Tibial Tubercle Apophyseal Stage to Determine Skeletal Age in Pediatric Patients Undergoing ACL Reconstruction

A Validation and Reliability Study

Mihir S. Dekhne,[*] MS, Isabelle D. Kocher,[†] Zaamin B. Hussain,[†‡] MD, EdM, Aliya G. Feroe,[*†] MPH, Saritha Sankarankutty,[†] MBBS, MPH, Kathryn A. Williams,[§] MS, Benton E. Heyworth,[*†] MD, Matthew D. Milewski,[*†] MD, and Mininder S. Kocher,[*†||] MD, MPH

Investigation performed at Boston Children's Hospital, Boston, Massachusetts, USA

Background: Anterior cruciate ligament (ACL) injuries demand individualized treatments based on an accurate estimation of the child's skeletal age. Wrist radiographs, which have traditionally been used to determine skeletal age, have a number of limitations, including cost, radiation exposure, and inconvenience.

Purpose: To evaluate the reliability and validity of a radiographic staging system using tibial apophyseal landmarks as hypothetical proxies for skeletal age to use in the preoperative management of pediatric ACL tears.

Study Design: Cohort study (diagnosis); Level of evidence, 2.

Methods: The study included children younger than 16 years of age who underwent ACL reconstruction between July 2008 and July 2018 and received both skeletal age radiography and knee radiography within 3 months of each other. Skeletal age was calculated from hand and wrist radiographs using the Greulich and Pyle atlas. Tibial apophyseal staging was categorized into 4 stages: cartilaginous stage (stage 1), apophyseal stage (stage 2), epiphyseal stage (stage 3), and bony/fused stage (stage 4). Data were collected by 2 independent assessors. The analysis was repeated 1 month later with the same assessors. We calculated descriptive statistics, measures of agreement, and the correlation between skeletal age and apophyseal stage.

Results: The mean chronological age of the 287 patients included in the analysis was 12.9 ± 1.9 years; 164 (57%) of the patients were male. The overall Spearman r between skeletal age and tibial apophyseal staging was 0.69 (0.77 in males; 0.60 in females). The interrater reliability for the tibial apophyseal staging was substantial (Cohen $\kappa = 0.66$), and the intrarater reliability was excellent (Cohen $\kappa = 0.82$). The interrater reliability for skeletal age was excellent (intraclass correlation coefficient [ICC] = 0.93), as was the intrarater reliability (ICC = 0.97).

Conclusion: The observed correlation between skeletal age and tibial apophyseal staging as well as observed intra- and interrater reliabilities demonstrated that tibial apophyseal landmarks on knee radiographs may be used to estimate skeletal age. This study supports the validity of knee radiographs in determining skeletal age and provides early evidence in certain clinical presentations to simplify the diagnostic workup and operative management of pediatric knee injuries, including ACL tears.

Keywords: bone age; skeletal age; Greulich and Pyle atlas; anterior cruciate ligament (ACL) injuries

Skeletal age, distinct from chronological age, takes into account individualized rates of physiological development and is the mainstay for measuring developmental status.[26] Skeletal age is a crucial factor in the optimal management of pediatric orthopaedic patients. Therefore, an accurate determination of skeletal age via high intra- and interobserver agreement is important in guiding treatment. One of the most commonly used methods for the assessment of skeletal age is the Greulich and Pyle atlas method,[11] which compares the left wrist, hand, and finger radiograph of the patient under investigation to the nearest standard radiograph in the atlas.

Anterior cruciate ligament (ACL) injuries, which have been reported with increasing frequency in skeletally immature patients,[10,30] demand individualized treatments based on an accurate estimation of the child's skeletal age. The main goal in assessing skeletal age is to determine remaining growth potential. These estimates guide

The Orthopaedic Journal of Sports Medicine, 9(9), 23259671211036897
DOI: 10.1177/23259671211036897

treatment selection—nonoperative or operative—as well as surgical timing and technique. Protecting the open physis is central to preventing growth arrest and deformity, and even the recommended surgical approaches for pediatric ACL injuries do not completely mitigate this risk.[4,15,31] Indeed, at the time of writing, standard practice for knee surgery involved the use of preoperative hand radiographs to estimate pediatric skeletal maturity.

The use of preoperative hand radiographs in knee surgery has clear drawbacks. First, additional radiographs increase cumulative radiation, which is especially harmful to the developing structures of young children. Second, these radiographs can complicate operative planning, posing emotional, physical, and economic burden to the patient and caregiver. A functionally similar method to assess skeletal age while circumnavigating these drawbacks may demonstrate clinical utility in the setting of knee surgery.

