index obtained at tarsus, called tarsal index. Journal of the Seminar of the Department of Medical Pathology A Barcelona. Spanish Archives of Internal Medicine. 1977;10:721-24.
2. Ebrí Torne B. Numeric and radiological study of the tarsal bones in a human population from the fetal period to puberty. Proceedings of X Congress of the SAE, Zaragoza. 1978;175-181.
3. Ebrí Torné B. Statistical study Ebrí Torne and pace of ossification of the tarsal bones in children. RIMT. 1979;6:128-138.
4. Ebrí Torne B. Presentation of a new biometric method (IVO) for the assessment of bone age in children. Klink Medizinische. 1979;214:50-56.
5. Ebrí Torne B. Maturation on Tarsus and carpal bone (Clinical-radiological study Child) Editorial Heraldo de Aragon. Zaragoza; 1988.
6. Ebrí Torne B. Radiographic atlas of carpo and tarso. Editorial Heraldo of Aragon. Zaragoza; 1988.
7. Ebrí Torné B. Biometric method adaptation al Basic. Acta Pediátrica Scandinavica. 1990; 79(12):1242-1243.
8. Ebrí Torne B. New equations to calculate bone age in Tarsus by the tarsal Ebrí method in children from birth to two and four years. Aragones III congress of medicine. Royal Academy of Medicine. Zaragoza. 1992;1:170.
9. Ebrí Torné B. Biometric method for the ossification evaluation of children since birth up to the ages of two and four, applied to the Tarsus. Acta Paediatrica Scandinavica. 1993; 82:872.
10. Ebrí Torne B. Bone maturation. Chronological sequence analysis and differential nuclei of ossification of Tarsus, from the population of the Provincial Maternity Zaragoza. Munchener Medizinische Wochenschrift. 1979;3:129-139.
11. Ebrí Torne B. Study Spanish population of 5225 and 540 children of both sexes by the set method of Carpo (IVOC) and Tarsus (IVOT). Basic program. Adaptation bone age bone age Ebrí to Greulich-Pyle and Tanner Whitehouse for height prediction. Speech at the Royal Academy of Medicine of Zaragoza. Vol LII communications conference and the Royal Academy of Medicine of Zaragoza. Course. 1988-89;9-31.
12. Ebrí Torné B. New index valuation the ossification of Carpe (IVOC) 5225 Study on Children Spanish. Pediatrics. 1993;48:813-817.
13. Ebrí Torné B. New equations to calculate bone age Carpal in the carpal Ebrí method in children from birth to two and four years. Spanish Pediatric Act. 1994;52(2):79-82.
14. Ebrí Torne B. Contribution in numerical and graphical tables of maximum diameters carpal ossification centers. Spanish study population of 5225 children. Magazine Spanish Mano. 1989 of Surgery. 1989;38(16):55-62.
15. Ebrí Torne B. Determination of bone age by a new numerical method: IC (Index Carpal) longitudinal population in Switzerland. XVIII Extraordinary Congress of the Alape. Sevilla. Spanish Annals of Pediatrics. 1992;169.
16. Ebrí Torné B. Predicción de Talla adulta en población española (836 niños) a través del método de valoración osificativo Ebrí-carpal. Acta Pediátrica Española. 1995;53(7):424-427.
17. Ebrí Torne B. Exposure percentile carpal size index and population Switzerland from the longitudinal study of Zurich. Child compared to Spanish. Spanish Pediatric Act. 1993; 51(9):589-593.
18. B. Ebrí Torne. Statistical and descriptive study in Swiss child in the carpal bone age by Tanner and methods Ebrí. Spanish Journal of Hand Surgery. 1994;21(47):67-75.
19. Ebrí Torne B. Bone metacarpalpalanx assessment index. Swiss longitudinal study. Rus compared with tanner II study. Spanish Pediatric Act. 1996;54(2):94-102.
20. Ebrí Torne B. Comparative study of bone-rus ages tanner, tanner carpal, ebrí- carpal, metacarpalpalanx ebrí and greulich and pyle. Pediatric Española Act. 1997;55(8):369-374.
