

Serum bone and mineral metabolism markers in CBCT-confirmed degenerative versus non-degenerative temporomandibular disorders

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Received: 26 June 2026 / Accepted: 6 October 2026

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Abstract

Background Bone and mineral metabolism markers, particularly vitamin D, have been linked to temporomandibular disorders, but rarely to objectively documented joint degeneration. We examined whether serum bone and mineral metabolism markers, particularly 25-hydroxyvitamin D and magnesium, differ between temporomandibular disorder patients with versus without cone-beam computed tomography-documented osseous degeneration, and whether they track with condylar erosion severity.

Methods In this single-centre prospective cross-sectional study of consecutively enrolled patients, sixty temporomandibular disorder patients with cone-beam computed tomography-confirmed degenerative joint disease were compared with forty symptomatic patients without cone-beam computed tomography-detectable osseous degeneration. Serum 25-hydroxyvitamin D, magnesium, parathyroid hormone, calcium, phosphorus and alkaline phosphatase were measured. The two markers of primary interest were 25-hydroxyvitamin D, the established candidate, and magnesium, the novel one; all remaining comparisons were secondary or exploratory. Groups were compared with parametric or non-parametric tests as appropriate, and with a Firth penalized logistic regression adjusted for age and sex only.

Results Degenerative patients had lower 25-hydroxyvitamin D (16.4 versus 25.6 ng/mL) and magnesium (1.66 versus 2.00 mg/dL) and higher parathyroid hormone ($p < 0.001$, $p < 0.001$ and $p = 0.005$, respectively); calcium did not differ. No degenerative patient was vitamin D-sufficient, whereas the comparison group was predominantly insufficient. After adjustment, 25-hydroxyvitamin D and magnesium remained associated with degeneration independently of age and sex, whereas parathyroid hormone did not. Within degenerative patients, erosion severity correlated inversely with 25-hydroxyvitamin D and positively with parathyroid hormone; magnesium separated the groups but showed no severity gradient.

Conclusions Lower serum 25-hydroxyvitamin D and magnesium were associated with cone-beam computed tomography-documented joint degeneration independently of age and sex, most strongly for 25-hydroxyvitamin D; the magnesium association is the novel element and requires confirmation. Comparing degenerative with non-degenerative patients reduces confounding by the presence of the disorder itself, although the groups also differed in their DC/TMD profiles and adjustment was possible for age and sex only. These cross-sectional associations

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do not establish causality and do not support any screening or treatment recommendation; they identify bone and mineral metabolism status as a hypothesis for prospective study in temporomandibular joint osteoarthritis.

Keywords Temporomandibular joint · Osteoarthritis · Cone-beam computed tomography · Vitamin D · Magnesium · DC/TMD

Background

Temporomandibular disorders (TMDs) are a heterogeneous group of conditions of the masticatory muscles and the temporomandibular joint (TMJ), with a female predominance and a multifactorial aetiology. Degenerative osseous changes of the condyle—erosion, osteophytes, subchondral cysts and generalized sclerosis—are the radiographic hallmarks of TMJ osteoarthritis, and cone-beam computed tomography (CBCT) is the validated cross-sectional reference for their assessment, with image-analysis criteria standardized within the RDC/TMD framework [1].

Beyond calcium–phosphorus homeostasis, vitamin D has immunomodulatory and anti-inflammatory roles relevant to joint health, yet the TMD evidence is inconsistent. A 2025 systematic review and meta-analysis reported lower 25(OH)D and more frequent deficiency in TMD, together with a higher prevalence of vitamin D receptor polymorphisms [2]; a multi-centre cohort linked deficient 25(OH)D to incident TMD (pooled hazard ratio 1.50, 95% CI 1.07–2.12) [3]; and earlier reviews were broadly concordant [4, 5]. Calcium-metabolism markers have likewise been related to TMD in clinical series [6], and bone diseases more broadly have been causally linked to TMD [7]. In contrast, a recent case–control study found no significant 25(OH)D difference [8], and a Mendelian-randomization analysis suggested a non-linear relationship [9]. Two gaps persist: most studies relate vitamin D to a clinical TMD label rather than to objectively quantified degeneration, and magnesium—essential for chondrocyte function, extracellular-matrix mineralization and the regulation of low-grade inflammation, and linked to radiographic osteoarthritis and cartilage loss elsewhere in the skeleton [10–13]—is rarely examined in the TMJ. To our knowledge, no previous study has evaluated serum magnesium against CBCT-confirmed TMJ degeneration.

To address these gaps while reducing confounding by the presence of TMD itself, we compared bone and mineral metabolism markers between TMD patients with versus without CBCT-documented degeneration, and tested, within the degenerative group, whether these markers track with condylar erosion severity. Because both groups are symptomatic TMD patients drawn from the same clinical population, this contrast reduces confounding by the presence of TMD itself. It does not remove all differences between the groups: their DC/TMD symptom profiles differ, and determinants of bone and mineral metabolism that were not recorded may differ with them.

Materials and methods

Design and participants

This was a single-centre, prospective, cross-sectional observational study of consecutively enrolled patients, conducted at the Department of Orthodontics, Faculty of Dentistry, Istanbul Kent University. The study protocol was approved by the ethics committee before any patient was enrolled (see Declarations), and enrolment ran from February 2026 to May 2026. All consecutive patients who presented during this period and met the eligibility criteria below were enrolled; no patient group was selected after inspection of the data.

Eligible patients were adults (≥ 18 years) who presented with TMJ complaints and fulfilled Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) Axis I criteria for a TMD diagnosis, and for whom both an adequate cone-beam computed tomography (CBCT) examination and a complete serum bone and mineral

panel obtained within four weeks of that CBCT were available. Exclusion criteria were active inflammatory or rheumatologic disease, known parathyroid disease or advanced renal disease, prior condylar surgery, incomplete biochemistry, and inadequate CBCT quality.

