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Mandibular condyle bone density and cortical bone thickness in subjects affected by juvenile idiopathic arthritis assessed with cone-beam computed tomography: a cross-sectional study

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Abstract

Background The aim of this cross-sectional study was to analyze the cortical and trabecular bone density, as well as the cortical bone thicknesses of the mandibular condyles in subjects with Juvenile Idiopathic Arthritis (JIA) and compare them with the condyles of control subjects.

Materials and methods Patients aged between 7 and 16 years were included in the study. A total of 75 CBCTs were analyzed, including 25 from patients with unilateral JIA (mean age 11.1 ± 2.2), 25 from patients with bilateral JIA (mean age 11.9 ± 2.6), and 25 from control subjects (mean age 11.7 ± 2.5). Mimics® (Materialise software BV, Leuven, Belgium) was used for measurements of bone density and cortical bone thicknesses. Total (DTo), cortical (DCo), and trabecular bone density (DTr), as well as cortical bone thicknesses at the medial (MCBT), lateral (LCBT), and upper (UCBT) poles of the condyle's head, were analyzed. The Paired t-test was used to compare the condyles within each group, and the independent t-test was performed to assess differences between the healthy condyles of unilateral JIA subjects and the controls. A three-group multiple regression model, weighted by sex, age, side, and clinic of the condyles (whether healthy or affected), was computed to perform a between-groups comparison.

Results A statistically significant difference ($p=0.02$) was found in DTr (-23.26 ± 48.61 HU) and UCBT (-0.35 ± 0.24 mm) between the affected and unaffected sides in the unilateral JIA group. In bilateral JIA patients, a statistically significant difference in total bone density ($p < 0.01$) and trabecular bone density ($p < 0.01$) of the condylar head was noticed between the right and left sides, with significantly higher values on the right side. The multiple regression model

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showed a significant influence of the pathology on DTr (-23.53 ± 8.70 HU) and UCBT (-0.35 ± 0.03 mm) of the affected condyles.

Analyzing the differences between the control group and the Bilateral JIA subjects, it was found that there was a statistically significant reduced thickness of MCBT ($0.11 \text{ mm} \pm 0.05$), LCBT ($-0.13 \text{ mm} \pm 0.05$), and UCBT ($-0.11 \text{ mm} \pm 0.04$). The affected side of unilateral JIA subjects showed a statistically significant reduction in UCBT (-0.06 ± 0.03 mm) compared to the controls.

Conclusions The results suggest that in affected JIA condyles, the rheumatic disease has a significant impact on the bone structures, impairing trabecular bone density and cortical bone thickness, particularly at the level of the upper pole.

Keywords Juvenile idiopathic arthritis, Temporomandibular joint, Cone-Beam Computed Tomography, Bone density, Bone thickness

Introduction

Juvenile idiopathic arthritis is one of the most significant rheumatic diseases affecting childhood and adolescence, both due to the severity of its clinical manifestations and its prevalence. The precise etiology remains unidentified, and its clinical presentation is highly variable [1]. It is characterized by joint inflammation, affecting one or more joints, resulting in pain, swelling, and limited movement. Onset typically occurs before the age of 16, with symptoms persisting for at least 6 consecutive weeks in the same joint(s) [1]. The temporomandibular joint (TMJ) is frequently affected, with prevalence ranging from 38% to 72%, depending on the diagnostic method and JIA subtype [2, 3]. Joint damage caused by JIA tends to be more severe than that seen in adults with rheumatoid arthritis (RA) since affected joints are in the growth phase, leading to alterations in the quantity and quality of mandibular ramus growth. Notably, the primary site of mandibular growth is the articular surface of the condylar head, making the TMJ particularly vulnerable to damage at the bone surfaces [4].

Moreover, chronic inflammation and damage to the condylar cartilage during developmental stages are considered primary factors in mandibular growth abnormalities and severe malocclusions. In cases of unilateral TMJ involvement, patients may develop marked facial asymmetry, with the affected side's mandibular ramus appearing reduced in length, resulting in chin deviation towards the affected side [5, 6].

Condylar surface damage is often asymptomatic, progressing without subjective or clinical expression. This frequently leads to delayed diagnoses and, consequently, complicated therapeutic approaches. Additionally, the lack of pain and palpable swelling makes reliable follow-up during therapy challenging [3, 7].

Early diagnosis of JIA is crucial to prevent condylar destruction before clinical and morphological signs, such as retrognathia, short mandibular ramus, decreased posterior facial height, mandibular post rotation, increased

hyper-divergence, anterior facial convexity, and facial asymmetry, become irreversible [8–10].

The severity of condylar head involvement in joint damage ranges from small erosions and osteophytes to the complete absence of the condylar head, resulting in varying degrees of functional impairment [6, 11].

Studies by Huntjens et al. [12] and Koos B et al. [13], conducted using cone-beam computed tomography (CBCT), have shown that mandibular asymmetry in JIA-affected children results from significant alterations in the volume and morphology of the condylar head and mandibular ramus.

CBCT and magnetic resonance imaging (MRI) are widely used techniques for early detection and follow-up of disease activity in JIA patients [14, 15].

CBCT provides an accurate representation of the TMJ and joint space without the typical distortions of conventional 2D radiology. It allows for early diagnosis of degenerative joint disease, with higher sensitivity in detecting small bony structure alterations compared to conventional radiology and MRI. MRI is particularly useful for rapidly controlling active synovitis and preventing structural damage [12, 16, 17].

