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ORIGINAL PAPER

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The use of medial clavicular epiphysis ossification stages for bone age determination

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ABSTRACT

Introduction. Bone age determination is a radiological method investigating the compatibility of ossification processes of bones with chronological ages.

Aim. We aimed to investigate the use of CT staging of the medial clavicular epiphyseal ossification in bone age determination in Turkish adolescents and young adults.

Material and methods. Chest CT exams of 2018 patients between 11 and 35 years of age were retrospectively evaluated for epiphyseal ossification stages of the bilateral medial clavicles (4036 clavicles) on both axial&coronal images and compared with the sex and chronologic age of the individuals in Turkey.

Results. For stage 2,3 and 4 the ages of women were greater than men and it was statistically significant. For an individual classified as stage 4,it can be said with certainty that he or she has already reached the age of 18.There was no statistically significant difference between left&right sides and between the axial&coronal images.In addition, it was found that the medial clavicular head epiphyses showed a lot of variation.

Conclusion. CT evaluation of the medial clavicular epiphysis ossification stages is helpful in determination of the individuals over the age of 18. Regardless of the sex, the stage 4 can be used as a criterion to make the prediction that an individual is older than 18 years.

Keywords. bone age, clavicle, medial clavicular epiphysis, skeletal age

Introduction

Age estimation has an important role in both diagnosis and treatment and also decision making processes in forensic applications in which the accuracy of age determination is an important subject in criminal issues.[1] The age determination methods include mainly bone ossification, dental mineralization and sexual maturation characteristics. Bone age (skeletal age) determination is a radiological examination method investigating the compatibility of ossification processes of bones with chronological ages. The most commonly used method is hand bone ossification. However, completed hand and wrist bone ossification in cases over 18 years of age makes bone age estimation difficult. Sexual maturation and mineralization of teeth in these cases have also been completed. Because the clavicular medial head has the most lately fused epiphysis in the entire body, by looking at the union of the medial clavicular epiphysis (sternal end), bone age determination can be made up to a certain age, even after the age of 18.[2] The utility of radiological imaging methods primarily radiograhy and computed tomography (CT) and also magnetic resonance imaging (MRI) have been examined in various studies. In a study conducted in Korean adolescents and young adults chest ra-

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diographs were used to estimate the age with marginally moderate interobserver agreement and high diagnostic accuracy.[3] However, CT has advantages of more accurate evaluation of ossification centers with lack of artifacts due to soft tissue superposition. It is a method recommended by Forensic Age Diagnostics of the German Association of Forensic Medicine (AGFAD).[4]

Aim

In this study, we investigated the use of CT staging of the medial clavicular epiphyseal ossification in bone age determination in adolescents and young adults by retrospectively examining the CT images of 2018 patients in Turkey, using a modified staging system.

Material and methods

This retrospective study was approved by the local ethics committee of the hospital with the IRB number of 621. Chest CT and chest high resolution CT (HRCT) examinations of a total of 2018 patients between 11 and 35 years of age were retrospectively evaluated for epiphyseal ossification stages of the bilateral medial clavicles (4036 clavicles) and compared with the sex and chronologic age of the individuals. Patients with diseases affecting bone development, with clavicle fracture and mass lesions involving the medial head of the clavicle, patients who could not be evaluated clearly due to motion or contrast material artifacts were excluded from the study. The final study population consisted of 2018 patients; 43.4% (876) female and 56.6% (1142) male cases between 11 and 35 years of age. Examinations were carried out with 16 slice Philips and 64 slice Toshiba multidetector CT scanner with parameters of 220 kV, 120 mAs and a collimated slice width of a 1 mm. The slice thicknes varied between the range of 0.3-7 mm. In both gender, the ossification stage of both left and right medial clavicular epiphysis were classified with a modified staging system based on Schmeling and his colleagues staging at both axial and coronal planes, seperately (fig. 1-7).[5] In addition, presence of variations were also noted.