21. Ebrí Torné B. Adult height prediction in Swiss child through predictive methodical Ebrí incorporated into bone ages. Spanish Pediatric Act. 1997;55(7):330-333.

22. Ebrí Torne B, Ebrí Verde I. Metacarpalphalanx and numerical indices to calculate carpal bone age and adult height prediction. *An Pediatr (Barc)*. 2012;76(4):199-213.
23. Ebrí Torne B, Ebrí Verde I. New rating index bone ebrí-carpo metacarpalphalanx and adult height prediction. *Integral Pediatr*. 2012;XVI(10):822.e1-822.e9
24. Ebrí Torné B, Ebrí Verde I. Biometric method for the ossification evaluation of children from birth up to the ages of two and four – applied to the metacarpal and phalanxes in Spanish longitudinal series. *Cureus*. 2013;5(12):e151. DOI: 10.7759/cureus.151
25. Ebrí Torne B, Ebrí Verde I. And comparative study between bone age Greulich-Pyle and Tanner-W2 and Ebrí, between predictions and adult height. *Integral Pediatr*. 2012; XVI(9):741.e1-741.e7.
26. Ebrí Torné B, Ebrí Verde I. Studies in Spanish children to calculate bone age and predict adult height: Forty years of own investigation. *Pediatr Therapeut*. 2015;5:227. DOI: 10.4172/2161-0665.1000227
27. Peña E, Cardenas E, JL del Olmo. Bone growth and maturation athletes tweens and teens. Galvan and Ramos R (Eds). *Antro is Biol. II Colloquium Antro. Physical. J. Comas, Mexico City: Antro Inv Inst*. 1982;453-466.
28. Eiben OG, Panto E, Cyenis G, Frohlich J. Physique of young female gymnasts. *Anthrop Kazl*. 1986;30:209-220.
29. Osterback LL, Viitasalo. Growth selection of young boys participating in different sports. J Rutenfranz, R Mocellin and F. Klimt (eds). *Children and Exercise XII Champaign, IL. Human Kinetics*. 1986;373-380.
30. Brooks-Gunn J, Warren MP. Mother-daughter differences in menarcheal age in adolescent girls attending national dance company schools and non- dancers. *Ann Hum Biol*. 1988;15:35-43.
31. Theinz GK, Howald H, Allemann Y, Sizonenko PC. Growth and puberal development of young female gymnasts and swimmers: A correlation with parenteral data. *Int J Sports. Med*. 1989;10(2):87-91.
32. Espina de Ferreira A, Ferreira J, Céspedes M, Barrios F, Ortega A, Maldonado Y. Using the dental age and bone age for calculating the chronological age for forensic purposes, in school children with height and weight values not appropriate for their age and sex, in Maracaibo. Zulia State. Preliminary study. *Home Editions*. 2007;45(1).
33. Ferrández Longás A. The bone maturation as a fundamental element forecast human development. *Clinical Medicine*. 1975;64:97-10.
34. Sobradillo B. Prediction of adult height. monograph on nutrition, growth and development. Research Institute Growth and Development. Faustino Orbegoza Foundation. Bilbao. 1979;55-63.
35. Martí Henneberg C. Roy MP, Passe NP. Analysis of skeletal maturation in man. *Methodology. Clin Med*. 1975;2(64):49.
36. Sappey PH. Descriptive anatomy treaty. Madrid; 1874.
37. Hartman MJ. Manual of descriptive anatomy. Barcelona; 1883.
38. Cruvelhier J. Anatomy descriptive treaty. Paris; 1887.
39. Pryor JW. The hereditary nature of variation in the ossification of bones. *Anat Rec*. 1907;1:84.
40. Pryor JW. The cronology and order of ossification of the bones of the human carpus. *Bull Univ. Kentucky*. 1909;23.
41. Tood TW. Atlas of skeletal maturation. Part I. the hand, C. V. Mosby S. Luis; 1937.
42. Greulich W, Pyle SJ. Radiographic atlas of skeletal development of the hand wrist. 2 Ed California: Stanford University Press; 1959.
43. Andersen E. Comparison of tanner-whitehouse and greulich-pyle methods in a large scala danish survery. *Amer J Phys Anthropol*. 1971;35:373-8.
