Use of digital panoramic radiographs as a screening tool for diagnosis of osteoporosis in Thai postmenopausal women

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A Thesis Submitted in Partial Fulfillment of the Requirements
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การใช้ภาพรังสีปริทรรศน์ดิจิตอลเป็นเครื่องมือในการตรวจคัดกรองโรคกระดูกพรุนในผู้หญิงไทยวัยหมดประจำเดือน

ว่าที่ ร.อ.หญิงเนตณฎา จงเรืองศรี

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เนตณฎา จงเรืองศรี :

การใช้ภาพรังสีปริทรรศน์ดิจิตอลเป็นเครื่องมือในการตรวจคัดกรองโรคกระดูกพรุนในผู้หญิงไทยวัยหมดประจำเดือน. (Use of digital panoramic radiographs as a screening tool for diagnosis of osteoporosis in Thai postmenopausal women) อ.ที่ปรึกษาหลัก : รศ. ทพ. ดร.พรชัย จันศิษย์ยานนท์, อ.ที่ปรึกษาร่วม : อ.ทญ. ดร.วรรณาภรณ์ ชื่นชมพูนุท

วัตถุประสงค์: เพื่อหาความสัมพันธ์ของดัชนีจากภาพรังสีปริทรรศน์ และโรคกระดูกพรุน รวมถึงหาว่าภาพรังสีปริทรรศน์สามารถใช้เป็นเครื่องมือคัดกรองโรคกระดูกพรุนในผู้หญิงไทยวัยหมดประจำเดือนได้หรือไม่ *วิธีดำเนินการวิจัย*: งานศึกษาแบบตัดขวางในผู้หญิงไทยวัยหมดประจำเดือนจำนวน 60 คนทั้งที่เป็นและไม่เป็นโรคกระดูกพรุน โดยผู้เข้าร่วมงานวิจัยได้ถูกแบ่งเป็น 3 กลุ่มกลุ่มละ 20 คน ตามการวินิจฉัยโรค โดยแบ่งเป็น ปกติ,กระดูกบาง และเป็นโรคกระดูกพรุน ซึ่งวินิจฉัยจากการตรวจความหนาแน่นของมวลกระดูก (BMD) แบบใช้รังสีเอกซ์ชนิดสองพลังงาน (Dual Energy. X-ray Absorptiometry, DXA) การวัดค่าดัชนีจากภาพรังสีปริทรรศน์จะวัด 2 ดัชนี คือ Mental index (MI) และ Mandibular cortical index (MCI) และใช้การวิเคราะห์สหสัมพันธ์แบบเพียร์สัน เพื่อหาความสัมพันธ์ของ MI, MCI และ BMD และใช้ Receiver Operating Characteristic curve (ROC curve) เพื่อหาความสามารถในการแยกโรค ความสามารถในการทำนายโรค ของ MCI และ MI รวมถึงหาจุดตัดของค่า MI ในการทำนายโรคกระดูกพรุน โดยมีค่านัยสำคัญทางสถิติที่ P=0.05 *ผลการวิจัย*: MCI มีความแตกต่างอย่างมีนัยสำคัญทางสถิติระหว่าง 3 กลุ่ม มีความสัมพันธ์กันระหว่างดัชนีจากภาพรังสีปริทรรศน์และค่าความหนาแน่นของมวลกระดูกทั้งในบริเวณกระดูกสะโพกและกระดูกสันหลัง โดยพบว่า MI มีความสัมพันธ์เป็นเชิงบวกกับความหนาแน่นของมวลกระดูกทั้ง 3 ตำแหน่งดังต่อไปนี้ กระดูกสันหลังส่วนเอว r= 0.566, ส่วนคอของกระดูกสะโพก r=0.554 และส่วนสะโพก r=0.524 สำหรับ MCI มีความสัมพันธ์เป็นเชิงลบกับความหนาแน่นของมวลกระดูกทั้ง 3 ตำแหน่ง ดังต่อไปนี้ กระดูกสันหลังส่วนเอว r= -0.514, ส่วนคอของกระดูกสะโพก r=-0.507 และส่วนสะโพก r=-0.513 ค่าตำแหน่งจุดตัดของ MI ที่เหมาะสมในการวินิจฉัยภาวะความหนาแน่นของมวลกระดูกต่ำ (กลุ่มกระดูกบางและกระดูกพรุน) คือ 3.9 มม. และสำหรับการวินิจฉัยโรคกระดูกพรุนอยู่ที่ 3.8 มม. *สรุป*: จากผลการศึกษาในงานวิจัยนี้พบว่า MI และ MCI สามารถใช้เป็นเครื่องมือคัดกรองโรคกระดูกพรุนในผู้หญิงไทยวัยหมดประจำเดือนได้

สาขาวิชา	ศัลยศาสตร์ช่องปากและแม็กซิลโลเฟเชียล	ลายมือชื่อนิสิต .....
ปีการศึกษา	2562	ลายมือชื่อ อ.ที่ปรึกษาหลัก .....
		ลายมือชื่อ อ.ที่ปรึกษาร่วม .....

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KEYWORD: Panoramic radiographs, Osteoporosis, Bone mineral density, Postmenopause, Radiographic indices

Net-nada Chongruangsri : Use of digital panoramic radiographs as a screening tool for diagnosis of osteoporosis in Thai postmenopausal women. Advisor: Assoc. Prof. Pornchai Jansisyanont, D.D.S., M.Sc., Ph.D. Co-advisor: VANNAPORN CHUENCHOMPOONUT, D.D.S., Ph.D.

Purpose: To investigate the correlation between panoramic radiographic indices and osteoporosis, and to determine whether digital panoramic radiographs could be used as a screening tool for the diagnosis of osteoporosis in Thai postmenopausal women.

Materials and Methods: A cross-sectional study of sixty Thai postmenopausal women with and without osteoporosis. The subjects were divided into three groups based on diagnosis by dual-energy X-ray absorptiometry (DXA): normal, osteopenia, and osteoporosis equally in each group. The panoramic radiographic indices measured were mental index (MI) and mandibular cortical index (MCI). Pearson's correlation test was performed to analyze any correlation between MI, MCI, and BMD (Bone Mineral Density) T-scores. To determine the ability of the indices to classify disease and investigate the cut-off value of MI for diagnosis of osteoporosis, the receiver operating characteristic analysis was performed. The P value was set at 0.05.

Results: The MCI was significantly different in the 3 different groups ($p<0.001$). There were correlations between the panoramic radiographic indices and BMD in the regions of the hip bone and the lumbar spine. MI was positively correlated with BMDs: lumbar spine: r=0.566, femoral neck: r= 0.554, and total hip: r= 0.524 ($p<0.001$). The MCI was negatively correlated with BMDs: lumbar spine: r= -0.514, femoral neck: r= -0.507, total hip: r=-0.513 ($p<0.001$). The cut-off value of MI for the reduced skeletal bone mineral density groups (both osteopenia and osteoporosis groups) was 3.9 mm and for the diagnosis of osteoporosis was 3.8 mm.

Conclusion: The results of this study suggest that MI and MCI can be used as a screening tool for diagnosis of osteoporosis in postmenopausal women.

Field of Study:	Oral and Maxillofacial Surgery	Student's Signature .....
Academic Year:	2019	Advisor's Signature .....
		Co-advisor's Signature .....

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Net-nada Chongruangsri

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Chapter 1 Introduction

Background and rationale

Osteoporosis is a disease which has low bone mass and structural weakening of bone tissue. Osteoporosis will effect to bone fragility and increases risk of fractures. The fractures often happen in hip, spine, and wrist. Osteoporosis may not been known until the bones become fragile. When their bones are fragile, the minor accident or fall causes a hip to fracture or a vertebra to breakdown [1].

The diagnosis of osteoporotic is defined when T-score of skeletal bone mass density (BMD) is 2.5 standard deviations under the average peak bone density. The average peak bone density came from BMD of the early adults matched by gender and ethnicity [2] [3]. Hence, detection of osteoporosis, evaluation of bone quantity, and identification of fracture risk are important goals when assessing patients for osteoporosis [4] [5].

Numerous techniques are used for BMD evaluation. For now, the gold standard method for BMD evaluation is Dual x-ray absorptiometry (DXA) [6].

The prevalence of the disease as defined by low BMD increases with age. Hence, mostly osteoporosis will be seen in postmenopausal women. There is the international guidelines suggest that female who over sixty-five years old should achieve bone densitometry and female with related risk factors who had earlier in postmenopausal stage [7].

Although elderly population usually visit their doctor for annual physical check-up but mostly do not include bone densitometry. Meanwhile, the dentist is a doctor who older

patients regularly visit. Furthermore, dental radiographic images are generally use for these patients.

For initial diagnosis as well as treatment planning, the dentists regularly requested panoramic radiograph. Numerous evaluation methods have been suggested for the identification and assessment of bone alterations in panoramic radiograph for predicting osteoporosis [8]. Klemetti et al. [9] investigated the relationship between mandibular cortical morphology and low BMD. This index is called the Klemetti index (KI) or mandibular cortical index (MCI). This index is evaluated the mandibular cortical bone below the mental foramen region for observing resorptive changes of cortical bone. The mandibular cortical bone in osteoporotic patients showed a lessened thickness and more porous at the inferior border because of higher resorptive activity [10].

Accordingly, there were several studies that investigated the correlation of digital panoramic radiograph and BMD score to identify patients with osteoporosis. Some studies investigated only in the osteoporosis group [11] [12] or osteopenia and osteoporosis[13] that did not compare the indices to the normal group. There was a study classified patients as low BMD if they were osteopenia or osteoporosis and all other patients were classified as normal[14]. Nevertheless, there were studies that compared the panoramic radiographic indices in osteoporosis, osteopenia and normal but did not clarify that their subjects were already treated osteoporosis or not[15] [16]. Moreover, until now, previous studies were developed in Caucasian[9] [17] [18] [19] and other Asian [12, 20] [21] [22] [23] such as Korean, Japanese, Indian but have not been reported in Thai population. This study assessed the correlation between panoramic radiographic indices and BMD score in Thai postmenopausal women and considered to define whether panoramic radiograph would be useful in diagnosis of osteoporosis.

Research question

Does the panoramic radiograph can be a screeningl tool for diagnosis of osteoporosis in Thai postmenopausal women?

Objective

To investigate the correlation between panoramic radiographic indices and BMD score in Thai postmenopausal women.

Research hypothesis

There are correlation between panoramic radiographic indices and BMD score in Thai postmenopausal women.

