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Relationship between radiographic changes in the temporomandibular joint and bone mineral density: A population based study

Oksana Jagur, Mart Kull, Edvitar Leibur, Riina Kallikorm, Dagmar Loorits, Margus Lember, Ülle Voog – Oras

SUMMARY

Objective. The aim of this population based study was to compare radiographic changes in the temporomandibular joint (TMJ) with the lumbar spine and femoral neck BMD. To find whether there is any relationship between TMJ radiographic changes, vitamin D (25(OH)D) and bone markers levels and the number of missing teeth.

Material and methods. The study included 95 randomly selected participants. Bilateral TMJ images were obtained using an orthopantomograph (OPTG) and were evaluated for presence of radiographic signs. BMD was measured by dual energy X-ray absorptiometry (DXA). BMD of the lumbar spine (LT score) and femur (FT score) was detected by DXA. The level of type I collagen telopeptide fragments (P1NP), of C-telopeptide crosslaps of type I collagen (CTX-1) and of 25(OH)D were also measured.

Results. Subjects with a lower LT score had significantly fewer occluding pairs of teeth ($p=0.018$) and were more frequent users of removable prostheses ($p=0.008$). Radiographic changes were negatively correlated with P1NP ($p=0.041$). CTX-1 correlated positively with P1NP ($p<0.001$) and negatively with 25(OH)D ($p=0.042$). Occluding pairs of teeth were positively correlated with the LT score ($p=0.012$) and FT score ($p<0.001$). Radiography showed changes in the TMJ of 57% of participants. Out of 95 participants, 60% demonstrated an abnormally low LT value.

Conclusions. This population based study indicates that TMJ radiographic changes and teeth loss seems to be related to the low level of BMD and 25(OH)D level.

Key words: bone mineral density, dental occlusion, osteoporosis, temporomandibular joint, vitamin D.

INTRODUCTION

The association between osteoporosis and oral bone disease was identified already in 1960 [1]. Osteoporosis is one of the most significant risk factors for potential failure of initial surgical treatment of painful and dysfunctional temporomandibular joint derangement [2]. Osteoporosis is generally characterized by a reduction of bone mass and micro – architectural deterioration of bone tissue. It results in increased bone fragility and susceptibility to fracture. Osteoporosis usually develops through a condition known as osteopenia – reduction in bone mass due to a rate of bone resorption that exceeds bone formation.

Studies have shown that mandibular cortical shape as shown on orthopantomograms (OPTGs) may provide an indication of bone turnover and spine BMD. A significant relationship has been demonstrated between biochemical markers and spinal BMD, i.e. mandibular cortical erosion has

[1]*Department of Stomatology of the University of Tartu*
[2]*Department of Internal Medicine of the University of Tartu*
[3]*Department of Radiology of the University of Tartu, Estonia*

Oksana Jagur[1] *– DDS, PhD student*
Mart Kull[2] *– MD, PhD, researcher*
Edvitar Leibur[1] *– MD, PhD, Dr Med Sc, prof. emer , senior reseacher.*
Riina Kallikorm[2] *– MD, PhD, assoc. prof.*
Dagmar Loorits[3] *– MD*
Margus Lember[2] *– MD, PhD, Dr Med Sc, prof.*
Ülle Voog-Oras[1] *– DDS, Lic Med , Dr Med, Sc assoc. prof*

Address correspondence to Dr. Oksana Jagur, Department of Stomatology, University of Tartu, 8 L. Puusepa St, 51014 Tartu, Estonia.
E-mail address: oksana.jagur@kliinikum.ee

been significantly associated with increased N-telopeptide cross-links of type I collagen and alkaline phosphatase levels [3]. Bone loss occurs when the balance shifts toward excess resorption [4, 5].

There are several markers that characterise bone metabolism. Still, it is not easy to distinguish various mechanisms of bone resorption. Type I collagen telopeptide fragments, C – telopeptide crosslaps of type I collagen (CTX-1) and C-terminal telopeptides of type I collagen (1CTP) are currently considered to be the most sensitive markers of bone resorption. They are released from type I collagen in the bone – by different enzymatic pathways. CTX-1 is generated by cathepsin K, the key osteoclastic enzyme for systemic bone resorption. In contrast, 1CTP is generated by matrix metalloproteinases whose activity plays an important role in collagen degradation associated with systemic inflammatory disease [6, 7].