Pennock et al[25] described the use of magnetic resonance imaging (MRI) to visualize ossification centers and obtain accurate bone age calculations. However, to our knowledge, no studies have examined the utility of knee radiographs for the same purpose, which have also been shown to capture ossification centers.[1,22,23] Because knee radiographs are routinely performed to diagnose knee injuries (eg, ACL tears), these radiographs may be able to serve a double role in both diagnosis and skeletal-age estimation, providing a feasible alternative to preoperative hand radiographs in certain contexts. As such, the purpose of this study was to evaluate the reliability and validity of a radiographic staging system using tibial tubercle apophyseal landmarks as hypothetical proxies for skeletal age. Wrist radiographs assessed by the Greulich and Pyle atlas acted as the reference standard to compare with estimates of skeletal age using tibial apophyseal landmark findings on lateral knee radiographs. We hypothesized that the correlation between estimates of skeletal age and tibial apophyseal landmarks derived by this staging system would demonstrate sufficient reliability and validity to warrant the use of knee radiographs to guide operative management for select knee injuries.

METHODS

Study Sample

After institutional review board approval was received, study patients were identified from an operative departmental database. Patients included in this study had to have undergone ACL reconstructive surgery between July 2008 and July 2018, be younger than 16 years of age, and have records of skeletal age and a knee radiograph within a 3-month span (Figure 1). No other specific exclusion criteria were applied. Application of these criteria resulted in a sample of 373 patients. To maximize external validity and to ensure an even representation across the larger study sample, the size of each age subgroup (6-year-olds, 7-year-olds, etc) and sex subgroup (female and male) was restricted to a maximum of 30 patients. When >30 patients fit subgroup criteria, a random number generator was used to select the 30 patients to include. The final sample consisted of 287 patients.

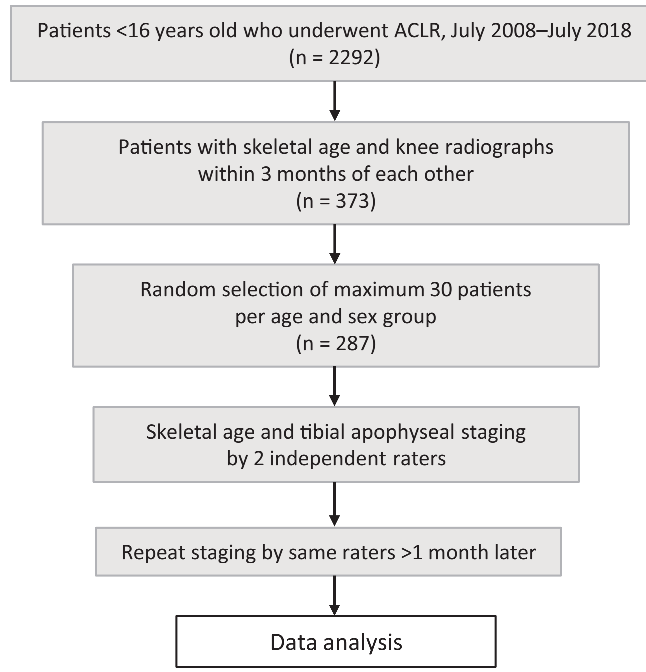

Figure 1. Flowchart of study sample and application of study design.

Radiographic Features

Skeletal age was determined using the Greulich and Pyle atlas method by using the left wrist, hand, and finger radiograph of the patient and comparing it to the nearest standard radiograph in the atlas.[11] In the case of imperfect

‖Address correspondence to Mininder S. Kocher, MD, MPH, Boston Children's Hospital, 300 Longwood Avenue, Boston, MA, 02115, USA (email: Mininder.Kocher@childrens.harvard.edu).
*Harvard Medical School, Boston, Massachusetts, USA.
†Division of Sports Medicine, Department of Orthopaedic Surgery, Boston Children's Hospital, Boston, Massachusetts, USA.
‡Department of Orthopaedic Surgery, Emory University School of Medicine, Atlanta, Georgia, USA.
§Biostatistics and Research Design Center, ICCTR, Boston Children's Hospital, Boston, Massachusetts, USA.
Final revision submitted April 12, 2021; accepted May 13, 2021.
One or more of the authors has declared the following potential conflict of interest or source of funding: B.E.H. has received education payments and consulting fees from Arthrex. M.D.M. has received education payments from Kairos Surgical. M.S.K. has received consulting fees from Best Doctors, OrthoPediatrics, Ossur, and Smith & Nephew and royalties from OrthoPediatrics, Ossur, Saunders/Mosby-Elsevier, and Wolters Kluwer Health–Lippincott Williams & Wilkins. AOSSM checks author disclosures against the Open Payments Database (OPD). AOSSM has not conducted an independent investigation on the OPD and disclaims any liability or responsibility relating thereto.
Ethical approval for this study was obtained from Boston Children's Hospital (protocol No. IRB-P00030381).