Research design

A cross-sectional study

Expected benefits and application

Panoramic radiograph will be one of a method for screening osteoporosis in Thai postmenopausal women

Conceptual framework

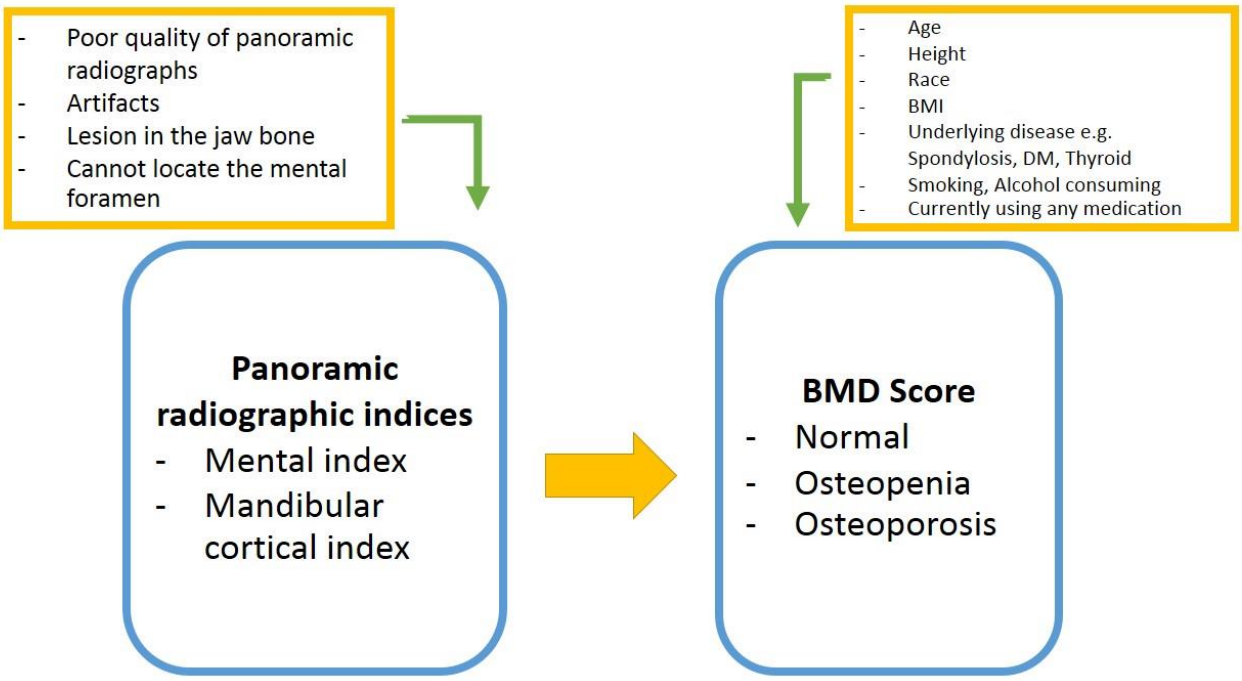

Figure 1 Conceptual framework

Chapter2 Review of literature

Osteoporosis

Osteoporosis is a disease that has low bone mass, weakening of bone tissue, and disruption of bone microarchitecture. It can increased the risk of bone fractures[2]. Osteoporosis one of the major public health problem. Osteoporosis affects a massive quantity of population, of both genders and all ethnicities. The prevalence of osteoporosis will rise when the ages increase. The fractures occur after osteoporosis can cause significant secondary health problems and even death. [24]

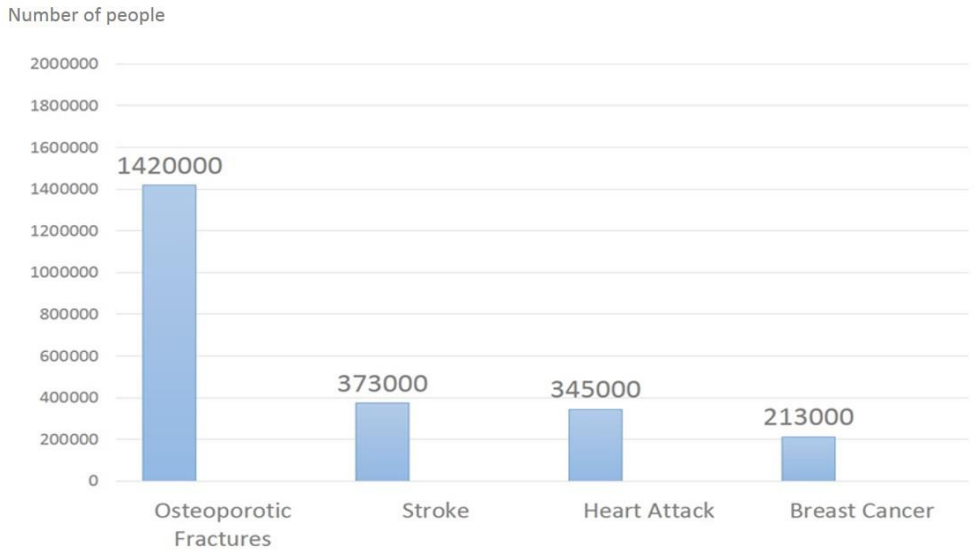

Figure 2 Showed comparative incidences of osteoporotic fractures, strokes, heart attacks, and breast cancer in women in the United States.

Adapted from Watts NB et al[25]

Osteoporosis causes more than 8.9 million fractures yearly. In each 3 seconds, osteoporotic fracture was found worldwide. Following the hip fractures, about 20% of patients dead in the first year, mostly because of their own earlier medical conditions. The research showed that less than 1/2 of patients who survived the hip fracture regained their prior function[26]. European and Americans people accounted for 51% of all these fractures, while most of the remainder happened in the Western Pacific region and Southeast Asia. There was a study in European population showed that the disability due to osteoporosis was greater than that caused by cancers (with the exception of lung cancer) and was comparable or larger than that lost to a multiplicity of chronic non-transmitted diseases [27].

Osteoporosis was a major health problem in Asia as well. There was a multicenter study which document and compare the incidence of hip fracture in four Asian countries. The study shown that the prevalence of hip fracture had risen when there was more economic development. The adjusted rates in Hong Kong and Singapore were almost identical to those seen in American Caucasians (at 19 per 10,000). The rates in Thailand was 2/3 and the rates in Malaysia was 1/2 of the Hong Kong rate [28].

Osteoporosis was also a significant health problem in Thailand because of increasing of older population. There was a study in 2008 showed that the Thai males had a life expectancy of 69.5 years and 76.3 for females [29]. The resent study showed that the life expectancy of Thais had increased to 78.4 years for females and 71.6 years for males[30]. There was a study that reviews of the incidence of osteoporosis[31] indicated 19–21% of lumbar spine osteoporosis and 11–13% of femoral neck osteoporosis in females aged more than 40 years old in Thailand. The most common and most clinical complications osteoporotic fracture was hip. There was a study during 2012-2013 showed an escalation in post hip fracture death rates. Throughout the first year after hip fracture, the average death rate was about 9 times higher than that of the general population[32].

Osteoporosis happens when the resorption rate of bone is more than the formation rate. Bone remodeling is a process which has deletion of older bone to replace with newly formed bone. It is used to prevent macrofractures and repair microfractures. Bone mass reaches its peak at puberty. It is called peak bone mass (PBM). The hereditary factors, healthiness, nutrition, hormonal status, gender, and physical activity are the factors that determine PBM[33].

The reason why osteoporosis is common in female at postmenopausal stage was menopause and progressing age causes a discrepancy between resorption and formation rates of bone. When resorption becomes further than formation, the possibility of fracture will increase. The significantly reduced bone mass happens when individual trabecular plates of bone are lost lead to a deteriorated structure. This process increases possibility of fracture which is intensified by other aging-related falloffs in functioning [33].

Although, the fixed risk factors of osteoporosis are age 50 and older, female, previous fracture or family history of fracture, menopause, long term glucocorticoid, and rheumatoid arthritis. The study of ethnicity and osteoporosis reported that osteoporosis is more common in Caucasian and Asian populations. Fractures occur when damaged bone is overloaded especially by falls[34].

The measurement of bone mineral density (BMD) is recognized the diagnosis of osteoporosis. BMD is gained by means of dual X-ray absorptiometry (DXA). The BMD is expressed in absolute terms of grams of mineral (primarily, as g/cm^2 of calcium) per square centimeter of the scanned bone. The BMD measurements are usually done in the hip and spine regions. They used to found or approve the diagnosis of osteoporosis, predict future fracture possibility and observe patients. The difference between the patient's BMD and mean BMD of young females aged in the range of 20–29 years which divided by the standard deviation (SD) of the reference population earnings the T-score. As defined by the World Health Organization (WHO) criteria. The osteoporosis is present

when BMD is 2.5 SD or more below the average value for young healthy women (a T-score of < -2.5 SD). Osteopenia or Low bone mass is defined when a T-score is between -1 and -2.5 SD. Severe or established osteoporosis has been defined in the presence of one or more fractures (Table 1) [27].

Table 1 Represented WHO definitions of osteoporosis based on BMD [27]

Diagnosis	T-score
Normal	at -1.0 and above
Low bone mass (Osteopenia)	between -1.0 and -2.5
Osteoporosis	at or below -2.5
Severe or established osteoporosis	at or below -2.5 with one or more fractures

Panoramic radiographic image and Osteoporosis

Dental panoramic radiograph produces an image of maxilla, mandible and dentitions on one radiography that has simple process and less time consuming.

The weighted dose equivalent from a panoramic examination was calculated to be 80 μSv corresponding to a lifetime risk of fatal cancer of 1.3×10^{-6}. There had a change of the design of panoramic radiograph machine over the same period of time. For reducing the radiation doses, rare earth film have becomes more commonly used [18]. White et al. calculated the average effective dose for a panoramic examination to be 6.7 μSV. This number is associated with an estimated risk of deadly malignancy of 0.21×10^{-6} [35].

Although the dose of panoramic radiograph is low and reasonable to use in screening, the panoramic image had several superimpositions and distortions. It may be worsened by procedural errors in processing the image. Moreover, one of the interpretation challenges is the panoramic radiograph contains various anatomic structures outside of the jawbones. The key to successful interpretation is to understanding the anatomy of head and neck and how it is represented in the panoramic radiograph.

There was a study provides the steps for an approach to analyzing the panoramic radiograph:

1. Assess the boundary and corners of the image

• The structures in this area may contain: – orbits – articular processes of the temporal bones (at the temporomandibular joints) – cervical spine – styloid processes – pharynx – hyoid bone.

2. Observe the outer cortices of the mandible

• Trace the periphery of the bone starting at one spot and completing a circuit which includes: – anterior and posterior rami – coronoid processes – condyles and condylar necks – inferior border.

• Look for continuity and evenness of the cortices.

3. Observe the cortices of the maxilla

• This includes the posterior and medial walls and floor of each maxillary sinus.