The primary objective of TMJ imaging is to obtain a precise evaluation of cortical and trabecular bony structure involvement, assessing disease extent and progression. Consequently, CBCT is the preferred radiographic diagnostic examination for evaluating TMJ bone changes. Recently, interdisciplinary consensus-based recommendations have endorsed the use of cone-beam computed tomography (CBCT) for the evaluation of temporomandibular joint (TMJ) disorders and dentofacial deformities [18].

Regarding the evaluation of cortical and trabecular bone quality and morphology, studies by Kim et al. [19] and Lo Giudice et al. [20] analyzed bone density and cortical thicknesses of mandibular condyles in patients to evaluate bone changes in different skeletal patterns.

To the best of our knowledge, no study has yet considered these parameters in subjects affected by rheumatic

diseases. Therefore, the current investigation aimed to analyze cortical and trabecular bone densities and cortical bone thicknesses at the medial, lateral, and upper poles of the mandibular condyles' head in JIA subjects. It sought to identify any differences between JIA patients with unilateral TMJ involvement, those with bilateral TMJ involvement, and control subjects to determine how the pathology could influence bone variables.

Materials and methods

Study design

The current investigation is a cross-sectional study conducted on CBCT scans of subjects with Juvenile Idiopathic Arthritis (JIA) and subjects with no JIA serving as controls. To carry out an anonymous analysis of their children's medical history for research purposes, written informed consent was obtained from the parents of the patients.

The study protocol (protocol n.573/15) was approved by the Ethical Committee of the Fondazione IRCCS Ca'Granda, Ospedale Maggiore, Milan - Italy. The study was conducted in compliance with the Declaration of Helsinki guidelines for human studies, ensuring ethical standards were maintained throughout the research process.

Types of participants and inclusion criteria

The CBCT scans analyzed in this research were retrospectively sourced from the digital archive of the Department of Hidden. Medical records of Juvenile Idiopathic Arthritis (JIA) patients were scrutinized, and the following data were collected: gender, age, disease subtype, number of affected joints, and unilateral or bilateral Temporomandibular Joint (TMJ) involvement.

Each CBCT exam had been requested for diagnostic purposes by the dentist, in agreement with the rheumatologist who had diagnosed the disease. At the time of the visit and CBCT acquisition, no patient had undergone pharmacological treatment. No scan was acquired for the purpose of this investigation. All CBCTs taken between 2012 and 2022 that met the inclusion criteria were retrieved and analyzed.

Inclusion criteria for JIA subjects were: age 7–16 years; Caucasian ethnicity; JIA diagnosis per International League of Associations for Rheumatology (ILAR) criteria [21]; TMJ involvement; high-quality CBCTs covering the region of interest (ROI) from the glabella to the mandibular inferior border; and no prior orthodontic treatment.

For the control group, Caucasian subjects aged 7–16 years without JIA were selected based on: normal condylar morphology, symmetrical mandibular growth, good general health, hyperdivergent skeletal Class II (ANB > 4° per Riedel's cephalometry [22]); and increased intermaxillary divergence (Pns-Ans^Go-Me > 37°).

This selection was based on the craniofacial characteristics typically observed in JIA patients with TMJ involvement, which commonly include a high-angle skeletal Class II sagittal relationship, as previously reported by Hu et al. [34]. The adoption of a control group with comparable craniofacial features was intended to reduce potential selection bias and to ensure that the differences observed between groups were more likely attributable to the rheumatic condition rather than to underlying craniofacial morphology.

Exclusion criteria for both groups included: history of craniofacial trauma or congenital defects; bone metabolism disorders; craniofacial pathologies or malformations; personal/family history of rheumatic disease; and previous orthodontic treatment.

Seventy-five subjects met the inclusion criteria: fifty JIA patients (25 with bilateral and 25 with unilateral TMJ involvement) and twenty-five controls with no JIA.

CBCT scans in the control group were obtained for various clinical reasons, such as assessing impacted teeth, complex extractions, third molar gectomies, ENT evaluations, and 3D planning of orthodontic treatments involving temporary anchorage devices (TADs).

CBCT examination and postprocessing

CBCT images were acquired using the i-CAT FLX unit (Imaging Sciences International, Inc., <https://ct-dent.co.uk/i-cat-vision/>) with standardized settings: 360° rotation, 300 image frames, 120 kVp, 60 mAs, 17-second scan time, 0.39 mm voxel size, and a field of view (FOV) of 16 × 8 or 16 × 11 mm to limit radiation exposure. Radiological parameters were similar to those used by Kim et al. [19] for methodological consistency.

Scans were saved as DICOM files (Digital Imaging and Communications in Medicine).

Analysis was conducted using Mimics® software (Materialise NV, Leuven, Belgium; <https://www.materialise.com/en/medical/mimics-innovation-suite/mimics>) for segmentation, anatomical analysis, planning, and design. This software allowed measurement of bone density and cortical thickness in each mandibular condyle.