Procollagen type 1 contains N – and C – terminal extensions, which are removed by specific proteases during the conversion of procollagen to collagen. These extensions are the C- and N-terminal propeptides of procollagen type 1 (P1CP and P1NP), of which P1NP appears to be more sensitive as a marker of bone formation rate in osteoporosis [8].

Biochemical markers of bone turnover can be used to predict individual bone loss. They may help to alert patients to the risk of fracture and to assess the adequacy of osteoporosis therapy. Increased levels of these markers are associated with greater radial bone loss. Yet there is very little information on whether biochemical markers can function as a supplementary indicator (in addition to bone density scanning) in diagnosing osteoporosis [9].

Vitamin D (25(OH)D) plays an important role in calcium and bone metabolism. 25(OH)D has been found to inhibit cytokine production and cell proliferation in various tissues [10].

Non-invasive assessment of bone quality by dual energy X-ray absorptiometry (DXA) has received considerable attention [11-13]. There are studies which suggest that radiographic examination (e.g.ortopantomograph) could be an effective tool for early diagnosis of osteoporosis [9, 13-15] because primary osteoporotic changes may be visible in alveolar bone.

Several studies of on osteoporosis have sought to link the BMD of lumbar spine to mandibular cortical thickness. The results remain controversial: some of the authors report a correlation between skeleton BMD and mandible BMD [13, 16] and between BMD and interproximal bone loss [17], while others do not [18]. A significant correlation has been shown to exist between mandibular bone mass, structure and thickness [19]. A correlation between BMD and TMJ bone loss, periodontal disease and tooth loss has also been shown [20].

There are insufficient data with respect to the bone characteristics of patients with TMJ disorders. It is still an open question whether osteopenia in the mandible or in the TMJ area (dental osteopenia) is a local manifestation of osteoporosis – and will thus be characterised by a similar aetiology and by similar risk factors – or whether it is an independent process governed primarily by factors that cause changes in the bone structure of the TMJ.

The above points to the need for additional studies to evaluate the influence of potential contributing factors to further define the relationship between low BMD and TMJ disorders in population.

In view of the above, the aim of this population based study was to compare radiographic changes in the TMJ with the lumbar spine and femoral neck BMD. To find whether there is any relationship between TMJ radiographic changes, 25(OH)D and bone markers levels and the number of missing teeth.

MATERIAL AND METHODS

The study was approved by the Ethical Committee of the Faculty of Medicine, University of Tartu (140/18, 2005). All participants gave their informed consent before the start of the study.

The study was conducted in Väike-Maarja municipality of Estonia in 2006. A group of randomly selected participants (n=103) consisting of 61 females and 42 males from the patient register of a local family practitioner were invited to participate. Of those invited, 95 (92%) persons took part in the study (Table 1). Eight persons did not show up to perform the OPTG.

TMJ images were obtained with the orthopantomograph apparatus CRANEX 3 (Soredex orion corporation LTD, Finland) on the same day that blood sampling was performed. The OPTG images were evaluated for presence of such radiographic signs of structural bone changes as erosions, flattening and osteophyte formation on the condyle and the temporal bone [21] (Figure 1). Condyle erosion in the radiographs was scored according to Helenius et al. (2004) as follows: score 1 – very slight erosion; score 2 – erosion at the top of the condyle; score 3 – half of the condyle is eroded; score 4 – condyle totally eroded [22]. The number of missing teeth was also recorded. The relation between the number of missing teeth (excluding root remnants and third molars) and radiographic changes in the TMJ

