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ORIGINAL ARTICLE

Correlation in radiological bone age determination using the Greulich and Pyle method versus automated evaluation using BoneXpert software

Correlación en la determinación de la edad ósea radiológica mediante el método de Greulich y Pyle versus la evaluación automatizada utilizando el software BoneXpert

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Abstract

Objective: To determine the degree of correlation in the radiological bone age assessment using the Greulich and Pyle method versus automated assessment through BoneXpert® software between 2013 and 2016. **Material and Method:** Correlation study of diagnostic techniques of 1500 carpal X-rays to assess bone age in patients under 16 years of age from Clínica Alemana de Santiago. X-rays with bone age assessment using the Atlas of Greulich and Pyle (GP) by 1 out of 7 pediatric radiologists, were analyzed using the BoneXpert (BE) software for automated bone age assessment. 100 cases were taken at random for analysis/re-analysis using the BoneXpert method to determine its accuracy. The level of correlation of the measurements was analyzed using the correlation coefficient (Pearson's r) and the variability of the measurements using the Bland-Altman analysis. **Results:** 1493 cases were assessed, seven were excluded due to failure in the X-ray technique, 922 females (61.8%), with a median chronological age of 9.96 years and 11.12 years for males (p 0.001). The correlation between manual bone age (GP) and automated bone age using BoneXpert method among radiologists ranged from 0.91 to 0.93. The Bland-Altman analysis indicated an average difference between manual bone age and bone age using the BoneXpert method of 0.19 years (CI 0.13 to 0.25). In the analysis/re-analysis of 100 random cases using the BoneXpert software, the correlation was 1.00 (100% accuracy). **Conclusion:** The automated analysis using BoneXpert allows for standardized, low-variability, and high-concordance assessment.

Keywords:
Bone age measurement;
Greulich and Pyle;
BoneXpert

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Introduction

Bone age is a measure of a child's degree of skeletal maturation, that is, the extent to which the child has progressed in his/her skeletal development [(1)]. Skeletal maturation is controlled by hormones and these same hormones influence the onset of puberty, therefore a child with a late skeletal maturation, for example, is also likely to have late puberty [(2)].

Radiological evaluation of bone age, using carpal and wrist radiography, is a routine procedure in pediatric radiology and is an effective indicator for diagnosing different diseases and determining the best timing of their treatment, for example, children with early puberty and short stature, thus accuracy in the evaluation of bone age is very important [(3,4)].

In bone development during the fetal period, the radius, ulna, and phalanges have endochondral ossification, while carpal bones have intramembranous ossification. The rate of maturation of the carpal bones varies between individuals, however, full maturation occurs early in the carpal bones, which are less dependent on growth hormone compared to metacarpals and phalanges, which is why the carpal bones are not suitable for bone age assessment. Although the process of bone maturation is similar in all people, the rate of bone maturation differs among ethnic groups, due to the timing of the onset of puberty [(5,6)].

Several methods have been used to assess radiological bone age over time, the main problem is the inter- and intra-rater reliability [(7-14)]. The most commonly used methods are the Greulich and Pyle atlas (GP) and the Tanner-Whitehouse method (TW), both performed through the assessment of left hand x-rays. The reason for using the left hand is because most people are right-handed and the right hand is more likely to suffer more injuries than the left hand, and in the early 20th century, at a meeting of physical anthropologists, an agreement was reached and it was determined according to their observations that physical measurements should be made on the left side of the body [(4)].

Traditionally used manual bone age assessment methods are often time-consuming and can be inaccurate, which is why the need for automated methods to determine the bone age of patients with more accurate results has increased recently [(14)].

The Greulich and Pyle method consists of an atlas in which bone age is assessed by comparison of a patient's left hand x-ray with one of the closest standard x-rays in the atlas. This method was developed using x-rays of Caucasian children in Cleveland Ohio, United States of America, during the period 1931 to 1942 [(1)]. It has been reported that the secondary sexual characteristics of American children today begin earlier than several decades ago, therefore it may be difficult to accurately assess bone age in children today with this method [(15)].

One of the method for the automatic determination of bone age, called BoneXpert®, analyzes the X-ray automatically, independent of hand rotation, and both the left and right hand are accepted by the software. The age range for reading is 2.5 to 17 years for boys and 2 to 15 years for girls. BoneXpert® determines from the hand x-ray the edges of 13 bones automatically: radius, ulna and 11 short bones (metacarpal and phalanges of 1, 3 and 5 fingers). The system automatically rejects images with abnormal bone morphology or very poor image quality [(5,7)].