No investigation was performed for the purposes of this study. Neither additional imaging nor any invasive procedure was carried out: the CBCT examinations analysed here had been acquired on clinical indication as part of the diagnostic work-up, and the serum values were those of the bone and mineral metabolism panel that is requested in our department as part of the routine work-up of patients with suspected degenerative TMJ disease. Both were transcribed from the patients' clinical files into the study database after written informed consent had been obtained. Because neither investigation is performed in every patient presenting with a TMD complaint, the enrolled sample is a clinical subset of the TMD population attending the department rather than an unselected series, and the resulting selection bias is addressed in the Limitations. The flow of patients from eligibility assessment to the analysed sample, with the numbers excluded and the reasons for exclusion, is shown in Fig. 1.

The sample size was determined a priori in the study protocol using G*Power 3.1. For a two-sided correlation analysis ($\alpha=0.05$, power=0.80, expected effect size $r=0.40$), a minimum of 47 patients was required; a minimum of 50 was planned to allow for data loss, with the provision that enrolment could continue in order to increase statistical power. Enrolment continued to the end of the study period, yielding a final sample of 100 patients: 60 with CBCT-confirmed degenerative TMD and 40 with non-degenerative (CBCT-negative) TMD.

Group definition and CBCT assessment

Following the RDC/TMD imaging and DC/TMD criteria, degenerative joint disease (DJD) was defined by osseous changes on CBCT—erosion, osteophyte, subchondral cyst or generalized sclerosis—whereas isolated flattening was regarded as remodelling and not, in itself, diagnostic of osteoarthritis [1]. Accordingly, the degenerative group comprised patients with CBCT-confirmed DJD, and the non-degenerative group comprised symptomatic TMD patients lacking these osseous findings (normal or flattening-only). The label “non-degenerative” is used throughout in this strictly operational, imaging-based sense: it denotes the absence of CBCT-detectable osseous degeneration, not the absence of degenerative joint disease as such, since CBCT does not depict early cartilage or disc changes. Erosion severity was graded separately for each condyle on a four-point ordinal scale (0–3) adapted from Alexiou et al. [14]: 0, absent; 1, slight; 2, moderate; and 3, extensive. Right- and left-side scores were summed to obtain a bilateral erosion severity score ranging from 0 to 6, with higher scores indicating greater erosive involvement. Flattening, osteophyte, sclerosis and subchondral cyst were recorded as present/absent per side.

All CBCT images were independently evaluated by an experienced oral and maxillofacial radiologist and an orthodontist experienced in TMJ imaging, according to RDC/TMD imaging criteria. To assess intra-observer reliability, 20 randomly selected scans were re-evaluated by the radiologist after a two-week interval under blinded conditions; inter-observer reliability was determined from the same scans independently assessed by the orthodontist. Cohen's kappa was calculated for binary variables, weighted kappa for condylar erosion scores, and intraclass correlation coefficients (ICC) for continuous measurements. Intra-observer agreement was excellent ($\kappa=0.86$ –0.95; ICC=0.91–0.97), and inter-observer agreement ranged from good to excellent ($\kappa=0.82$ –0.92; ICC=0.88–0.95).

DC/TMD diagnoses and biochemistry

DC/TMD Axis I diagnoses (myalgia, arthralgia, headache attributed to TMD, disc displacement, DJD) were recorded for all patients. Because MRI was unavailable, disc displacement was diagnosed clinically and is reported as a provisional (non-imaging-confirmed) finding; the grouping axis is osseous (CBCT), for which CBCT is the validated reference. Serum 25(OH)D and PTH were measured by electrochemiluminescence, and ALP, calcium, phosphorus and magnesium by photometric assay.