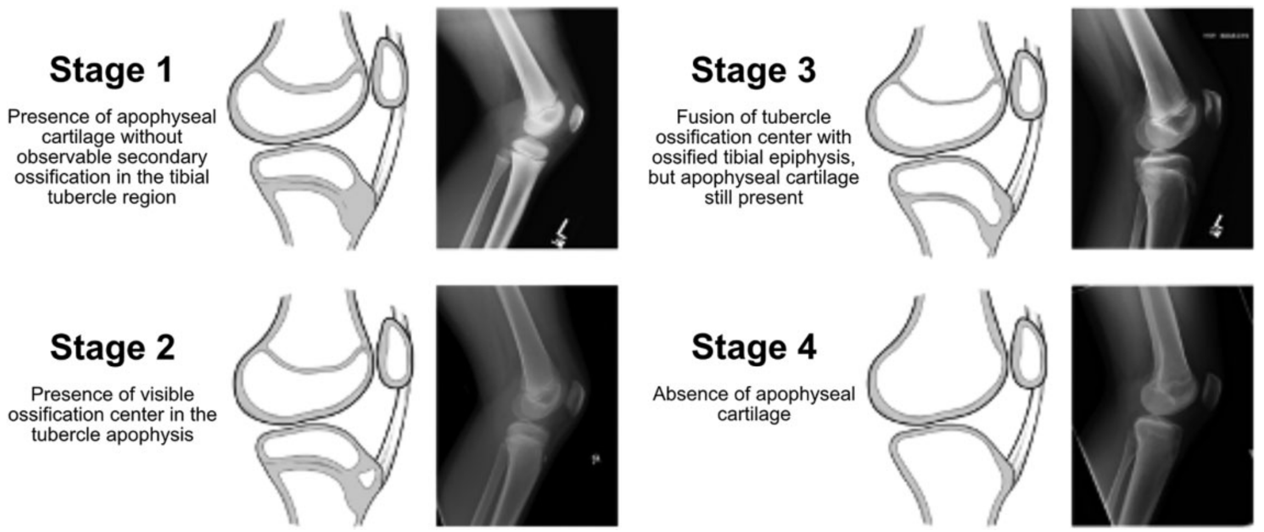

Figure 2. Tibial apophyseal staging schema.

matches, the closest matching template radiograph from the atlas was selected.

Lateral radiographs of the knee were then used to stage tibial apophyseal landmarks for each patient. We applied 1 of 4 stages (Figure 2): cartilaginous stage (stage 1), apophyseal stage (stage 2), epiphyseal stage (stage 3), and bony/fused stage (stage 4).[8] The cartilaginous stage (stage 1) was characterized by the absence of an ossification center without any observable secondary ossification in the tibial tubercle region. The apophyseal stage (stage 2) was characterized by the presence of a visible ossification center in the tubercle apophysis. The epiphyseal stage (stage 3) was characterized by the fusion of the tubercle ossification center with the ossified tibial epiphysis but with apophyseal cartilage still present. The bony/fused stage (stage 4) was characterized by the absence of apophyseal cartilage. Each stage corresponds with general skeletal ages: stages 1 and 2 with prepubescence, stage 3 with pubescence, and stage 4 with skeletal maturity or near skeletal maturity. The delineation of 4 tiers was thought to map tibial apophyseal stage and skeletal age to a clinically relevant degree of precision; further stratification was thought to not have notably more clinical utility.

Study Design

Both skeletal age and tibial apophyseal staging were recorded by 2 independent, blinded raters reading deidentified radiographs using a Synapse PACS system (Fujifilm Medical Systems), generating 4 recordings per patient. The same recordings were repeated at a minimum of 1 month apart by the same raters, generating a total of 8 recordings per patient, to analyze both inter- and intrarater reliability. The raters were students who had not yet undergone formal orthopaedic residency training (M.S.D. and I.D.K.). The raters were instructed on the overall hypothesis and study design and underwent rigorous study of the Greulich and Pyle atlas and thorough training by sports medicine surgeons on the radiographic features of tibial apophyseal staging. Before beginning data collection, the raters were required to exhibit strong interrater reliability with the attending surgeon to ensure rater proficiency. The raters were not involved in the clinical care of the patients and were blinded to each patient's chronological age and treatment course.

