Analysis of Beta-Crosslaps (B-Ctx) and Mandible Trabecular Parameters in Menopausal Women Using Cone Beam Computed Tomography (Cbct)

Silviana Farrah Diba[1]*, Azhari[2], Farina Pramanik[2], Sri Tjahajawati[3]

1.Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Universitas Gadjah Mada, Yogyakarta, Indonesia.
2.Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Universitas Padjadjaran, Bandung, Indonesia.
3.Department of Oral Biology, Faculty of Dentistry, Universitas Padjadjaran, Bandung, Indonesia.

Abstract

The purpose of this study was to analyze the correlation between Beta-CrossLaps (β-CTx) and trabecular structural parameters of menopausal women using CBCT

A total of 17 mandibular CBCT radiographs of menopausal women with laboratory tested of β-CTx were taken. Trabecular region of interest (ROI) sized 3 x 3 mm was choosen inferiorly from both side of mentale foramen make it a total of 34 ROI. Bone volume fraction (BV/TV), trabecular thickness (Tb.Th) and trabecular separation (Tb.Sp) was calculated using BoneJ on each ROI. Statistical analysis was done using SPSS. Pearson correlation to obtain the relationship of β-CTx with each parameter.

There is no significant correlation ($p > 0.05$) between β-CTx with BV/TV ($r = -0.252$) and Tb.Th ($r = 0.227$). Meanwhile β-CTx has a significant positive correlation ($p < 0.05$) associated with Tb.Sp ($r = 0.452$).

Increasing β-CTx level is not always followed by a decrease in BV/TV percentage and Tb.Th width. Tb.Sp is the most correlated parameter related to β-CTx.

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Introduction

Along with an increase of life expectancy reaching 70 years, women can spend around one third of their age in menopause. Bone loss in menopausal women can cause serious problem including fracture which results in reduced mobility also quality of life. The prevalence of menopausal women is increasing, so certain attention and early examination of bone quality is needed.[1]

The location of bone loss in menopausal women is more obvious in trabecular bone.[1] Besides bone mineral density, mechanical aspects also need to be considered to assess bone quality, examined from trabeculae parameters.[2] Several bone trabecular parameters that can describe bone architecture include bone volume fraction (BV/TV), trabecular thickness (Tb.Th), and trabecular separation (Tb.Sp).[3]

Dual energy X-ray absorptiometry (DXA) as a gold standard BMD assessment has been very popularly used yet there are some disadvantages including high costs and limited used in large-scale population. Compared with CBCT, bone quality evaluation using DXA is limited in 2-dimensional view only.[4] Analysis of trabecular structures can utilize micro computed tomography (μCT) and high-resolution peripheral quantitative computed tomography (HR-pQCT) but limited to the analysis of small animal bones or small biopsy specimens that are not appropiate when applied in clinical diagnosis.[5]

CBCT in dentistry field become a popular tool to diagnose dental and jaw areas, also used as bone assessment following implant application.[6] Three dimensional CBCT display allows images to be viewed from three different view with no superimposition.[7] Some studies utilize CBCT to evaluate osteoporosis, especially in the mental foramen region as a stable anatomic point.[8]

***Corresponding author:**
Silviana Farrah Diba
Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Universitas Gadjah Mada, Yogyakarta, Indonesia.
E-mail: silviana.farrahdiba@ugm.ac.id

Trabecular structure parameters on CBCT are highly correlated with (μCT) which observed in synthetic bone.[5] It is indicates that CBCT have a potential role through microstructural bone quality analysis as an alternative examinations in addition to examining bone quality through clinical laboratories.

Clinical laboratory examination of bone quality consists both of formation and resorption markers according to the bone turnover process. IOF recommend Beta crosslaps (β-CTx) as a bone resorption marker in study about osteoporosis, fracture risk, or treatment evaluation. Beta crosslaps is a fragment of type 1 collagen which is one of the most sensitive bone resorption markers.[9] An increase in the event of bone resorption is followed by an increase in the value of β-CTx in nano gram/ ml (ng/ml) as well.[10]

Some previous studies used CBCT radiographs of the jaw bone to assess bone quality in both cortical and trabecular but none has been associated with clinical laboratory examinations.[5,11,12] Bone density examination studies using CBCT have been carried out but in of 10-35 years old subjects.[13] So the purpose of this study was to analyze β-CTx and bone trabecular parameters on CBCT radiographs of menopausal women.