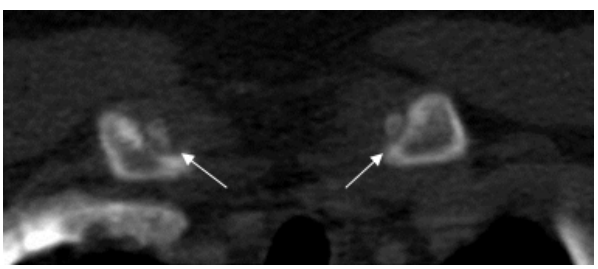


Fig. 1. CT image of medial clavicles of a14 year old female shows stage 2a ossification of bilateral epiphyseal cartilage (white arrows)

Stage 1: epiphyseal ossification is not yet visible (nonossified).

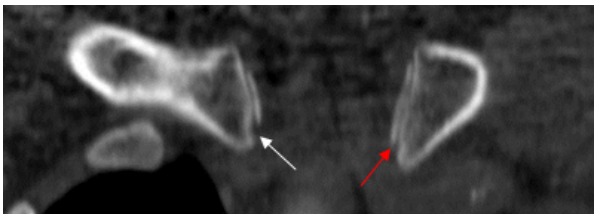


Fig. 2. CT image of medial clavicles of a 17 year old female shows stage 2a (white arrow) ossification of the right and stage 2c of the left epiphyseal cartilage (red arrow)

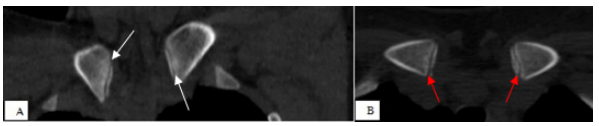


Fig. 3. (A, B) CT image of medial clavicles in a 17 year old female shows stage 2c ossification of bilateral epiphyseal cartilage on the coronal image (A, white arrow) and on the axial image (B, red arrows)

Stage 2a: epiphyseal ossification center has begun to appear but, its diameter is smaller than the 1/3 of the diameter of the metaphysis (Fig. 1, 2).

Stage 2b: the diameter of the epiphyseal ossification center is more than half the diameter of the metaphysis but less than its 2/3.

Stage 2c: the diameter of the epiphyseal ossification center is more than 2/3 of the diameter of the metaphysis but less than its 2/3 or has fully grasped the metaphysis, but fusion has not yet begun (Fig. 2, 3).

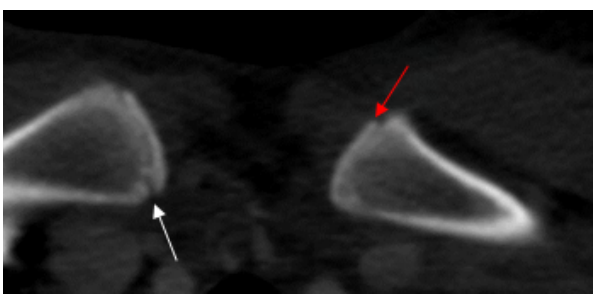


Fig. 4. CT image 18 year old female shows stage 3a ossification (white arrow) of the right and stage 3b of the left epiphyseal cartilage (red arrow)

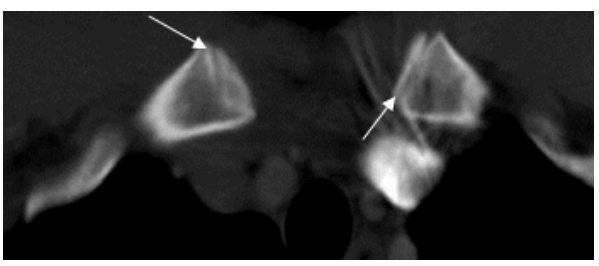


Fig. 5. CT image of medial clavicles of a19 year old male shows stage 3b ossification of bilateral epiphyseal cartilage (white arrows)

