Bone volume in human temporomandibular autopsy joints with and without erosive changes

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The aim was to compare the trabecular bone volume (TBV) and the total bone volume (TOBV) of human temporomandibular joints (TMJ) with erosive changes with those of joints without erosive changes. We examined 35 TMJ autopsy specimens from 19 individuals aged 66–88 years. Sagittal sections of the joints were analyzed microscopically for erosive hard-tissue changes. The TBV and the TOBV of the sections were assessed with the aid of computerized image analysis. A significant increase in trabecular and total bone volume was found in condyles with erosive changes (TBV = 21%, TOBV = 54%) as compared with condyles without erosive changes (TBV = 15%, TOBV = 40%). The trabecular bone volume of the temporal component was also increased (TBV = 24%) in joints with erosive changes in the condyle as compared with joints with unaffected condyles (TBV = 16%). The findings indicate that the relative bone mass may play a role in the development of erosive changes in the TMJ. □ *Bone density; image processing, computer-assisted; mandibular condyle; osteoarthritis; temporomandibular joint diseases*

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Studies of the bone tissue in patients with osteoarthrosis (OA) of the hip joint have shown that the bone mass in the skeleton far from the osteoarthrotic hip is increased (1–4), indicating that a generalized increase in bone mass might be an etiologic factor in OA. Gevers et al. (5) evaluated the physical and histomorphologic characteristics of iliac crest bone in patients with OA of the hands and found increased trabecular and cortical bone volume in patients with OA. Another finding indicating that OA may be part of a generalized bone disease is the negative correlation between osteoporosis and OA of the hip reported in several studies (1, 6–8).

In a histomorphometric study of the temporomandibular joint (TMJ) no significant differences in bone volume variables between dentate, edentulous, and denture wearer groups were found (9). Lubsen et al. (10), with the aid of histomorphometry, studied the cartilage and the cortical bone tissue in condyles of young human adults and found no cortical bone changes, either in thickness or in composition, between condyles with non-hypertrophic, hypertrophic, and hyperplastic cartilage. Other histomorphometric studies of the TMJ have focused on the soft tissues or descriptive macromorphologic observations (11–13). No studies on the bone volume including the trabecular bone tissue and changes indicative of OA in the TMJ have, however, been reported.

The aim of this study was to obtain a quantitative description of the fractional bone volume of the human TMJ with the aid of bone histomorphometry and to compare the bone tissue volume of TMJs with erosive changes with that of joints without erosive changes.

Materials and methods

Materials

The material examined consisted of TMJs from individuals who before death had donated their bodies to research. The specimens, removed as blocks, were fixed in a 10% neutralized buffered formaldehyde solution, then demineralized in 0.5M ethylenediaminetetraacetate (Na_2H_2-EDTA) for 16–20 weeks and finally embedded in paraffin. Sagittal microtome sections, with the microtome set at 6 μm, were taken at every millimeter from the most lateral aspect of the joint to the most medial one. The histologic sections were stained with Mayer's hemalun–eosin solution (14).

Of the original 42 joints, 4 joints were excluded owing to a diagnosis of rheumatoid arthritis. Of the 38 remaining joints, 35 were selected for analysis on the basis of the microscopic examination. The inclusion criterion was that the tissue preparation should be of high quality. The 35 joints used consisted of the bilateral joints of 16 individuals, 10 men (mean age, 74 years; range, 66–86 years) and 6 women (mean age, 78 years; range, 70–88 years), and of 3 unilateral joints from 2 men and 1 woman (aged 60, 80, and 67 years).

From the lateral, central, and medial thirds of each joint the sagittal section of best technical quality was selected.