Bone density operative protocol

For condylar bone density measurements, the protocol previously described by Kim K. et al. 2017 [19] served as the reference model. Each condyle was visualized by adjusting the contrast within the recommended bone density range (greyscale range of -1350 to 1650 HU) using the threshold function. In each patient, both condyles were measured individually using the same operational procedure, resulting in a total of 150 condyles. The "threshold" option was employed to highlight all bone structures within the recommended bone density range

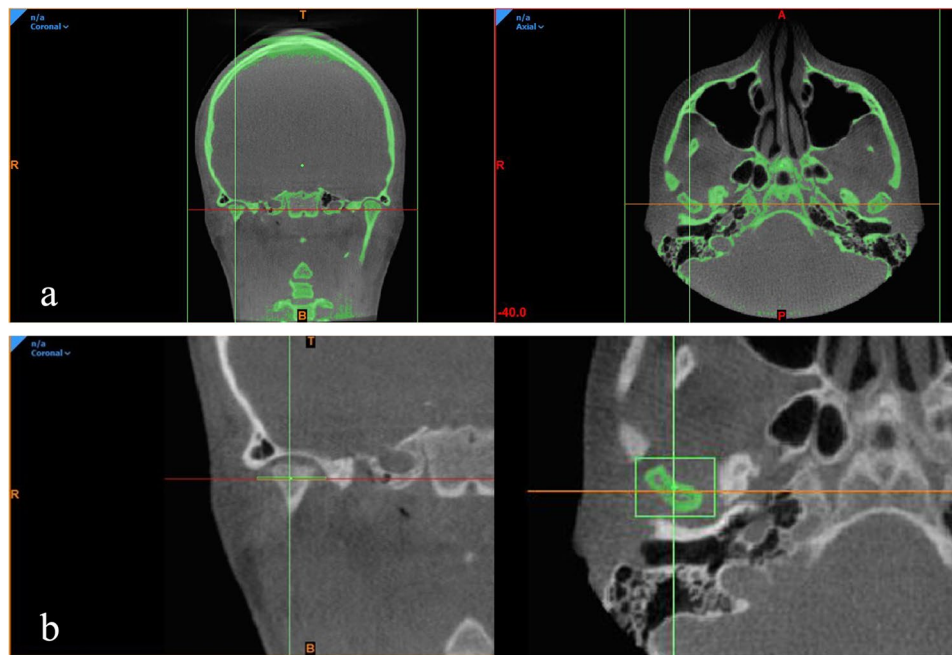


Fig. 1 Identification of the cranio-facial bone structures using the “threshold” command with a recommended bone density range of 226–3071 HU and isolation of the mandibular condyle in the reference slice in both (a) coronal and (b) axial projections

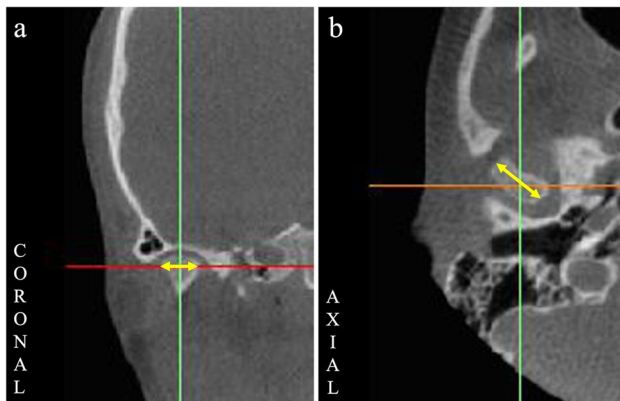


Fig. 2 The selected reference slice was the one with the greater medio-distal condylar diameter in both (a) coronal and (b) axial projections

of 226–3071 HU, aiming to isolate those of interest (Fig. 1a and b).

The slice presenting the largest mediolateral diameter of the mandibular condyle, both in axial and coronal projection, was selected for the measurements (Fig. 2a and b). A magnification of up to 400% was applied in each projection to enhance the identification of condylar morphology. The total bone density (DTo) of the condyles was determined by precisely delineating the condylar area in the axial projection using the “edit mask” function (Fig. 3a). Once the total density was identified, the “split mask” command was utilized to draw and then separate

the cortical bone from the trabecular part, always referencing the area used for the total density. In this manner, the average density was measured first for the cortical (DCo) (Fig. 3b) and then for the trabecular bone (DTr) (Fig. 3c). Bone densities were recorded in Hounsfield units (HU).

Cortical bone thicknesses operative protocol

For the measurements of the cortical bone thicknesses in the medial, lateral and upper poles, the protocol previously described by Lo Giudice A. et al. [20] was used as the reference model. Following the bone density measurements, maintaining the same magnification (400%) and utilizing the slice presenting the largest mediolateral diameter of the mandibular condyle in both axial and coronal projections, the cortical bone thicknesses were assessed.

Three condylar reference points were identified: Medial cortical bone thickness (MCBT), Lateral cortical bone thickness (LCBT), and Upper cortical bone thickness (UCBT) (Fig. 4a and b). For each reference point, the minimum distance between the outer and internal cortical surfaces was calculated using the “distance” command in the Mimics Research software. In the coronal view, median, lateral, and upper pole thicknesses were observed (Fig. 4a), while in the axial view, only the medial and lateral pole thicknesses were visible and analyzed (Fig. 4b).

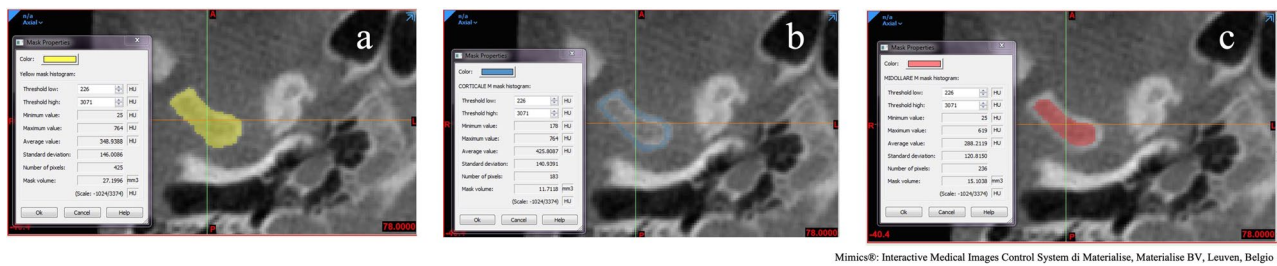


Fig. 3 Magnification in axial projection of 400% and delineation of total condylar area with detection of (a) total bone density (yellow), (b) cortical bone density (blue) and (c) trabecular (red) bone density