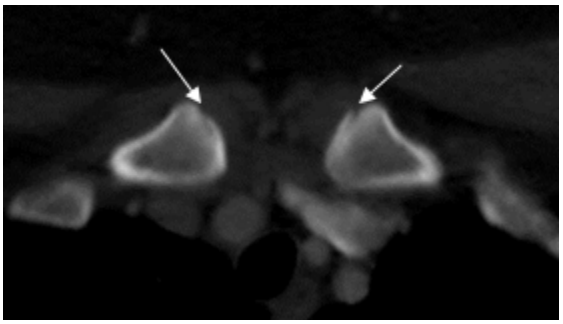


Fig. 6. CT image of medial clavicles of a 20 year old female shows stage 3c ossification of bilateral epiphyseal cartilage (white arrows)

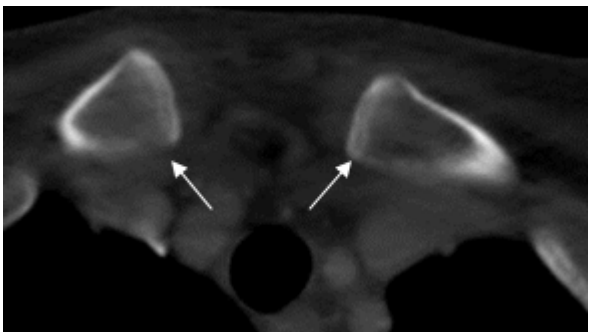


Fig. 7. CT image of medial clavicles of a 22 year old male shows stage 4a ossification of bilateral epiphyseal cartilage (white arrows)

Stage 3a: Epiphyseal fusion has begun, the fused part is less than the 1/3 of the diameter of the epiphysis (Fig. 4).

Stage 3b: Epiphyseal fusion is more than half the diameter of the epiphysis but less than its 2/3 (Fig. 4, 5).

Stage 3c: Epiphyseal fusion is more than 2/3 of the diameter of the epiphysis but it is not completed (Fig. 6).

Stage 4: Epiphyseal fusion is complete but epiphyseal scar (epiphyseal line) can be detected.

Stage 5: Epiphyseal scar can not be detected.

In our study, the stage 4 has been subdivided into 2 groups;

Stage 4a: Epiphyseal fusion is complete but an obvious epiphyseal scar (epiphyseal line) can be detected (Fig.7).

Stage 4b: Epiphyseal fusion is complete and some of the epiphyseal scar (epiphyseal line) can be detected.

Statistical analysis

In the descriptive statistics of the data, the mean, standart deviation, frequency and ratio values were used. The distribution of the variables was controlled with the Kolmogorov Simirnov test. Kruskal-wallis, Mann-Whitney u test for the analysis of quantitative data and Kappa test for the aggrement analysis was applied. SPSS 21.0 program was used in the analyzes.

Results

The ages of all stages differed significantly from each other. The age increased significantly ($p<0.05$) with each increasing stage (Table 1).

Table 1. The ages of the stages

	Age			p
	The lowest	The higest	Mean ± SD	
Stage 1	11	20	13.22 ± 1.92	<0.00001
Stage 2	11	24	16.78 ± 2.32	
Stage 3	14	27	20.59 ± 2.42	
Stage 4	18	35	25.48 ± 4.57	
Stage 5	21	35	29.30 ± 3.49	
Kruskal-Wallis/Mann-Whitney U test				

SD – standard deviation

Table 2 shows the mean ages and standard deviation values among the stage 2, 3 and 4 subgroups themselves. In stage 2a, the age of the patients was significantly ($p<0.05$) lower than stage 2b and 2c. The age of the patients in stage 2b and 2c did not differ significantly as in stage 3b and 3a did not differ significantly ($p>0.05$). In stage 3c, the age of the patients was significantly ($p<0.05$) higher than stage 3a and stage 3b. In stage 4b the age of the patients was significantly ($p<0.05$) higher than stage 4a (Table 2).