Microscopic analysis

First, all sections were examined microscopically for erosive changes on the basis of the definition presented in a previous paper (15). An erosive change was defined as a hard-tissue change with loss of cortical lining, absence of a calcified cartilage layer, and signs of osteoclastic resorption such as a scalloped bone surface with osteoclast lacunae and occasional osteoclasts (15). Then, the total bone volume (TOBV), defined as ((Cn-BV + Ct-BV)/TtV), and the trabecular bone volume (TBV), defined as (Cn-BV/TtV), were determined in both the condyle and the temporal component with the aid of computer-assisted image analysis (Cn = cancellous; Ct = cortical; BV = bone volume; and TtV = total volume, following the abbreviations suggested by Parfitt et al. (16)). A semiautomatic threshold setting based on the gray-scale of the image was applied. The image analysis equipment and the semiautomatic threshold setting have been described in detail in another study (17). The region of interest (ROI) of the condyle was defined by inserting a vertical line, corresponding to 5 mm and following the long-axis of the condyle, from the most superior point of the condyle. A horizontal line was then automatically drawn perpendicular from the lowest point of the vertical line, thereby delineating the ROI of the condyle. The vertical distance of the ROI in the condyle was chosen as an approximation to provide a large enough ROI to include the bone changes indicative of OA and still be within the limits of the condylar process. In the temporal component, the ROI was defined by drawing a horizontal line tangential to the most superior point of the fossa and another vertical line automatically perpendicular to the horizontal line. The vertical line was inserted so as to cross the most inferior point of the tubercle. The vertical distance of the ROI in the temporal component was thus determined by the height and angle of the posterior slope. The outer border of the cortical bone and

Table 1. Mean, standard deviation (*s*), and range of trabecular bone volume (TBV), total bone volume (TOBV), and TBV/TOBV fraction of the condyle and the temporal component of 35 temporomandibular joints

	Condyle			Temporal component		
	Mean	*s*	Range	Mean	*s*	Range
TBV*	17	7	7–34	18	6	8–34
TOBV*	44	11	23–70	57	12	30–78
TBV/TOBV (×100)	37	12	16–61	34	12	11–62

* TVB and TOBV are expressed in percentage (%) of total volume.

Table 2. Mean, standard deviation (*s*), and significance level of difference in trabecular bone volume (TBV), total bone volume (TOBV), and TBV/TOBV fraction of the condyle and the temporal component of 35 temporomandibular joints with and without erosive changes

	Group Ia, Joints without changes (n = 17)			Group Ib, Joints with erosive changes (n = 18)			Group IIa, Condyles without changes (n = 25)			Group IIb, Condyles with erosive changes (n = 10)			Group IIIa, Temporal components without changes (n = 19)			Group IIIb, Temporal components with erosive changes (n = 16)		
	Mean	*s*		Mean	*s*		Mean	*s*		Mean	*s*		Mean	*s*		Mean	*s*	
Condyle																		
TBV*	18	7	NS†	17	8		15	5	$P = 0.041$	21	8		17	5	NS	17	8	
TOBV*	39	11	NS	47	12		40	7	$P = 0.0012$	54	11		41	7	NS	47	13	
TBV/TOBV (×100)	39	10	NS	36	12		37	11	NS	39	13		41	11	NS	35	12	
Temporal component																		
TBV	17	4	NS	20	7		16	5	$P = 0.0023$	24	6		17	5	NS	20	7	
TOBV	59	13	NS	58	10		58	14	NS	57	5		57	13	NS	58	11	
TBV/TOBV (×100)	31	11	NS	36	13		31	11	$P = 0.012$	42	11		34	12	NS	35	13	

* TBV and TOBV are expressed in percentage (%) of total volume.
† NS = no significant difference between groups ($P \geq 0.05$).

another line approximately one and a half times the width of the bone trabecula inside the interface between the cortical and trabecular bone were traced in each ROI. The outer border delineated the total bone and the inner line the trabecular bone regions. The measurement values were presented as fractional bone area—that is, percentage of bone within the defined ROI (17).

Statistical analysis

The material was classified on the basis of the microscopic findings of erosive changes:

I. Findings of the whole joint:
   a) Joints without erosive changes.
   b) Joints with erosive changes in any joint component.