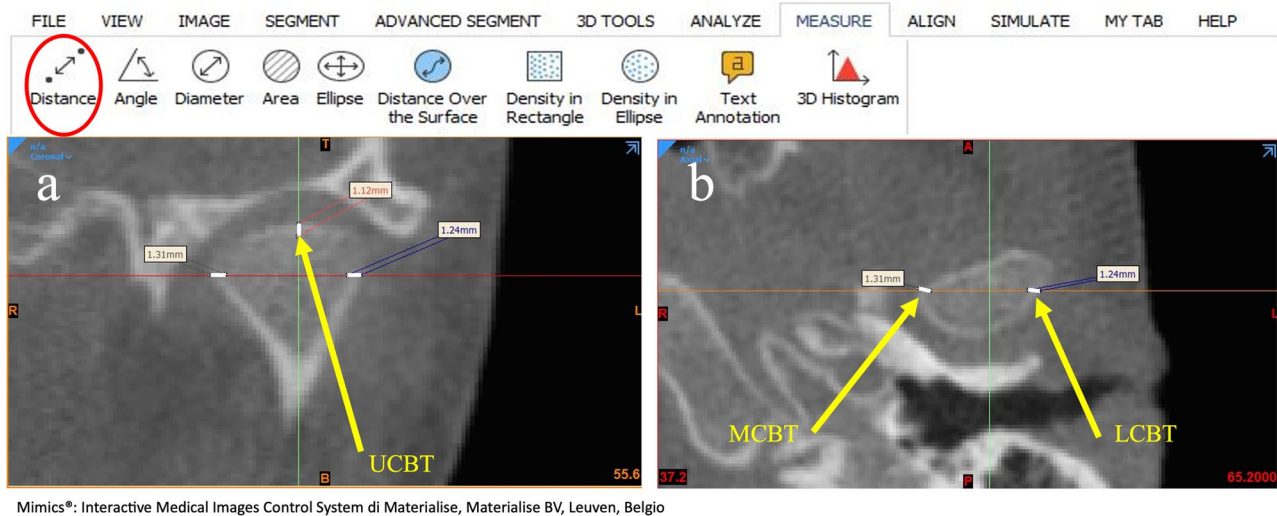


Fig. 4 Condylar bone thickness measurement: (a) The medial (MCBT) and lateral (LCBT) pole thicknesses were measurable in both axial and coronal projections; (b) the upper cortical bone thickness (UCBT) has been measured in its coronal projection

Statistical analysis and sample size calculation

A priori sample size calculation was conducted using G*Power (version 3.1.9, <http://www.psychologie.hhu.de/arbeitsgruppen/allgemeine-psychologie-und-arbeitspsychologie/gpower.html>). Since no previous studies have reported data on bone density and cortical bone thickness in JIA and unaffected subjects, reference values from Cavagnetto et al. [23] for condylar volume of affected (1007.82 ± 384.27) and unaffected condyles (1424.69 ± 417.64) were used.

The entire statistical analysis was performed using Stata 17 software (StataCorp 2021). Subjects in the JIA group were categorized based on unilateral or bilateral TMJ damage. Variations in total condylar bone density, cortical bone density, trabecular bone density, and cortical bone thickness of mandibular condyles in subjects with unilateral and bilateral JIA were analyzed and compared with a control group. Compatibility between JIA and control groups was assessed concerning age, ANB angle, and intermaxillary divergence (Pns-Ans^{Go}-Me angle) using the independent sample t-test and gender using a Chi-squared test.

Normal distribution of data was assessed using the Shapiro–Wilk test. Since data were normally distributed, parametric tests were used for analysis. The sample was organized into three groups: (1) bilateral JIA subjects, (2) unilateral JIA subjects, and (3) control subjects. Descriptive statistics were calculated for each group and mean and standard deviation were reported for all variables. Paired t-tests were employed to compare each variable between affected and non-affected sides in unilateral JIA subjects, right and left sides in bilateral JIA subjects, and in the control group. Subsequently, an independent t-test was performed to compare the unaffected side condyles of unilateral JIA subjects with the unaffected condyles of non-JIA subjects.

A three-group multiple regression model (bilateral JIA subjects, unilateral JIA subjects, control group) was used to compare bone characteristics between the three groups, weighted by age, sex, and side, and also by the clinical condition of the condyle (whether healthy or affected).

A Pearson correlation analysis was conducted to assess the correlation between bone density and cortical bone

thickness, evaluating whether a reduction in bone density in JIA patients could be related to damage to cortical thickness or vice versa.

The significance level for both t-tests and multiple regression models was set at $p < 0.05$.

Method error

Dahlberg's formula [24] was used to assess method error, and the intra-class correlation coefficient (ICC) was employed to evaluate intra- and inter-operator reliability. All CBCTs were acquired by the same dental radiologist, and measurements were performed by a single 3D imaging expert (M.D.). After a two-week interval, 20 CBCT scans were randomly selected and re-evaluated by a second expert (A.A.), then re-assessed by the first investigator (M.D.) to determine inter- and intra-observer reliability. Both investigators were blinded to patient identities.