Materials and methods

A total of 17 healthy menopausal women aged between 55-79 years (mean = 65.4, SD = 7.3) conducted CBCT examinations in the Radiology Department of UNPAD dental hospital based on the referring dentist. The exclusion criteria specified are menopausal female patients who consume drugs or suffer from systemic diseases associated with bone metabolism such as diabetes, hyperparathyroidsm, hypoparathyroidsm. Patients who agreed to participate in this study were asked to sign an informed consent. This research has been approved by the ethics commission of the Universitas Padjadjaran Indonesia (No. 941/ UN6.KEP/ EC/ 2018).

Laboratory tests for β-CTx were performed using the Electrochemiluminescence Immunoassay (ECLIA) method at Elecsys 2010 (Roche Diagnostic, USA) according to manufacturer's procedure. The patient was asked to fast for 12 hours before blood sampling procedure.[14]

Region of interest (ROI) trabecular analysis

CBCT Picasso-Trio E-Woo Technology (Gyeonggi-do, Republic of Korea) was used in this study with the following spesification: field of view (FOV) 8 x 8 cm, 6 mA, 75 kVp, 0.202 x 0.202 x 0.202 mm voxel so that it can display the entire mandibular body. Image reconstruction was carried out using EzImplant Basic software (3-D image viewer) for subsequent determination of ROI. In axial view, the sagittal axis was directed parallel to the buccal and lingual cortical mandible. The coronal axis was directed to the mental foramen as far as it clearly visible on the coronal view. In coronal view, axis is positioned so that the orifice of mental foramen is clearly visible (figure 1). A 3 x 3 mm ROI is positioned between the inferior border of the mental foramen and the superior margin of mandible cortical. Seen from the axial view, a 3 x 3 mm ROI would form a 3-dimensional cuboidal volume consisting of 17 image slices. Each radiograph was taken bilateral cuboid ROI on the right and left so that there are 34 ROI to be analyzed.

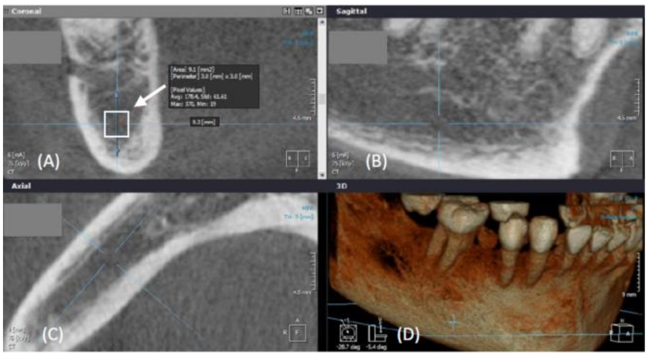

Figure 1. Multiplanar View of Sampling Location. A. Region of interest sized 3x3 mm was located between inferior margin of mental foramen and superior margin of mandibular cortical (white arrow). B. Region of interest location from (B) sagittal view, (C) axial view and (D) 3D image.

Radiograph data as axial slices were imported into BoneJ (1.51v, National Institutes of Health, Bethesda, USA). Image sequence of ROI opened in BoneJ and then applied the optimized threshold to distinguish between images of bone and bone marrow also determine the level of minimal connectivity. Three bone trabecular structure parameters which assessed were BV/TV, Tb.Th., and Tb.Sp. Bone volume fraction is the ratio of bone voxel to tissue in 1 ROI, calculated by voxel counting methods in percentage. Tb.Th analysis measures the average trabecular thickness while Tb. Sp measures the average distance between trabecules, both in millimeters.[5]

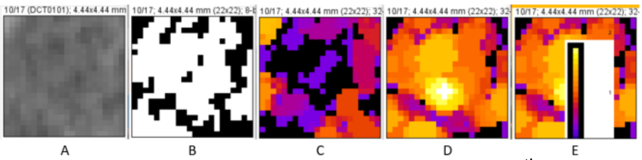

Figure 2. The image is taken on the 10th slice of a total of 17 slices in one region of interest, gathered from BoneJ. A. Raw image before tresholding process. B. 'optimized threshold' converts trabecula into black and bone marrow into white. C. Trabecular thickness measured in areas other than black, D. Trabecular separation measured in areas other than black. E. Color scale from the thinnest (purple) to the thickest (yellow).

Statistical analysis

Normality and Pearson correlation test were performed using SPSS 16 (SPSS Inc, Chicago, USA) for Windows. Pearson correlation test was conducted to observed whether any correlation between β-CTx and each trabecular bone parameter on mandibular CBCT radiographs of menopausal women. The correlation coefficient value gets stronger when it approaches 1 and gets weaker when it approaches 0. Significance value less than 0.05 were considered statistically significant.