II. Findings of the condyle:
   a) Joints with condyles without erosive changes.
   b) Joints with erosive changes in the condyle only.

III. Findings of the temporal component:
   a) Joints with temporal components without erosive changes.
   b) Joints with erosive changes in the temporal component only.

Some joints were included in more than one group but not in two mutually compared groups. Differences in TBV, TOBV, TBV/TOBV fraction, and size of the ROI between the two groups in categories I, II, and III described above were assessed with the Wilcoxon–Mann–Whitney rank sum test (two-tailed); such comparisons were performed both with the joint and with the individual as observational unit. The two individuals with one joint with erosive changes and the other joint without erosive changes were included among the individuals with joints with erosive changes. A P values less than 0.05 was considered statistically significant. In each group the correlation coefficient between age and TBV, TOBV, or TBV/TOBV fraction, respectively, was calculated.

Results

Microscopically, 31 erosions with and 36 erosions without overlying cartilage were found. These erosions were distributed over 11 condyles and 18 temporal components. The TBV, the TOBV, and the TBV/TOBV fraction of the condyle and the temporal component are presented in Table 1. The range and the variation of the variables were high for both the condyle and the temporal component. There was no difference in the size of the regions of interest between the different subgroups.

Table 2 presents the TBV, TOBV, and TBV/TOBV fraction of the condyle and the temporal component in joints with and without erosive changes. The variation was high for all variables both in joints with and those without erosive changes. The TBV and TOBV of condyles with erosive changes were significantly higher than the TBV and TOBV of condyles without erosive changes. In joints with condyles with erosive changes the TBV and TBV/TOBV fraction of the temporal component were also higher than in joints with condyles without changes. There was no statistically significant difference in the TBV, TOBV, or TBV/TOBV fraction between joints with and without erosive changes when the findings were based on the whole joint or on the temporal component.

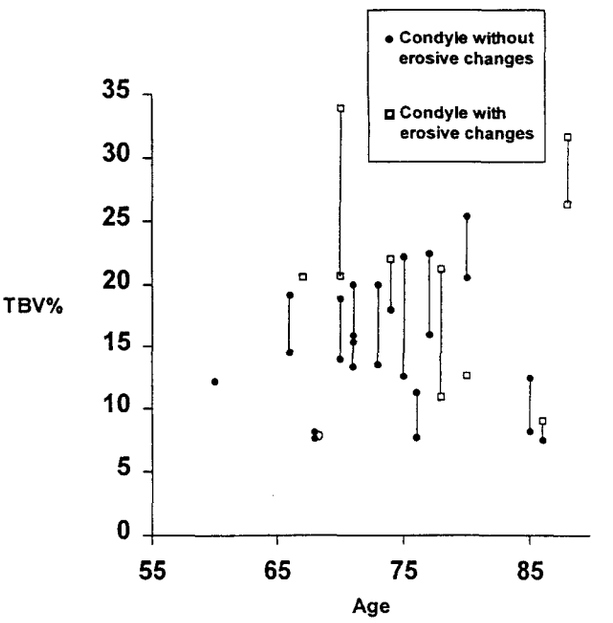

Fig. 1. Age of the individual and the trabecular bone volume (TBV%) in condyles with and without erosive changes in 35 temporomandibular joints from 19 individuals aged 60–88 years. Joints from the same individual are connected with a thin line.

Fig. 1 presents the TBV and Fig. 2 the TOBV of condyles with and without erosive changes in relation to the individual's age. The age distribution of individuals with condyles with erosive changes was comparable to that of individuals with condyles without erosive changes. As shown in Fig. 2, the three individuals in whom erosive changes were found bilaterally presented the highest TOBV. The two individuals with one TMJ with and the contralateral joint without erosive changes presented a TOBV that was comparable to that of individuals with bilateral joints without changes.

Significant differences were found between individuals with erosive changes of any condyle and individuals without erosive changes for TOBV of the condyle ($P = 0.043$) and TBV of the temporal component ($P = 0.0088$).