• While examining the posterior wall of the sinus, also look at the: – zygomatic process of the maxilla – pterygomaxillary fissure

4. Observe the zygomatic bones and arches

• Follow where they extend posteriorly from the zygomatic processes of the maxilla to the temporal bones.

5. Evaluate the internal density of the maxillary sinuses

• Compare left and right sides.

• Opacification is most commonly a sign of inflammatory disease but could be a sign of more serious pathology.

6. Evaluate the structures of the nasal cavity and the palates

• Observe the floor of nose or hard palate and conchae which located horizontally along left and right sides of the radiograph.

• In the midline, nasal septum should be noticed.

• The soft palate can be seen on both sides extending from the posterior aspect of the hard palate and into the oropharynx.

7. Observe the bone shape of both jaws

• The pattern and density of the trabeculae will be evaluated

• Evaluated the dimensions, location, cortication and evenness of the: inferior alveolar nerve canals – mandibular foramina – mental foramina[36].

The widespread use, practicality, and low cost of dental panoramic radiograph are great conceivable of being a screening tool. The healthiness of mandible can be observed from a panoramic radiograph. The possible role of panoramic radiograph is can be help identifying especially high-risk postmenopausal women [35].

The changes of mandible due to the reduction of BMD have been examined in several studies. One of the most cited index for mandible was mandibular cortical index (MCI) by Klemetti et al. Klemetti et al. [9] investigated the correlation between mandibular cortical morphology and skeletal low BMD in 1994. This index qualitatively classifies the mandibular cortex distally to the mental foramen.

This index categorized mandibular cortex into 3 category:

C1 is defined when the endosteal margin is even and sharp.

C2 is defined when the endosteal margin shows lacunar resorption or cortical remains on one or both sides.

C3 is defined when the cortical layer is clearly porous, with heavy endosteal cortical remains (Fig.3).

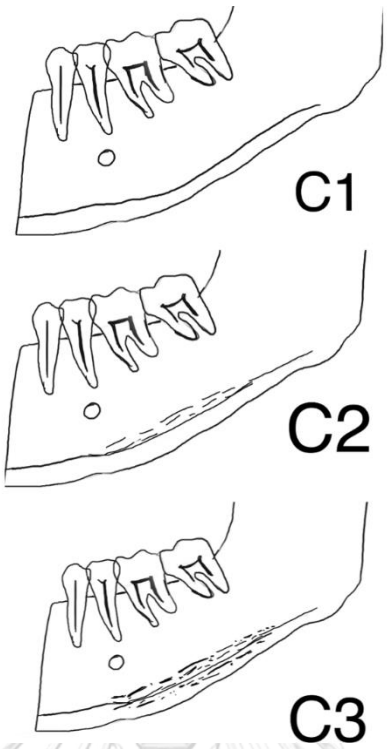

Figure 3 Showed the classification of mandibular cortex (C1-3) based on changes in inferior cortex on panoramic x-ray images. (C1, when the endosteal margin is even and sharp; C2, when the endosteal margin presents lacunar resorption or cortical residues on one or both sides; and C3, when the cortical layer is clearly porous, with heavy endosteal cortical residues)

There are many studies supported that MCI could be used for detecting patients with low BMD. Gulsahi et al.[37] found that the thickness and patterns of intracortical resorption of the mandible, the validity of an MCI was noticed. They demonstrated that this index could be beneficial in screening for low bone mass or osteoporosis compared with BMD at the lumbar spine as evaluated by DXA. The study by Taguchi et al.[38] also suggested that MCI classification based on panoramic radiographs may be useful index for the diagnosis of osteoporosis. In accordance with the study by Horner and Devlin[10] which previously shown that mean mandibular bone density assessed by DXA has a significant relationship with the MCI. They found that the mandibles which categorized as

C3 having the lowest bone density. There was a study shown that MCI had significant relationship with lumbar spine BMD as measured with quantitative computed tomography (QCT) [4]. The method that practically useful should be reproducible. The study by Klemetti et al. [9], interobserver agreement of MCI was 98% which was highly repeatable. Taguchi et al. [38] found that MCI had overall agreement of 92% and kappa index of 0.86 for intraobserver performance.

And besides the mandibular cortical index, mental index was also most used. Mental index (MI) is a cortical width below the mental foramen. MI is measured by draw a line perpendicular to this tangent intersecting the inferior border of the mental foramen was constructed, along which mandibular cortical width was measured [20] (Fig. 4).

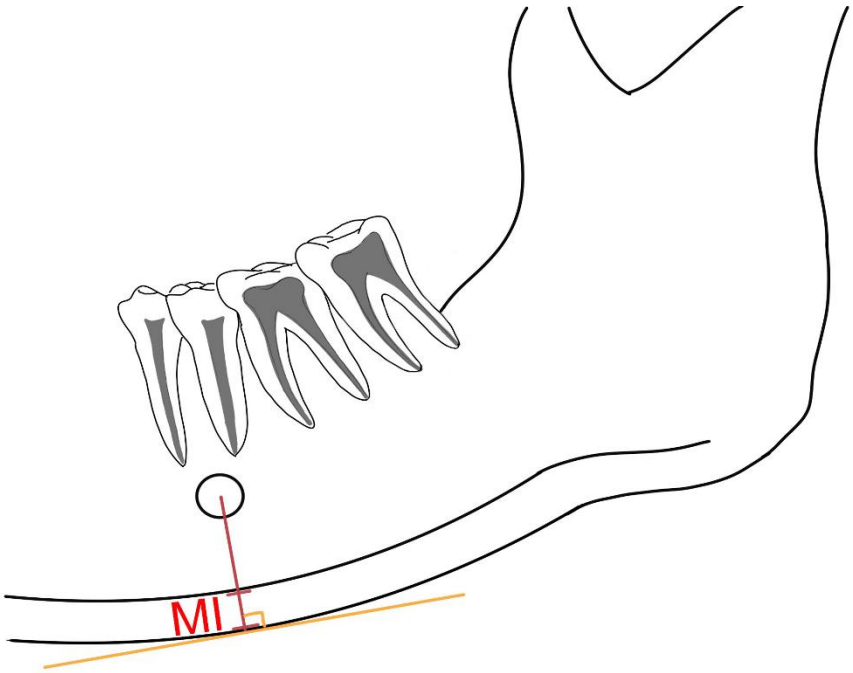

Figure 4 Represented the measurement of MI (Mental index) on panoramic radiograph.

There are also several studies support that MI could be used for detecting patients with low bone mineral density. Monsour et al. [15] found that there was a significant correlation between the MI and BMD. They mentioned that MI could be an accurate index for determining BMD in female with osteoporosis. Kim et al. [12] reported that MI had association with BMD and MI may be beneficial in osteoporosis predictors. There was also a study found that the ROC values of MI as an indicator of the occurrence of osteoporosis ranged between 0.80-8.87 which could realistically assumed that MI was a reliable indication [39].

In addition, several panoramic radiographic indices were used in many studies such as antegonial index (AI), gonial index (GI), mandibular cortical index (MCI), mental index (MI), panoramic mandibular index (PMI), and simple visual estimation (SVE). Antegonial index (AI) by Ledgerton et al. [40] as a measurement of cortical thickness in the

area anterior to the gonion at a point identified by extending a line of "bestfit" on the anterior border of the ascending ramus down to the lower border of the mandible (Fig. 5).

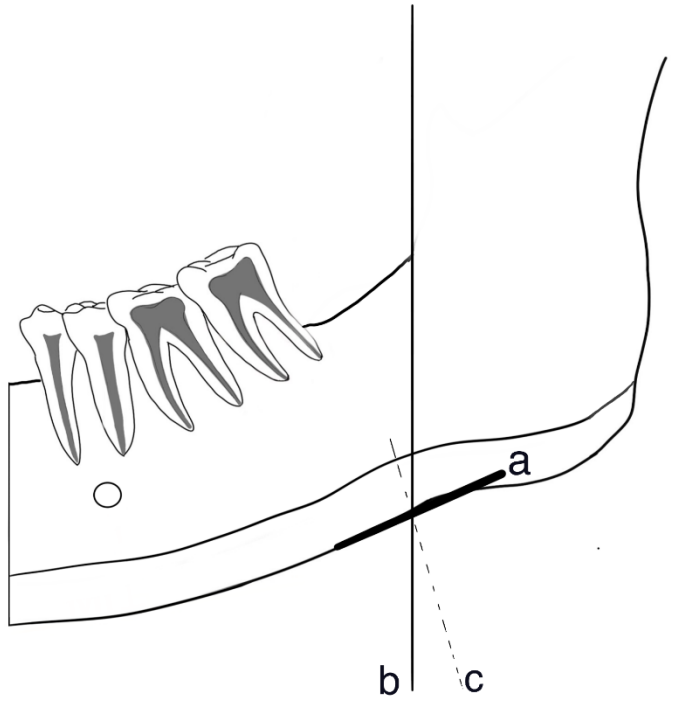

Figure 5 Antegonion index

The "best fit" straight line (b) was plotted along the anterior border of the ascending ramus and extended down to cross the mandibular lower border. The tangent to the lower border (a) was drawn and a perpendicular to the tangent plotted, dotted line (c). Measurement of antegonion cortical thickness (antegonion index) was made along this perpendicular[40].

According to the study by Leite et al. [17], they found that AI had poor replicability, and no significant differences among BMDs. Thus, they concluded that AI should not be used as a radiographic tool in diagnosis of osteoporosis and low bone density. This result was consistent with the study by Taguchi et al. [41] that AI was suggested had no beneficial because of problems related with repeatability and the accuracy.

Gonial index (GI) was found by Bras et al. [42] as the thickness of the mandibular angular cortex. Thickness of the mandibular angular cortex on the panoramic radiographs was measured. To determine the location of the gonion, a vertical tangent to the posterior border of ramus was drawn. The angle made by this line with the tangent to the lower mandibular border at mental foramen was divided. At a point of intersection of this bisector line with the angle of mandible, the thickness of angular cortex was measured (Fig.6).

