YEDİTEPE UNIVERSITY
INSTITUTE OF HEALTH SCIENCES
DEPARTMENT OF DENTOMAXILLOFACIAL RADIOLOGY

COMPARISON OF PANORAMIC RADIOGRAPHY AND CONE BEAM COMPUTED TOMOGRAPHY (CBCT) IMAGES OF EIGHT RADIOLOGICAL INDICES OF HIGH RISK OSTEOPOROTIC WOMEN IN RELATION TO AGE

MASTER'S THESIS

Prepared By:
EMAN. A. B. AGUORI
B.D.S

ISTANBUL - 2015

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I. THESIS APPROVAL

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APPROVAL

This thesis has been deemed by the jury in accordance with the relevant articles of Yeditepe University Graduate Education and Examinations Regulation and has been approved by Administrative Board of Institute with decision dated 24.12.2015, and numbered 2015/32-1

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Director of Institute of Health Sciences

II. DECLARATION

I hereby declare that this thesis is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person nor material which has been accepted for the award of any other degree except where due acknowledgment has been made in the text.

Date

Signature

Name Surname

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VII. LIST OF SYMBOLS AND ABBREVIATIONS

AACE	American Association of Clinical Endocrinologists
AD	Antegonial Depth
AGA	Antegonial Angle
AGI	Antegonial Index
BMC	Bone Mineral Content
BMD	Bone Mineral Density
BMI	Body Mass Index
BQI	Bone Quality Index
CA	Condylar Angle
CBCT	Cone Beam Computed Tomography
CI	Cortical Index
cm	Centimeter
CT	Computed Tomography
CTCI	Computed Tomography Cortical Index
CTI"I"	Computed Tomography Mandibular Index "Inferior"
CTX	Collagen Type I cross - linked C telopeptide
CTMI	Computed Tomography Mental Index
DXA	Dual X - ray energy Absorptiometry
D - PYR	Urinary Deoxypyridinoline

Era Estrogen receptors A

Erb Estrogen receptors B

FACIT Family of Fibril - Associated Collagens with Interrupted Triple Helices

GA Gonial Angle

GI Gonial Index

ICC Intraclass Correlation Coefficient

ICSI Institute for Clinical Systems Improvement

IGF-I Insulin Growth Factor - I

IL Interleukin

KI Klemetti Index

kVp Kilovolts peak

L Left

mA Milliamper

MCI Mandibular Cortical Index

M-CSF Macrophage Colony - Stimulating Factor

MCW Mandibular Cortical Width

MI Mental Index

mm Millimeter

NTX Collagen Type I cross - linked -N -telopeptide

OPG Osteoprotegrin

PICP C - terminal Propeptides of type I Collagen

PICP	Procollagen I Carboxy terminal Propeptide
PINP	N - terminal Propeptides of type I Collagen
PMI	Panoramic Mandibular Index
PTH	Parathyroid Hormone
PYR	Urinary Pyridinoline
QCT	Quantitative Computed Tomography
QUS	Quantitative Ultrasound
r	Pearson Correlation Coefficient
R	Right
RA	Radiographic Absorptiometry
RANKL	Receptor Activator of Nuclear factor Kappa B Ligand
RANK	Receptor Activator of Nuclear factor Kappa
SPSS	Statistical Package for Social Sciences
SXA	Single X - ray Absorptiometry
SD	Standard Deviation
TGF	Transforming Growth Factor
TMJ	Temporomandibular joint
TNF	Tumor Necrosis Factor
USA	United States of America
WHO	World Health Organization
3D	Three Dimensional

2D Two Dimensional

VIII - ABSTRACT

Eman. A. B. Aguori. (2015). **COMPARISON OF PANORAMIC RADIOGRAPHY AND CONE BEAM COMPUTED TOMOGRAPHY (CBCT) IMAGES OF EIGHT RADIOLOGICAL INDICES OF HIGH RISK OSTEOPOROTIC WOMEN IN RELATION TO AGE**. Yeditepe University, Institute of Health Sciences, Faculty of Dentistry, Department of Dentomaxillofacial Radiology, Master's Thesis, Istanbul. This study was conducted to compare the value of Gonial Angle (GA), Mental Index (MI), Cortical Index (CI), Antegoinal Index (AGI), Panoramic Mandibular Index (PMI), Antegonial Angle (AGA), Antegonial Depth (AD), and Condylar Angle (CA) in both panoramic and CBCT images of high risk osteoporotic femal patients in relation to age. Sixty nine panoramic and CBCT images taken from the women with age range between 44 - 80 years, were included in this study. On CBCT images, MI, CI, AGI, and PMI were measured on cross - section images on the both sides. GA, AGA, AD, and CA were measured using panoramic representations of the mandible on both sides. Intraclass Correlation Coefficient (ICC) test was used to evaluate the agreement between the first and the second measurements. The relationship between the right and the left sides for GA, MI, AGI, PMI, AGA, AD, and CA was examined by using Pearson's Correlation Coefficient test. The relationship between the right and the left sides for CI was examined by using Contingency Coefficient test. Chi - Square test was used to compare CI classification between two independent samples. t - test was used to compare the mean different of other indices between two independent samples.

The results show that, there was agreement between the first and the second CBCT and panoramic radiography measurements. There was a significant correlation between the right and the left measurements of CBCT for all indices ($P < 0.05$), except GA ($P > 0.05$). There was a significant correlation between the right and the left measurements of panoramic radiographs for all indices ($p < 0.05$). We found that there was no significant difference between the measurement of panoramic radiography and CBCT in MI, CI, AGI, PMI, AGA, AD, and CA in both the right and left sides ($P > 0.05$). Also, there was no significant difference in GA between two groups in the right side ($p > 0.05$). But there was a significant difference in GA between two groups in the left side ($p < 0.05$). There was no significant difference between two age groups in all indices measured on CBCT or on panoramic images on both sides ($P > 0.05$). In conclusion, in the attempt to reduce initial cost and the dose of radiation for the detection of osteoporosis with larger numbers of osteoporotic patients

attending dental clinics; panoramic images can be used for evaluation of the bone changes instead of CBCT images.