Table 2. The mean ages and standard deviation values among the stage 2, 3 and 4 subgroups

	Age			p
	The lowest	The highest	Mean ± SD	
Stage 2a	11	20	15.56 ± 2.27	<0.00001
Stage 2b	12	22	17.72 ± 1.82	
Stage 2c	14	24	17.87 ± 1.81	
Stage 3a	14	22	19.03 ± 1.83	<0.00001
Stage 3b	17	25	19.86 ± 2.03	
Stage 3c	17	27	21.52 ± 2.32	
Stage 4a	19	35	24.39 ± 3.91	<0.00001
Stage 4b	18	35	26.92 ± 4.98	
Kruskal-Wallis/Mann-Whitney U test				

SD – standard deviation

Table 3 shows the mean and standard deviation values of the earliest and the latest ages of the medial clavicular epiphyseal ossification stages. In stage 1, 2a, 2b, 3a, and 3c the average age of the men was significantly ($p<0.05$) higher than the women. In other stages, the ages of the men and women did not differ significantly ($p>0.05$) (Table 3).

There was a significant agreement between the right and left sides with accordance of the 89.1% of the stages on the axial images ($p=0.000$ <0.001; Kappa: 0.855) and with accordance of 89.3% of the stages on coronal images ($p=0.000$ <0.001; Kappa: 0.858) (Table 4). There was

also a significant agreement between the axial and coronal images with accordance of 98.9 % of the stages of the right side (p=0.000 <0.001; Kappa: 0.985) and with accordance of 99.1 % of the stages of the left side agreement (p=0.000 <0.001; Kappa: 0.989) (Table 5).

Table 3. The mean and standard deviation values of the earliest and the latest ages of the medial clavicular epiphyseal ossification stages

Age	Female	Male	
	Mean ± SD	Mean ± SD	p
Stage1	12.79 ± 1.94	13.39 ±1.89	0.004
Stage 2a	14.94 ± 1.94	15.97 ± 2.38	0.001
Stage 2b	16.58 ± 1.86	18.39 ± 1.43	<0.001
Stage 2c	17.44 ± 1.82	18.35 ± 1.68	0.007
Stage 3a	18.62 ± 1.84	19.58 ± 1.70	0.041
Stage 3b	18.91 ± 2.26	20.44 ± 1.69	0.052
Stage 3c	20.59 ± 2.14	22.14 ± 2.24	<0.001
Stage 4a	24.25 ± 4.20	24.57 ± 3.52	0.195
Stage 4b	27.69 ± 5.29	26.46 ± 4.77	0.484
Stage 5	29.44 ± 3.50	29.18 ± 3.47	0.194

Mann-Whitney U test

SD – standard deviation

Table 4. The aggreement between left anf right sides on axial and coronal images

	Left axial/right axial	
	accordance	difference
n	1799	220
%	89.1%	10.9%

	Left coronal/right coronal	
	accordance	difference
n	1803	216
%	89.3%	10.7%

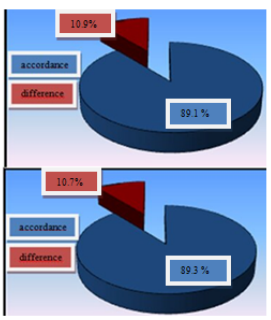
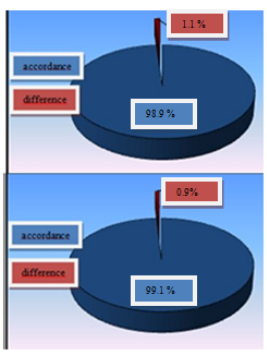


Table 5. The aggreement on axial/coronal images regarding the right and left sides

	Right axial/Right coronal	
	accordance	difference
n	1996	23
%	98.9%	1.1%

	Left axial/Left coronal	
	accordance	difference
n	2001	18
%	99.1%	0.9%



In table 6, the lowest and the highest ages, mean age, standard deviation and median values of women and men in each stages were shown.