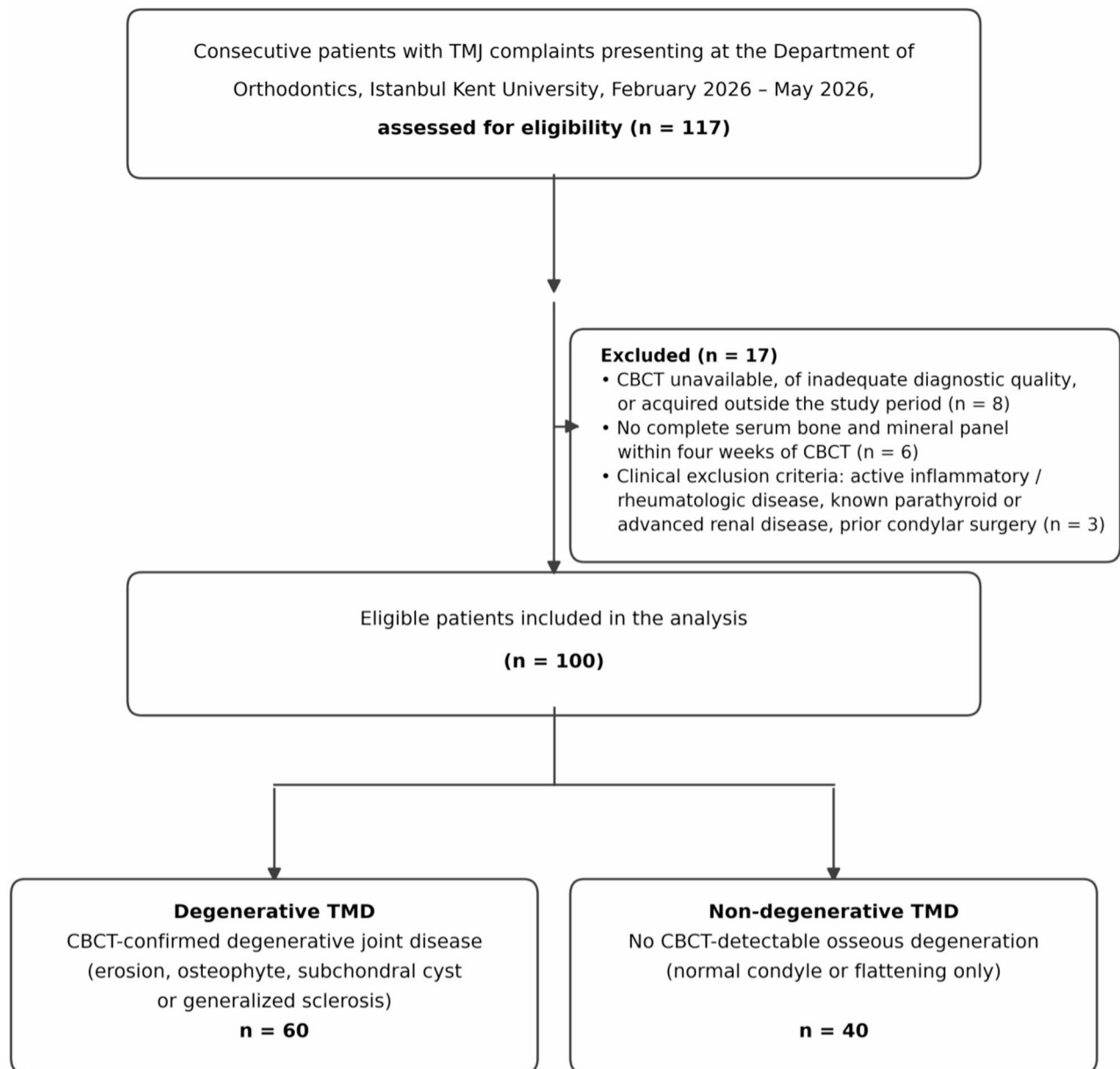


Fig. 1 Flow of patients through the study. Consecutive patients presenting with temporomandibular joint complaints at the Department of Orthodontics between February 2026 and May 2026 were assessed for eligibility; the numbers excluded because an adequate CBCT examination or a complete serum bone and mineral panel within four weeks of the CBCT was unavailable, and because of the clinical exclusion criteria, are shown, together with the composition of the two analysed groups

Serum 25(OH)D status was categorized according to the Endocrine Society clinical practice guideline [15] and the Turkish Society of Endocrinology and Metabolism (TEMED) guideline [16] as severe deficiency (< 10 ng/mL), deficiency (10 – < 20 ng/mL), insufficiency (20 – < 30 ng/mL) and sufficiency (≥ 30 ng/mL). The 2024 Endocrine Society guideline reframed vitamin D recommendations around disease prevention and no longer endorses specific serum cut-points [17]; the established 2011/TEMED operational thresholds were retained here for categorical comparability with the prior observational TMD and osteoarthritis literature.

Statistical analysis

Normality was assessed with the Shapiro–Wilk test; groups were compared with the Welch t-test (PTH, phosphorus, calcium) or Mann–Whitney U test (age, 25(OH)D, magnesium, ALP), with Hedges *g* as the effect size. Categorical distributions were compared with the Fisher exact test, and the ordinal 25(OH)D status distribution with a chi-square test for trend. Within the degenerative group, associations between markers and condylar erosion severity were examined with Spearman correlation. Because the group sizes are modest and unpenalized maximum-likelihood estimates can be biased away from the null in samples of this size, a multivariable Firth penalized logistic regression (degenerative/non-degenerative ~ 25(OH)D + magnesium + PTH + age + sex) was used to obtain bias-reduced odds ratios (OR) with 95% confidence intervals (CI); ORs are reported both per measurement unit and per 1-SD increment to aid interpretation. As a sensitivity analysis for the age imbalance, each non-degenerative patient was matched 1:1 to the nearest-age degenerative patient (caliper 3 years) and the marker comparison repeated. Because the further determinants of bone and mineral metabolism listed in the Limitations were not recorded, the model could be adjusted for age and sex only; the term “independent” is therefore used throughout in this restricted sense. Analyses were ordered in an explicit hierarchy. The principal analysis reported here is the comparison of serum markers between patients with and without CBCT-confirmed osseous degeneration, in which 25(OH)D and magnesium were the two markers of primary interest; both retained significance after Bonferroni correction across the seven markers examined. Where degeneration severity was analysed, the summed bilateral erosion score (0–6) served as the severity measure. The dichotomisation of the cohort into a degenerative and a non-degenerative group was an analysis decision taken within the cross-sectional framework of the protocol and was not itself specified in advance. Secondary analyses comprised the remaining serum markers, the multivariable Firth model, the within-group correlations between markers and condylar erosion severity, and the age-matched sensitivity analysis. The comparison of DC/TMD Axis I diagnoses and the description of CBCT finding types were exploratory. Secondary and exploratory analyses were not corrected for multiplicity and are interpreted as hypothesis-generating. Significance was set at $p < 0.05$. Because complete serum biochemistry within four weeks of CBCT and adequate image quality were inclusion requirements, no missing data were present for the analysed variables.

Results

Participant characteristics

The degenerative group comprised 49 women and 11 men, and the non-degenerative group 26 women and 14 men (82% vs. 65% female; $p = 0.099$). Age differed modestly (degenerative median 22 years, IQR 21–26, mean 26.0 ± 9.6 ; non-degenerative median 28 years, IQR 24–32, mean 27.8 ± 5.6 ; Mann–Whitney $p = 0.006$), with the degenerative group slightly younger—an inverse-to-expected pattern that argues against age alone driving degeneration. This imbalance was addressed by the multivariable model and an age-matched sensitivity analysis (Table 1). Of 117 consecutive patients assessed for eligibility, 17 were excluded: eight because a CBCT examination of adequate diagnostic quality acquired within the study period was not available, six because a complete serum bone and mineral panel obtained within four weeks of the CBCT was not available, and three on the clinical exclusion criteria. The remaining 100 patients constituted the study sample (Fig. 1).

Between-group marker comparison

Serum 25(OH)D and magnesium were substantially lower, and PTH higher, in the degenerative group, whereas calcium was indistinguishable between groups (Table 1; Fig. 2).