Key words: Osteoporosis, Gonial Angle, Mental Index, Mandibular Cortical Index or Computed Tomography Cortical Index, Antegonial Index, Panoramic Mandibular Index or Computer Tomography Mandibular Index "Inferior, Antegonial Angle, Antegonial Depth, Condylar Angle, Panoramic and CBCT images.

1. INTRODUCTION

1.1. The normal bone anatomy and physiology:

1.1.1. Bone function and structure:

Bone tissue or osseous tissue, is the most significant structural and supportive connective tissue of the body. Bone tissue forms the rigid part of the bones that make up the skeleton. The function of these bones may include:

- Structural support for the rest of the body (the skeleton), also support against forces of gravity, and posture. Movement and locomotion as they provide lever points for the muscles.
- Protection of vital internal organs and structures.
- Provision and maintenance of mineral homeostasis and acid - base balance.
- Storage of growth factors and cytokines.
- Provision of good environment for hematopoiesis in marrow spaces (1, 2).

The adult human skeleton is composed of 80% cortical bone and 20% trabecular bone. Different bones and skeletal sites within bones have different percentages of cortical and trabecular bone. This proportion affects in the bone strength independently (2).

Cortical bone is a dense solid shell that surrounds a honeycomb like network of trabecular bone, which circumscribes the bone marrow. The trabecular bone is composed of a network of trabecular plates and rods that scattered in the bone marrow compartment.

The surface area of the trabecular bone is more than that of the cortical bone, so it responds more quickly to hormonal changes; like decrease in estrogen concentrations, increases in parathyroid hormone or administration of corticosteroids (1, 2).

Both cortical and trabecular bone are composed of osteons. The unit of cortical osteon is called Haversian system. Under the microscope, the walls of Haversian system are formed of concentric lamellae. Trabecular osteons are called packets; these consist of plates and rods which are coated by lining cell, and composed of concentric lamellae (1, 2).

Cortical bone is surrounded by the periosteum from the outer surface and by endosteam from the inner surface. The periosteum is a fibrous connective tissue sheath, which contains blood vessels, nerve fibers, and osteoblasts and osteoclasts. It is attached to the outer cortical surface of bone by Sharpey’s fibers. The endosteum is a membranous structure which lines the inner surface of trabecular bone, cortical bone and blood vessel canals (Volkman’s

canals) and is in contact with the bone marrow space and contains blood vessels, osteoblasts, and osteoclasts (2).

The activity of the periosteal surface is essential for appositional growth and fracture repair. The rate of the bone formation is higher than the rate of bone resorption on the periosteal surface. So, the bones normally increase in diameter with aging. On the contrary to the endosteum, the rate of the bone resorption is more than the rate of the bone formation in endosteal surface. So, the marrow space normally expands with aging (1, 2).

In the cortical bone and trabecular bone, the collagen fibrils arrangement is in a regular alternating manner similar to plywood that gives the cortical and the trabecular bone lamellar pattern which is significant in increasing the bone strength. This lamellar pattern is not present in woven bone, because the collagen fibrils are arranged in an irregular manner. That is why the woven bone strength is less than that of the lamellar bone (2).

The remodeling activity of the endosteal surface is more than the remodeling activity of the periosteal surface because of the greater exposure of the endosteal surface to cytokine from the neighboring bone marrow compartment. The rate of remodeling in cortical bone increases with age, that is why the cortical bone becomes more porous and thin with age (2).

1.1.2. Bone Cells:

1.1.2.1. Osteoblasts:

Osteoblasts are flattened bone - lining cells that make the endosteum on trabecular and endosteal surfaces beneath the periosteum on the mineralized surface, where synthesis and secretion of type I collagen and other matrix proteins takes place (2).

They are involved in the synthesis of collagen and other proteins of the bone matrix. On the outer surface of the osteoblasts there are receptors for hormones, such as estrogen, which produce the first signals to initiate bone remodeling (1, 3).

1.1.2.2. Osteocytes:

Osteocytes originate from osteoblasts; however, osteocytes are different from osteoblasts; they are spidery cells with nuclei and main cell bodies lying within lacunae in mineralized bone. As neurons, osteocytes transmit signals of stresses or micro-damage in bone to other bone cells (1). Osteocytes release osteocalcin, galectin 3, and CD44; a cell adhesion receptor for hyaluronate, as well as several other bone matrix proteins that help in intercellular

adhesion (2). Osteocytes have estrogen receptors on their surface for binding of estrogen, which stimulate the osteocytes for bone formation (3).

1.1.2.3. Osteoclasts:

These are differentiated from the monocyte and macrophage cells. Osteoclasts are the only cells known to be capable of dissolving and reabsorbing bone (1).

Osteoclasts have estrogen receptors (Era, Erb) on their surface. Estrogen has an inhibitory effect on osteoclasts; when it binds to estrogen receptors on the osteoclasts, it stimulates protein formation. This protein inhibits bone resorption by decreasing the formation of mature osteoclasts and increasing osteoclast apoptosis (3).

1.1.3. Bone tissue composition and properties:

Bone is composed of 50 - 70% mineral, 20 - 40% organic matrix, 5 to 10% water, and < 3% lipids. The mineral phase is mainly calcium and phosphor in the form of hydroxyapatite crystals and the organic phase is collagen, non - collagenous proteins and cells. The organic phase of bone provides post - yield behavior, strength, elasticity and flexibility, whereas the mineral phase provides mechanical rigidity and load - bearing strength to bone, which is known as the stiffness of the tissue. The mechanical properties of the bone are determined by the quantity and mechanical integrity of each phase (2).

1.1.3.1. Collagen:

Osteoblasts synthesis the collagen fibrils, which provide a scaffold for bone minerals and give strength for the bone. Various types of the collagen in bone; mainly type I collagen, III, IV and VI, and FACIT (family of Fibril - Associated Collagens with Interrupted Triple Helices) are also present. FACIT collagens are members of a group of non fibrillar collagens that serve as molecular ridges that are important for the organization and stability of extracellular matrices (2, 3)**.**

1.1.3.2. Mineral:

Mineral content of the bone includes calcium hydroxyapatite, which is a collection of calcium, phosphate, and hydroxyl groups that bind to bone proteins; and they control the strength and hardness of bone (2).