In our study, no statistically significant difference was found between the right and left side on axial and coronal images of the same case in terms of the stage (Table 4, 5).

Table 6. The lowest and the highest ages, mean age, standard deviation and median values of women and men in each stages

		The lowest	The highest	Mean ± SD	Median (Q1/Q3)		
Stage 1	female	11	20	12.79 ± 1.94	12.0	11.0	14.0
	male	11	20	13.39 ± 1.89	13.0	12.0	14.0
Stage 2a	female	11	19	14.94 ± 1.94	15.0	14.0	16.0
	male	11	20	15.97 ± 2.38	17.0	14.0	18.0
Stage 2b	female	12	20	16.58 ± 1.86	16.0	15.3	18.0
	male	15	22	18.39 ± 1.43	19.0	17.5	19.0
Stage 2c	female	14	24	17.44 ± 1.82	18.0	16.0	18.0
	male	15	23	18.35 ± 1.68	18.0	17.0	20.0
Stage 3a	female	14	22	18.62 ± 1.84	19.0	17.0	20.0
	male	15	22	19.58 ± 1.70	20.0	18.0	21.0
Stage 3b	female	17	23	18.91 ± 2.26	18.0	17.0	21.0
	male	18	25	20.44 ± 1.69	21.0	19.0	21.0
Stage 3c	female	17	26	20.59 ± 2.14	20.0	19.0	22.0
	male	17	27	22.14 ± 2.24	22.0	20.8	24.0
Stage 4a	female	19	35	24.25 ± 4.20	23.0	21.3	25.8
	male	21	33	24.57 ± 3.52	23.0	22.0	25.8
Stage 4b	female	20	35	27.69 ± 5.29	28.0	22.0	33.0
	male	18	35	26.46 ± 4.77	25.0	23.0	31.0
Stage 5	female	21	35	29.44 ± 3.50	30.0	27.0	32.0
	male	21	35	29.18 ± 3.47	29.0	26.0	32.0

SD – standard deviation, Q1 – Quartile 1, Q3 – Quartile 1

In addition, there are some difficulties encountered during the evaluation in our study. The most common problem among these was the pronounced notching at the head of the clavicle (Fig. 8). In almost all of these cases the epiphyses were hypoplastic or evaluated as a smaller stage despite the advanced age. Another problem was the appearance of more than one small ossification centers (Fig. 9). In addition, the sclerotic bands parallel to the metaphysis, formed in relation with growth in pediatric cases create an appearance similar to the physeal scars observed in stage 4a (Fig. 10). In such cases, it will be necessary to know the estimated age of the person and to evaluate accordingly. Another important point to note is that, the occurance of accessory ossicle which is very rare, imitates the epiphyseal ossification center. In our study, it was found adjacent to the medial head of the right clavicle in two cases (Fig. 11). In addition, the diameter of the epiphysis is about half the diameter of the metaphysis in some cases, but the fusion is complete (Fig. 12). In our study, these cases were evaluated as stage 3c. If these cases came before the

fusion, they would be considered as stage 2a due to the small diameter of the epiphysis.