The image analysis is divided into three layers: the A layer reconstructs the edge of the bones and validates it. The B layer determines the bone age of each bone and validates it. In the C layer, the system involves a potentially nonlinear transformation of the intrinsic bone ages into Greulich and Pyle bone ages or Tanner Whitehouse stages [(7)]. The results are immediately available to the radiologist and/or requesting clinician through the PACS system and can be read directly from the image (Figure 1).

The objective of this study was to establish the correlation of bone age assessed using the manual method through the Greulich and Pyle atlas, versus automated assessment using the BoneXpert® software.

Material and Method

Retrospective analysis approved by the Ethics Committee of the study's host institution, Clínica Alemana de Santiago de Chile, which grants exemption from informed consent. A correlation study of diagnostic techniques was performed for which 1,500 consecutive carpal X-rays of the PACS system of the imaging department of our institution were selected for bone age determination in children under 16 years of age during the period January 2013 to January 2016. They were anonymized and then stored in DICOM format, assigning them a sequential number to each study. X-rays that had previously been assessed for bone age using the Greulich and Pyle Atlas by one of our seven pediatric radiologists of the institution were submitted to the BoneXpert® software for automated bone age assessment.

The bone age report was extracted from the radiological report in years and months with its respective standard deviation and also the results of the bone age assessment from the BoneXpert® software. All data were recorded in an Excel database and then analyzed with the STATA statistical software version 13.1.

In addition, 100 random cases are sampled for analysis/re-analysis of the BoneXpert® technique. Sub-

Figure 1. Radiographic assessment by BoneXpert Method.

BA (GP):	Greulich-Pyle bone age with decimals (M or F indicates the gender)
BA SDS:	Standard deviation score (SDS, also known as Z-score) of GP bone age, based on Healthy Dutch children 1997 BA SDS > 0 indicates advanced bone age BA SDS < 0 indicates delayed bone age
BA (TW3):	Tanner-Whitehouse-3 bone age, TW2 can also be shown
Age:	Chronological age with decimals
BHI:	Bone health index, based on cortical thickness of the metacarpals
BHI SDS:	Standard deviation score of BHI

sequently, the correlation levels of the measurements were analyzed using the Pearson correlation coefficient and the levels of variability of the measurements using Bland-Altman analysis and calculated 95% confidence intervals.

Results

Out of the 1,500 analyzed x-rays, seven cases were excluded due to a technical failure that prevents automatic quantification, such as a finger of the technologist and/or parents projected on the radius and/or ulna, the system did not indicate the bone age. The final sample corresponds to 1,493 cases of which 922 were girls (61.6%) and 571 boys (38.4%), with a median chronological age of 9.96 years (IQR 8.51-11.29) in girls and 11.12 years (IQR 8.72-12.71) in boys (p 0.001) (Figure 2).

Correlation levels between manual bone age and automated bone age BoneXpert® among different raters ranged from 0.91 to 0.93 (Figure 3).

Bland-Altman analysis indicated an average difference between manual bone age and BoneXpert® of 0.19 years (CI 0.13 to 0.25), corresponding to 2.2 months (Figure 4). In the analysis/re-analysis of 100 random cases using the BoneXpert® method to assess the accuracy of the software, the correlation was 1.00 (perfect correlation, that is to say, 100% accuracy).

Discussion

The correlation in bone age assessment through the BoneXpert® method compared to manual assessment by pediatric radiologists in our study was very good, ranging from 0.91 to 0.93 when comparing different raters, with an average difference between the measurements of 0.19 years or 2.2 months between the methods. 61.6% of our series are girls, with a median age of 9.9 years, figures that are probably influenced by the concern of mothers and patients themselves to know what their final height will be and to consult a doctor early on. In a series of studies published to date in different countries and populations, similar results to ours were observed, for example, in the study conducted in Japan by Martin in 284 patients, the variation between measurements was 0.71[11]. Another study in Chinese population conducted by Shao-Yan, which included 6,026 images, the degree of agreement between BoneXpert® and manual reading was 0.64[10]. Van Rijn's study, in German population (405 cases) was 0.71[13] and Thodberg's study[15], where the BoneXpert® method was validated in 1,390 American children of four ethnicities (Hispanic, African-American, Caucasian and Asian), the correlation between the methods was 0.74. In Chile, in 2010 Moënne, K et al conducted a comparative analysis of bone age between manual reading, BoneXpert® and Bone-age ultrasound in a cohort of 194 children aged 5 to 7 years, which showed a good correlation of 0.69 between methods [15]. Our results allow us to validate the automated assessment of bone age through the BoneXpert® software in an important sample of the Chilean population. The radiologist assessment is always important to determine abnormalities beyond the simple quantification of the