Results

Descriptive β-CTx and structural bone parameters data were presented in table 1. A total of 17 menopausal women with ages ranging from 55 to 79 years. The average β-CTx value was 0.475 ng/ml while the average of BV/TV , Tb.Th, and Tb.Sp were 0.410%, 1.122 mm and 0.891 mm, respectively.

The correlation between β-CTx and each bone trabecular parameter were shown in table 2 and clarified in Figure 3 linear graph. There were no significant correlation (p> 0.05) between β-CTx and BV/TV (p= 0.150) and Tb.Th (p= 0.197). Both showed a weak correlation, negative for BV/TV (r = -0.252) and positive for Tb.Th (r = 0.227). there was a significant positive correlation between β-CTx and Tb. Sp (r = 0.452, p <0.05).

	Age	β-CTx (ng/ml)	BV/ TV (%)	Tb.Th (mm)	Tb.Sp (mm)
Mean	65.4	0.475	0.410	1.122	0.891
SD	7.3	0.177	0.083	0.283	0.235
N	17	17	17	17	17

Table 1. Mean and standard deviation (SD) of β-CTx and bone trabecular parameters.
BV/TV: Bone Volume/ Tissue Volume, Tb.Th: trabecular thickness, Tb.Sp: trabecular separation.

Bone Turnover Marker	N	BV/TV		Tb. Th		Tb. Sp	
		Pearson correlation (r)	p	Pearson correlation (r)	p	Pearson correlation (r)	p
β-CTx	34	-0.252	0.150	0.227	0.197	0.452	0.007*

Table 2. Pearson correlation between β-CTx and BV/TV, Tb.Th, Tb.Sp respectively.
*p <0.05, BV/TV: Bone Volume/ Tissue Volume, Tb.Th: trabecular thickness, Tb.Sp: trabecular separation.

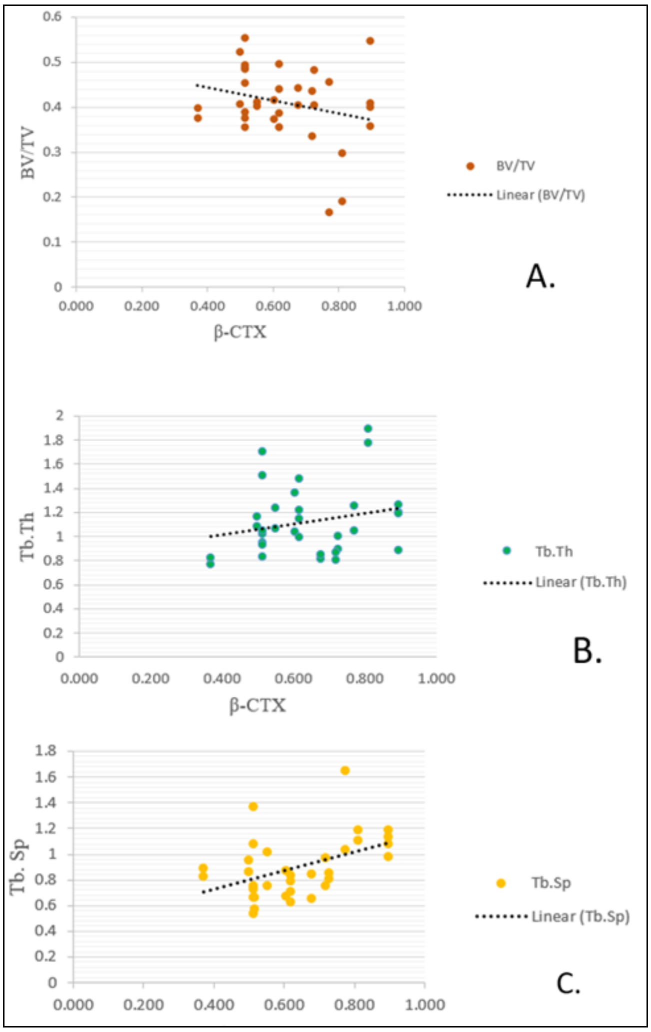

Figure 3. Linear correlation graph between β-CTx and (a) BV/TV, (b) Tb.Th, (c) Tb.Sp respectively.