Statistical Analyses

Descriptive statistics were reported. The Cohen kappa (κ) was used to calculate the inter- and intrarater reliability for tibial apophyseal staging (ordinal variable), and the intraclass correlation coefficient (ICC) was used to calculate the inter- and intrarater reliability for bone age (continuous variable). The lowest ICC or κ value was reported. The Landis and Koch criteria were used to measure the magnitude of the reliability coefficient: 0-0.2 = poor, 0.21-0.4 = fair, 0.41-0.6 = moderate, 0.61-0.8 = substantial, and 0.81-1.0 = excellent agreement.[18] Guidelines by Koo et al[17] for interpreting ICCs were used. The strength of the correlation between mean skeletal age and modal apophyseal age was indicated with the Spearman correlation coefficient (r_S). All statistical analyses and generation of figures were performed using R Version 3.6.1 (R Foundation).

RESULTS

The sex-stratified distribution of chronological and skeletal age for the 287 study participants, shown in Figure 3, was normal overall with minimal left-sided skew. The mean chronological age was 12.9 ± 1.9 years, and male patients comprised 164 (57%) of the study sample. The relationship between tibial apophyseal stage and skeletal age for male and female participants is illustrated in Figure 4 and

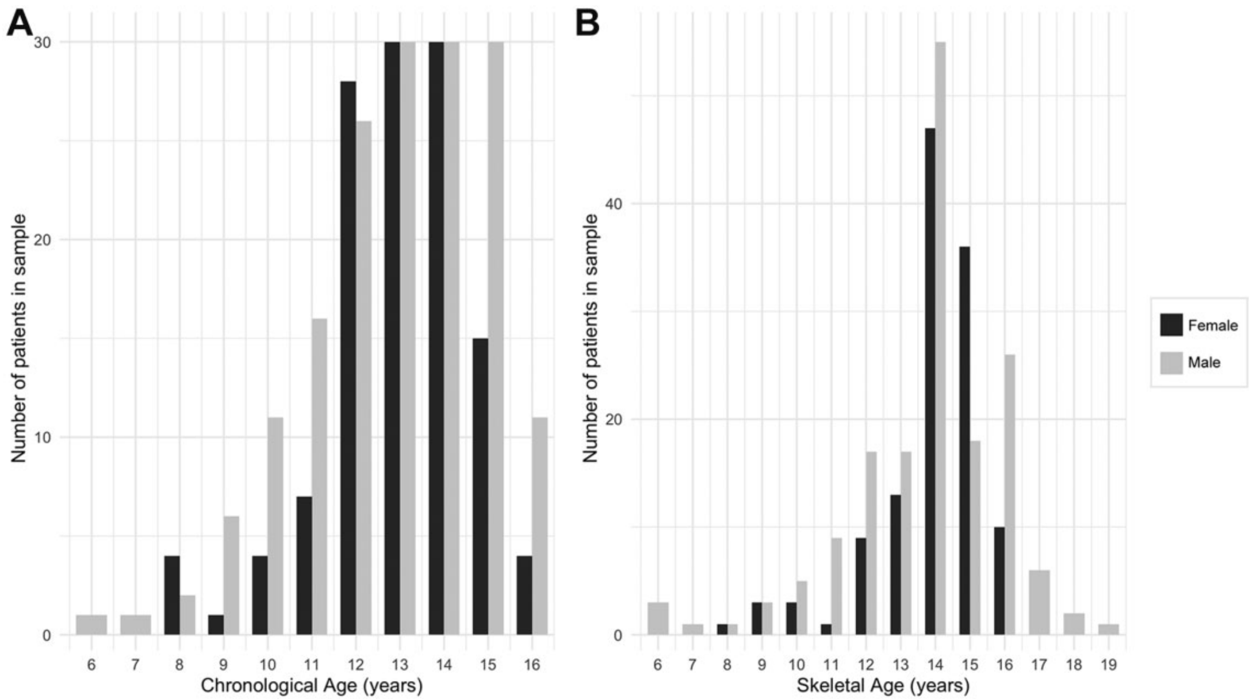

Figure 3. Bar charts demonstrating (A) chronological and (B) skeletal age distributions for the 287 included patients grouped by sex.