Results

The JIA groups comprised fifty Caucasian subjects diagnosed with JIA and TMJ involvement, including 25 with bilateral TMJ involvement (15 females with a mean age of 11.8 ± 2.5 years and 10 males with a mean age of 13.6 ± 1.1 years) and 25 with unilateral TMJ involvement (15 females with a mean age of 10.9 ± 2.1 years and 10 males with a mean age of 11.4 ± 2.5 years). The control group included twenty-five Caucasian subjects with no known rheumatic comorbidities (14 females with a mean age of 11.9 ± 2.3 years and 11 males with a mean age of 11.8 ± 2.1 years).

The calculation of the sample size indicated that 23 subjects per group were needed to reject the null hypothesis of equal population means for the JIA and control groups with a 95% confidence interval and a margin of error of 5 units (type I error of 0.05).

The statistical analysis conducted for the compatibility assessment between the JIA and the control group revealed no statistically significant differences, suggesting a reduction in biases when comparing the two groups (Table 1).

Descriptive statistics and statistical comparisons for bone densities and cortical bone thickness measurements

between affected and unaffected condyles in unilateral JIA subjects and between the right and left condyles of bilateral JIA subjects and the control group are presented in Table 2. No statistically significant differences were observed for any variable between right and left condyles of the control group (Table 2). In bilateral JIA patients, a statistically significant difference in total bone density ($p < 0.01$) and trabecular bone density ($p < 0.01$) of the condyle was found between the right and left sides, with significantly higher values on the right side (Table 2). Additionally, in unilateral JIA patients, a statistically significant difference in trabecular bone densities ($p = 0.02$) and upper cortical bone thicknesses ($p < 0.001$) was observed, with a decrease in density of -23.26 HU and thickness of -0.35 mm in the affected side condyles (Table 2).

Statistical comparisons for each condylar bone measurement between the unaffected condyles of unilateral JIA subjects and the control group are reported in Table 3. There were no statistically significant differences for any bone density variable, whereas a statistically significant difference in cortical thickness in the lateral ($p = 0.001$) and superior ($p < 0.001$) poles was observed (Table 3).

Table 4 presents the 3-group multiple regression model weighted by age, sex, side, and clinic of the condyle between JIA groups and the control group. The unaffected condyles of unilateral JIA patients and the healthy condyles of the control group were not merged in the multiple regression model.

No statistically significant differences were found in the total, cortical, and trabecular bone densities when comparing JIA groups with the control one (Table 4). Comparing the bilateral JIA group and the control group, all cortical bone thickness variables showed a statistically significant difference (Table 4); the Medial pole thickness was found to be lower in patients with bilateral JIA by -0.11 mm ($p = 0.026$), the Lateral pole thickness was -0.13 mm ($p = 0.007$), and the Upper pole thickness was lower on average by -0.11 mm ($p = 0.011$). Furthermore, the comparison between the unilateral JIA group and the control group did not reveal statistically significant differences in any cortical bone thickness variables.

Table 1 Demography and clinical characteristics of the patients with the relative statistical analysis calculated by means of *t* test for the age group, ANB angle and intermaxillary divergence comparison and Chi-squared test for differences in proportion

Sample characteristics	Total (N = 75)	JIA group (N = 50)	Control group (N = 25)	Significance (p value)
Mean $\pm$ SD	12.7 $\pm$ 1.8	12.7 $\pm$ 1.7	11.9 $\pm$ 2.3	0.326
Sex				
Male	41	30	11	0.065
Female	34	20	14	
Skeletal Class				
ANB angle	7.03 $\pm$ 1.9	7.23 $\pm$ 1.8	6.84 $\pm$ 1.5	0.184
Intermaxillary divergence	38.09 $\pm$ 1.8	38.7 $\pm$ 2.6	37.3 $\pm$ 1.6	0.225

Table 2 Descriptive statistics and Paired *t* test between affected (Uni-Aff) and unaffected (Uni-UnAff) sides in Unilateral JIA patients and between right and left sides in bilateral JIA patients (Bil-Aff) and control group (Ctrl)

	Unilateral JIA			Bilateral JIA			Ctrl		Δ (Uni-Aff – Uni-UnAff)			Δ (Right – Left Bilateral JIA)			Δ (Right – Left Ctrl)		
	Uni-Aff	Uni-UnAff		Right-Bil-Aff	Left-Bil-Aff		Right	Left	Mean ± SD	P value	Mean ± SD	P value	Mean ± SD	P value	Mean ± SD	P value	
		Mean ± SD			Mean ± SD												Mean ± SD
DTot (HU)	238.50±60.84	248.95±71.53	254.80±61.24	233.49±65.87	258.58±75.75	254.49±71.01	-10.45±40.35	0.208	21.31±35.17	0.006*	4.08±33.88	0.552					
OCot (HU)	329.72±66.53	319.97±70.10	344.04±78.94	327.58±78.06	326.09±73.35	326.53±77.70	9.75±45.76	0.297	16.46±60.57	0.187	-0.44±41.98	0.959					
DTTr (HU)	190.12±69.08	213.38±80.65	201.53±61.08	176.64±62.67	216.63±64.63	212.55±75.90	-23.26±48.61	0.025*	24.89±40.56	0.005*	4.08±37.15	0.588					
MCBT (mm)	1.32±0.18	1.33±0.17	1.13±0.20	1.21±0.17	1.29±0.11	1.28±0.10	-0.01±0.16	0.676	-0.08±0.19	0.054	0.0048±0.12	0.839					
LCBT (mm)	1.27±0.13	1.24±0.15	1.19±0.19	1.17±0.19	1.28±0.11	1.31±0.08	0.02±0.18	0.558	0.02±0.18	0.494	-0.032±0.10	0.136					
UCBT (mm)	0.73±0.16	1.08±0.13	0.68±0.14	0.69±0.15	1.13±0.12	1.14±0.08	-0.35±0.24	0.0000*	-0.01±0.13	0.691	-0.01±0.08	0.486					

**p* value < 0.05 was considered statistically significant

Considering the results weighted for the clinic of the condyles, DTr of the affected ones was found to be statistically significantly lower ($p=0.007$) compared to the control ones. Moreover, there was a statistically significant difference in the UCBT, with a mean reduction of -0.35 mm ($p<0.001$) in the affected condyles.