Discussion

This study investigated the correlation analysis between β-CTx and mandibular trabecular structural parameters of menopausal women. Bone density did not undergo many changes in the group of young adults aged of 25-35 years old but then began to decline at the aged of 40-49 years.[13] Estrogen deficiency increases the bone resorption process and slowly changes the trabecular architecture from plate-like to rod-like. Bone mass decrease would increases the future risk of fracture in postmenopausal women so that early detection is needed to prevent fractures due to osteoporosis.[12]

Bone trabeculae have a high bone turnover rate and blood supply. Besides, most fractures also occur in this part so it is important to assess trabecular bone structure.[15,16] Evaluation of bone microstructure parameter analysis through trabeculae is important to predict bone strength and fracture risk.[3] Compared with cortical bone, trabeculae is more sensitive to detect bone metabolic changes thus providing relevant information related to early detection of bone quality and treatment evaluation.[11] There are several parameters for quantitative trabecular architecture counting but in this study only used three measurement parameters namely BV/TV, Tb.Th, and Tb.Sp. Those three variables are a minimum set that must be included in the measurement of trabecular morphometry also often used by researchers.[17] The selection of ROI in this study was trabecular between the mentale foramen and cortical bone so that the structural analysis was completely carried out on the trabecula without any cortical involvment.

CBCT is popularly used in dentistry especially for disease diagnosing with its advantages of 3-dimensional image presentation in more affordable price than conventional CT.[11] CBCT identify bone as a homogeneous object and does not have porosity by using grayscale values to assess bone density.[5] The measurement of microstructural parameters of bone trabecular using CBCT can be used as a reference for practical dentists in analyzing jaw structure in menopausal women. In this study analysis of trabecular structural parameters from CBCT radiographs was processed using BoneJ. BoneJ is a plugins from ImageJ with its advantages include being validated for bone morphometry software, designed to measure bone geometry, and can be applied in image sequences such as CBCT and μCT.[18]

Based on the analysis of the trabecular structure that has been carried out, it was found that there was no significant correlations between β-CTx with BV/TV and Tb.Th even though their correlation is weak. It is indicate that BV/TV and Tb.Th parameters have low sensitivity to be correlated with β-CTx in menopausal women. β-CTx level is negatively correlated with BV/TV which means that the value of β-CTx increases, the percentage of BV/TV bone would decreases as in figure 3. This finding is in line with a study conducted by of Yingling et al. using ovariectomy rats as a postmenopausal model. Increased bone resorption is indicated by increased β-CTx levels accompanied by a decrease in BV / TV. The percentage of BV/TV can also decrease because of the wide trabecular (Tb.Sp) separation.[19] This unsignificant correlation is contrast to what was stated by Barngkgei[20] that BV/TV is the most correlated parameter compared to Tb.Sp. It might be because not all trabecular bone structure measurements using CBCT correlate strongly with gold standards.

Slightly different from the results of this study, correlation between β-CTx and Tb.Th is positive, which is the increase in trabecular thickness (Tb.Th) would increase β-CTx level as well. This is likely to occur because the CBCT that being used in this study has a large voxel size when scanning. As a result, thin trabeculae are not detected so that the size of Tb.Th is increasing.[5] Another factor that might influence is a partial volume effect (PVE). The binarization process will change the voxel into black (bone) and white (marrow) depending on the gray value. Voxel with gray value between bone and marrow values is difficult to predict, wether they will appear as bone or marrow in the image after the threshold process. Large voxel size affected by PVE causes trabeculae become thicker or thin trabeculae will loss.[2]

As age increases especially in postmenopausal women, BV/TV and Tb.Th tend to decrease while Tb.Sp is increase, seen in the mandibular condyle through CBCT. These changes indicate a decrease in bone quality related to age, especially postmenopausal women due to the effect of estrogen hormones deficiency.[12] In osteoporotic women, trabecular width decrease occur due to thinning and loss of inter-trabecular connectivity.[19]

There is a positive significant correlation between β-CTx and Tb.Sp so that a wider Tb.Sp will increases β-CTx level (figure 3). It means that Tb.Sp as a microstructural parameter is more sensitive in detecting bone resorption or the presence of bone loss through CBCT in menopausal women associated with β-CTx. Bone loss is identical to a wider space between the trabeculae or Tb.Sp.[10]

Conclusions

The shortcoming of this study include the limited number of samples, limited size of ROI and nutritional variables that are negligible. From this study we can conclude that the increase of β-CTx is not always followed by a decrease of BV/TV percentage nor Tb.Th width associated with a weak correlation with both trabecular parameters. β-CTx increases was followed by the size of Tb. Sp which is also become wider. The parameter Tb.Sp is the most correlated parameter among the three trabecular structural parameters studied.

Declaration of Interest

The authors have nothing to disclose.

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