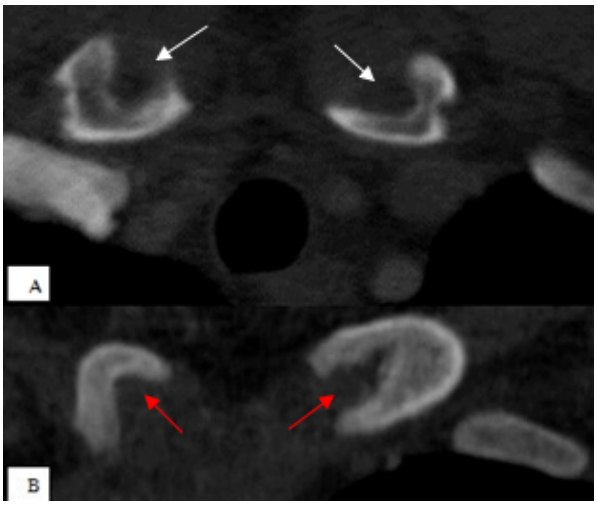


Fig. 8. (A, B) CT images of medial clavicles. A significant notching is seen on the heads of both clavicles on the axial image (A, white arrows) and the coronal image (B, red arrows). The epiphyseal ossification center is not visible

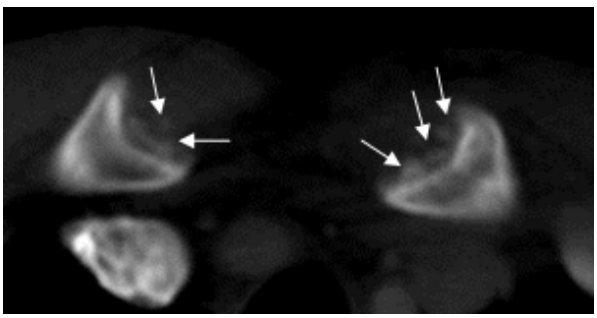


Fig. 9. CT image of medial clavicles of a18 year old male shows more than one ossification center on both sides (white arrows)

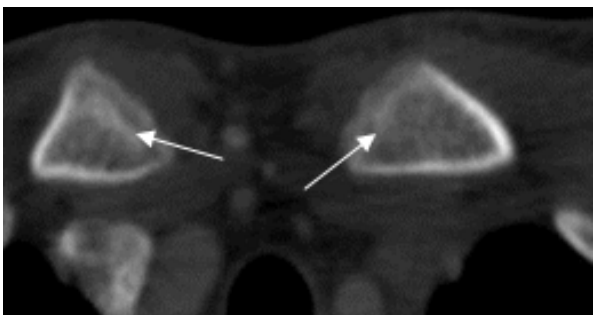


Fig. 10. CT image of medial clavicles of a13 year old male shows sclerotic band associated with growth (white arrows) creating an appearance similar to the physeal scars seen in stage 4a

Discussion

In legal cases, the chronological age is tried to be estimated with different methods. The most important marker showing the development from the birth to the maturity is the bone age.[6] In Turkey, the most commonly used method for determination of age is the left hand and wrist radiographs. Studies have been conducted in the literature to suggest that the ossification stage of medial clavicular head can be used for age determination in people over 18 years of age with closed hand skeletal epiphysis, especially in forensic issues.[3,7,8] Since long, in various studies, it was investigated whether there is any difference by using various methods such as, X-ray, CT and MRI. In the study conducted by Kreitner et al. in 1998 by using CT, ossification of the clavicle was divided into 4 stages (the 4 stage classification system).[9]

Stage 1: The epiphyseal ossification center is not seen.
Stage 2: Ossification center is started to be seen.
Stage 3: There is partial epiphyseal fusion.
Stage 4: The fusion is completed.