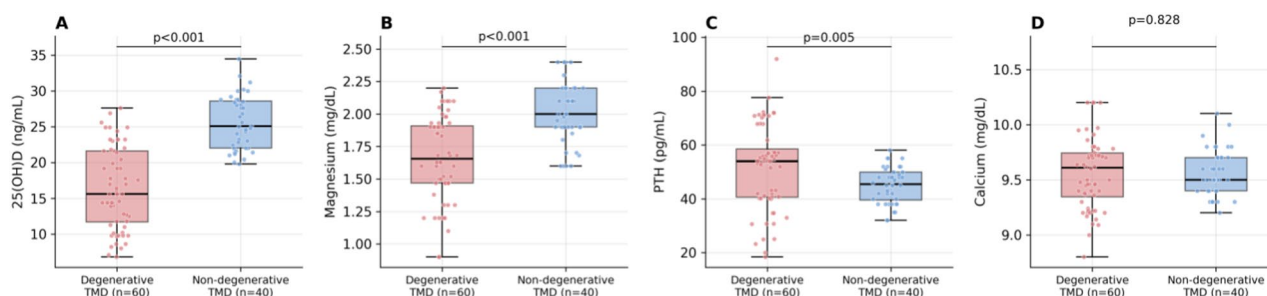
Table 1 Demographic characteristics and bone and mineral metabolism markers

Variable	Degenerative (<i>n</i> = 60)	Non-degenerative (<i>n</i> = 40)	<i>p</i>	Hedges <i>g</i>
Age (years), mean ± SD	26.0 ± 9.6	27.8 ± 5.6	0.006 b	−0.21
Female, <i>n</i> (%)	49 (82)	26 (65)	0.099 c	—
25(OH)D (ng/mL)	16.40 ± 5.73	25.56 ± 3.77	< 0.001 b	−1.80
Magnesium (mg/dL)	1.66 ± 0.33	2.00 ± 0.23	< 0.001 b	−1.15
PTH (pg/mL)	51.63 ± 15.81	45.08 ± 6.68	0.005 a	+ 0.50
Phosphorus (mg/dL)	3.33 ± 0.69	3.53 ± 0.17	0.034 a	−0.37
Calcium (mg/dL)	9.56 ± 0.32	9.57 ± 0.20	0.83 a	−0.04
ALP (U/L)	104.0 ± 49.3	92.1 ± 27.2	0.20 b	+ 0.28

Data are mean ± SD

Effect size: Hedges *g*. 25(OH)D and magnesium separate the groups most strongly; calcium does not differ. Age was non-normally distributed (right-skewed in the degenerative group); medians (IQR) were 22 (21–26) versus 28 (24–32)a Welch *t*-testb Mann–Whitney *U* test

c chi-square test

**Fig. 2** Bone and mineral metabolism markers in degenerative versus non-degenerative TMD. The groups overlap but differ in central tendency for 25(OH)D and magnesium; calcium is indistinguishable**Table 2** Distribution of serum markers by clinical thresholds

Category / threshold	Degenerative <i>n</i> (%)	Non-degenerative <i>n</i> (%)	<i>p</i>
25(OH)D severe deficiency (< 10)	11 (18.3)	0 (0)	< 0.001*
25(OH)D deficiency (10–<20)	31 (51.7)	1 (2.5)	
25(OH)D insufficiency (20–<30)	18 (30.0)	33 (82.5)	
25(OH)D sufficiency (≥ 30)	0 (0)	6 (15.0)	
Magnesium < 1.7 mg/dL	33 (55)	5 (12.5)	< 0.001
PTH > 65 pg/mL	14 (23)	0 (0)	0.001

*Chi-square test for trend across the four ordinal 25(OH)D categories; Fisher exact test for magnesium and PTH thresholds. 25(OH)D thresholds per Endocrine Society [15] and TEMD [16] guidelines

Vitamin D status categories

When 25(OH)D was classified by Endocrine Society/TEMD thresholds, the groups separated sharply across the ordinal severity scale (chi-square for trend $p < 0.001$). No degenerative patient reached sufficiency (≥ 30 ng/mL); 18% were severely deficient and a further 52% deficient. The non-degenerative group was not “healthy” but predominantly insufficient (82.5% in the 20–<30 band), with only 15% sufficient and a single patient deficient (Table 2; Fig. 3). This pattern is consistent with the high background prevalence of hypovitaminosis D in the Turkish adult population.

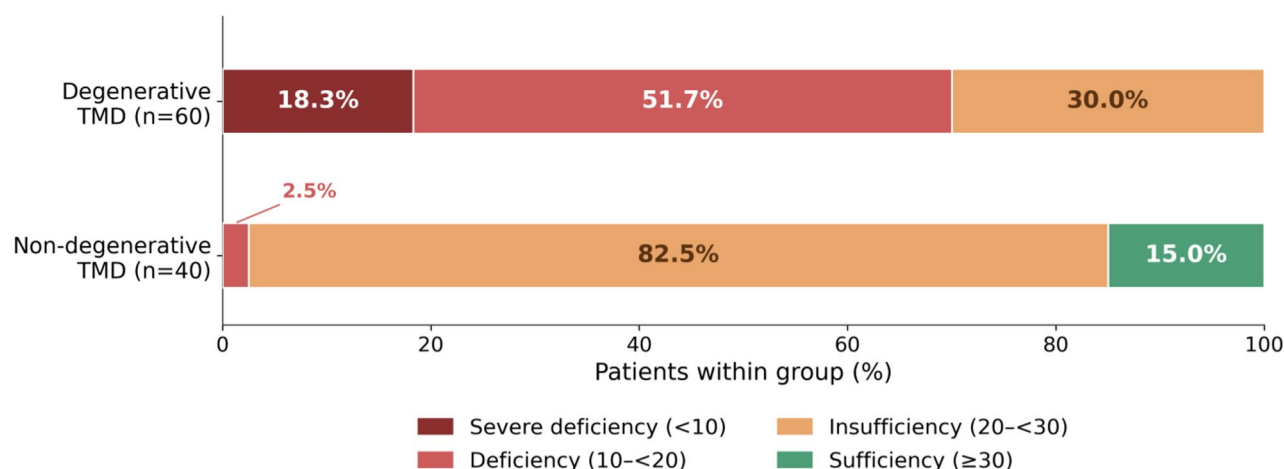


Fig. 3 Serum 25(OH)D status distribution by group (TEMED/Endocrine Society thresholds). No degenerative patient is sufficient; the non-degenerative group is predominantly insufficient

Table 3 Within-case correlations between serum markers and condylar erosion severity (degenerative group, $n=60$)