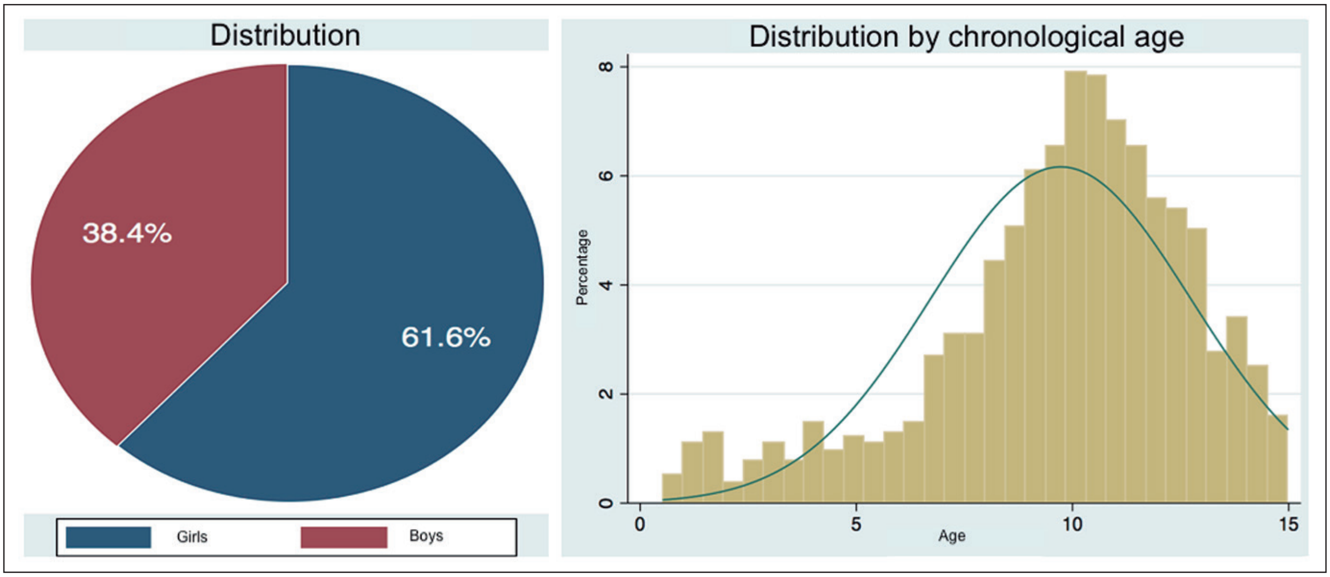

Figure 2. Distribution of patients according to chronological age.