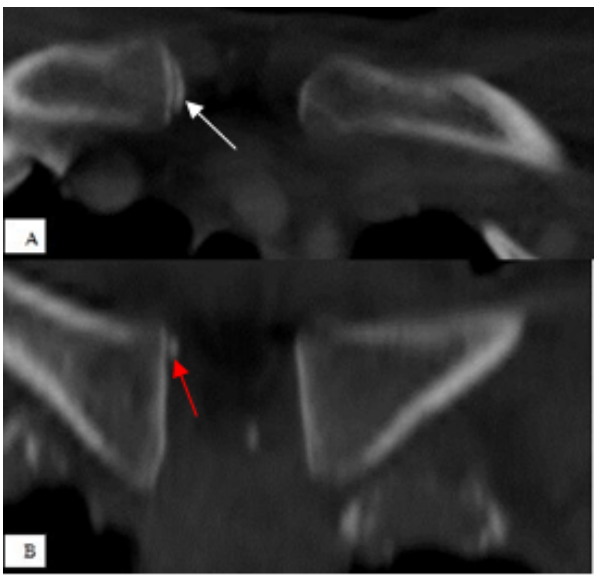


Fig. 11. (A, B) CT images of medial clavicles of a 31 year old female show the accessory ossicle imitating the epiphyseal ossification center on the right side on axial (A, white arrow) and coronal (B, red arrow) images

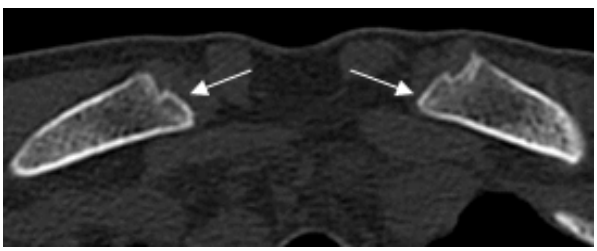


Fig. 12. CT image of medial clavicles of 20 year old male shows that the diameter of the epiphysis is about half the diameter of the metaphysis but the fusion is complete (white arrows)

In this study, it was stated that stage 1 was seen up to the age of 16, stage 2 was seen between the ages of

13 and 22, stage 3 was seen between the ages of 16 and 26 and the age of first appearance of the stage 4 was 26. However, since no gender discrimination was made, its use in forensic medicine was limited. This 4 stage classification system was also used in the study conducted by Zhang et al. analyzing the CT scans of 752 individuals in 2015.[10] They found that the epiphysis was observed to commence fusion in females at 16.28 years and 16.74 years in males and be fully ossified by 25.97 years in females and 25.81 years in males, suggesting that ossification of medial clavicular epiphyseal cartilage can be used in age estimation for West China Han population with the age threshold of 18 years. However, in many of the studies performed on the ossification stages of the medial clavicular head, Schmeling's 5-stage system is used (the 5 stage classification system).[5]

Stage 1: Non-ossified epiphysis.

Stage 2: ossification is started without growth plate ossification.

Stage 3: Growth plate is partially fused.

Stage 4: complete fusion of the epiphysis and metaphysis; physeal scar is visible.

Stage 5: complete fusion of the epiphysis and metaphysis; the physeal scar is no longer visible.

In the study conducted by Patil et al. in 2018, CT images of 462 individuals aged between 10 and 30 years were evaluated retrospectively in an Indian population using the 5 stage classification mentioned by Schmeling.[7] They concluded that the clavicular maturation stage 2 represent age >13 years, stage 3 represent age >16 years, stage 4 represent age >22 years and stage 5 represent age >25 years for an Indian. The study conducted on 142 subjects by El Morsi et al. in Egyptian population evaluating multislice CT on the medial end of clavicles of both sides recommended using stage 1 to be 15 years; Stage 3 to be >15 years; stage 4 of maturation to be >19 years and stage 5 to be >21 years.[8] This study revealed no significant differences between males and females (except for stage 1) or right and left sides as regard age of ossification of medial end clavicles.