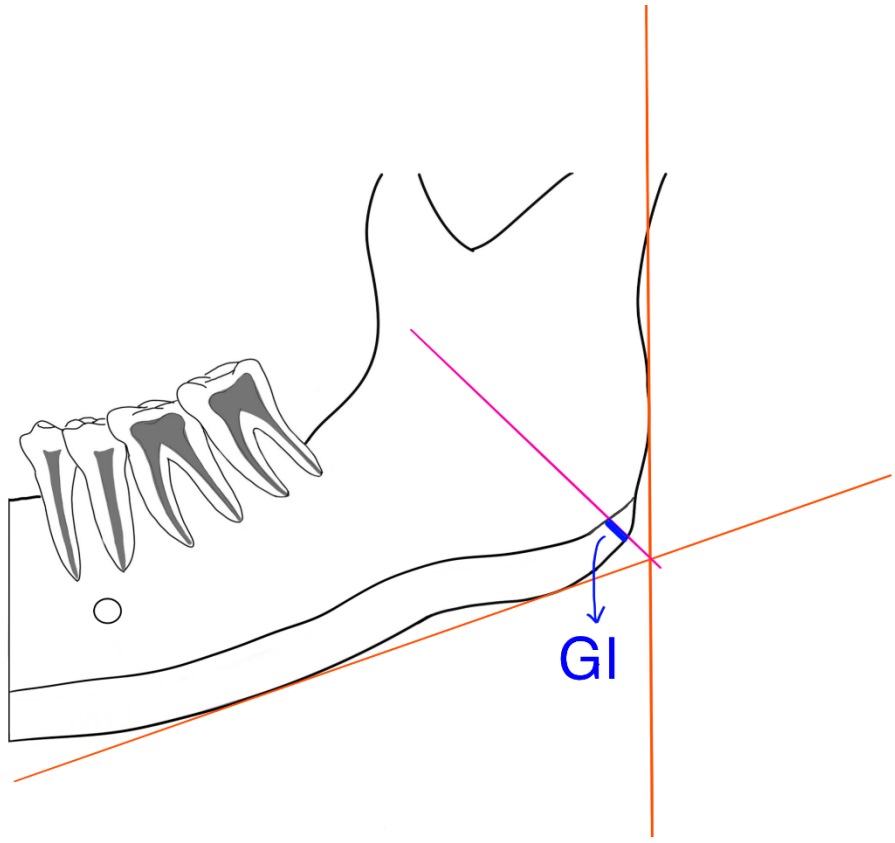

Figure 6 Gonial index (GI)

Ledgerton et al. [40] found that GI had very poor levels of precision, probably because of the moderately small proportions of cortical thickness in this area. They concluded that GI should not be reliable method of assessing bone mineral status. Similar to the study by Taguchi et al. [41], the precision of GI measurements was very poor due to the small dimension at the gonial region, unstable horizontal magnification, the site of measurement was unclear, and the occlusal force from masseter and medial pterygoid

muscles which attach to the angle of mandible may effect the measurement. They concluded that GI was not used for identifying osteoporosis in elderly.

Panoramic mandibular index (PMI) was first described by Benson et al. [43]. PMI is a ratio of thickness of mandibular cortex at mental foramen region and the length between inferior border of mental foramen to inferior border of the mandible (Fig.7).

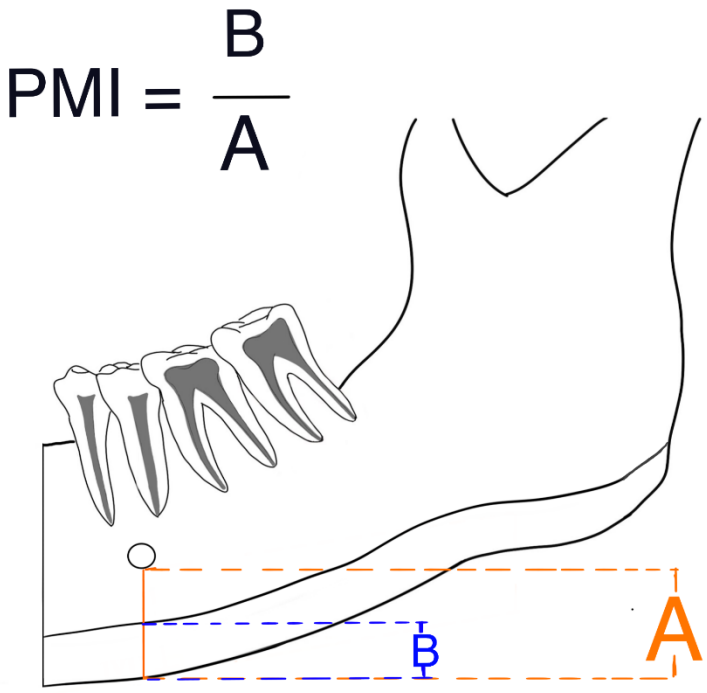

Figure 7 Diagram of the mandible illustrating measurement of PMI.
Line A: distance between inferior cortex of mental foramen and outer cortex of mandible.
Line B: distance of inferior border at mental foramen.

Some studies[9] [10] [44] suggested that PMI had no different benefits over MI in the role for BMD measurement of mandible. Watson et al. [45] found that there was no significant differences in the mean PMI between healthy and osteoporotic female. They suggested that PMI lacked of sensitivity for use as a screening tool for discovery of early osteoporosis. There was a study [46] also noted that there was no correlations of PMI and

DXA, so it should not be used as indicators of skeletal status and this index was more time-consuming and complicated than MCI which did not differ significantly in variables measured.

Simple visual estimation (SVE) is the index that classified qualitative of mandibular cortex in three categories. The categorizes are defined by simple visual estimations of inferior cortex thickness of mandible: normal, intermediate, and very thin [17]. Although, the study by Leite et al. [17] concluded that the most precise indices were the mental index, mandibular cortical index, and visual estimation of cortical width. Nevertheless, Lee et al. reported that the mean sensitivity of simple visual estimation in identifying females with skeletal low BMD was low. About ½ of the females in the study with low skeletal BMD were not recognized by the simple visual estimation because of overall low mean sensitivity[21].

Thus, according to the aim of this study, the indices were used in the present study had to be the most practical and reproducibility for screening. The present study decided to use one of the most sited indices for screening which are MCI and MI [47]. MI is a quantitative index, whereas MCI is a qualitative index.

Chapter 3 Materials and Methods

This study is a cross-sectional study evaluated the correlation of indices of 60 digital panoramic radiographs from Thai postmenopausal women and BMD scores at lumbar spine, femoral neck and total hip.

Ethical approval

This study was approved by the human research ethics committee of the Faculty of Dentistry, Chulalongkorn University (HREC-DCU 2019-055) and Police General Hospital IRB (Nq 262881/62), Bangkok, Thailand. All participants signed an informed consent agreement

Sample size calculation

Sample size estimation was perform by G*power version 3.1.9.2. The effect size (f) of 0.42 was calculated from previous study [48] with significance level (α) of 0.05 and power (1-β) of 0.8. The calculated samples were 57. However, in case for losing the data at any period of time, the total sample size in this study was 60 patients and allocated into three groups. Each group comprises of 20 patients.

F tests – ANOVA: Fixed effects, omnibus, one-way

Analysis: A priori: Compute required sample size

Input:	Effect size f	= 0.4228352
	α err prob	= 0.05
	Power (1−β err prob)	= 0.8
	Number of groups	= 3
Output:	Noncentrality parameter δ	= 10.1910076
	Critical f	= 3.1682460

Numeration df	=	2
Denomination df	=	54
Total sample size	=	57
Actual power	=	0.8000497

Methods

The subjects were postmenopausal women who came into Police General Hospital for performing bone densitometry tests for the first time. All BMD scans were conducted with Horizon® (Marlborough, MA, USA) DXA System by certified radiologist using standardized procedures and following protocols recommended by the manufacturer. The T-score was calculated and the diagnosis was based on WHO criteria. Osteoporosis was defined as a BMD T score of –2.5 or less, low bone mass (osteopenia) as a BMD T-score between –1 and –2.5 and normal as a BMD T-score above -1. All panoramic radiographs were taken at Faculty of Dentistry, Chulalongkorn University using Carestream Kodak 9000C (60-90 kVp, 2-10 mAs, 15.1 s).

ELIGIBILITY CRITERIA

The inclusion criteria were as follows:

1. Patient who is a female.
2. Patient who is healthy.
3. Patient who is in postmenopausal stage (no period for at least one year).
4. Panoramic radiograph displays adequate quality for locating the mental foramen.
5. The radiograph which has no bony pathology lesion at the mandible, hip or spine.

The exclusion criteria were as follows:

1. Patient who has uncontrolled or severe systemic condition such as cardiovascular disease, endocrine disorders, neoplastic disease, renal failure, rheumatoid arthritis, parathyroid, multiple myeloma or other metabolic bone diseases.
2. Patient who is smoking and/ or alcohol consuming.
3. Patient who has a history of radiation treatment or surgery in the head and neck region.
4. Patient who currently uses some medications such as steroid, chemotherapy, thyroid hormone and bisphosphonate or any antiresorptive and antianabolic drugs.
5. Patient who has lesion or prostheses at the hip area.
6. Patient who has vertebrae or hip fracture.
7. Patient who has previously jaw surgery and/or trauma to the mandible.
8. Any scan of BMD which is poor quality.

DATA COLLECTION

All subjects were divided into 3 groups based on diagnosis of osteoporosis: normal (n= 20), osteopenia (n= 20) and osteoporosis (n= 20). Ages, heights, weights, BMI, and BMD scores were recorded.

In this study was measured two panoramic radiographic indices, mental index (MI) and mandibular cortical index (MCI) by the main researcher under the close supervision of an experienced oral radiologist, using INFINITT® software (INFINITT Healthcare Co., Ltd. Ver. 3.0.11.3 BN8.2). MI was assessed by measuring the lower border mandibular cortical width in the mental foramen region on both sides of mandible. A line parallel to the long axis of the mandible and tangential to the inferior border of the

mandible was drawn. A line perpendicular to this tangent intersecting the inferior border of the mental foramen was constructed, along which mandibular cortical width was measured [20] (Fig 8). MCI was measured by detected mandibular cortical pattern on both sides of the mandible at a distal edge of the mental foramen. Subjects were classified into 3 groups according to the following classification of Klemetti [9]: C1= the endosteal margin is even and sharp, C2= the endosteal margin presents lacunar resorption or cortical residues, C3= the cortical layer is clearly porous, with heavy endosteal cortical residues (Fig 9).