Marker	Spearman ρ	p
25(OH)D	-0.41	0.001
PTH	+0.36	0.005
Phosphorus	-0.28	0.028
Magnesium	-0.14	0.28
Age	+0.16	0.23
Calcium	+0.09	0.50
ALP	+0.08	0.56

Spearman rank correlation. Erosion severity=summed right + left condylar erosion score (0–6), used here as the measure of osseous degeneration severity

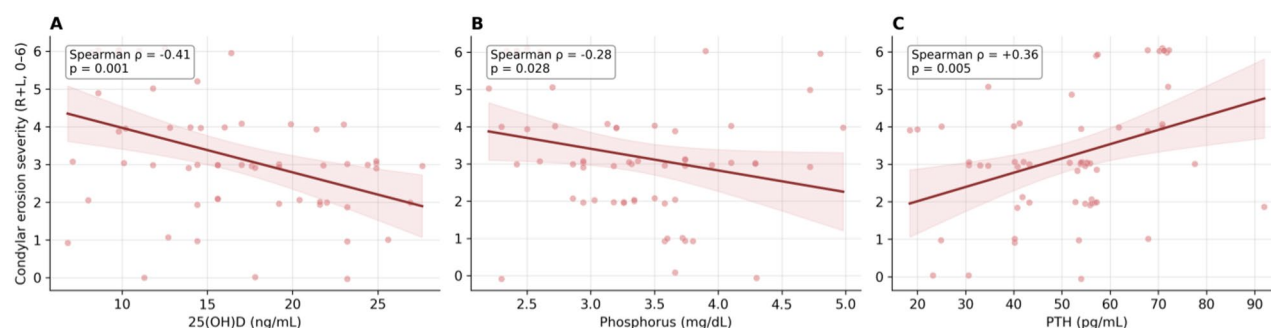


Fig. 4 Serum markers and condylar erosion severity within the degenerative group ($n=60$). Lower 25(OH)D (A) and phosphorus (B) and higher PTH (C) accompany greater condylar erosion severity; the line indicates a linear fit with its 95% confidence band, shown for visualization only. The associations are cross-sectional and are not evidence of a causal dose-response relationship. Associations were tested using Spearman rank correlation

Serum markers and condylar erosion severity within the degenerative group

Within the degenerative group, condylar erosion severity correlated inversely with 25(OH)D ($\rho=-0.41$; $p=0.001$) and phosphorus ($\rho=-0.28$; $p=0.028$) and positively with PTH ($\rho=+0.36$; $p=0.005$); magnesium, calcium, ALP and age were not significantly correlated (Table 3; Fig. 4). These are cross-sectional rank associations within a

Table 4 Multivariable Firth penalized logistic regression for degenerative status, adjusted for age and sex ($n=100$)

Variable	OR (per unit)	OR (per SD)	95% CI (per SD)	<i>p</i>
25(OH)D	0.72	0.11	0.04–0.35	<0.001
Magnesium	0.028	0.30	0.13–0.68	0.004
PTH	1.01	1.20	0.46–3.14	0.71
Age	0.92	0.51	0.23–1.11	0.09
Sex (female)	0.53	0.76	0.38–1.50	0.42

OR < 1 indicates that lower values increase the odds of degenerative TMD. 25(OH)D and magnesium are independent of age and sex; PTH is not
OR odds ratio, CI confidence interval

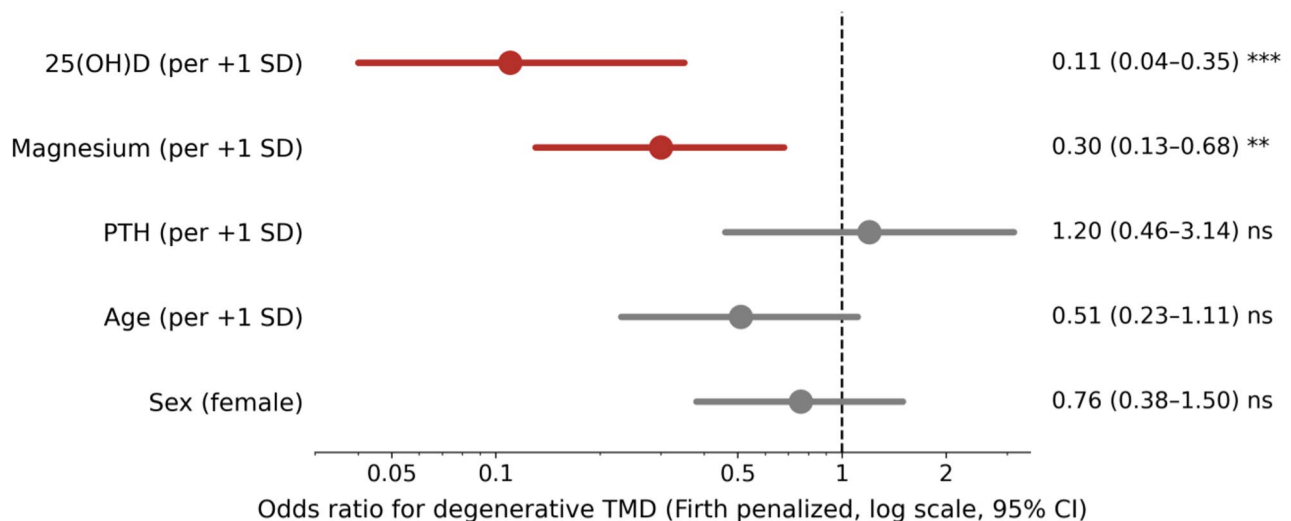


Fig. 5 Forest plot of the age- and sex-adjusted Firth penalized regression (per 1-SD increment). 25(OH)D and magnesium remain associated with degenerative status independently of age and sex; PTH, age and sex do not. The model was adjusted for age and sex only, so the estimates are not adjusted for other determinants of bone and mineral metabolism

single group; they describe how marker levels vary with erosion severity and do not demonstrate a dose–response relationship in the causal sense.