It is widely accepted that the stiffness and brittleness of bone tissue are determined by mineral content, and the mineral content increase with age. However, some studies found that the amount of mineral reduced after age 50 (4). When mineral crystals are deposited by osteoblasts on the organic matrix, bone mineralization occurs (3).

1.1.4. Normal bone physiology:

The bone remodeling is the procedure of resorption of the old bone and formation of new bone to avoid accumulation of bone micro-damage and to preserve bone strength and mineral homeostasis. The bone remodeling cells are osteoclasts and osteoblasts that are responsible for resorption of old bone and formation of new bone. The highest rate of bone remodeling occurs in perimenopausal and early postmenopausal women and then reduces with further aging, but stays at a faster rate than that in premenopausal women (2, 5).

During normal bone remodeling, there is a number of cytokines and growth factors that control the activity of bone cells, like cytokines and growth factors, namely the Receptor Activator of Nuclear factor Kappa B Ligand (RANKL) and Macrophage Colony - Stimulating Factor (M - CSF) and Osteoprotegrin (OPG) which are released from osteoblasts and bone - lining cells. RANKL and M - CSF control the osteoclast activity by binding the Receptor Activator of Nuclear factor Kappa (RANK) on osteoclast precursors and stimulating proliferation and differentiation into mature osteoclasts. OPG binding to RANKL and blocking RANK acts to stop osteoclast differentiation at the end of the resorption process (3, 6).

As osteoclasts form a resorption cavity, the osteoblasts follow along behind filling in the cavity with osteoid. This process tends to minimize stress in the bone tissue relatively to its weight (5). When bone resorption is complete, at which the multinucleated osteoclasts undergo apoptosis, new bone starts to form as resorption cavities containing monocytes, osteocytes secreted from bone matrix, and preosteoblasts recruited to begin new bone formation. Transforming Growth Factor (TGF) released from bone matrix inhibits RANKL production by osteoblasts, whish lead to decreases osteoclast resorption activity(2, 3).

As osteoblasts synthesize new collagenous organic matrix and regulate mineralization of matrix, the osteoblasts are buried within the matrix and then become osteocytes (2, 3). At the end of bone formation, about 50 - 70% of the osteoblasts expire and the remaining become osteocytes or bone - lining cells, which control the movement of mineral ions into and out of

bone extracellular fluid, and maintain the ability to redifferentiate into osteoblasts upon exposure to parathyroid hormone or mechanical force (2).

1.1.5. Bone changes with aging and menopause:

Aging is a complex process; its effect is myriad and insidious, leading to progressive deterioration of various organs, including the skeleton (7). As the bone is a composite material consisting of collagen fibrils, mineral phase, and water. Changes in each of the constituents may cause significant effects on the fragility of bone (8). The follows are the most common bone changes with age:

1- Changes in the dynamics of bone cell populations, causing unbalance of the normal process of bone resorption and formation.
2- Alterations in bone architecture (e.g., reorganization of trabecular structures) and cross - sectional geometry (expansion of subperiosteal and widening of the medullary cavity).
3- Increase of microfractures.
4- Inconsistency in the concentration of deposited minerals, with hypomineralization in some areas and hypermineralization in others.
5- Alterations in the crystalline properties of mineral deposits.
6- Alterations in the protein content of matrix material.
7- Changes in the level of phosphate regulating hormones which certainly affect the maintenance of normal bone homeostasis: parathyroid hormone (PTH) increases, and production of the most active metabolites of vitamin D 3 decreases.
8- Decrease in the physical activity and dietary inadequacies of the elderly can effect bone status (7, 9).
9- The density of osteocyte lacuna reduces exponentially with age. This is related with the increase in micro-damage as well as increase in porosity with ages. Recent studies use osteocyte density as a fracture indicator, revealing that it is more accurate than bone mineral density (BMD) alone (10).
10- The elastic modulus, the stiffness and strength of the collagen phase in bone are decreases with aging in both longitudinal and transverse directions. Such changes are due to multiple factors:

A. Increases in collagen porosity with age may be directly related to decreases in the stiffness and strength of the collagen phase.

B. Decreases in concentration of collagen fibrils significantly from middle aged to elderly donors may make the collagen phase more compliant and weaker.
C. Increases in the amount of advanced glycation end products with age in bone matrix may associate with decreases in the stiffness and strength of the collagen phase (8).

11- Increase in the bone loss, there are three major age - related processes that lead to bone loss as follows:

A. The decrease in trabecular bone; caused by thinning of the trabeculae and, specifically in early postmenopausal women, by disruption of the trabecular microstructure and loss of trabecular elements, can contribute to bone loss.
B. The decrease in cortical bone; mainly caused by increasing the porosity from both an increase in resorption cavities and an accumulation of incompletely closed osteons with aging, can contribute to bone loss.
C. The continuous net resorption at the endocortical surface lead to bone loss (7).

These processes are accelerated after menopause in women (9)." A period of transformation in women's lives in which they are faced with medical and psychological problems, including: hot flushes, headaches, sweating, fatigue, sexual dysfunction and reduction of estrogen, and accordingly may cause a rapid loss of bone mass. Women usually go through menopause between age 45 and 55 " (11).

The estrogen plays a significant role in the maintenance of bone mass and regulation of the remodeling balance between osteoblastic and osteoclastic activity. After menopause, dropping of estrogen levels leads to 0.5% to 2% bone loss yearly. As a net result of increased resorption and reduced formation. These changes lead to osteoporosis and increased osteoporotic fracture risk (7, 12, 13).

These can be explained by that; osteoclast, osteoblasts and osteocytes have receptors for estrogen on their surface. Therefore, their function may be affected when estrogen production changes. when estrogen levels are decreased, causing osteocyte apoptosis, hypermineralization of the surrounding bone, altered organization of the osteocyte, and osteocyte density increases. Moreover, osteoblasts produce less bone per cell, the number of osteoclast progenitors increase, inducing prolonged bone resorption, trabecular perforation, fragility of bone, and eventually bone fracture (3).

There is evidence of effect of estrogen deficiency on osteoclasts activity:

The molecules that stimulate osteoclast activity (Tumor Necrosis Factor - a [TNF - a], MCS - F, RANKL, Interleukins [IL]) increase, whereas those that inhibit osteoclasts (OPG, TGF - b) decrease during estrogen deficiency. So, osteoclast synthesis increases and osteoclast apoptosis decreases, leading to deeper resorption for an extended period, reduced bone mass, and microdamage (3).