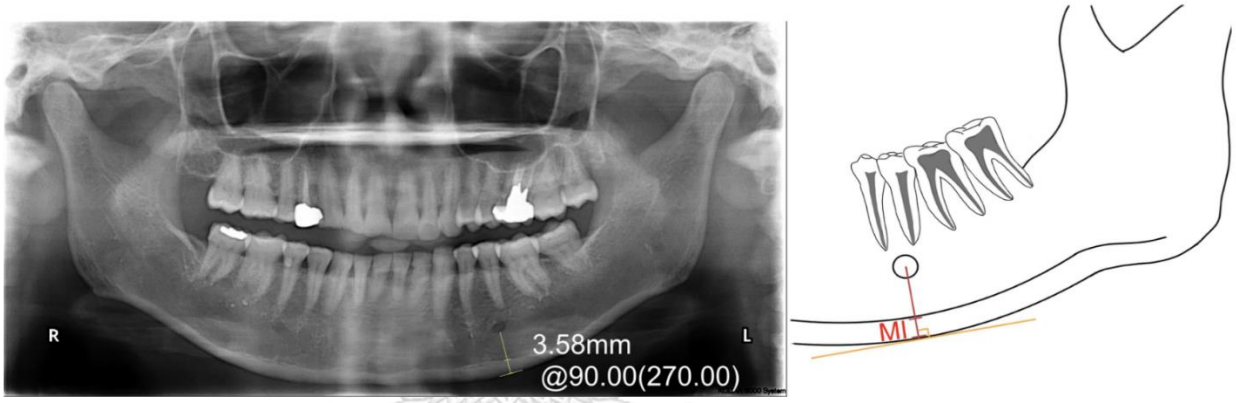

Figure 8 A panoramic radiograph showing MI measurement. A line parallel to the long axis of the mandible and tangential to the inferior border of the mandible was drawn. A line perpendicular to this tangent intersecting the inferior border of the mental foramen was constructed, along which mandibular cortical width was measured.

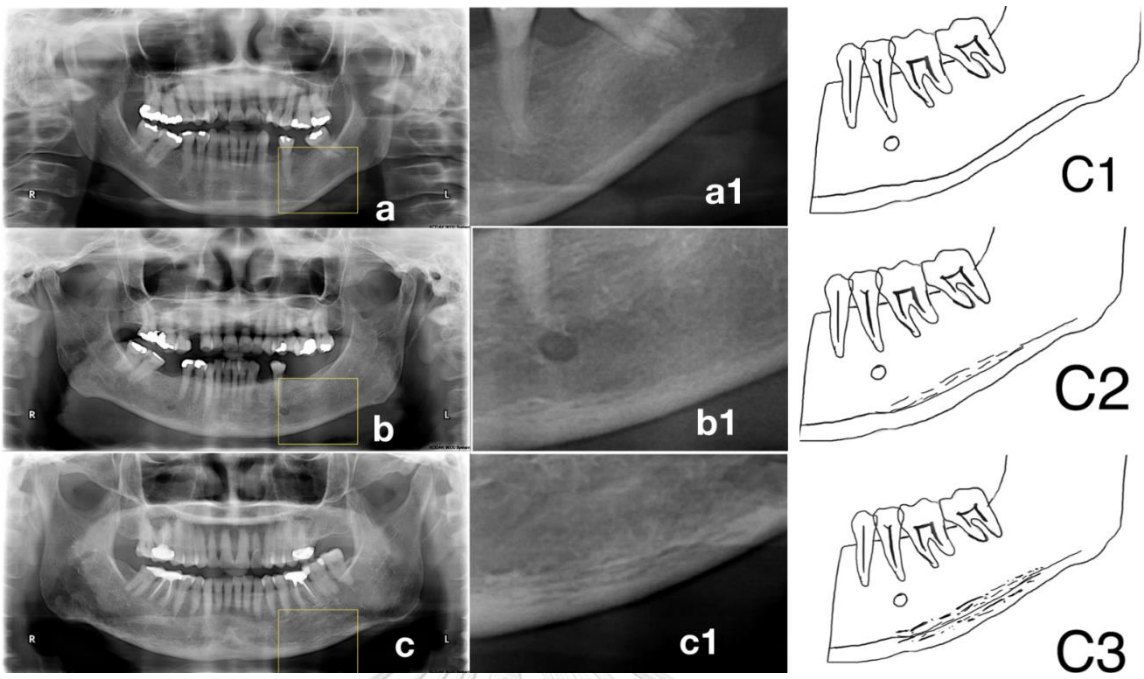

Figure 9 Example of radiographic appearance of mandibular cortical morphology classified by mandibular cortical index (MCI). a, C1: the endosteal margin is even and sharp, a1, magnification of C1 panoramic radiograph. b, C2= the endosteal margin presents lacunar resorption or cortical residues, b1, magnification of C2 panoramic radiograph, c, C3= the cortical layer is clearly porous, with heavy endosteal cortical residues, c1, magnification of C3 panoramic radiograph.

STATISTICAL ANALYSIS

The collected data were analyzed for the mean (±SD) and percentage. Each MI measurement was done twice on the right and the left side. The average value was calculated. MCI measurement was calculated both the right and the left side separately. Intraclass correlation coefficient (ICC) was used to quantify intraobserver agreements. The correlation between panoramic radiographic indices and BMDs was used Pearson's correlation analysis. One-way ANOVA test was used to determine statistically significant difference between MI and the osteoporosis group and the osteopenia and the normal group. The difference between MCI and the osteoporosis group and the osteopenia and the normal group was used Kruskal-Wallis test to determine statistically significant. The receiver operating characteristic (ROC) analysis was used to evaluate the ability of MI and MCI to diagnosis of osteoporosis or osteopenia. The optimal MI cut-off values for diagnosis of osteoporosis and osteopenia were determined by using Youden's index. All statistical analysis were conducted with SPSS statistic software (version 21 software SPSS Inc., Chicago, IL.). The statistical significance level of 5% was considered.

Chapter 4 Results

Intraobserver agreement

Intraclass correlation was done for measuring the reliability of measurement for data that has been collected as groups or sorted into groups. The intraclass correlation was also done to investigate that the measurements could be replicated. Intraclass correlation coefficient values for intraobserver agreement in this study were 0.988 and at 95% CI was 0.980-0.993 (Table2, 3).

Table 2 Intraclass Correlation Coefficient

	Intraclass Correlation[b]	95% Confidence Interval		F Test with True Value 0		
		Lower Bound	Upper Bound	Value	df1	df2
Single Measures	.976[a]	.961	.985	82.475	67	67
Average Measures	.988[c]	.980	.993	82.475	67	67

Table 3 Intraclass Correlation Coefficient

	F Test with True Value 0[b]
	Sig
Single Measures	.000[a]
Average Measures	.000[c]

Two-way mixed effects model where people effects were random and measures effects are fixed.

a. The estimator was the same, whether the interaction effect was present or not.

b. Type C intraclass correlation coefficients using a consistency definition-the between-measure variance was excluded from the denominator variance.

c. This estimate was computed assuming the interaction effect was absent, because it was not estimable otherwise.

Demographic Data

The study subjects' characteristic were shown in table4. The mean age of the subjects in this study was 58.62±10.03 (range 49-87). When divided by the diagnosis group, the mean age of the normal group was 56.95±5.89 (range 49-73), the osteopenia group was 64.9±9.06 (range 51-82), and the osteoporosis group was 69.75±10.4 (range 51-87) (Table 4). There were significant differences of ages between normal and osteopenia ($p= 0.014$), normal and osteoporosis ($p< 0.001$), but no significant difference between osteopenia and osteoporosis group.

The mean height of the subjects in this study was 156.37 cm (SD=6.23). The mean height of the normal group was 160.72 cm, the osteopenia group was 153.64 cm, and the osteoporosis group was 154.75 cm (Table 4). There were significant differences of height between normal and osteopenia ($p< 0.001$), normal and osteoporosis ($p= 0.003$), but no significant difference between osteopenia and osteoporosis group which was the same as the results of age and weight.

The mean weight of the subjects in this study was 58.62 kg (SD= 12.46). The osteoporosis group had the lowest mean weight which was 49.74 kg (Table 4). There were significant differences of weight between normal and osteopenia ($p< 0.001$), normal and osteoporosis ($p< 0.001$), but no significant difference between osteopenia and osteoporosis group.

The mean BMI of the subjects in this study was 23.9 (SD=4.39). The osteoporosis group had the lowest mean BMI which was 20.76 (Table 4). There were significant differences of BMI between 3 groups, normal and osteopenia ($p= 0.016$), normal and osteoporosis ($p< 0.001$), and osteopenia and osteoporosis ($p= 0.024$).

Table 4 Basic characteristics of participants

	Normal (N= 20)	Osteopenia(N=20)	Osteoporosis (N=20)
	Mean ± SD	Mean ± SD	Mean ± SD
Age (years old)	56.95±5.89[a]	64.9±9.06[b]	69.75± 10.4[b]
Weight (kg)	69.87± 11.94[a]	56.27±8.21[b]	49.74±7.06[b]
Height (cm)	160.72±6.08[a]	153.64±5.37[b]	154.75±4.91[b]
BMI	27.09±4.63[a]	23.83±3.11[b]	20.76±2.76[c]

([a,b ,c] Different letters show significant differences, $p < 0.05$)

Bone mineral density (BMD) of the participants

The mean lumbar spine, femoral neck, total hip BMD t-score of the participants in this study were -1.41, -0.86, and 3.87 respectively.

The mean lumbar spine BMD t-score of normal, osteopenia and osteoporosis were 0.83, -1.32, and -2.54 respectively (Table 5). There were significant differences of lumbar spine BMD t-score between 3 groups, normal and osteopenia ($p< 0.001$), normal and osteoporosis ($p< 0.001$), and osteopenia and osteoporosis ($p= 0.002$).

The mean femoral neck BMD t-score of normal, osteopenia and osteoporosis were -0.04, -1.58, and -2.61 respectively (Table 5). There were significant differences of femoral neck BMD t-score between 3 groups, normal and osteopenia ($p< 0.001$), normal and osteoporosis ($p< 0.001$), and osteopenia and osteoporosis ($p= 0.001$).

The mean total hip BMD t-score of normal, osteopenia and osteoporosis were 0.54, -1.18, and -1.94 respectively (Table 5). There were significant differences of total hip BMD t-score between 3 groups, normal and osteopenia ($p< 0.001$), normal and

osteoporosis ($p< 0.001$), and osteopenia and osteoporosis ($p= 0.015$). The mean BMD t-score at femoral neck was the lowest among lumbar spine and total hip in the osteopenia and osteoporosis group.

Table 5 Parameters of participants

	Normal (N= 20) Mean ± SD	Osteopenia (N=20) Mean ± SD	Osteoporosis (N=20) Mean ± SD
BMD t-score			
Lumbar Spine	0.83 ± 1.47^{a}	-1.32 ± 0.92^{b}	-2.54 ± 0.79^{c}
Femoral Neck	-0.04 ± 0.98^{a}	-1.58 ± 0.49^{b}	-2.61 ± 0.90^{c}
Total Hip	0.54 ± 1.05^{a}	-1.18 ± 0.52^{b}	-1.94 ± 0.83^{c}
MI (Average)	4.53 ± 0.60^{a}	4.00 ± 0.57^{b}	3.08 ± 0.47^{c}

(^{a,b,c} Different letters show significant differences, $p < 0.05$)

The panoramic radiographic indices

The panoramic radiographic indices in this study were MI and MCI. The mean MI which were the average value of the right and left site of the mandible in normal, osteopenia, osteoporosis groups were 4.53, 4.00, and 3.08 respectively (Table 5). The MI which were the average value of the right and left site of the mandible were used for statistically analysis in this study. For MCI, this study evaluated this index both right and left site of the mandible separately. The MCI was classified the morphology of cortical border of the mandible into 3 groups: C1, C2, and C3. The results of MCI in this study were similar both right and left site of the mandible. In the normal group, C1 was the most found index (90%) and followed by C2 (10%). C3 was absent in the normal group. In the osteopenia, the most found index was

C2(60%) and followed by C1(30%). In the osteoporosis group, C2(55%) was also the most found index and followed by C3(40%) as shown in Table 6.