44. Tanner J, Whitehouse R. Standards for skeletal maturation. Paris: International Children's Center; 1959.
45. Malina R, Little B. Comparison of TW1 and TW2 skeletal age differences in American Black and White and in Mexican children 6-13 years of age. *Ann Hum Biol*. 1981;8(6):543-548.
46. Tanner JM. Growth at adolescence. 2ª Edition. Black Well Scientific Puns. Oxford; 1962.
47. Tanner JM, Whitehouse RH, Healy MJR, Goldstein H. A revised system for estimating skeletal maturity from hand and wrist radiographs with separate standards for carpals and other bones (TW2 system). Standards for skeletal age. Paris: International Children's Centre; 1972.
48. Wenzel A, Melsen B. Replicability of assessing radiographs by the Tanner Whitehouse-2 Method. *Human Biol*. 1982;54: 575-81.
49. Kumi Ashizawa. Osseous maturation of Japanese children 6 to 18 years estimated by the Tanner-Whitehouse method of. *Bulletins*

- and memoirs of the Society d'antropologie de Paris. 1970;6(12):265-280.
50. Haavikko K, Kilpinen E. Skeletal development of Finish children in the light of hand-wrist roentgenograms. *Proc Finn Dent Soc.* 1973;69(5):182-190.
51. Fry EJ. Tanner-Whitehouse and Greulich-Pyle skeletal age velocity comparisons. *Am J Phys Anthro.* 1971;35L377.
52. Tanner J, Whitehouse R, Cameron N, Marshall W, Healy M, Goldstein H. Assessment of skeletal maturity and prediction of adult height (TW3 method). 3a ed. London: W.B. Saunders; 2001.
53. Ahmed ML, Warmer T. TW2 and TW3 bone ages: Time to change? *Arch Dis Child.* 2007; 92:371-375.
54. Lopez P, Moron, Urdaneta O. Bone maturation of school children (7-14 years) of the Wayúu and Creole ethnic groups in the Municipality of Maracaibo, Zulia State. *Comparative study. Riv Vin Oit.* 2007;24.1.
55. Moron A, Rivera L, Rojas F, Pirona M, Santana, Suarez I, et al. Contributions to the study of dental epidemiology Wayuu. *Dental Science.* 2004;1(1):18-29.
56. Foundation Study Center for Human Growth and Development Venezuelan population (FUNDACREDESA): Atlas of the Venezuelan bone maturation. Caracas, Venezuela. Offset intense C.A; 2003.
57. Ebrí Torné B. Nouvelle indice de valorisation de l'ossification du carpe (IVOC). Étude sur 5225 Enfants Espagnoles. *Pédiatrie.* 1993;48:813-817.
58. Sontag LW, Lipford J. The effect illness and other factors on appearance pattern of skeletal epiphyses. *J Pediatr.* 1943;7(23):391.
59. Pyle SI, Hoerr NL. Radiographic atlas of skeletal development of the knee. Springfield, I, 11, Charles C Thomas; 1955.
60. Sempé M Capron JP. Chronos: Analysis of skeletal maturation by an automated digital method. *Pediatrics.* 1979;34:834.
61. Baccetti T, Franchi I, McNamara JA Jr. The cervical vertebral maturation method for the assessment of optimal treatment timing in dentofacial orthopaedics. *Semin Orthod: Elsevier.* 2005;11:119-129.
62. Hernández M, Sánchez E, Sobradillo B, Rincón JM. Bone maturation and adult height prediction. Atlas and numerical methods. Ed Diaz de Santos. Madrid; 1991.
63. Gill GG, Abbott LC. Practical method of predicting the growth of femur and tibia in the child. *Arch Surg Chicago.* 1942;45:286.
64. Bayley N. Tables for predicting adult height from skeletal age and present height. *J Pediatr.* 1946;28:49.
65. Roche AF, Wainer H, Thissen D. The RET method for the prediction of adult stature. *Pediatrics.* 1975;56(6):1033.
66. Longás Ferrández A. Normal longitudinal study Spanish children from birth to adulthood. Anthropometric, pubertal, radiological and intellectual data. Andrea Prader Foundation. Zaragoza; 2005.