1.2. Osteoporosis:

1.2.1. Definition of osteoporosis:

In 2000, the United States National Institutes of Health consensus conference modified the osteoporosis definition as " a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture. Bone strength reflects the integration of two main features: bone density and bone quality ". BMD can be referred to as grams of mineral per area or volume and is determined by highest bone mass and total of bone loss (14). Also, the BMD can be defined as a quantitative measure of bone mass and represents the total mineral in a selected volume of bone in the hip or in the spine. Measurements assessed with Dual - energy X - ray Absorptiometry (DXA) (3). Bone quality is regarded as trabecular bone architecture, turnover, damage accumulation (e.g., microfractures), and mineralization (14, 15).

According to the World Health Organization (WHO), fragility fracture is defined as "a fracture caused by injury that would be insufficient to fracture normal bone: the result of reduced compressive and/or torsional strength of bone" (13). When minimum force (e.g. trauma) is applied to osteoporotic bone, fractures may happen. Thus, osteoporosis is a major risk factor for fracture, and a difference between both risk factors for fracture and risk factors that affect bone metabolism must be established (14).

The WHO provides criteria for both diagnostic and intervention threshold for osteoporosis, by defining it as a BMD that lies 2.5 standard deviations or more below the average value for young healthy women (T - score of < - 2.5 SD) (16, 17). The same definition is further explained in the terms of osteoporosis classification.

1.2.2. Classification of osteoporosis:

The WHO definition of osteoporosis in 2004 was updated in 2008 to include both of bone mass (BMD and Bone Mineral Content [BMC]) and the fracture. Based on this definition, osteoporosis can be classified into 4 general diagnostic categories (Table 1.1).

Table 1.1: WHO classification of osteoporosis.

Category	BMD level	T-score
Normal	BMD or BMC value not more than 1 SD below young adult mean	T - score: > - 1
Osteopenia	BMD or BMC value between 1 and 2.5 SD below the young adult mean	T - score: between - 1 and - 2.5
Osteoporosis	BMD or BMC value is 2.5 SD or more below the young adult mean	T - score : ≤ - 2.5
Established or Severe osteoporosis	BMD or BMC value is 2.5 SD or more below the young adult mean	T - score: ≤ - 2.5and the presence of one or more fragility fractures

BMD: Bone Mineral Density. BMC: Bone Mineral Content. SD: Standard Deviation. T - score: the number of SD above or below the average BMD value for young healthy white women. (18, 19, 20, 21).

Furthermore, the orthopedic specialists classified the osteoporosis into 4 type (Table 1.2):

Table 1.2: Orthopedic classification of osteoporosis.

Type of osteoporosis	Prevalence	Age group	Cause
Primary osteoporosis	Women (most common) Men	45 - 50 year	Physiological change
Osteogenesis imperfecta	-	Any age	Certain medical condition or drug treatment
Secondary osteoporosis	Rare	At birth	Congenital
Idiopathic osteoporosis	Rare	8 - 14 year	Unknown

Adapted by orthopedic specialist of South Canada (22).

Moreover, it is mentioned in the literature that osteoporosis can be further classified as either primary or secondary osteoporosis (3, 14, 23, 24).

The primary osteoporosis is further classified in to two types:

Type I : Bone loss occurring in postmenopausal women due to estrogen deficiency.

Type II : Bone loss as a result of the normal ageing process.

Secondary osteoporosis is bone loss resulting from a secondary effect of diseases or drug treatment (3).

Type I osteoporosis, which usually called involutional osteoporosis, is founded in the women at the first 15 - 20 years after menopause. During this period, there are severe and uneven loss of cancellous bone over cortical bone, which can cause acute vertebral compression fractures and distal forearm (colles) fractures (23, 24).

Type I osteoporosis is a consequences of estrogen deficiency and some additional factors, which effective only in the presence of estrogen deficiency and act as paracrine mediators of estrogen action in bone such as IL - 1, IIL - 6, TNF, and prostaglandin E2 (23, 24).

Type II osteoporosis, which usually called senile osteoporosis, affects both men and women over 75 and is usually associated with the slow phase of age - related bone loss and comparable losses of both cancellous and cortical bone. This process occurs in the entire population of aging women and men and as more and more bone is lost, the greatest risk for fracture. The common fractures associated with this process are those of the proximal femur and wedge fractures of the vertebrae (23, 24).

In 2010, the AACE identified the most common causes of secondary osteoporosis (Table 1.3) (21).

1.2.3. The prevalence of osteoporosis:

In many regions of the world, the prevalence of osteoporosis, and incidence of fracture vary by gender, race, ethnicity, and age. As a result of the ageing population, the estimated number of osteoporotic fractures in both men and women is increased by more than three folds over the next 50 years (14, 16).

It is mentioned in the literature that osteoporosis has a higher incidence in the female population for the reason of gender differences in muscle mass (9), differences in amount of bone mass, rate of bone loss, bone geometry, frequency of falls (14) and the consequences of menopause (11).

Table 1.3: The most common causes of secondary osteoporosis.

Endocrine or metabolic causes	Nutritional/ gastrointestinal conditions	Drugs	Disorders of collagen metabolism	Other
Acromegaly Diabetes mellitus Type 1 Type 2 Growth hormone deficiency Hypercortisolism Hyperparathyroidism Hyperthyroidism Hypogonadism Hypophosphatasia Porphyria Pregnancy	Alcoholism Anorexia nervosa Calcium deficiency Chronic liver disease Malabsorption syndromes/ malnutrition (including celiac disease, Crohn disease, and gastric resection or by pass) Total parenteral nutrition Vitamin D deficiency	Antiepileptics Aromatase inhibitors Chemotherapy/ Immunosuppressants Depo - Provera Glucocorticoids Gonadotropin - releasing hormone agonists Heparin Lithium Proton pump inhibitors Selective serotonin reuptake inhibitors Thiazolidinediones Thyroid hormone Warfarin	Ehlers -Danlos syndrome Homocystinuria due to cystathionine deficiency Marfan syndrome	AIDS / HIV Ankylosing spondylitis Chronic obstructive pulmonary disease Gaucher disease Hemophilia Hypercalciuria Immobilization Major depression Myeloma and Cancers Organ transplantation Renal insufficiency Renal tubular acidosis Rheumatoid arthritis mastocytosis Thalassemia

Adapted by the American Association of Clinical Endocrinologists (AACE) 2010 (21).
(HIV / AIDS): Human Immunodeficiency Virus / Acquired Immune Deficiency Syndrome.