Table 6 Mandibular cortical index (MCI) distribution of participants

	Normal (N=20) N (%)	**Osteopenia (N=20)** N (%)	**Osteoporosis (N=20)** N (%)
MCI			
C1	18 (90%)	6 (30%)	1 (5%)
C2	2 (10%)	12 (60%)	11 (55%)
C3	0 (0%)	2 (10%)	8 (40%)

The results for comparing between MI and age in cases classified as C1, C2, and C3 were shown in table 7. We found that the lowest mean MI was C3 group followed by C2, and C1. There were significant differences between MI in C1 and C3 group ($p< 0.001$), and C2 and C3 group ($p= 0.01$). But, no significant differences of MI between C1 and C2 group. This study revealed that C3 group showed lowest mean age followed by C2, and C1. There were significant differences between age in C1 and C2 ($p= 0.001$) group and C1 and C3 ($p< 0.001$) group. But, no significant differences of age between C2 and C3 group.

Table 7 The results for comparing between MI and age in cases classified as C1, C2, and C3 (^{a,b} Different letters show significant differences, $p < 0.05$)

	C1	C2	C3
MI (Mean ± SD)	4.24 ± 0.59^{a}	3.83 ± 0.82^{a}	3.03 ± 0.66^{b}
Age (Mean ± SD)	57.52 ± 6.86^{a}	66.40 ± 8.42^{b}	73.40 ± 10.68^{b}

The distribution of the indices in this study were normal. There was a statistically significant difference of MCI between the normal, osteopenia and osteoporosis group ($p < 0.001$). There was a statistically significant difference of MI between 3 groups ($p < 0.001$) as well. The analysis of Pearson's correlation between radiographic indicators of mandible and BMD t-score are both correlated. MI was positively correlated with BMDs: lumbar spine: $r = 0.566$, femoral neck: $r = 0.554$, and total hip: $r = 0.524$ ($p < 0.001$), respectively. MCI was negatively correlated with BMDs: lumbar spine: $r = -0.514$, femoral neck: $r = -0.507$, total hip: $r = -0.513$ ($p < 0.001$), respectively as shown in Table 8.

Table 8 Correlation between radiographic indicators of mandible and bone mineral density (BMD)

Correlation coefficient; r (p-value)	**BMD t-score at lumbar spine**	**BMD t-score at femoral neck**	**BMD t-score at total hip**
MI	0.566 (< 0.001)	0.554 (< 0.001)	0.524 (< 0.001)
MCI	-0.514 (< 0.001)	-0.507 (< 0.001)	-0.513 (< 0.001)

We found the correlation between radiographic indicators of mandible and age. MCI was positively correlated with age: $r = 0.590$ ($p < 0.001$), but MI was negatively correlated with age: $r = -0.346$ ($p = 0.007$).

The area under the ROC curve were used for evaluating the ability of MI and MCI to classify the reduced bone mineral density group (both osteopenia and osteoporosis) which were 0.845 and 0.875 (Fig 10, 11) and the ability of MI and MCI to classify the osteoporosis group were 0.934 and 0.831, respectively (Fig 12, 13).

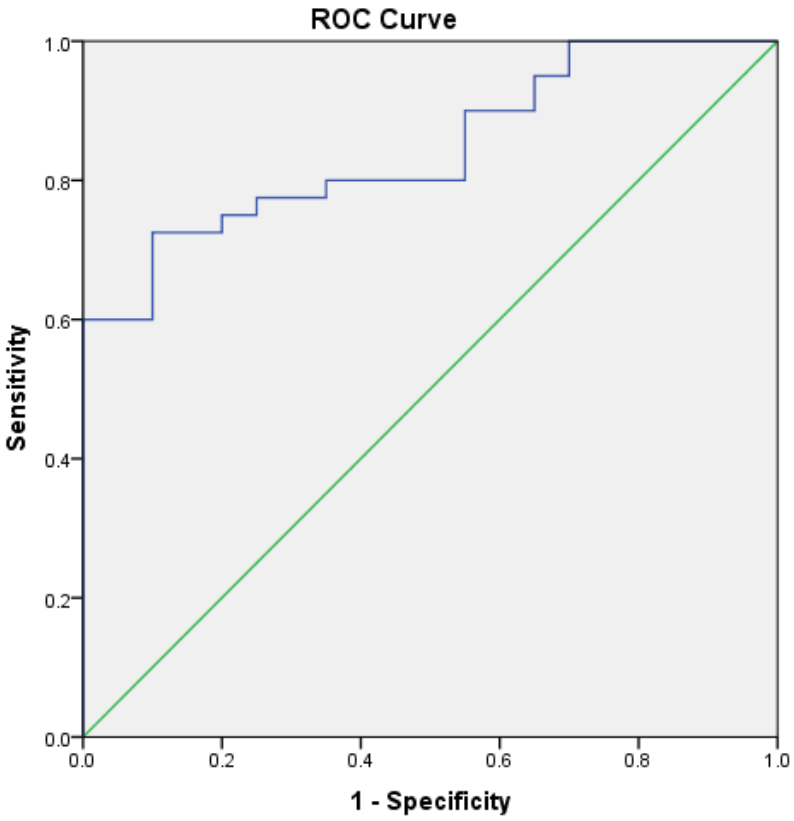

Figure 10 The receiver operating characteristic (ROC) curve to determine the ability of mental index (MI) to evaluating reduced bone mineral density group (Osteopenia and osteoporosis). Area under the ROC curve = 0.845

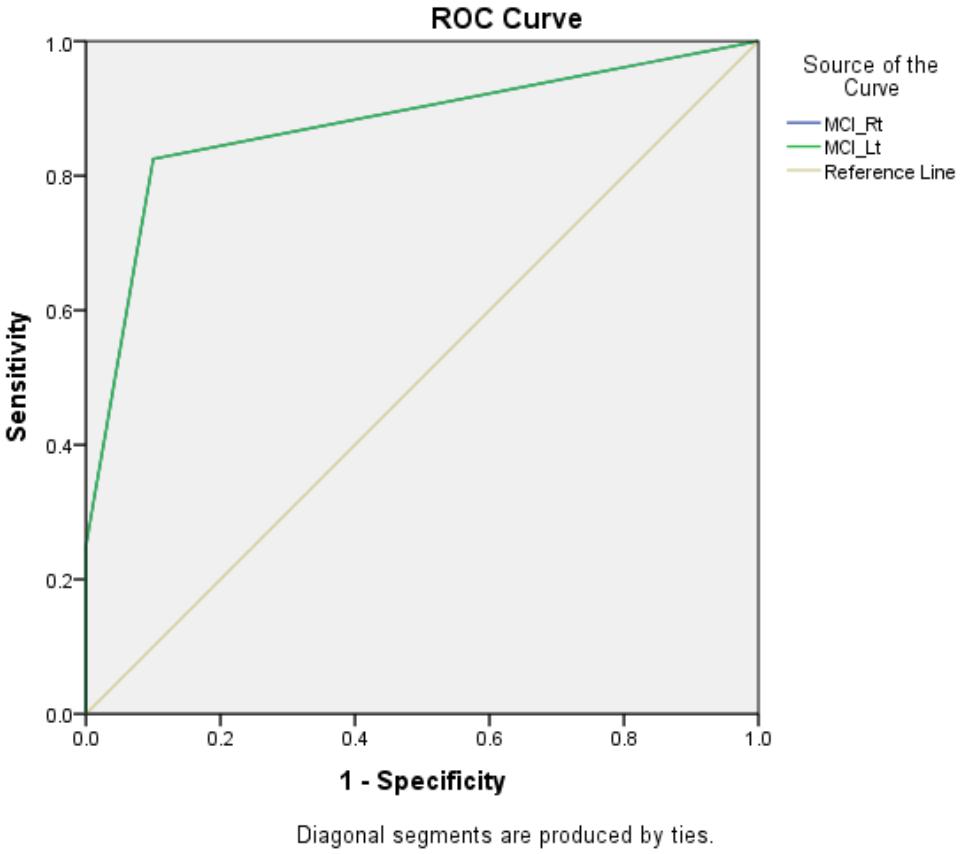

Figure 11 The receiver operating characteristic (ROC) curve to determine the ability of mandibular cortical index (MCI) to evaluating reduced bone mineral density group (Osteopenia and osteoporosis). Area under the ROC curve = 0.875.

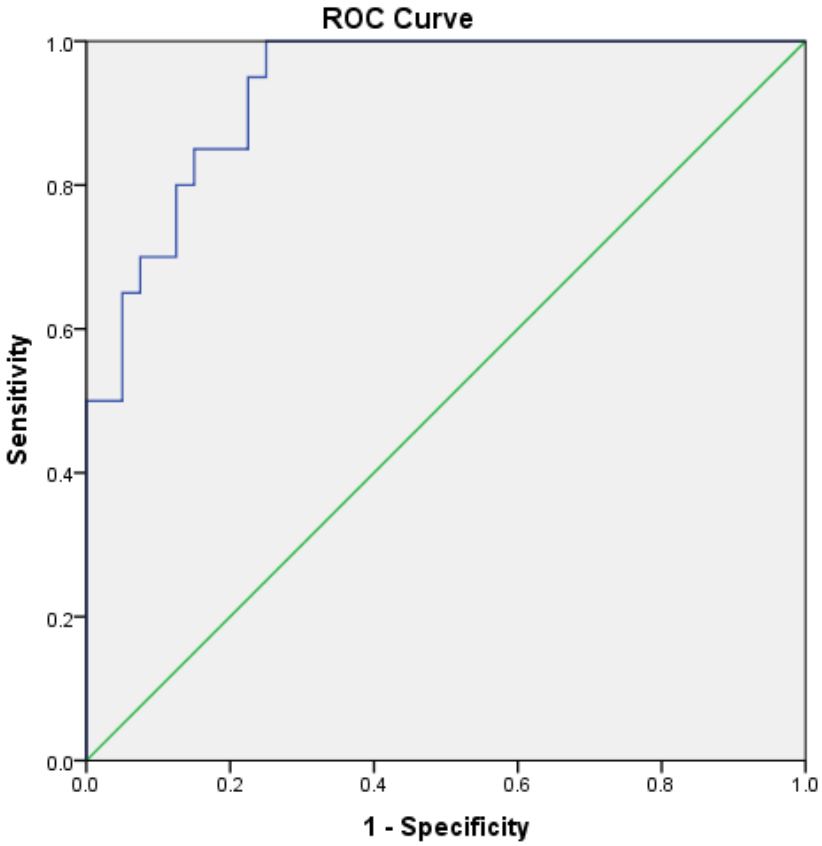

Figure 12 The receiver operating characteristic (ROC) curve to determine the ability of mental index (MI) to evaluating osteoporosis. Area under the ROC curve = 0.934