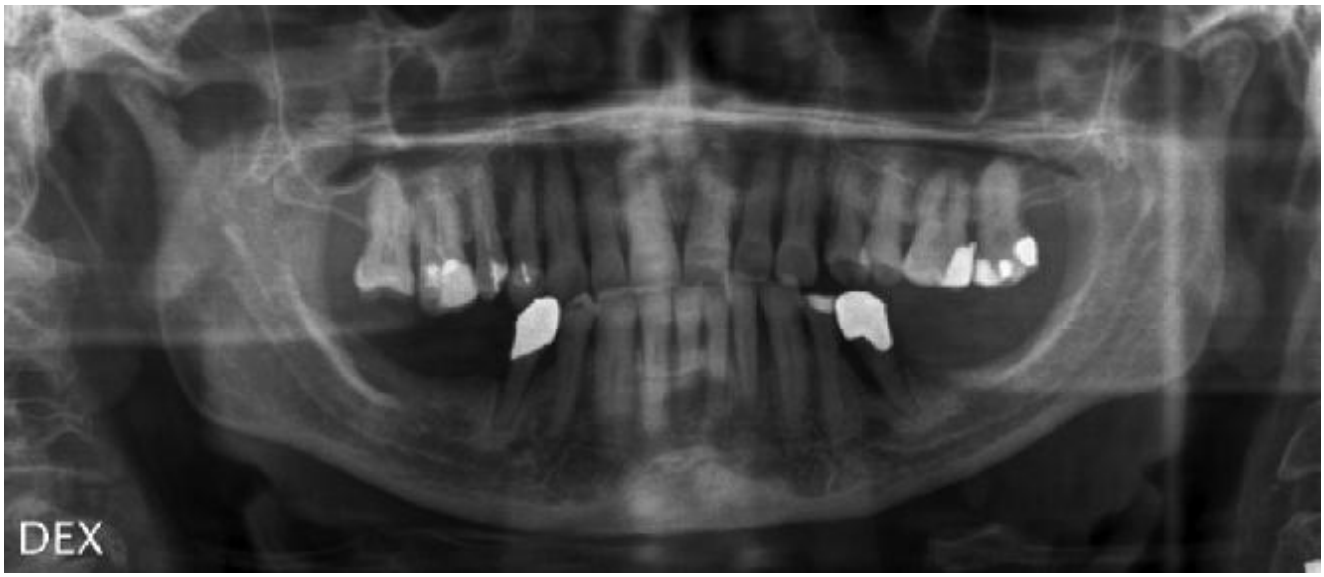

Fig. 1. Ortopantomograph. Subchondral bony erosions of the right mandibular condyles are visible. Narrowing of both temporomandibular joint spaces and an irregularity of joint surfaces is observed.

was compared. All OPTG images were examined by three independent investigators who were not presented with the underlying laboratory or clinical data. To allow for intraobserver error assessment, thirty percent of OPTGs were re-examined three months after the first examination by an independent investigator who recorded her assessment on a separate form.

BMD of the lumbar spine (LT score) and femur (FT score) were measured at each centre by DXA with a densitometer (GE – Lunar Progidy, Madison, Massachusetts, USA) at the lumbar spine (L2 to L4) with anterior-posterior view and at the left hip (femoral neck) [23]. BMD was expressed in grams of bone mineral per square centimeter (g/cm^2), as the number of standard deviations (SD) from the mean of healthy individuals matched to the participants in age and sex (the Z-score), and as the number of SD from the mean of healthy young sex-matched individuals (the T-score). The reference values were obtained from Lunars combined European/US reference population [24].

T-score was used for analysis based on World Health Organization (WHO) criteria.

The universally accepted WHO criteria for assessing BMD contrast individual T –scores to peak BMD in healthy adult control populations. In this scheme, "osteoporosis" refers arbitrarily to T-values below -2.5, "osteopenia" to values between -1.0 and -2.5, and "normal" to values above -1.0 [25].

The subjects were divided into two groups such that the BMD values of group one were normal and those of group two abnormal.

All samples were taken in the morning (after an overnight fast) between 8 a.m. and noon using pre-cooled tubes. Serum was separated and the samples were stored at -20°C until analyzed. All samples were analyzed simultaneously and in duplicates to minimize inter-assay variations. Analyses were performed at the United Laboratories of the University of Tartu Clinic.