No significant correlation was found between age and TBV, TOBV, or TBV/TOBV fraction, with a correlation coefficient (r) below 0.37 in all groups.

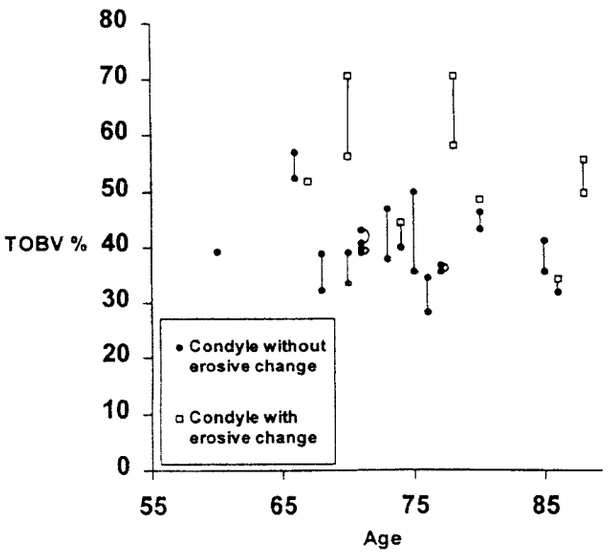

Fig. 2. Age of the individual and the total bone volume (TOBV%) in condyles with and without erosive changes in 35 temporomandibular joints from 19 individuals aged 60–88 years. Joints from the same individual are connected with a thin line.

Discussion

Osteoarthrosis was for decades considered to be primarily a disease of the cartilage with secondary bone changes such as bone erosion, osteophyte formation, and subchondral sclerosis (18). Several authors have, however, suggested that the initial events in OA can occur in the subchondral tissues (19–23). For the TMJ the relationship between remodeling and OA have been much debated (24, 25). Deviation in form of the joint under intact articular surface is often regarded as physiologic, non-pathologic remodeling (26), and hard tissue erosive changes are considered a part of regressive remodeling (27, 28). However, macroscopic and histologic analyses in numerous studies have shown that subchondral bone changes may precede the cartilage changes in OA of the TMJ (15, 24, 25, 27–32). Thus, the findings from studies on the TMJ and on other synovial joints indicate that erosive changes, the extensive ones in particular, could be considered histopathologic evidence of OA. Erosive changes are also a feature in rheumatoid arthritis. Joints from patients with known rheumatoid arthritis were, however, excluded from this study.

The technique applied in this study enables quantitative analysis of the bone tissue. No information is, however, obtained on the bone structure, such as how the bone mass is spatially distributed. The condyle and the temporal component differ embryonically both in bone structure and in bone formation. The postnatal bone formation of the condyle, with a thin trabecular network underlying a cartilaginous growth zone (33), to some extent resembles the endochondral ossification of other synovial joints (34). The bone formation of the tubercle is different (35). Ingervall et al. (33) reported the mineralization of the tubercle to occur in discrete centers that coalesce to form a continuous bony layer. These differences between the condyle and the temporal component in embryologic origin should be considered when interpreting the present results.

The trabecular bone tissue has a higher metabolic activity and a larger surface area involved in remodeling throughout life than the cortical bone tissue (36). In bone histomorphometry this is reflected by the TBV being a better indicator of osteoporosis and, presumably, of sclerosis than the TOBV in iliac bone biopsy specimens (37). The mechanical properties of the bone tissue are, however, not only dependent on bone mass but also on bone structure. Accordingly, analysis of vertebral trabecular bone demonstrated that biomechanical competence is dependent on both the continuity of the trabecular lattice and the bone mass (38). The bone architecture of the condyle seems to be similar to that of iliac biopsy specimens as presented in figures by Boyce et al. (37). Even so, we considered it of interest to measure both TBV and TOBV, since two variables might be more indicative of active bone changes than one and because these variables were previously not known for the TMJ. The definition of the measurement regions made it possible to achieve reproducible and standardized ROI in each joint (17). One might argue that the quality and the quantity of bone tissue would determine the quality of the histologic section, thus introducing bias to the section selection. However, the variation and the range of all variables were large in all subgroups, even in joints without erosive changes. Thus, the sections were more likely to be excluded for reasons other than the quantity of bone tissue. Sections were excluded because of poor impregnation of the embedding medium into the block or because of folding.