During menopause, the increasing prevalence of osteoporosis and associated fractures depend on the length of hormonal disorder and the woman's age. In age ranging from 50 - 59 years, the prevalence of osteoporosis at the lumbar spine is around 15.8% (20% prevalence of fracture) and in women over the age of 80 years is around 54.5% (82% prevalence of

fractures) (11). In early years of menopause, women's high risk for fractures may be due to rapid bone loss during this period (14).

At the age of 50, the possibility of a hip fracture during the lifetime is 14 % for a white female and 5 - 6 % for a white male. The probability of this type of fracture for the same age in both African American women and men is much lower (6% and 3%, respectively) (14).

After the age of 50, risks of hip and spine fracture in white women are about 2 to 3times greater than those for men, because the women have smaller bones and tend to have lower bone density as they age (1).

At the age of 60, the frequency of femoral neck fractures doubles in women every 5years and in men every 7 years (25).

The rate of bone loss slows down during menopause, and then it accelerates again after the age of 70. In women older than 80 years of age, there is about 1 - 2% of bone loss per year, and the reason for that is not known (1).

In the United States, about 1.5 million fractures are due to osteoporosis each year (26).

By 2030, the number of menopausal and postmenopausal women in the world is estimated to increase to 1.2 billion, with 47 million of them will have osteoporosis each year (27).

By 2035, the number of hip fractures in Turkey is expected to increase to nearly 64,000. The prevalence of osteoporosis at the femoral neck is 7.5% and 33.3% in men and women aged 50 years or more, respectively (28).

1.2.4. Pathogenesis of osteoporosis:

During osteoporosis, there are two new unitary models of pathophysiology of involutional osteoporosis. These are the early - accelerated, and the late - slow phases of bone loss in postmenopausal women. The estrogen deficiency is the main cause of these phases.

During the early - accelerated phase (first 4 - 8 years after menopause), the loss of preventive effect of estrogen on bone resorption may be one of the reasons that increases outflow of skeletal calcium into the extracellular fluids and compensatory decreases PTH secretion.

The estrogen deficiency has more skeletal effects then extraskeletal effects, because estrogen treatment during this phase leads to an increase in serum PTH level (23).

During menopause, the acute loss of the restraining effects of estrogen on bone cells activity leads to an accelerated phase of loss of predominantly cancellous bone (3- to 5- fold greater than the loss of cortical bone), due to the large increase in the number and activity of osteoclasts, resulting in perforative resorption of trabecular plates with loss of structural

elements that decreases after about 4 - 8 years and disappears after about 15 - 20 years when severe depletion of cancellous bone stimulates counter - regulatory forces that limit further loss (23).

During the late - slow phase of bone loss, the effect of estrogen deficiency on extraskeletal calcium becomes prominent, leading to continuous increases in PTH secretion and slow bone loss. This involves loss of both cancellous and cortical bone and continues throughout the remaining life. It is caused by the loss of estrogen effects on extraskeletal calcium homeostasis leading to decreased intestinal calcium absorption, increased renal calcium wasting, and perhaps also effects on vitamin D metabolism and loss of direct effect on the parathyroid gland that decreases PTH secretion. So, this increases the level of dietary calcium intake required to prevent secondary hyperparathyroidism and increases bone turnover. These manifestations can be reversed by either estrogen replacement (which restores extraskeletal calcium fluxes to premenopausal levels) and decreases serum PTH levels, or by large increases in dietary calcium, which offsets the net calcium losses induced by postmenopausal abnormalities in extraskeletal calcium fluxes (23).

In addition, during postmenopausal osteoporosis, both of Insulin Growth Factor - I (IGF - I) and TGF - b, which normally are released from the extracellular matrix for recruited and activated osteoblasts to begin collagen synthesis, and OPG levels are decreased, while IL - 7 level and the IL - 7 receptor numbers are increased (3).

Moreover, TNF - a production is increased, IL - 1 and IL - 6 expression are upregulated in human osteoporotic bone (3, 29).

1.2.5. Osteoporosis and its oral implications:

The relation between osteoporosis and oral bone loss was founded in 1960 (27). Osteoporosis is associated with periodontal bone loss, tooth loss, and temporomandibular joint (TMJ) bone loss (30). Osteoporosis can lead to decrease in the residual ridge height in edentulous patients (31).

Systemic bone loss and BMD were found to be related to alveolar bone loss and to a lesser extent to clinical loss of attachment in postmenopausal Caucasian women (30, 32, 33).

The most sensitive site for differentiating osteoporotic patients from the normal people is the anterior maxilla due to the relatively large amount of trabecular bone and the relatively low cortical bone thickness at this site. Moreover, the density of maxillary alveolar process is significantly related to the density of the mandibular alveolar process, lumbar spine, coxa,

and radius in healthy women and the density of maxillary alveolar process declines with age (30).

1.2.6. Osteoporosis characteristic and consequences:

The osteoporosis is an asymptomatic disease until the fractures occur. The most common sites of fracture include the spine, hip, forearm and proximal humerus (16, 20).

Consequences of osteoporosis and osteoporotic fracture includes: the financial, physical, social and psychosocial factors, which significantly affect the individual, as well as the family and community (14).

The problem is likely to be dangerous as the population ages, and as a continued movement of population from rural areas, where more sun light exposure that help in production of endogenous vitamin D to urban areas with less sun exposure (34).

1.2.7. Bone strength during osteoporosis:

Bone strength is the ability of the bone to resist a force. The overall mechanical strength of bone is determined by two features, bone mass and bone quality (trabecular bone architecture, turnover, damage accumulation [e.g., microfractures], and mineralization) (18, 20). Each of these features is responsible for mechanical properties of the bone (3).