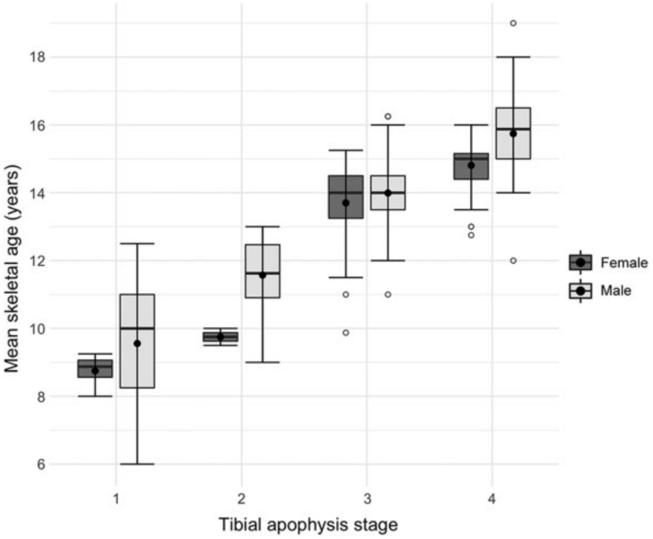

Figure 4. Boxplot demonstrating the relationship between tibial apophyseal stage and skeletal age for male and female participants. Boxes display median and interquartile range (IQR), and whiskers represent up to 1.5× IQR. Filled points represent sample mean, and unfilled points represent outliers.

Table 1. A moderate linear positive correlation was present, and the total Spearman correlation coefficient between tibial apophyseal stage and skeletal age was 0.69 (0.77 in male participants [strong]; 0.60 in female participants [moderate]).

TABLE 1
Correlation of Skeletal Age and Apophyseal Stage by Sex

	Skeletal Age, y, mean ± SD (range)	
	Males (n = 164)	Females (n = 123)
Apophyseal stage		
1	9.6 ± 2.0 (8.6-10.6)	8.8 ± 0.5 (7.9-9.6)
2	11.6 ± 1.3 (10.9-12.3)	9.8 ± 0.4 (6.6-12.9)
3	14.0 ± 1.1 (13.8-14.3)	13.7 ± 1.1 (13.4-13.9)
4	15.7 ± 1.3 (15.2-16.1)	14.8 ± 0.8 (14.6-15.0)
Correlation (r_S)[a]	0.77	0.60

[a]Combined $r_S = 0.69$.

TABLE 2
Reliability Assessment (N = 287)[a]

Measure	Interrater Agreement	Intrarater Agreement
Apophyseal stage, κ	0.66 (0.59-0.74)	0.82 (0.76-0.88)
Skeletal age, ICC	0.93 (0.91-0.95)	0.97 (0.96-0.97)

[a]Values in parentheses are 95% confidence interval. ICC, intraclass correlation coefficient..

Results from the reliability analyses are shown in Table 2. The interrater reliability for the tibial apophyseal staging was substantial (κ = 0.66), and the intrarater reliability was excellent (κ = 0.82). The interrater reliability for skeletal age was excellent (ICC = 0.93), as was the intrarater reliability (ICC = 0.97).

DISCUSSION

The present study demonstrated a strong correlation between tibial apophyseal stage and pediatric skeletal age in boys but only a moderate correlation in girls. This suggests that apophyseal landmarks on lateral knee radiographs may provide an adequate preoperative estimate of skeletal age for boys but that the possible role of such landmarks in girls requires further evaluation.

Although radiography of the left wrist, hand, and fingers is the most common method for estimating skeletal age, alternative methods have been described examining the pelvis,[21] elbow,[7] spine,[27] and calcaneal radiographs[21]; also, knee MRIs routinely obtained in surgical evaluation have been validated as a radiation-free imaging alternative.[25] Our study suggests that tibial apophyseal landmarks from knee radiographs may provide an additional option for estimating skeletal maturity, having demonstrated substantial to excellent intra- and interrater agreement. Although not an absolute replacement for other methods of measuring skeletal maturity, routine knee radiography performed for most knee injuries may provide an adequate alternative when other methods (eg, preoperative hand radiographs) are not a ready option. In these cases, the use of existing knee radiographs may have the additional benefits of lessening pediatric radiation exposure, simplifying patient preoperative procedures, and reducing health care costs.