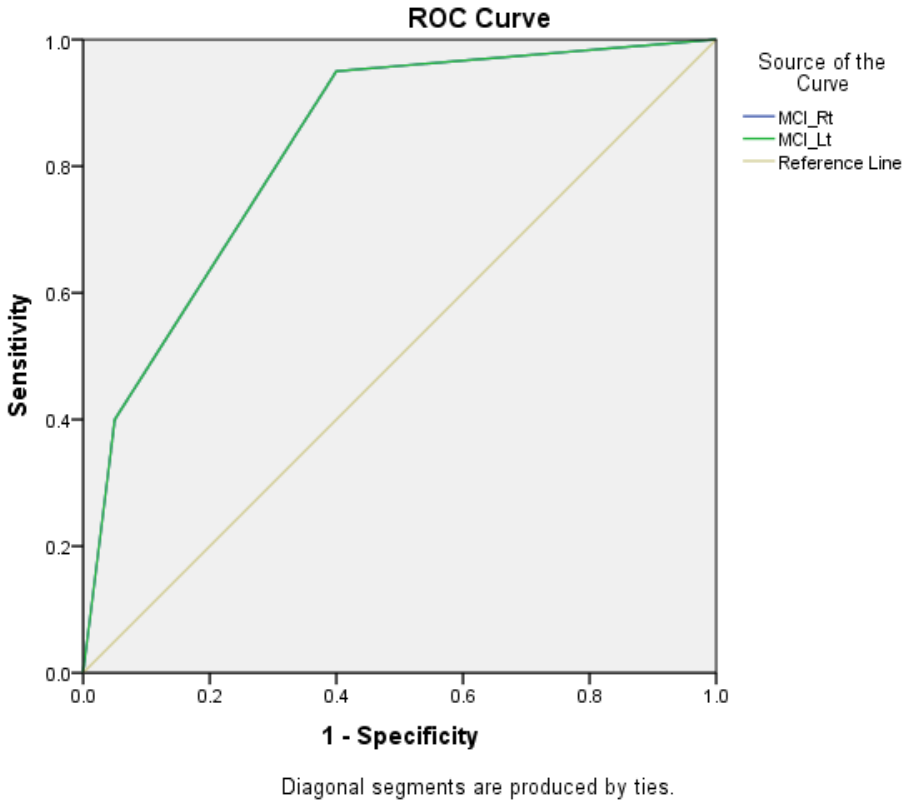

Figure 13 The receiver operating characteristic (ROC) curve to determine the ability of mandibular cortical index (MCI) to evaluating osteoporosis.

Area under the ROC curve = 0.831.

For calculating the optimal cut-off value of the panoramic mandibular indices, Youden's index were used. The result was shown in Table 9-12.

Table 9 Youden's index of MI for diagnosis of the reduced bone mineral density group

MI	Sensitivity	1-specificity	Specificity	Youden's index
3.9175	0.725	0.1	0.9	0.625
3.56	0.6	0	1	0.6
3.8075	0.7	0.1	0.9	0.6
3.745	0.675	0.1	0.9	0.575
3.5275	0.575	0	1	0.575
3.9725	0.725	0.15	0.85	0.575
3.4875	0.55	0	1	0.55
3.7375	0.65	0.1	0.9	0.55
4.0475	0.75	0.2	0.8	0.55
3.63	0.6	0.05	0.95	0.55
3.445	0.525	0	1	0.525
3.72	0.625	0.1	0.9	0.525
4.005	0.725	0.2	0.8	0.525
4.24	0.775	0.25	0.75	0.525
3.4225	0.5	0	1	0.5
3.6925	0.6	0.1	0.9	0.5
4.1475	0.75	0.25	0.75	0.5
3.39	0.475	0	1	0.475
4.265	0.775	0.3	0.7	0.475
4.3275	0.8	0.35	0.65	0.45
3.36	0.45	0	1	0.45
3.345	0.425	0	1	0.425
4.2875	0.775	0.35	0.65	0.425
3.32	0.4	0	1	0.4
4.37	0.8	0.4	0.6	0.4
3.2925	0.375	0	1	0.375
3.27	0.35	0	1	0.35
4.52	0.9	0.55	0.45	0.35
3.2125	0.325	0	1	0.325
4.4475	0.875	0.55	0.45	0.325
3.1625	0.3	0	1	0.3
4.38	0.8	0.5	0.5	0.3
4.5875	0.9	0.6	0.4	0.3
4.825	1	0.7	0.3	0.3
4.4075	0.85	0.55	0.45	0.3
4.6875	0.95	0.65	0.35	0.3
3.15	0.275	0	1	0.275
4.3975	0.825	0.55	0.45	0.275
4.665	0.925	0.65	0.35	0.275
4.7625	0.975	0.7	0.3	0.275

3.1225	0.25	0	1	0.25
4.39	0.8	0.55	0.45	0.25
4.635	0.9	0.65	0.35	0.25
4.71	0.95	0.7	0.3	0.25
4.8825	1	0.75	0.25	0.25
3.035	0.225	0	1	0.225
2.945	0.2	0	1	0.2
5.0325	1	0.8	0.2	0.2
2.8925	0.175	0	1	0.175
2.835	0.15	0	1	0.15
5.15	1	0.85	0.15	0.15
2.745	0.125	0	1	0.125
2.605	0.1	0	1	0.1
5.2025	1	0.9	0.1	0.1
2.4875	0.05	0	1	0.05
5.6825	1	0.95	0.05	0.05
2.2575	0.025	0	1	0.025
1.07	0	0	1	0
7.115	1	1	0	0

Table 10 Youden's index of MCI for diagnosis of the reduced bone mineral density group

MCI	Sensitivity	1-Specificity	Specificity	Youden's index
0	1	1	0	0
1.5	0.825	0.1	0.9	0.725
2.5	0.25	0	1	0.25
4	0	0	1	0

Table 11 Youden's index of MI for diagnosis of osteoporosis

MI	Sensitivity	1-specificity	Specificity	Youden's index
3.8075	1	0.25	0.75	0.75
3.7375	0.95	0.225	0.775	0.725
3.9175	1	0.275	0.725	0.725
3.5275	0.85	0.15	0.85	0.7
3.745	0.95	0.25	0.75	0.7
3.9725	1	0.3	0.7	0.7
3.445	0.8	0.125	0.875	0.675
3.72	0.9	0.225	0.775	0.675
4.005	1	0.325	0.675	0.675
3.56	0.85	0.175	0.825	0.675
3.4875	0.8	0.15	0.85	0.65
3.63	0.85	0.2	0.8	0.65
4.0475	1	0.35	0.65	0.65
3.345	0.7	0.075	0.925	0.625
3.4225	0.75	0.125	0.875	0.625
3.6925	0.85	0.225	0.775	0.625
4.1475	1	0.375	0.625	0.625
3.2925	0.65	0.05	0.95	0.6
3.36	0.7	0.1	0.9	0.6
4.24	1	0.4	0.6	0.6
3.32	0.65	0.075	0.925	0.575
3.39	0.7	0.125	0.875	0.575
4.265	1	0.425	0.575	0.575
4.2875	1	0.45	0.55	0.55
3.27	0.6	0.05	0.95	0.55
4.3275	1	0.475	0.525	0.525
3.1225	0.5	0	1	0.5
3.2125	0.55	0.05	0.95	0.5
4.37	1	0.5	0.5	0.5
3.15	0.5	0.025	0.975	0.475
3.035	0.45	0	1	0.45
3.1625	0.5	0.05	0.95	0.45
4.38	1	0.55	0.45	0.45
4.39	1	0.575	0.425	0.425
2.945	0.4	0	1	0.4
4.3975	1	0.6	0.4	0.4
4.4075	1	0.625	0.375	0.375
2.8925	0.35	0	1	0.35
4.4475	1	0.65	0.35	0.35
4.52	1	0.675	0.325	0.325

2.835	0.3	0	1	0.3
4.5875	1	0.7	0.3	0.3
4.635	1	0.725	0.275	0.275
2.745	0.25	0	1	0.25
4.665	1	0.75	0.25	0.25
4.6875	1	0.775	0.225	0.225
2.605	0.2	0	1	0.2
4.71	1	0.8	0.2	0.2
4.7625	1	0.825	0.175	0.175
4.825	1	0.85	0.15	0.15
4.8825	1	0.875	0.125	0.125
2.4875	0.1	0	1	0.1
5.0325	1	0.9	0.1	0.1
5.15	1	0.925	0.075	0.075
2.2575	0.05	0	1	0.05
5.2025	1	0.95	0.05	0.05
5.6825	1	0.975	0.025	0.025
1.07	0	0	1	0
7.115	1	1	0	0

Table 12 Youden's index of MCI for diagnosis of osteoporosis

MCI	Sensitivity	1-specificity	Specificity	Youden's index
1.5	0.95	0.4	0.6	0.55
2.5	0.4	0.05	0.95	0.35
0	1	1	0	0
4	0	0	1	0

Thus, from the results of this study, the optimal cut-off value of MI for the reduced bone mineral density group is 3.9 mm at sensitivity = 72.5% and specificity = 90%, and for the diagnosis of osteoporosis group is 3.8 mm at sensitivity 100% and specificity = 75% (Table 13). For MCI, the sensitivity of the index was 82.5% and specificity was 90% for the diagnosis of reduced bone mineral density group. The sensitivity and specificity of MCI for the diagnosis of osteoporosis group were 95% and 60% respectively (Table 14).