Due to osteoporosis or estrogen deficiency, the mechanical properties (apparent elastic modulus, stress and strain, compressive strength, stiffness, yield strength) of the bone are considerably low in comparison with normal people to a degree that bone fractures occur under normal loading conditions (3, 35, 36, 37).

1.2.7.1. Bone mass during osteoporosis:

The bone mass is reduced as estrogen level reduced. Since BMD is a quantitative measure of bone mass and bone mass is a quantitative measurement of the whole bone present in a definite size of bone. BMD has become the gold standard for the clinical diagnosis of osteoporosis (see page 15) (3).

1.2.7.2. Bone micro-architecture and morphology during osteoporosis:

Micro-architecture is the microscopic morphology and organization of both trabecular and cortical bone. Stereology is helpful to recognize bone micro-architecture, cortical porosity, cortical thickness, trabecular number, trabecular thickness and trabecular connectivity (3).

After menopause, consequently to either increased remodeling activation, or estrogen deficiency, rapid loss of trabecular bone, thinning, and disconnection of trabeculae leads to loss of strength (38).

1.2.8. Diagnosis of osteoporosis:

As osteoporosis is painless disease, the diagnosis of asymptomatic individuals may be beneficial before the onset of fracture by:

- Medical evaluation:
  - History of osteoporosis.
  - Physical examination risk.
- Risk assessment:
  - Identify women at risk of low bone mass.
  - Identify women at risk of fragility fracture.
- Bone turnover.
- Laboratory test.
- BMD measurement.
- Radiography assessment (26).

1.2.8.1. Medical evaluation:

According to National Osteoporosis Foundation, in order to recognize the medical conditions that cause bone loss, the overall medical evaluation, including complete history taking and general physical analysis, is essential for all postmenopausal women and men age 50 and older, before making a diagnosis of osteoporosis on the basis of a low BMD alone. In patients with suspected secondary cause of osteoporosis, biochemical testing (such as serum calcium, creatinine, etc.) and radiographic assessment should be considered (20).

1.2.8.1.A. History of osteoporosis:

The patient with osteoporosis is typically a Caucasian woman, in her sixties, or 10 - 20 years postmenopausal. The patient usually has a positive family history of symptomatic osteoporosis, and usually presents with complaints related to fracture of a limb, (colles, hip, or humeral fracture), that is due to seemingly minor trauma, or with symptoms related to the back (25).

A history of medication use, smoking, dietary sources of calcium and vitamin D, past and present medical and surgical problems have potential etiologic significance. Many of these features are also felt to be significant indicators of the population at risk (25).

1.2.8.1.B. Physical Examination:

The general characteristics of primary osteoporosis include: tendency of patient to be thin; loss of several inches of height, tendency to lose average body hair, an arm span greater than, or equal to height, and tender spinous process (25).

1.2.8.2. Risk Assessment:

In order to detect high - risk persons for osteoporosis, Osteoporosis Society of Canada recommends two stages of assessment. The first stage: the risk factors identification for those, who should be assessed with a BMD test. The second stage: the risk factors identification for those with risk of osteoporotic (fragility) fracture, who should be considered for treatment (39).

The selected key risk factors should aid physicians in identifying those who require further assessment and investigation to determine whether medical intervention is needed to reduce their risk of osteoporotic (fragility) fracture. The risk assessment includes:

- Identification of women at risk of low bone mass.
- Identify women at risk of fragility fracture.

1.2.8.2.A. Women at risk of low bone mass:

Low bone mass is one characteristic feature of postmenopausal osteoporosis and the primary indicator of fracture risk in women without fractures, but the bone mass is not sufficiently sensitive for diagnosis or exclusion of osteoporosis. 70% to 80 % of peak bone mass is primarily determined by genetics, but may also be modified by other factors, such as physical activity, diet (e.g. inadequate calcium intake), concomitant diseases (for example hyperthyroidism), adverse lifestyle (e.g. smoking) (21**)**, body size, and gender general health (18).

During the first three decades of life, bone mass increases and reaches its peak around age 30 years. After adolescence, individuals with the highest peak bone mass have the most protective benefit as inevitable declines in bone density associated with increasing age **(**14). There are many factors responsible for increase and decrease of bone mass as is shown in Table (1.4).

During the menopause period, there is a rapid and large amount of bone loss throughout the whole skeleton due to the increase in number of remodeling bone sites. In the early postmenopausal period, estimated bone loss is about 1 to 2% per year. However, bone loss can be also attributable to estrogen deficiency and aging. It may be more rapid and marked in the cancellous bone, such as in the lumbar spine; the bone mass loss in the cancellous bone is more than that in the cortical bone. That can be attributed to the fact that the rate of remodeling is greater in cancellous bone than in cortical bone (14, 21).

Table 1.4: General risk factors associated with decreased bone mass.

Risk factors (1, 14, 21, 40, 41)
• Female gender • Inadequate calcium intake • White race • Increased age • Body Mass Index (BMI) • Estrogen deficiency • Low body weight
• Low muscle strength • Family history of osteoporosis
• Smoking • Use of alcohol and caffeine containing beverages • History of prior fracture • Late menarche and early menopause • Anorexia nervosa

1.2.8.2.B. Women at risk of fragility fracture:

Fragility fracture is defined as “ a fracture that occurs spontaneously or following a minor trauma ” (39).

Osteoporosis - associated fractures are common in sites of low bone mass, but they may occur in any site with high mortality and morbidity rate. As the number of risk factors increase, the risk of the fracture increases. The secondary complications of fragility fractures are loss of height, decreased rib - to - pelvis distance, kyphosis, crowding of internal organs, back pain (acute and chronic), prolonged disability, poor self - image, social isolation, depression, and increased mortality rate (21).

In general, the objectives of assessment of risk factors in fractures can be summarized as follows:

- Recognizing women, who are at high risk of fractures.
- Clinical awareness of osteoporosis.
- Formation of general policies for both the prevention of fracture and treatment of osteoporosis (42).

The person, who have a history of low - trauma fracture, the risk of another fracture depends on the age, number of prior fractures and the site of the incident fracture (13). Also, the risk of hip fracture increases if the person has a history of hip fracture in a maternal grandmother (43).