Age- and sex-adjusted analysis (Firth penalized regression)

In the Firth penalized model, 25(OH)D (OR 0.72 per ng/mL, 95% CI 0.61–0.86; OR 0.11 per SD; $p<0.001$) and magnesium (OR 0.028 per mg/dL, 95% CI 0.003–0.32; OR 0.30 per SD, 95% CI 0.13–0.68; $p=0.004$) remained associated with degenerative status independently of age and sex, whereas PTH lost significance (OR 1.01 per pg/mL; $p=0.71$), as did age (OR 0.92; $p=0.09$) and sex ($p=0.42$). Penalized estimation removed the implausibly wide confidence interval that ordinary logistic regression produced for magnesium, while preserving the direction and significance of the effect. The PTH association did not persist once 25(OH)D and magnesium were entered into the model. This is compatible with PTH elevation being secondary to hypovitaminosis D rather than an independent factor, but the cross-sectional design cannot establish such a sequence, and the observation is reported here as a description of model behaviour (Table 4; Fig. 5).

DC/TMD diagnoses and CBCT findings

DC/TMD Axis I diagnoses characterized the two groups (Table 5). Arthralgia predominated in the degenerative group (78% vs. 30%; $p<0.001$), whereas headache attributed to TMD predominated in the non-degenerative

Table 5 DC/TMD Axis I diagnoses by group

Diagnosis	Degenerative <i>n</i> (%)	Non-degenerative <i>n</i> (%)	<i>p</i>
Myalgia	51 (85)	40 (100)	0.010
Arthralgia	47 (78)	12 (30)	<0.001
Headache attributed to TMD	23 (38)	33 (82)	<0.001
Disc displacement (clinical) ¹	58 (97)	31 (78)	0.006

(Fisher exact test). ¹Disc displacement was diagnosed clinically per DC/TMD (no MRI) and is therefore a provisional, non-imaging-confirmed diagnosis. CBCT-confirmed DJD is not shown, as it defines group membership

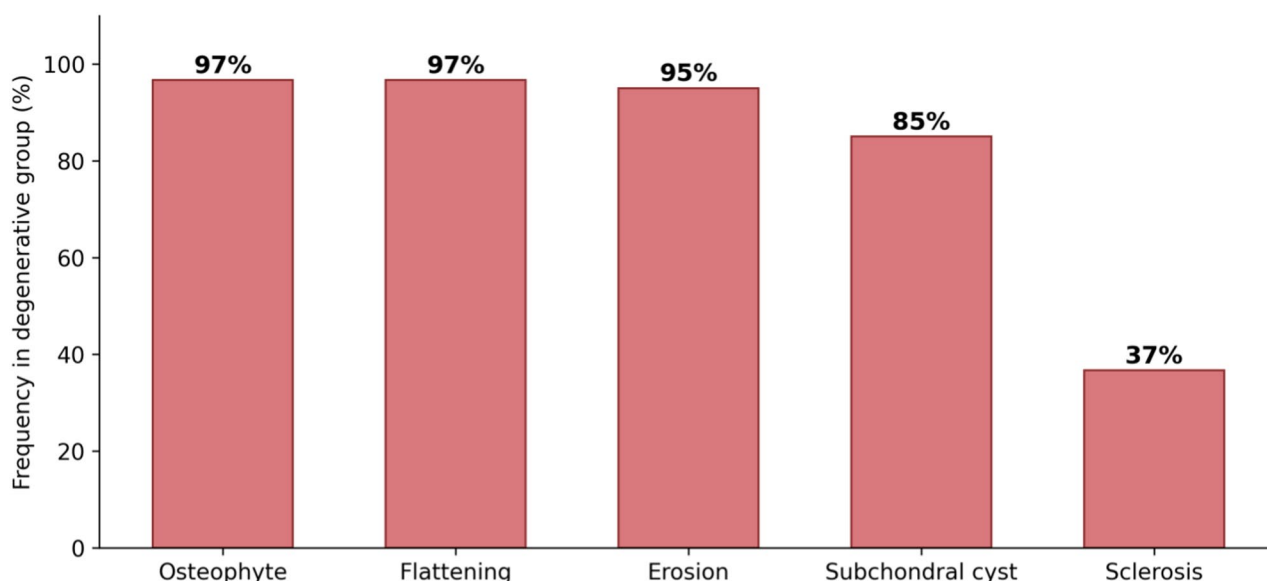


Fig. 6 Frequency of CBCT degenerative finding types in the degenerative group (*n* = 60). Flattening alone was not used to define degeneration but frequently co-occurred with other degenerative findings

group (82% vs. 38%; $p < 0.001$); myalgia was near-universal in both. Disc displacement was frequent in both groups (97% vs. 78%). Because MRI was unavailable, this diagnosis rests on clinical DC/TMD criteria alone, the accuracy of which against MRI is limited; the between-group difference is therefore provisional and should not be read as an imaging-verified difference in disc position. CBCT-confirmed DJD is not tabulated, since it defines group membership and its comparison between the groups would be tautological.

Among degenerative patients, osteophytes and flattening (each 97%), erosion (95%) and subchondral cysts (85%) were the most frequent CBCT findings and sclerosis the least frequent (37%), consistent with large CBCT series of TMD patients [18] (Fig. 6).

Age-matched sensitivity analysis

Because the degenerative group was younger, each non-degenerative patient was matched 1:1 to the nearest-age degenerative patient (caliper 3 years), yielding 29 age-balanced pairs in which age no longer differed (25.6 ± 5.5 vs. 25.8 ± 5.2 years; $p = 0.25$). In this matched subset, the differences in 25(OH)D (16.05 ± 5.70 vs. 25.08 ± 3.82 ng/mL; $p < 0.001$; $g = -1.84$) and magnesium (1.65 ± 0.36 vs. 2.01 ± 0.22 mg/dL; $p < 0.001$; $g = -1.19$) persisted essentially unchanged, and the PTH difference was, if anything, larger (53.9 ± 14.1 vs. 44.0 ± 6.7 pg/mL; $p = 0.001$; $g = +0.89$). This indicates that the marker associations are not driven by the age imbalance (Table 6).