The 25(OH)D level in serum was measured by radioimmunosorbent assay produced by DiaSorin (Stillwater, Minnesota, USA). The intra and inter-assay CVs were 4.1% and 5.7% respectively. For group discrimination, we used 25 nmol/L as the critical value for deficiency and 50 nmol/L as the cut-off value for insufficiency. 75 nmol/L was considered to be the optimal 25(OH)D level. Serum PTH was measured with an Immulite 2000 analyser (DPC). P1NP was used as a marker of bone formation, and CTX-1 as a marker of bone degradation. P1NP was determined by Elecsys 1010/2010 total P1NP serum kit (Roche Diagnostics, Mannheim, Germany),

Table 1. Correlation between saliva buffer capacity detected by different tests and caries prevalence

			Median	IQR
Age		years	55	24
Gender	Female	%	58	
	Male	%	37	
Occlusion	Occluding pair of teeth	number	8	9
	Removable prosthesis	%	32	
TMJ	Pain episodes	%	47	

IQR – interquartile range. Occluding pair of teeth – number of occluding pair of teeth, Removable prosthesis – percentage of patients wearing removable prosthesis, TMJ – percentage of patients having current or present pain episodes in the TMJ area

which employs the electrochemiluminescence immunoassay (ECLIA) technique (measuring range 5 to 1200 μg/L).

CTX-1 was determined by Elecsys 1010/2010 β-CrossLaps/serum kit (Roche Diagnostics, Mannheim, Germany) whose sensitivity of assay is 0.01 ng/mL. The mean (SD) and mean+2SD figures are: for premenopausal women, 0.299 (0.137) ng/mL and 0.573 ng/mL; for postmenopausal women, 0.556 (0.226) ng/mL and 1.008 ng/mL; for men, 30 to 50 years, 0.300 (0.142) ng/mL and 0.584 ng/mL; for men aged 50 to 70, 0.304 (0.200) ng/mL and 0.704 ng/mL; and for men older than 70, 0.394 (0.230) ng/mL and 0.854 ng/mL.

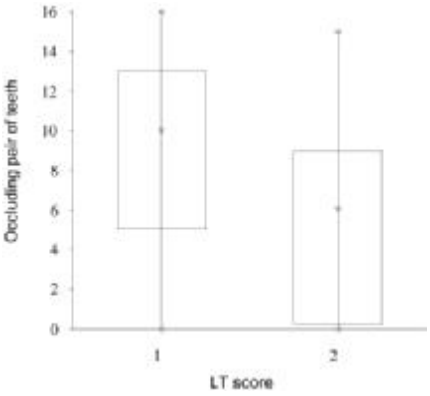

Fig. 2. Relationship between occluding pair of teeth and LT score.
Box plot is showing the relationship between occluding pair of teeth and LT score. Box number 1 – subjects with normal mineral density. Box number 2 – subjects with lower LT score.

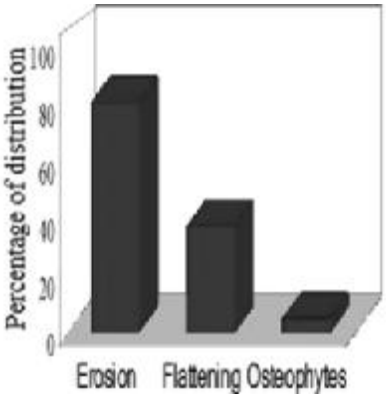

Fig. 4. Distribution of radiographic changes. Distribution of radiographic changes observed in 57% of participants. The most frequent radiographic signs were erosion – 80%, flattening 37% and osteophytes 5 of participants.

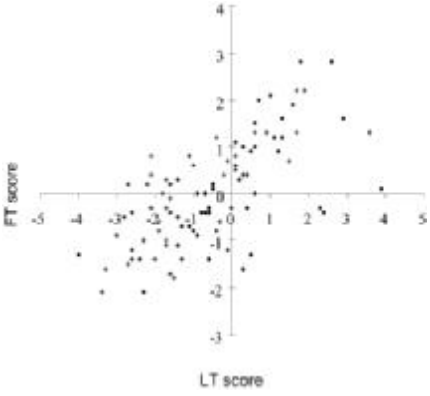

Fig. 3. Relationship between LT score and FT score.