In the study conducted by Kellinghaus et al. using thin slice CT in 2009, the difference between the genders was found to be significant for stage 2.[11] It was determined that female cases reached stage 2, 18 months earlier than male cases. It was also stated that the race has no effect on ossification but low socioeconomic status delays the ossification. Since our study is a retrospective study, no information was obtained about the socioeconomic levels of the cases. In 2010 Kellinghaus et al. divided each of the ossification stages 2 and 3 into an early, intermediate and late phase (a, b, c; respectively) by evaluating thin-slice CT scans of 185 patients aged between 13 and 26 years and formed the '9 stage classification system'.[12] In this study, no significant difference was found between genders. It was determined that the earliest age of appearance of stage 3c was 19.5 in women and 19.7 in men and the average age of this stage was 22.5 in women and 22.9 in men. Based on these findings, it was emphasized that even if the epiphyseal fusion of the case is incomplete, if the ossification stage is 3c, it is possible to say that the individual has already reached the legally important age threshold of 18 years. We used the Schmeling's 5 stages in our own modified form by subdividing the stage 4 into two subgroups. We found that the age of the first appearance of stage 4a is 19 for females and 21 for males. Based on this findings, for the individual who is classified as stage 4, it can be said with certainty that he or she has already reached the age of 18. The age of the last appearance of the stage 3b was found to be 23 for females and 25 for males. Based on this findings, it can be said that the age of the person with stage 3b is less than 22 years old. Since the other age ranges in the epiphyseal development and closure stages of the medial clavicular head were very wide, we can give a certain bone age range for a given individual but it was imposible to determine the exact bone age precisely by looking at the medial clavicular head epiphyseal development. In addition, we also found that after 20 years old or older, that is after the closure of iliac and iscial epiphysis (when we actually need to use medial clavicular ossification method) the standard deviation is higher in comparison to the earlier stages. The first and the latest seen age ranges of each seperate stage in our study are shown in table 6. In our study, the ages of the males in stage 1, 2a, 2b, 2c, 3a and 3c was significantly higher than females. No statistically significant difference between left and right sides was found. In the study conducted by Schulz et al. by using CT in 2005, the difference between genders was found to be significant for stage 2. In addition, in this study the age of the first appearance of stage 5 was found to be 21 in women and 22 in men.[13] In terms of the effect of CT slice thickness on the stage, a study conducted by Mühler et al. was published in 2005. In this study, it was determined that increasing the slice thickness (between 1 mm and 3 mm, between 3 and 5 mm, between 5 mm and 7 mm) caused evaluation differences and it was stated that the most appropriate slice thicknes should be 1 mm.[14]

Limitations

The main limitation of our study is its retrospective design, which caused differences in CT slice thickness among the study patients and made us accept the officially recorded age as the real chronological age of the study participants. In addidion we could not evaluate the effect of socioeconomic or nutrition status on the epiphyseal ossification, although low socioeconomic or nutrition status affecting skeletal maturation is a quite rare possibility in Tukey. Nevertheless, we think that our study is valuable in terms of having a very large patients series that has a power to reflect the general population.

In addition, our study is also different in terms of revealing the anatomical variations that may interfere the estimation of the medial clavicular ossification stages.

Conclusion

CT evaluation of the medial clavicular epiphysis ossification stages is helpful in determination of the individuals over the age of 18 and can be used in forensic medicine. Regardless of the sex, the stage 4 can be used as a criterion to make the prediction that an individual is older than 18 years. However, it is not possible to determine the bone age clearly, as the development and closure stages of the medial clavicle epiphysis are seen in a wide age range and the variations are common. Therefore a certain bone age range can be given, but, in this regard it should be taken into account that the standard deviation is higher after the closure of the iliac and ischionic epiphyses (20 years and over) compared to the previous periods.

Declarations

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Author contributions

Conceptualization, N.N.W.; Methodology, N.N.W.; Validation, N.N.W. and B.E.; Formal Analysis, B.E., N.N.W.; Investigation, B.E. and N.N.W.; Data Curation, N.N.W.; Writing – Original Draft Preparation, B.E.; Writing – Review & Editing, B.E. and N.N.W.; Supervision, B.E. and N.N.W.

Conflicts of interest

The authors declare no conflict of interest.

Data availability

All data generated or analyzed during this study are included in this article [and/or] its supplementary material files. Further enquiries can be directed to the corresponding author.

Ethics approval

This retrospective study was approved by the local ethics committee of the Istanbul Medical Faculty with the IRB number of 621.

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