Table 6 Age-matched sensitivity analysis (1:1 nearest-age matching, caliper 3 years)

Variable	Degenerative (<i>n</i> = 29)	Non-degenerative (<i>n</i> = 29)	<i>p</i>	Hedges <i>g</i>
Age (years), mean ± SD	25.6 ± 5.5	25.8 ± 5.2	0.25	—
25(OH)D (ng/mL)	16.05 ± 5.70	25.08 ± 3.82	< 0.001	−1.84
Magnesium (mg/dL)	1.65 ± 0.36	2.01 ± 0.22	< 0.001	−1.19
PTH (pg/mL)	53.93 ± 14.11	43.97 ± 6.67	0.001	+ 0.89
Phosphorus (mg/dL)	3.14 ± 0.67	3.55 ± 0.17	0.004	−0.83
Calcium (mg/dL)	9.50 ± 0.31	9.60 ± 0.21	0.105	−0.36
ALP (U/L)	96.4 ± 34.0	95.6 ± 31.3	0.592	+ 0.03

Paired comparison (Wilcoxon signed-rank or paired *t*-test per Shapiro–Wilk). After matching, age no longer differed, yet the 25(OH)D and magnesium differences persisted essentially unchanged

Discussion

Among symptomatic TMD patients, those with CBCT-documented degeneration had substantially lower serum 25(OH)D and magnesium and higher PTH than those without osseous degeneration, and, within the degenerative group, lower 25(OH)D and higher PTH accompanied greater condylar erosion severity. Both 25(OH)D and magnesium remained associated with degenerative status independently of age and sex after Firth penalized regression, while PTH did not, and calcium was essentially identical between groups. Because the comparison is between TMD patients with versus without CBCT-detectable degeneration—rather than patients versus healthy controls—it reduces confounding by the presence of a TMD itself. It does not isolate degeneration completely: the two groups also differed in their DC/TMD symptom profiles, and unmeasured metabolic and lifestyle determinants of the markers may differ along with them. Notably, the degenerative group was younger than the non-degenerative group, contrary to the age-related pattern of classic osteoarthritis. Our data do not explain this observation. Disease duration, clinical course, progression and TMD subtype were not recorded, and an age difference alone cannot identify a phenotype; a younger-onset degenerative or condylar-resorptive presentation in this referral population is therefore offered strictly as a hypothesis for longitudinally phenotyped studies. What the finding does support is the narrower statement that the marker associations were not explained by greater age in the degenerative group.

The vitamin D findings align with the larger recent literature [2–5]. Our study extends this work by anchoring the comparison to an objective imaging phenotype and by showing that, within the degenerative group, 25(OH)D and PTH levels vary with erosion severity — a cross-sectional gradient rather than a dose–response relationship in the causal sense. The discordant evidence must also be acknowledged: a recent case–control study found no significant 25(OH)D difference, attributing the disorder largely to metabolic and behavioural factors [8], and a Mendelian-randomization analysis raised the possibility of a non-linear relationship [9]. Two interpretive safeguards are warranted. First, the 25(OH)D distributions overlap (degenerative 6.8–27.6, non-degenerative 19.8–34.5 ng/mL), indicating a shift in central tendency rather than categorical separation. Second, the non-degenerative group was itself predominantly vitamin-D-insufficient (82.5%); only 15% were sufficient. This is concordant with the high background prevalence of hypovitaminosis D among Turkish adults and indicates that the contrast reflects relative depletion within an already-insufficient population rather than comparison against a vitamin-D-replete control [16].

The magnesium result is among the few TMJ-specific observations and is consistent with a broad osteoarthritis literature [10–13]. Mechanistically, magnesium is a cofactor for extracellular-matrix mineralization and chondrocyte metabolism and helps restrain systemic low-grade inflammation, offering a plausible basis for its association with osseous degeneration. Among the markers examined, 25(OH)D showed the strongest and most consistent association with degeneration, separating the groups and tracking erosion severity within the degenerative group; magnesium, by contrast, is the novel element of these findings, since bone and mineral metabolism studies of the TMJ have concentrated almost exclusively on vitamin D. Notably, magnesium discriminated the presence

of degeneration strongly (independently of age and sex in the adjusted model) yet did not track erosion severity within the degenerative group ($\rho = -0.14$; $p = 0.28$), whereas 25(OH)D did both. This threshold-versus-gradient pattern has, to our knowledge, not been described for the TMJ, and it may indicate that magnesium relates to whether osseous degeneration is present rather than to its graded severity. It should be stressed, however, that the contrast between a significant and a non-significant association is not itself a formal test of a difference, and that a null within-group correlation in 60 patients is compatible with a modest true association; the pattern therefore requires confirmation in larger samples before it is interpreted mechanistically. A further caution is that serum magnesium reflects only the small extracellular fraction of total body magnesium and is an imperfect index of magnesium status, so the observed difference should be read as a difference in circulating concentration rather than as established magnesium depletion. Other serum biomarkers, such as CCL5, have likewise been investigated for degenerative joint disease of the TMJ [19], whereas routinely available bone and mineral metabolism markers had not previously been tested against CBCT-confirmed degeneration.

The behaviour of PTH invites a mechanistic reading, which the present design can support only as a hypothesis. Serum 25(OH)D below ~ 20 ng/mL triggers a compensatory PTH rise that accelerates bone resorption—vitamin-D-dependent secondary hyperparathyroidism, in which PTH typically remains below 100 pg/mL [20]. That PTH was elevated and correlated with erosion severity in unadjusted analyses yet lost significance once 25(OH)D and magnesium were modelled is compatible with, though not evidence of, PTH lying downstream of hypovitaminosis D; a cross-sectional design cannot establish the direction of this relationship. The unchanged calcium concentrations fit this interpretation: in early secondary hyperparathyroidism, normocalcaemia is maintained at the expense of increased PTH-driven bone turnover, consistent with reports linking calcium-metabolism markers to TMD [6].

Mechanistically, vitamin D may act on the TMJ through both systemic and local pathways. Systemically, the hypovitaminosis-D / secondary-hyperparathyroidism axis promotes subchondral bone resorption [20]. Locally, 1,25-dihydroxyvitamin D requires vitamin D receptor (VDR) binding to drive osteoclast formation [21]; VDR polymorphisms are associated with osteoarthritis across joints [22] and specifically with TMJ disease in a Turkish cohort [23]; and deletion of the VDR exacerbates TMJ degeneration in vivo, with normocalcaemic Vdr-null mice showing more severe condylar degeneration under mechanical loading [24]. These convergent lines provide a biological rationale for the lower 25(OH)D in degenerative patients and for the within-group gradient.