Table 2. Background factors of 95 persons

		Median	IQR
LT score		-0.6	2.3
FT score		0	1.6
25(OH)D	nmol/L	43	22
P1NP	ng/L	39.9	24.3
CTX-1	ng/L	0.3	0.2

IQR – interquartile range, LT score – T score of lumbal spine, FT score – T score of femoral neck, 25(OH)D – Vitamin D in nmol/L, P1NP – Procollagen-1N-collagen in ng/L, CTX-1 – C-telopeptide of type I collagen in ng/mL.

Background factors of 95 persons are presented in Table 2.

Considering statistical analyses the variables were tested for differences between groups with the Mann-Whitney U-test. The significance of the correlations was tested by the Spearman rank correlation coefficient (rs). A significance level of less than 0.05 was considered as significant.

RESULTS

Differences based on BMD

Analysis of the data showed differences between the LT scores of the two groups (Table 3).

Participants with a lower LT score had significantly fewer occluding pairs of teeth ($p = 0.018$), i.e. the lower the number of occluding pairs of teeth, the lower the BMD value (Figure 2).

Participants with lower LT scores had significantly more removable prostheses ($p=0.008$), i.e. participants with a removable prosthesis showed lower BMD values.

Participants with a low LT score also demonstrated a low FT score ($p<0.001$; Figure 3).

Table 3. Distribution of 95 persons between two groups based on LT score values

		Bone mineral density					Occlusion	
		LT score	FT score	25(OH)D	P1NP	CTX-1	Occluding pair of teeth	Prosthesis
Group I	Median	-1,9	-0,75	43	40,79	257	6	
	IQR	875	1325	13	25,94	189	8,25	
	Sum							19
Group II	Median	0,4	0,7	43	39,96	276	10	
	IQR	1,5	1575	25	21,41	204	8	
	Sum							12

IQR – interquartile range, LT score – T-score of lumbal spine, FT score – T-score of femoral neck, 25(OH)D – Vitamin D in nmol/L, P1NP – Procollagen-1N-Terminal Peptide reference in μg/L, CTX-1– C-telopeptide of type I collagen reference in ng/mL, Occluding pair of teeth – number of occluding pair of teeth, Prosthesis – percentage of patients wearing removable prothesis, Group I – subjects with low value of bone density (-2.5 to -1.0), Group II – subjects with normal value of bone density (above -1.0).

There were no differences between radiographic changes and BMD values between the two groups.

Contributing factors

Radiographic changes in the TMJ correlated negatively with P1NP (r_s=-0.217, n=95, p=0.041) i.e. the higher the number of radiographic changes the lower the value of P1NP.

CTX-1 correlated positively with P1NP (r_s= -0.6449, n=95, p<0.001) and negatively with 25(OH) D (r_s=-0.207, n=95, p=0.042), i.e. the higher the values of CTX-1, the lower the values of 25(OH)D.

Occluding pairs of teeth were positively correlated with the LT score (r_s=0.254, n=95, p=0.012) and the FT score (r_s=0.325, n=95, p<0.001), i.e. the more occluding pairs of teeth the higher the values of LT score and FT score.

Removable prostheses were negatively correlated with the LT score (r_s=-0.303, n=95, p=0.001); and the FT score (r_s=-0.33, n=95, p<0.001), i.e. subjects with a removable prosthesis had lower values of LT score and FT score.

Occluding pairs of teeth were negatively correlated with removable prostheses (r_s=-0.529, n=95, p<0.001); i.e. subjects with a prostheses had fewer occluding pairs of teeth.

Radiographic changes in the TMJ were observed in 57% of participants. Erosions were identified in the OPTGs of 80% of the participants, flattening in 37% and osteophytes in 5% (Figure 4).

There was no statistically significant difference between male and female subjects in terms of the extent and nature of radiographic changes in the TMJ.

Out of the 95 participants, 42% had abnormally low values of the LT score. Among them, osteoporosis was observed in 10.4% and osteopenia in 31.6% of participants.