The finding that both TBV and TOBV were increased in condyles with erosive changes as compared to unaffected condyles can be interpreted as signs of different biologic changes. The differences in bone volume found in the condyle may be an expression of a primarily dense joint as part of a generalized bone alteration, which will predispose to OA. On the basis of the observation that patients with OA tend to have higher bone mineral density than individuals without OA, it has been suggested that generalized OA is the result of a generalized bone alteration (8). This hypothesis is supported by findings in patients with OA of the hand (5) and the hip joint (1–4), who have been found to have increased bone mass in the skeleton, far from the affected joints and in areas where wear and tear phenomena are less likely, as compared with age-matched controls. Both increased amounts of cortical bone (1, 2) and increased amounts of trabecular bone tissue (4, 39) have been found in OA patients. In the present material the individuals with bilateral joints with erosive changes presented the highest TBV and TOBV.

The two individuals with one joint with erosive changes and the contralateral joint without changes may represent another type of OA. The increased bone volume of these condyles with erosive changes as compared with the contralateral joint might be an expression of a local subchondral sclerosis secondary to OA in the articular cartilage. Thirdly, the increased bone volume might indicate a local trabecular sclerosis preceding osteoarthrotic cartilage changes (20, 21). On the basis of animal experiments, Radin et al. (20, 21) put forward the hypothesis that low impulse loading of the joint causes trabecular microfractures that will heal with callus formation. Such a repair would, according to Radin et al. (20, 21), increase the stiffness gradient of the subchondral bone and result in subsequent cartilage breakdown and OA. The increase in TBV and TOBV in joints with erosive hard-tissue changes might also represent progressive remodeling, as described for the TMJ by Moffet et al. (27). In progressive remodeling of the TMJ the calcified cartilage layer is thickened and the tidemark advances into the articular tissue. Subsequently, the deeper parts of the calcified cartilage layer are replaced by bone tissue and the cortical bone is thickened (27). The fact that the TBV/TOBV fraction was comparable in joints with and without erosive changes contradicts, however, these latter two hypotheses. If the increase in TBV and TOBV in joints with erosive changes was the result of either repair of trabecular microfractures or of progressive remodeling, then the TBV/TOBV fraction should be different. Thus, in the case of repair of trabecular microfractures with callus formation the TBV/TOBV fraction should be higher and in the case of progressive remodeling the TBV/TOBV fraction should be lower than in joints without erosive changes.

There was a high interindividual variation of the TBV and the TOBV for both the condyle and the temporal component, in accordance with the findings of studies on bone tissue of the iliac crest (40) and of load and non-load bearing areas of the femoral head (41). The bone volume of the TMJ has previously been reported only in one histomorphometric study on the effects of denture wearing by Taddei et al. (9). Standardized measurements of the fractional bone volume and the trabecular bone volume as proposed by Parfitt et al. (16) were, however, not applied. Instead, the size of the joints was measured. As the measurement methods and definitions of bone volume were quite different, the values presented by Taddei et al. (9) cannot be compared with our results.

In conclusion, it was demonstrated that the average bone volume was higher in TMJs with condyles with erosive changes than in condyles without erosive changes. Our findings indicate that a generalized bone alteration could be of importance in the development of changes indicative of OA also in the TMJ. To validate such a hypothesis and exclude possibilities of local secondary bone sclerosis, further studies, measuring the bone mass in other parts of the skeleton far from the affected joints, should be performed in patients with and without TMJ bone changes indicative of OA.

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