The DC/TMD characterization adds clinical coherence. Both groups were genuine TMD patients, but their diagnostic profiles differed in an interpretable way: arthralgia predominated where the joint was degenerated, whereas headache attributed to TMD and near-universal myalgia characterized the non-degenerative group—consistent with a muscle-predominant, earlier-stage presentation. The non-degenerative group may include patients at an earlier stage of disease; however, the cross-sectional design cannot establish temporal progression.

Limitations

Several limitations apply. The cross-sectional, single-centre design precludes causal inference; prospective and, ideally, vitamin-D-supplementation studies are needed to establish directionality. The degenerative group was younger and comprised a higher proportion of women; neither variable was a significant predictor in the age- and sex-adjusted model, and a 1:1 age-matched sensitivity analysis reproduced the 25(OH)D and magnesium differences, indicating the findings are not age-driven. MRI was unavailable, so disc displacement could not be confirmed and was diagnosed clinically; the grouping axis, however, is osseous (CBCT), for which the modality is validated, although CBCT does not capture early cartilaginous degeneration and limited misclassification of the non-degenerative group cannot be excluded. Furthermore, non-degenerative TMD patients may represent an earlier stage of disease and could develop osseous degeneration over time despite the absence of CBCT-defined degenerative changes at the time of imaging. Longitudinal studies are needed to clarify the temporal progression from non-degenerative to degenerative TMD. Nevertheless, comparing symptomatic TMD patients with and

without CBCT-defined degeneration reduces confounding attributable to the presence of TMD itself, even though it does not remove the other differences between the groups discussed below.

Three further limitations bear directly on interpretation. First, although patients were enrolled consecutively, the analysed sample is a clinical subset rather than an unselected TMD series: eligibility required that both an adequate CBCT examination and a complete serum panel obtained within four weeks of it were available, and both investigations had been performed on clinical indication rather than by study protocol. Patients with more pronounced joint complaints are therefore likely to be over-represented (Fig. 1). Second, the division of the cohort into a degenerative and a non-degenerative group was an analysis decision rather than a design specified in advance, and adjustment was possible for age and sex only. Season of blood sampling, sun exposure, body-mass index, diet, physical activity, vitamin D or magnesium supplementation, renal function and serum albumin, medication use and systemic inflammatory status are all established determinants of the markers examined and were not recorded; although clinically overt parathyroid disease and advanced renal disease were exclusion criteria, renal function and albumin were not systematically measured. “Independently associated” in this study therefore means independent of age and sex alone, and residual confounding by broader metabolic and lifestyle factors remains a plausible partial explanation for the observed differences. Third, “non-degenerative” denotes the absence of CBCT-detectable osseous change only; early cartilage and disc degeneration cannot be excluded by CBCT, so some patients in that group may have had degenerative disease invisible to this modality, which would bias the contrast toward the null.

Serum magnesium, moreover, reflects total-body magnesium status only imperfectly. Secondary correlational and diagnostic comparisons were exploratory and not adjusted for multiplicity. The non-degenerative group was itself largely vitamin-D-insufficient, which conservatively biases the contrast toward the null. Because the study population comprised symptomatic TMD patients attending a university-based specialist (tertiary) clinic, generalisation to the general population should be made with caution.

Finally, the design supports statements about association only. Neither the diagnostic accuracy of any marker for CBCT-confirmed degeneration, nor its prognostic value, nor the effect of correcting a deficiency was evaluated. No recommendation for screening, supplementation or clinical management can be derived from these data, which should be read as hypothesis-generating for prospective and interventional studies.

Conclusions

Among TMD patients, lower serum 25(OH)D and magnesium were associated with CBCT-documented joint degeneration independently of age and sex; the association was strongest for 25(OH)D, which alone also tracked condylar erosion severity within the degenerative group. The magnesium association, which separated the groups without a severity gradient, is the novel element of these findings and requires confirmation. Comparing degenerative with non-degenerative TMD—rather than patients with healthy controls—reduces confounding by the presence of the disorder itself, although the groups still differed in their DC/TMD profiles and adjustment was possible for age and sex only. PTH was higher in the degenerative group but was not independently associated with degenerative status after adjustment, whereas calcium did not differ between groups. These are cross-sectional associations in a selected single-centre sample: they do not establish causality and do not support any screening or treatment recommendation. Prospective, age-matched and interventional studies with fuller metabolic and lifestyle data are required.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1186/s13005-026-00657-3>.

Acknowledgements Not applicable.

Authors' contributions G.A.: Conceptualization, Methodology, Investigation (cone-beam computed tomography assess-

ment), Validation, Formal analysis, Visualization, Writing – original draft, Writing – review and editing, Project administration; E.Z.: Investigation, Data curation, Writing – review and editing; F.Y.: Investigation (cone-beam computed tomography image assessment), Validation (intra- and inter-observer reliability), Writing – review and editing; Y.E.A.: Formal analysis (serum bone and mineral metabolism markers), Methodology, Writing – review and editing; S.B.: Conceptualization, Supervision, Writing – review and editing. All authors approved the final version of the manuscript.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Data availability The de-identified datasets analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate The study was approved by the Non-Interventional Clinical Research Ethics Committee of Istanbul Aydin University (Decision No. 58/2026, 4 February 2026; application submitted 21 January 2026) and was conducted in accordance with the Declaration of Helsinki. Approval was obtained before the enrolment of the first patient, and all data were collected between February 2026 and May 2026. No additional imaging and no invasive procedure were performed for the purposes of the study; all imaging and laboratory investigations analysed here had been carried out on clinical indication as part of routine diagnostic care. Written informed consent to participate, and for the use of the corresponding clinical data for research purposes, was obtained from all participants, and all data were anonymised before analysis.

Consent for publication Not applicable; this study does not contain any data or images relating to an individual identifiable person.

Competing interests The authors declare no competing interests.

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