DISCUSSION

The population based random study reported in this article demonstrates a significant relationship between low BMD and radiographic changes in the TMJ, as well as between low BMD and the number of occluding pairs of teeth. Subjects with lower BMD values have fewer occluding pairs of teeth and are more likely to have a removable prosthesis. This is in accordance with the study performed by Sato et al 1998, whose authors found that bite force and the number of residual teeth were significantly correlated with the BMD of trabecular mandibular condyle. The study also confirmed the importance of having a BMD within the normal limits in order to avoid loss of teeth and eventual temporomandibular disorders (TMD) [26] – our findings indicate that radiographic changes that occur in the TMJ appear to be related to the BMD. In addition, our findings support the importance of functional loading and dental state for mandibular condyle.

Radiographic changes in the TMJ were negatively correlated with P1NP, which has been shown to be a sensitive marker of bone formation. Radiographic changes in the TMJ were observed in 57% of participants. This suggests that decreased levels of P1NP interfere with bone formation in the TMJ, causing erosions, flattening and osteophytes.

The above mentioned marker correlated with CTX-1, which is currently considered as one of the most sensitive markers of bone resorption. A correlation between these two markers is probably due to equal shift / balance in a normal bone metabolism, where osteoblasts are acting simultaneously with osteoclasts.

High levels of CTX-1 in our data correlated with low levels of 25(OH)D. This association could be due to the fact that cases of more pronounced bone resorption are accompanied by a deficiency of 25(OH)D. Based on the results described above an indirect correlation may be suggested between radiographic changes in the TMJ and the level of 25(OH)D. This finding points to the possibility of 25(OH)D lowering BMD in the TMJ and eventually leading to osteoporosis.

These findings indicate that decreasing BMD may be regarded as one of the predictors of TMJ bone destruction. A low 25(OH)D level can also predict TMJ bone destruction. Therefore, the destruction of mineralized tissues in the TMJ might be slowed or counteracted by correcting the patient's 25(OH)D levels. Further research is necessary to confirm this hypothesis.

Among the participants who had radiographic changes in the TMJ, erosions were found in 80%. TMJ bone erosion, which is caused by demineralization of articular bone tissue, is generally considered to be an indicator of active bone resorption resulting either from inflammation or remodelling [27, 28]. Flattening was observed in 37% of participants. The erosive process in the TMJ is likely to result in flattening of the mandibular condyle and the articular eminence, which, if bilateral and pronounced, is likely to cause very severe malocclusion. Flattening of the mandibular condyle or the temporal articular eminence could thus either be the result of a loss of hard tissue due to inflammation or it could be caused by hard tissue remodelling due to age or trauma or a low level of 25(OH)D, or a combination of these factors (it is impossible to differentiate determine the underlying reason from radiography). It

has been reported that changes due to remodelling or arthrosis mainly appear after the age of 45 – thus, the fact that the median age in study was 55 years suggests these as the most likely factors.

In our study we did not find any statistical differences between the sexes in the frequency of osteoporosis. This is in accordance with the DXA data collected by Lochmüller et al. (1998) whose analysis suggests that no significant decrease in bone density or structure occurs in men due to age, and with the study of Eckstein et al. (2007) which did not report significant sex differences either.

Osteoporosis has been linked to the loss of teeth calcium and vitamin D supplements can bolster bone density in the jaws [10]. Low skeletal BMD induces changes in mandibular bone structure and bone mass. This in turn increases susceptibility to diseases of the teeth and the periodontium and may result in the loss of teeth and in bone loss in the TMJ [17, 20].

Early detections of TMJ pathologies together with antiresorptive therapy for osteoporosis merit future consideration in TMD prevention. Diagnosis and evaluation of risk factors may in due course necessitate the selection of a specific initial procedure that minimizes the influence of concomitant risk factors for long-term success. Lofman et al. [30] reports that biochemical markers of bone turnover are related to current bone mass and provide information about future bone loss.

The results of an investigation carried out by examining a patient's OPTG, BMD and the biochemical markers of bone turnover may differ from those of an assessment of any one of these factors in isolation. When the clinical interpretation, reliability, and validity of the images-derived outcomes have been established, the TMJ pathology may be detected at an earlier stage.

Thus, OPTG could be useful as a screening method to see whether changes are taking place in TMJ bone structure. Yet it is unlikely that radiographic findings and biochemical markers will be able to replace bone density scanning.

CONCLUSIONS

This population based study indicates that TMJ radiographic changes and teeth loss seems to be related to the low level of BMD and 25(OH)D level.

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