There is a positive association between the amount of height loss and the risk of a new vertebral fracture. Determination of height loss is a powerful method in assessing the risk of vertebral fracture (44). Also, increased body weight is an important step that may decrease the risk of falling and accordingly the risk for hip fracture (30, 45). Moreover, by ageing, people change dietary habits and this can affect both their weight and BMD (9). In obesity, the circulating and tissue proinflammatory cytokines may encourage osteoclast activity and bone resorption by altering the RANK / RANKL / OPG pathway (see page 11) (46).

The amount of BMD can predict the fracture risk, but cannot detect if someone will have a fracture (47). According to the WHO, BMD can be used to predict the fracture risk; in other terms when BMD decrease, fracture risk increases (1, 16), which depends on the age, the number of prior fractures and the site of the incident fracture (13).

The increase in bone turnover during menopause and/or other certain diseases, such as hyperthyroidism and calcium imbalance, can lead to large amount of bone occupation with remodeling units and less bone mineralization. Accordingly, acceleration of bone resorption, perforation of the trabecular rod and plate, and decreased bone mass can occur. As a result, there is an increased possibility of the risk of bone fracture. It is important to highlight that

the increase of bone resorption markers is associated with increased vertebral and non-vertebral fractures independently of BMD (18).

The age is a major risk factor for fracture, because BMD decreases with the age (9, 13, 16, 42). As people become old, the risk of fracture increases due to the increased possibility of bone loss, weakening of the bone quality, and the increased risk of fallings (1). For each standard deviation of BMD below a baseline level (either the mean peak bone mass or the mean for the reference population of the person's age and sex), the fracture risk increases. This risk changes according to the person's age. For example, risk of fracture for a 25 year - old person with a low BMD (e.g. a T - score of - 2.5) is not more than that of a 25 year - old with a high BMD. Nevertheless, a risk fracture for the person with the same BMD at the age of 65 has a considerably higher 10 - year risk of fracture (13). Generally, the fracture risk is 2 to 5 folds higher in the elderly than that in the young (18).

In addition, increased probability of falling is considered as risk factor of fracture.
The most common causes for increased falling probability are:

1- General risk factors: e.g. muscle weakness, impaired balance, low body mass, reduced visual acuity, slower gait, frailty, and deconditioning (13, 18, 20, 21, 48).
2- Neurologic disorders: e.g. Parkinson' disease, proximal myopathy, autonomic dysfunction with orthostatic hypotension, hypotension, and poor balance (18, 20, 21).
3- Medications: e.g. Sedatives and hypnotics, antihypertensive agents, and anticonvulsants (18, 20, 21).
4- Environmental factors: e.g. Poor lighting, stairs, slippery floors, obstacles in the walking path, and positioning in a wet or dry bathtub (21).
5- Other factors: e.g. Prior fall, more than three fall in the previous year, sideways fall, and previous fall with injury (18).

1.2.8.3. Role of biochemical markers of bone turnover:

The bone turnover can be evaluated by measurement of the biochemical markers of the bone resorption and formation, or quantities bone histology. The markers of bone turnover can be classified as bone formation and resorption markers. The two forms are coupled and they change in parallel (18). The bone remodeling is natural process that maintain bone strength. The bone remodeling units are osteoclasts and osteoblasts that resorbs old bone and forms new bone to prevent accumulation of bone microdamage (2). Osteoblasts release serum, osteocalcin, bone - specific alkaline phosphatase, procollagen I carboxy terminal

propeptide (PICP), and the C - and N - terminal propeptides of type I collagen (PICP, PINP) into the circulation. Their concentration reflects the rate of bone formation and bone turnover rates (18, 39).

Osteoclasts produce bone degradation products, including: urinary hydroxyl proline, urinary pyridinoline (PYR), urinary deoxypyridinoline (D - PYR) as well as collagen Type I cross - linked N telopeptide (NTX), and collagen Type I cross - linked C telopeptide (CTX) which act as bone resorption markers that are released into the circulation (13, 18, 39). The bone resorption marker levels may be effected by age, gender, menopausal status, diet, diurnal ariation, and certain medications, and can cause extreme variability (13).

During perimenopausal and early postmenopausal periods, the bone remodeling and biochemical markers increase and then reduce with advanced aging, but remain faster in premenopausal women (2).

The relation between bone turnover rate and BMD is adversely proportional. Higher levels of bone formation and resorption markers are significantly associated with faster and greater BMD loss. Thus, biochemical markers may be used to identify fast bone loss (13).

1.2.8.4. Laboratory test:

Osteoporosis is a symptomatic disease. It has a long preclinical course before the onset of fracture. There are many reliable tests that can help to establish the diagnosis and treatments of osteoporosis and reduce the risk of fractures (26).

There is general consensus among osteoporosis specialists that a minimum number of laboratory tests should be considered for all osteoporosis diagnosed patient. The follows are the guidelines of Institute for Clinical Systems Improvement 2005 (ICSI) for laboratory testing in patients with newly diagnosed osteoporosis that should be measured for premenopausal or perimenopausal women, and postmenopausal women with comorbidities.

1- The patients with Z score above - 1.0 (less likely to have secondary causes of osteoporosis): Many laboratory tests can be done e.g. serum creatinine , liver function tests, serum calcium, alkaline phosphatase, serum phosphorus, serum 25- hydroxyvitamin D, and serum intact (whole-molecule), PTH, thyrotropin, thyroxine, and thyroid tests…. etc.
2- The patients with Z score below - 1.0 or premature osteoporotic fracture (higher risk of having secondary causes of osteoporosis): The above tests plus the following additional tests can be done e.g. Serum testosterone (total and free),

Serum estradiol, tissue transglutaminase antibodies, 24 - hour urinary free cortisol …etc .

For healthy postmenopausal women with no history of osteoporosis or any examination findings for secondary cause of osteoporosis, it may be rational to investigate for serum thyrotropin level only to rule out secondary causes of osteoporosis (26).