Regarding the results weighted by age, sex, and side, the multiple regression model showed that these three parameters did not influence the bone variables, neither in terms of density nor cortical bone thickness (Table 4).

Finally, the Pearson correlation analysis showed no statistically significant relationships between bone density and cortical bone thickness (Fig. 5), demonstrating that the two variables do not influence each other.

The ICC results reported high agreement for all bone variables measurements evaluated; for bone density, the average ($\pm$ SD, range) intra-operator and inter-operator ICC values were 0.96 ($\pm$ 0.07, 0.94–0.98) and 0.94 ($\pm$ 0.03, 0.92–0.97) respectively, and for cortical bone thickness, the average ($\pm$ SD, range) intra-operator and inter-operator ICC values were respectively 0.97 ($\pm$ 0.04, 0.95–0.98) and 0.94 ($\pm$ 0.03, 0.93–0.96).

The Dahlberg's formula reported that the random error for bone density measurements was about 13 HU, and for the cortical bone thicknesses, it was about 0.11 mm. Overall, the method error was considered negligible.

Discussion

Rheumatic disease affects bones and joints, and early childhood onset can impair growth and cause craniofacial dysmorphisms. In JIA patients with active TMJ involvement, growth leads to worsening craniofacial features such as reduced posterior facial height, mandibular retrognathia, open bite, and facial asymmetry [23]. Osteometabolic disorders in JIA progress gradually, influenced by factors such as sex, age, genetic predisposition, disease form and activity, number of affected joints, and disease duration. Accordingly, the present analysis used a multiple regression model incorporating age, sex, side, and condylar clinical status. Kjellberg et al. [25] pioneered the examination of TMJ changes in JIA patients, utilizing panoramic X-rays to measure condylar height, revealing significantly lower height and more frequent asymmetries. Subsequent studies, like Alexiou et al. [26] demonstrated that cone beam computed tomography (CBCT) imaging is useful not only for early diagnosis of TMJ degenerative processes but also for reliable localization of bone changes. Another study [27] showed that HU-CT (Hounsfield Unit Computed Tomography) in the isolated CBCT section at the condylar level can be used as a diagnostic tool to detect osteoarthritic processes in the TMJ.

The analysis of the density of the cortical and medullary bone has been previously described by Kim et al.

Table 3 Descriptive statistics and two-tailed independent T test between unaffected side's condyles (Uni-UnAff) of unilateral JIA subjects and healthy condyles of the control group (Ctrl)

	Uni-UnAff	Ctrl	$\Delta(\text{Ctrl} - \text{Uni-UnAff})$	
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	P value
DTo (HU)	248.95 $\pm$ 71.53	254.49 $\pm$ 71.01	5.55 $\pm$ 14.11	0.6951
DCo (HU)	319.97 $\pm$ 70.10	326.31 $\pm$ 74.78	6.56 $\pm$ 14.65	0.6554
DTr (HU)	213.38 $\pm$ 80.65	214.59 $\pm$ 79.59	-0.84 $\pm$ 15.50	0.9570
MCBT (mm)	1.33 $\pm$ 0.17	1.28 $\pm$ 0.10	-0.05 $\pm$ 0.03	0.0523
LCBT (mm)	1.24 $\pm$ 0.15	1.29 $\pm$ 0.10	0.06 $\pm$ 0.02	0.010*
UCBT (mm)	1.08 $\pm$ 0.13	1.13 $\pm$ 0.10	0.06 $\pm$ 0.02	0.0035*

*A p value < 0.05 was considered statistically significant

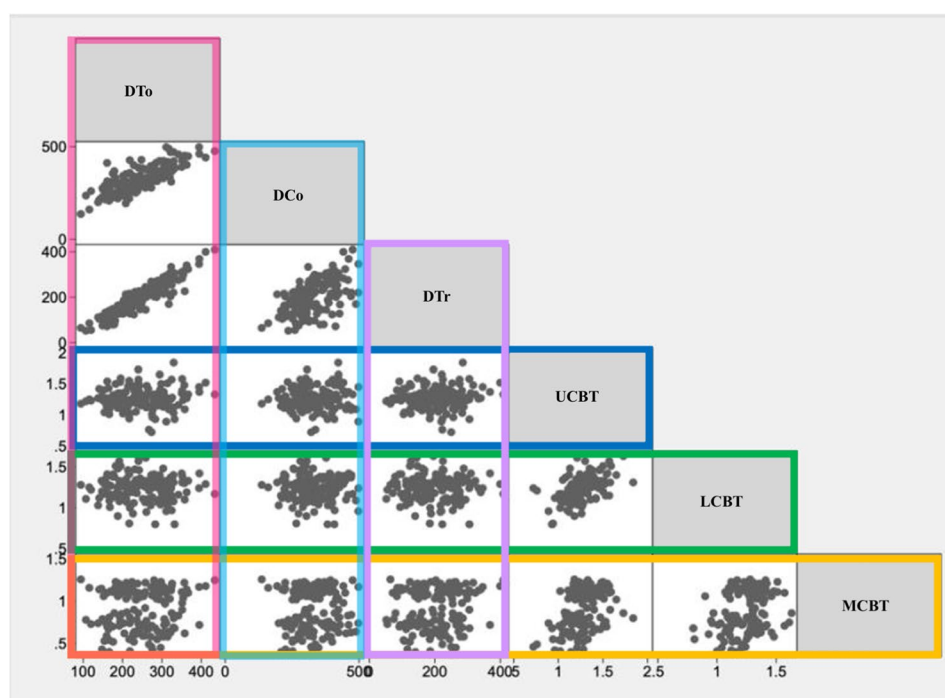
[19], who concluded that studying condylar bone density may be advantageous for predicting mandibular growth patterns in adolescents. A low bone density in the condyle could indicate reduced growth potential and a deficit in the response to functional stimuli following orthodontic treatment [19].