Table 13 Diagnosis performance of mental index (MI) in predicting reduced bone mineral density and osteoporosis

	Mental index (MI)	Sensitivity	1-Specificity	Specificity	Youden's index	Diagnostic accuracy
Reduced bone mineral density	3.9175	0.725	0.1	0.9	0.625	88.3%
Osteoporosis	3.8075	1	0.25	0.75	0.75	77.5%

Table 14 Diagnosis performance of mandibular cortical index (MCI) in predicting reduced bone mineral density and osteoporosis

	Sensitivity	1-Specificity	Specificity	Youden's index	Diagnostic accuracy
Reduced bone mineral density	0.825	0.1	0.9	0.725	89.3%
Osteoporosis	0.95	0.4	0.6	0.55	63.5%

Chapter 5 Discussion

The objective of the present study was to investigate whether the panoramic radiograph can be a screening tool for the diagnosis of osteoporosis in Thai postmenopausal women or not. From the results of this study, there were significant differences of ages between normal and osteopenia ($p= 0.014$) and normal and osteoporosis ($p< 0.001$). Because with increasing age, there was also a significant reduction in bone formation [49]. There was a study [50] showed that when a woman's estrogen levels dropped after menopause, and bone loss speeded up. Thus, the reason that there was no significant difference between osteopenia and osteoporosis group might be because the timing of the onset and the duration of the menopausal change and the timing of the final menstrual period were not the same in every women which was why the age of women with osteopenia and osteoporosis were not different.

The body mass index (BMI) is used your height and weight to identify if your weight is healthy. The BMI calculation divides an adult's weight in kilograms by their height in meters squared. For BMI and obesity, WHO defines obesity as a BMI ≥30, overweight as a BMI = 25 to 29.9 , and underweight as a BMI < 18.5 . There was a study reported that low BMI increases risk of osteoporosis fracture because low BMI is related to low BMD. The lesser of soft tissue, the decrease of muscle weakness [51]. In the same way as the results from this study, there were significant differences of BMI between 3 groups, normal and osteopenia ($p= 0.016$), normal and osteoporosis ($p< 0.001$), and osteopenia and osteoporosis ($p= 0.024$). However, the average BMI of the subjects in this study was not considered as an underweight. This data showed that not only postmenopausal women who were in the underweight group had a risk for osteoporosis but postmenopausal women who were in normal weight group could be at risk as well, so this means that BMI is not a good indicator.

The comparative results between MI in cases classified as C1, C2, and C3 were similar to the study by Mansour et al.[15]. They also found that the C3 group showed lowest mean MI followed by C2, and C1. There were significant differences between MI in C1 and C3 group, and C2 and C3 group. But there was no significant differences of MI between C1 and C2 group as well.

The results of the present study demonstrated that MI and MCI were correlated with BMD t-score which were in accordance with previous studies[12] [15] [41] that MI was positively correlated with BMD t-score and MCI was negatively correlated with BMD t-score. MI was positively correlated with BMDs: lumbar spine: $r = 0.566$, femoral neck: $r = 0.554$, and total hip: $r = 0.524$ ($p < 0.001$), respectively. Correlation was an effect size and could describe the strength of the correlation using the guideline for the absolute value of r. When r was between 0.40-0.59 it would be considered as moderate correlation. Thus, from this study, the strength of the correlations between MI and three BMD t-score were moderate positive relationship. MCI was negatively correlated with BMDs: lumbar spine: $r = -0.514$, femoral neck: $r = -0.507$, total hip: $r = -0.513$ ($p < 0.001$), respectively. We could concluded that the strength of the correlations between MCI and three BMD t-score were moderate negative relationship. Likewise, there was a study found that the BMD of the right calcaneus was significantly correlated with the MI ($r = 0.328$, $p < 0.001$). The reason they found lower correlation than our study might be because of the difference method in detecting BMD[41]. The study by Kim et al. [12] found that there was an association between MI and BMD only at lumbar spine and total hip. They found no association between MI and BMD at femoral neck of hip. Meanwhile, the association of MCI with BMD was found at lumbar spine, femoral neck, and total hip. The different results from their study might be because of different in statistical analysis method. They used multiple linear regression analysis for association between panoramic radiographic indices and BMD, but our study used Pearson's correlation. The study by Mansour et al. [15] also found similar result to our

study. They found that MI showed a statistically significant positive correlation with the BMD t score (r = 0.47) which was moderate positive correlation same as our result.

The results of this study showed that C3 group showed lowest mean age followed by C2, and C1. There were significant differences between age in C1 and C2 (p= 0.001) group and C1 and C3 (p< 0.001) group. But there was no significant differences of age between C2 and C3 group. We also found the correlation between radiographic indicators of mandible and age. MCI was positively correlated with age: r = 0.590 (p< 0.001) which was considered as a moderate positive correlation. Whereas, MI was negatively correlated with age: r = - 0.346 (p= 0.007) which was considered as a low negative correlation. These results were similar to the study by G Bozdag and S Sener [52]. They reported significant alterations in the values of MI according to age groups in females and found that when the age increased, MI values decreased. For MCI, they found that the most common category in young adult aged between 18-40 years old was C1. C2 was the most observable category when the age increased. There was a study also reported that the number of C3 cortices was common in older age groups [9]. However, the subjects of this study were lack of age group variables. The age range of this study was 49-87 years old because we included only postmenopausal women. Future studies should consider more variety of age groups in order to clarify the relationship between age and panoramic indices.

The area under the ROC curve were used for evaluating the capability of MI and MCI to classify the reduced bone mineral density group which were 0.845 and 0.875. The ability of MI and MCI to classify the osteoporosis group were 0.934 and 0.831, respectively. The results from this study were higher than other studies which meant the ability of the indices to classify the disease in this study were high accuracy. The study by C S Valerio et al. [53] reported that the area under the ROC curve in the appearance of MCI detected on digital panoramic radiographic images for the reduced bone mineral density group was 0.71. From the study by Leite et al. [17], the area under the ROC curve

for identifying women with reduced BMD and osteoporosis were 0.751 and 0.703 for MI. The study by Papamanthos et al. [39] reported that the ROC values of MI as an indicator of the presence of osteoporosis was between 0.80-0.87. According to the study by Devlin and Horner[14], they reported that the area under the ROC curve of MI in diagnosis of the reduced skeletal bone density was 0.733 which indicated moderate accuracy.

The optimal cut-off value of MI for diagnosis of osteoporosis in this study was 3.8 mm which had sensitivity 100%, specificity 75% and diagnostic accuracy 77.5% and for diagnosis of reduced BMD was 3.92 mm which had sensitivity 72.5%, specificity 90% and diagnostic accuracy 88.3%. From our results, Thai postmenopausal women with mandibular cortical thickness below than 3.9 mm should be referred for bone densitometry evaluation. These results were close to those found in other studies but had some differences. Devlin et al. [19] studied in the European population concluded that the thinnest MI ($\leq$ 3mm) should be referred for additional osteoporosis investigation. They found that MI $\leq$ 3mm would provide a sensitivity of 20% and specificity of 100% in diagnosis of the reduced BMD group, and specificity of 93.6% in diagnosis of osteoporosis. Leite et al. [17] reported that the MI optimal cut-off value for identifying women with osteoporosis was 3.15 mm and for reduced BMD was 3.38 mm. Mansour et al. [15] found that if the cut-off value of MI was $\leq$ 3mm considered abnormal, sensitivity, specificity and diagnostic accuracy were 10.3%, 98.4% and 64% respectively. But, when the MI cut-off point was changed to 4.5 mm, sensitivity, specificity and diagnostic accuracy were found to be 76.9%, 54.1% and 63% respectively. Kim et al. [12] reported the lower cut-off value of MI than other studies. They found that the optimal cut-off value of MI was 2.22 mm (sensitivity 67.9%, specificity 78.5%) for the diagnosis of osteoporosis. Although, statistically, our study found that the optimal cut-off value of MI for diagnosis of osteoporosis in this study was 3.8 mm and for diagnosis of reduced BMD was 3.92 mm. These two values were slightly different, which can lead to misinterpret in daily practice. Thus, from the result in this study, when the MI cut-off value was changed to 4.0 mm, the

sensitivity would be 72.5% and specificity would be 80% which were still higher than other study[12]. In accordance with the systematic review and meta-analysis by Calciolari et al. [54] They revealed that MI was more beneficial to exclude high risk for low BMD, since in 90% of the cases patients with a cortical width wider than 4 mm had a normal BMD. Hence, in daily practice, the suggestion would be use cut-off value of MI at 4.0 mm in order to screen the postmenopausal women with reduced bone mineral density. It was supposed that the reasons for difference cut-off value in every studies would be the difference of statistical analysis for determining cut-off value, the difference in the magnifying ratio of the panoramic radiographs, ethnic/races differences which were the important role of variation in BMD.

The sensitivity of MCI for diagnosis of reduced BMD was 82.5% which was close to the study by C S Velerio et al [53] in Brazil. According to the study from Navabi et al. [13] in Iran and comparing with the result from this study, the distribution of MCI tended to be similar. The most indices found in osteopenia and osteoporosis patients were C2, and followed by C1 and C3, respectively. However, there was a study by Kim et al. in Korean postmenopausal women with osteoporosis that found dissimilar distribution. Kim et al. [12] reported that MCI distribution was 48.9% for C2, 30.4% for C3, and 23.7% for C1. Nevertheless, C2 is still the most index that found in postmenopausal women with reduced BMD. Thus, the suggestion for the present study is Thai postmenopausal women who have mandibular cortical morphology that identified as C2 or C3 should be referred to evaluate the bone densitometry. Lee et al.[21] also reported the similar suggestion that women whose cortex was type C2 or type C3 had a high risk of low BMD. On the other hand, women whose cortex was type 1 had a low risk of low BMD. Kinalski et al. [47] reported the meta-analysis of MCI that it could be a reliable tool for screening the early BMD loss of osteopenia group in female with above 80% sensitivity and 60% of specificity. MCI for the reduced bone density group may have a possible value for screening because

of high sensitivity. The index that has high sensitivity will describe as hardly missing subjects with the disease via this index.

The present study had several limitations. First, this study only focused on postmenopausal women subjects not included the elderly men. Second, this study could not report the change of panoramic radiographic indices after the patient receives treatment with antiresorptive or antianabolic drugs. Further studies with the above considerations are needed to be done.

Chapter 6 Conclusion

The results of this study suggested that MI and MCI can be used as a screening tool for the diagnosis of osteoporosis in postmenopausal women. In daily practice, both MI and MCI can be useful tools for all specialist dentist even for general dentist. MI measurement will be easier when it is in a digital radiograph. MI may be time consuming in general dental practices to measure mandibular cortical widths. It may has to use with additional tools such as calipers or other tools. MCI will be more recommended if the digital panoramic radiograph is not available because it is feasible and does not require any measurement program.

Period of this study

Plan/Procedure	Feb 19	Mar 19	Apr 19	May 19	Jun 19	Jul 19	Aug 19	Sep 19	Oct 19	Nov 19	Dec 19	Jan 20	Feb 20	Mar 20	Apr 20	May 20	Jun 20
Literature review																	
Proposal presentation																	
Submitting research proposal for ethics review																	
Testing																	
Data analysis																	
Result and discussion																	
Report and presentation																	

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