Specifically, radiographic tibial tubercule apophyseal landmarks may improve the determination of optimal management for patients with ACL injuries. In prepubescent patients, corresponding to tibial apophyseal stage 1 and stage 2 patients in this study, physeal-sparing reconstruction is usually recommended. Physeal-sparing reconstruction includes the combined intra-articular/extra-articular iliotibial band technique described by Kocher et al[13,14] or an all-epiphyseal tunnel reconstruction as described by Anderson.[2,3] In pubescent patients, corresponding to tibial apophyseal stage 3, current recommendations include partial or complete transphyseal reconstruction with physeal-respecting techniques, such as soft tissue graft selection and physeal-sparing fixation implants.[6,12,16,20] Many approaches may be considered for patients who are at or near skeletal maturity, corresponding to tibial apophyseal stage 4, including complete transphyseal bone–patellar tendon–bone autograft or screw fixation of soft tissue grafts across the level of the physis. The latter technique is commonly pursued for adult patients.[5]

Importantly, the present staging criteria are less suitable for estimating skeletal maturity in girls as opposed to boys—where the correlation was strong. The lower correlation between tibial apophyseal staging in the present study may be a consequence of sex-specific differences in ossification center fusion in girls and boys.[1] In a large sample of Irish people, O'Connor et al[22,23] demonstrated sex differences in the estimation of skeletal age by tibial landmarks on knee radiographs, including lower precision of estimates in their female versus male participants (+2.0 to –1.9 years vs ±1.5 years of actual age, respectively). In addition to distinct degrees of skeletal age predictability in each sex, there has been evidence of sex-specific patterns in the rate that each stage of fusion occurs—boys may complete stage 2 six months earlier than girls, but girls will complete epiphyseal union earlier.[1] Similar findings have been characterized in the pediatric elbow as well.[24] These sex-specific biological differences in ossification require more evaluation to understand how to optimize the evaluation of tibial tubercules to improve estimates of skeletal age in girls.

Without question, the most useful determination of skeletal age incorporates a multifaceted approach that integrates patient history (eg, adolescent growth spurt, parental heights, and Tanner staging)[29] and diagnostic imaging specific to patient presentation. As such, tibial apophyseal staging by no means provides a universal replacement to current preoperative hand radiographs. There are settings where the precision of hand radiographs is necessary for operative management or where concurrent pathologies may make accurate tibial tubercle apophyseal staging (eg, Osgood-Schlatter disease) more challenging. Additionally, although lateral view knee radiographs have shown high sensitivity in evaluating a number of knee pathologies (eg, tibiofemoral narrowing associated with osteoarthritis, effusions),[19,28] variability in radiographic knee rotation may affect stage to age correlation in some patients. Supplemental imaging would be necessary in these cases. Furthermore, a clinician may benefit from complementary studies to the lateral knee radiograph, such as postinjury long-leg radiographs (hips to ankles) to establish a baseline for the assessment of subsequent angular deformity and leg length discrepancy.[4] Simplified skeletal age estimation systems may offer utility in research—especially retrospective—when other assessments of skeletal maturity were not performed.

This retrospective, single pediatric institution study had several limitations, primarily related to radiograph reads. First, the radiographs were reviewed by only 2 raters; rater blinding and an interval of >1 month between ratings were used to minimize potential bias. Second, neither rater was a trained orthopaedic surgeon, which likely affected their proficiency with radiographic interpretation. However, to diminish this influence, both raters underwent rigorous radiographic training by orthopaedic sports medicine surgeons and were required to demonstrate strong interrater agreement with the attending surgeons. Furthermore, reliability measurements by nonexperts may be more generalizable to a broader range of radiographic interpretation skill; this would be a greater limitation in highly specialized centers. Third, although using the Greulich and Pyle atlas as the standard for skeletal age estimation is common practice, the atlas was developed using radiographs of upper middle–class Caucasian children in Cleveland, Ohio, USA, between 1931 and 1942.[11] Given the increasing diversity of the United States and the reports that secondary sex characteristics in US boys and girls are developing earlier today than in previous decades,[9] bone-age assessments based on the Greulich and Pyle method may have an increased degree of inaccuracy.

CONCLUSION

The observed correlation between skeletal age and tibial apophyseal staging as well as observed intra- and interrater reliabilities demonstrates that tibial apophyseal landmarks on knee radiographs may be used to estimate skeletal age. This study supports the validity of knee radiographs in determining skeletal age and provides early evidence in certain clinical presentations to simplify the diagnostic workup and operative management of pediatric knee injuries, including ACL tears.

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