Concerning bone density, the comparison between affected and unaffected condyles in unilateral Juvenile Idiopathic Arthritis (JIA) patients revealed a statistically significant difference in trabecular bone density, indicating a decrease in the affected condyles. Moreover, there

Table 4 Descriptive statistics and 3 groups multiple regression model weighted for age, sex, side and clinics (whether pathological or healthy) of the condyles to compare Unilateral and Bilateral JIA groups with the controls

	DTo		DCo		DTr		MCBT		LCBT		UCBT	
	Mean $\pm$ SD	P Value	Mean $\pm$ SD	P Value	Mean $\pm$ SD	P Value	Mean $\pm$ SD	P Value	Mean $\pm$ SD	P Value	Mean $\pm$ SD	P Value
age	-0.43 $\pm$ 3.30	0.896	-0.22 $\pm$ 3.53	0.950	-0.53 $\pm$ 3.51	0.879	0.01 $\pm$ 0.01	0.187	0.01 $\pm$ 0.01	0.361	0.01 $\pm$ 0.01	0.224
sex ($\Delta M-F$)	9.97 $\pm$ 16.13	0.537	0.51 $\pm$ 17.27	0.977	13.36 $\pm$ 17.16	0.436	-0.02 $\pm$ 0.03	0.472	0.02 $\pm$ 0.03	0.441	-0.03 $\pm$ 0.03	0.273
side ($\Delta \text{sx-dx}$)	-6.56 $\pm$ 4.32	0.129	-7.79 $\pm$ 5.70	0.172	-6.74 $\pm$ 5.02	0.180	0.02 $\pm$ 0.02	0.274	0.02 $\pm$ 0.02	0.180	-0.01 $\pm$ 0.02	0.415
Clinics ($\Delta p-h$)	-10.71 $\pm$ 7.48	0.152	9.44 $\pm$ 9.88	0.339	-23.53 $\pm$ 8.70	0.007*	-0.01 $\pm$ 0.03	0.695	0.02 $\pm$ 0.03	0.471	-0.35 $\pm$ 0.03	0.000*
Unilateral JIA vs. Controls ($\Delta \text{Uni-Ctrl}$)	-6.17 $\pm$ 18.74	0.742	-6.26 $\pm$ 20.28	0.758	0.68 $\pm$ 20.02	0.973	0.05 $\pm$ 0.04	0.196	-0.04 $\pm$ 0.04	0.296	-0.06 $\pm$ 0.03	0.080*
Bilateral JIA vs. Controls ($\Delta \text{Bil-Ctrl}$)	2.15 $\pm$ 20.58	0.917	0.36 $\pm$ 22.79	0.987	3.14 $\pm$ 22.18	0.888	-0.11 $\pm$ 0.05	0.026*	-0.13 $\pm$ 0.05	0.007*	-0.11 $\pm$ 0.04	0.011*

*A p value < 0.05 was considered statistically significant

**Fig. 5** Correlation analysis between changes in cortical thickness and in mandibular condyle bone density

was a notable difference in the thickness of the upper pole, as outlined in Table 2. These observations align with the findings of a study by Wen et al. [28], which highlighted mandibular asymmetry as a primary factor influencing bone densities and thicknesses.

Simultaneously, the analysis of the research data revealed a statistically significant reduction in both total and trabecular density when comparing the right and left condyles of bilateral JIA subjects, indicating an asymmetrical involvement of the joints (Table 2). Typically, the degenerative process of the temporomandibular joint (TMJ) initiates in one joint and may subsequently progress to affect the other [4].

Furthermore, it is noteworthy that in the comparison between healthy condyles of patients with unilateral JIA and healthy condyles of the control group, a statistically significant difference in lateral and upper cortical thickness was observed (Table 3). It's important to acknowledge that this difference might be attributed to a very low standard deviation, rendering values like 0.06 mm statistically significant, although they may not be deemed clinically relevant.

Regarding the multiple regression model for the three groups, weighted for the clinic of the condyle, a statistically significant difference in trabecular bone density emerged. The comparison, involving all 75 healthy condyles and all 75 condyles affected by the pathology, showed a decrease in trabecular bone density in the affected ones (Table 4). The findings in this study align with Sušić et al. [29], who utilized dual-energy X-ray absorptiometry (DEXA) bone densitometry to assess osteodensitometric indicators in Juvenile Idiopathic Arthritis (JIA) patients. Sušić et al. reported a significant decrease in trabecular bone density. Similarly, Stagi et al. [30] identified significantly lower levels of trabecular bone mineral density (TrbBMD) in JIA patients compared to controls, while cortical bone mineral density (CortBMD) did not exhibit significant differences. Moreover, the current study supported these observations by demonstrating no significant difference in cortical densities between groups but revealing significantly lower levels of trabecular bone density in the condyles of JIA patients.