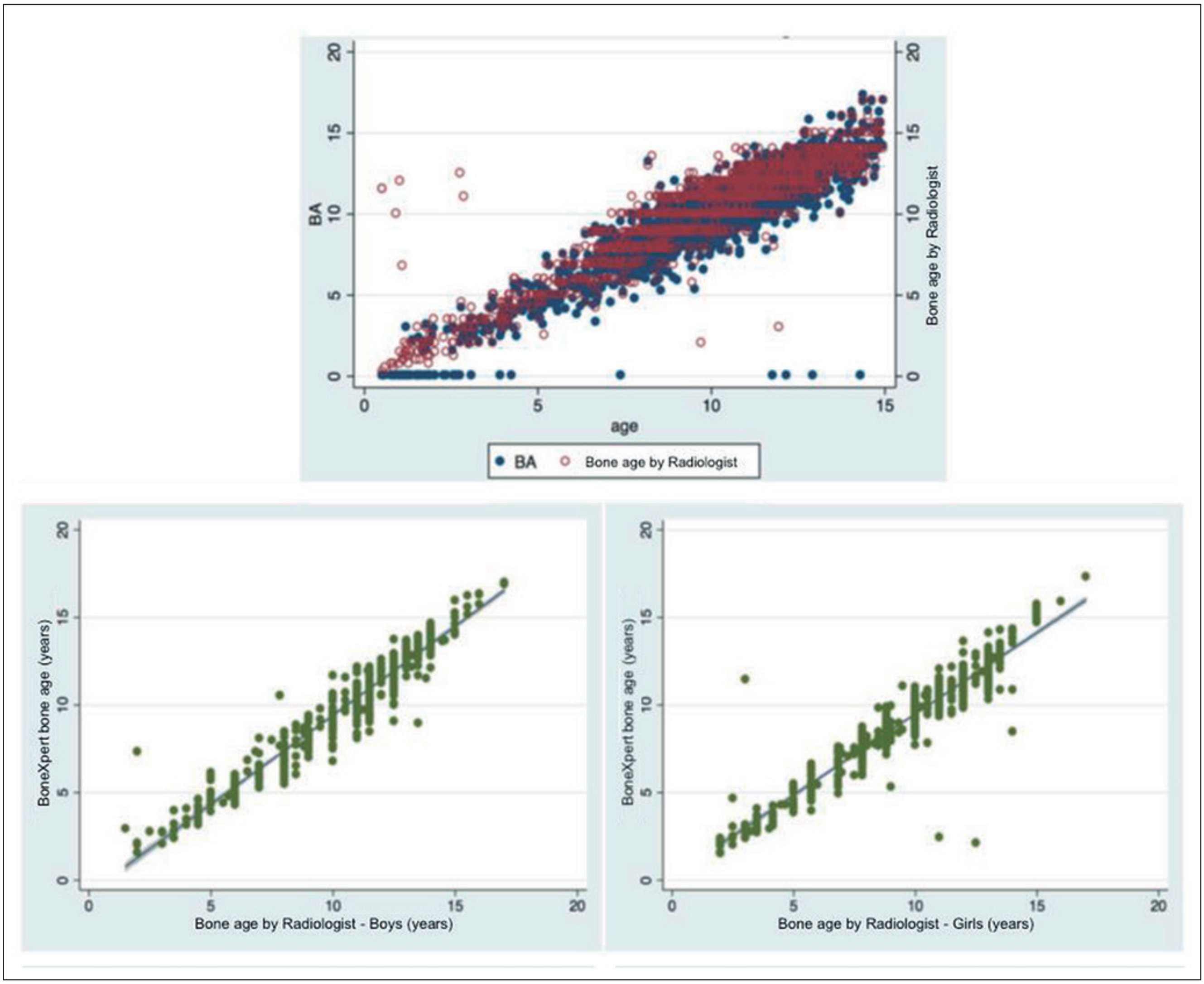

Figure 3. Correlation of radiological bone age versus automated bone age assessment BoneXpert.

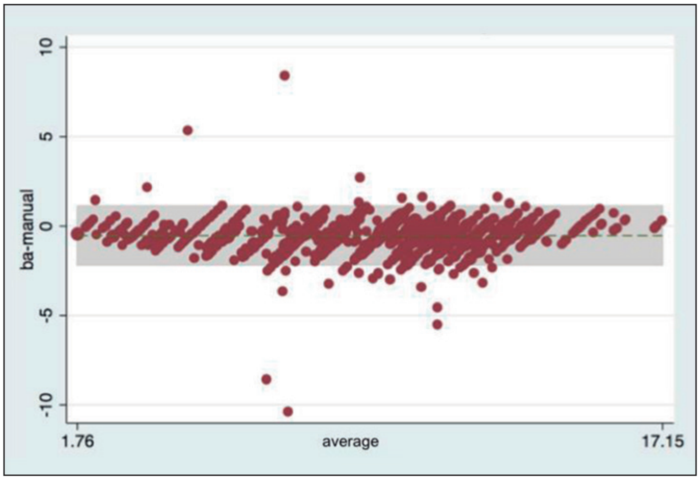

Figure 4. Bland-Altman plot. Difference between radiological bone age and automated bone age BoneXpert.

contours and in those cases of patients who are out of the range established by the software manufacturer 2.5 to 17 years in boys and 2 to 15 years in girls.

For the purposes of this study, the BoneXpert® software was used under an exclusive academic research license, but in the coming months it will be available as a regular clinical tool to support the actions of pediatric radiologists in those studies conducted at the Clínica Alemana-Santiago. Information about the software and how to obtain it can be found at www.bonexpert.com

Conclusion

Automated bone age assessment using the BoneXpert® software allows for a standardized, low-variability, and highly consistent assessment of bone age compared to manual reading by pediatric radiologists.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors state that the information has been obtained anonymously from previous data, therefore, Research Ethics Committee, in its discretion, has exempted from obtaining an informed consent, which is recorded in the respective form

Financial Disclosure

Authors state that no economic support has been associated with the present study.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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