Furthermore, the present study confirmed that condyles affected by JIA exhibited a statistically significant reduction in the thickness of the cortical bone, particularly in the upper pole of the condylar head. This is consistent with the findings of Billau et al. [2], in accordance with Pedersen et al. [31] who reported that temporomandibular joint damage, including minor cortical bone erosion progressing to the complete absence of the condylar head, is frequently observed in JIA patients, regardless of the disease subtype.

Chappard et al. [32] reported that changes in mechanical loading can decrease mineral content in bone cross-sections, leading to structural alterations, including changes in trabecular architecture. These morphological modifications align with Moss's functional matrix theory, which suggest that reduced muscle function may epigenetically influence bone growth and development. Such mandibular growth anomalies highlight the importance of early diagnosis and timely orthodontic intervention to prevent developmental disorders.

The clinical relevance of this study lies in the widespread use of CBCT for diagnosing TMJ involvement in juvenile idiopathic arthritis. Evaluating mandibular bone could serve as a complementary diagnostic tool for detecting signs of rheumatic pathology. Given the condyle's role in mandibular growth, assessing its bone density may help predict growth patterns in adolescents.

Moreover, understanding bone density is potentially essential for assessing the growth capacity of the condyle, which is particularly relevant given that this pathology affects growing patients. Given the condyle's key role in mandibular development, assessing its bone density may contribute to predicting growth patterns and planning orthodontic or orthopedic interventions accordingly.

Limitations and strengths of the study

Regarding the study's limitations, although the sample size was statistically adequate, evaluating the same parameters in a larger cohort of JIA patients would be beneficial. The study did not account for differences related to JIA subtype, disease duration at the TMJ level. In bilateral JIA cases, the timing of condylar involvement was unknown, raising the possibility that the disease began unilaterally and later became bilateral. A potential limitation of this study lies in the use of the intra-class correlation coefficient (ICC) to assess intra- and inter-observer reliability. While ICC is widely accepted, it only reflects the strength of association and may be influenced by the range of values within the sample. It does not account for possible systematic bias between observers. However, in line with established literature, we combined ICC with Dahlberg's formula for method error.

A longitudinal study design could provide valuable information on condylar growth and its changes over time. However, repeated CBCT scans pose radiation risks in pediatric populations, making this approach inadvisable according to DIMITRA guidelines [33]. The development of radiation-free imaging methods, such as MRI, is expected to address this limitation in the future.

As for the strengths, the study demonstrated high measurement reliability, with intra- and inter-observer ICC values exceeding 0.90 for both bone density and cortical thickness.

To our knowledge, this is the first study to assess these parameters in JIA patients. The studies by Kim, K et al. [19, 20], and Lo Giudice, A et al. [19, 20] demonstrated non-uniform bone density and cortical bone thicknesses in mandibular condyles across various skeletal patterns, in this research the authors opted for a control group matched for skeletal class and intermaxillary divergence (Table 1). This specific choice was guided by the craniofacial characteristics of JIA subjects with TMJ involvement, as reported by Hu et al. [34], which included a high-angle skeletal class II sagittal relationship. This decision aimed to minimize selection biases. Without this approach, it would have been challenging to discern whether the differences between JIA and non-JIA groups were linked to the rheumatic condition or the prevailing craniofacial characteristics of JIA patients, specifically the high-angle class II sagittal relationship.

Conclusions

In conclusion, the present study suggests that bone changes in JIA patients significantly reduce trabecular bone density and cortical thickness in the mandibular condyles.

The multiple regression model showed a statistically significant effect of the disease on the reduction of trabecular density and cortical thickness at the upper pole.

In unilateral JIA, affected condyles showed reduced trabecular density and thinner cortical bone at the upper pole, while in bilateral cases, cortical thickness was reduced at the medial, lateral, and upper poles of the condylar head. No positive correlation was found between bone density and cortical thickness, indicating that these two parameters are independent.

As the temporomandibular joint is highly susceptible to inflammatory bone changes during growth, even without symptoms, early diagnosis is essential to identify TMJ involvement and initiate targeted treatment of craniofacial alterations.

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Not applicable.

Informed consent

For this type of study, informed consent was obtained from all parents' patients or their guardians.

Authors' contributions

V. L. and C. M. equally contributed to this work Conceptualization: A.A., C. M., and M. D.; Methodology: A.A. and M. D.; Investigation: A.A. and M. D.; Validation: C. M. and A.A.; Software, A.A. and M. D.; Formal Analysis: V. L. and P. C.; Data Curation: A. U. and A. A.; Writing—Original Draft Preparation: C. M. and A.A.; Writing—Review And Editing: C. M., A. U., A.A. and V. L.; Supervision: V. L. and C. M. All authors have read and agreed to the published version of the manuscript.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Declarations

Ethics approval and consent to participate

A cross-sectional study was performed analyzing CBCT of patients affected by JIA and comparing them with controls. The study protocol was approved by the Ethical Committee of the Fondazione IRCCS Ca'Granda, Ospedale Maggiore, Milan - Italy (protocol n.573/15). All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. To carry out an anonymous analysis of their children's medical history for research purposes, written informed consent was obtained from the parents of the patients.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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