1.2.8.5. BMD measurement:

As the BMD has a positive relation with bone strength, BMD testing is the gold standard method for the diagnosis and management of osteoporosis and an excellent predictor of future fracture risk (20). Different people have different BMD, as a result of individual variations in body size, bone size, genetics, physical activities, habitual diets, certain health-related behaviors, and other factors that may influence BMD (49).
The objectives of BMD measurement are as follows:

1- Assessment of the risk of fracture.
2- Identification of the postmenopausal osteoporosis.
3- Identification of the patient for intervention.
4- Enhancement of the acceptance to treatment sites.
5- Identification of the alterations in bone mass over time in treated and untreated patients (21).

Evaluating the changes in BMD over time can measure the rate of bone loss, and assess whether there is a positive response to treatment or not. However, there is about 0.5 - 2% of bone loss per year and approximately 1 - 6% of BMD increases over the 3 years after treatment (13).

Prior to the BMD test, it is recommended to assess one major or two minor risk factors for osteoporosis to identify who should be screened for BMD test (Table 1.5).

As regarding females, the International Society for Clinical Densitometry provided the indications for BMD testing in 2013 as follows:

1- Women aged 65 and older.
2- For postmenopausal women younger than age 65, the bone density test is indicated if they have a risk factor for low bone mass such as:
    a. Low body weight.

b. Prior fracture.
c. High risk medication use.
d. Disease or condition associated with bone loss.

3- Women at the menopausal transition with clinical risk factors for fracture, such as low body weight, prior fracture, or high - risk medication use.

Women discontinuing estrogen should be considered for bone density testing according to the same indications (50).

The assessment of spinal bone mineral content from the conventional radiographs appears to be insensitive and inaccurate, if vertebral fractures are not present. Because the BMD must be decreased by about 35% before it can be detected on radiographs. That may be justified as the subjective assessment is influenced by many issues, such as: radiographic exposure factors, patient size, and film processing techniques. Therefore, objective methods of bone density measurements are required, which are accurate, precise, reproducible, sensitive, low - cost, and involves minimal exposure to ionizing radiation. Current techniques include:

1- Radiographic Absorptiometry (RA).
2- Single X - ray Absorptiometry (SXA).
3- Dual energy X - ray Absorptiometry (DXA).
4- Quantitative Computed Tomography (QCT).
5- Quantitative Ultrasound (QUS) (51).

1.2.8.5.A. Radiographic Absorption (RA):

Radiographic Absorption (RA) is one of the most favored methods for bone mass measurement, because it is cheap and can calculate bone loss quickly (52). It evaluates bone integrity (51), and it can provide basic measurements, such as cortical bone thickness and BMD (46). It can make a quantitative assessment of BMC restrictedly at the appendicular bones, such as the metacarpals, and phalanges, because they are surrounded by a relatively small amount of soft tissue (51).

While obtaining RA radiographs, an aluminum step - wedge is located on the film, and the image is analyzed using an optical densitometer (51, 52).

Table 1.5: Factors that identify people, who should be assessed for osteoporosis.

Major risk factors	Minor risk factors
• Age > 65 years • Vertebral compression fracture • Fragility fracture after age 40 • Family history of osteoporotic fracture (especially maternal hip fracture) • Systemic glucocorticoid therapy of > 3 months duration • Malabsorption syndrome • Primary hyperparathyroidism • Propensity to fall • Osteopenia apparent on x-ray film • Hypogonadism • Early menopause (before age 45)	• Rheumatoid arthritis • Past history of clinical hyperthyroidism • Chronic anticonvulsant therapy • Low dietary calcium intake • Smokers • Excessive alcohol intake • Excessive caffeine intake • Weight < 57 kg • Weight loss > 10% of weight at age 25 • Chronic heparin therapy

Adapted from the Canadian Consensus Conference on Osteoporosis 2006, 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada Update (13, 39).

1.2.8.5.B. Single X - ray Absorptiometry (SXA):

Single X - ray Absorptiometry (SXA) is low radiation exposure technique; suitable for measuring the BMD only at peripheral sites of the skeleton. The accuracy of SXA depends on the site. The calcaneus is the site of interest, because it is a load - bearing area and has a high cancellous bone content. However, more accurate results can be obtained at the shaft region, and the anatomic site at which BMD is being measured has to be surrounded by water, as water bags or water equivalent moldable materials (51). It is now widely considered not better than DXA, which uses a second energy beam to correct for absorption of x-ray energy by non - calcium containing tissues (52).

1.2.8.5.C. Dual energy X - ray Absorptiometry (DXA):

Dual - energy X - ray Absorptiometry (DXA) is a non - invasive (26), painless, fast, safe, cheap, and simple technique (9). DXA is the most accurate and widely available technique for BMD test. Therefore, it is the most recent and widely used technique for the measurement of bone density in clinical trials and epidemiological studies (51).

It can measure bone density at spine, hip, or total body. The evaluation of BMD in the hip and spine by DXA has a number of advantages, including: DXA is the most reliable way for assessing the bone quality and to determine BMD, which is one of the major method for diagnosis and predict risk for fractures in osteoporosis (16, 26, 53, 54). Also, It is used to assess effectiveness and monitor response to antifracture therapies (54).

The evaluation of BMD in the hip and spine by DXA has a number of disadvantages, including: Difficulty to distinguish between the cortical and trabecular compartments or image bone microstructure, because it has a low resolution (18, 55). It represents a two dimension (2D) areal BMD rather than a true three dimension (3D) volumetric bone density (18). Furthermore, DXA has an inadequacy in providing accurate measures of BMD in relation to information about bone strength, size, shape, and structure (15).

1.2.8.5.D. Quantitative Computed Tomography (QCT):

Quantitative Computed Tomography (QCT) has been principally employed to determine the true 3D volumetric density (mg/cm3) of cancellous or cortical bone at the spine and hip (18, 20, 35, 51, 55). The QCT scanners are very expensive, noninvasive, and high - resolution imaging technique (35). This technique may be more accurate in assessment of early bone loss. However, it is less used for patient follow up due to its higher radiation does and higher cost than that of DXA (18, 20, 51, 52).

1.2.8.5.E. Quantitative Ultrasound Densitometry (QUS):

Quantitative Ultrasound Densitometry (QUS) is used for measuring BMD at the patient's heel, and lasts for a minute. It gives alternative information about properties of bone, such as the speed of sound associated to bone density and structure (20, 52). It may give information about bone density, architecture, and elasticity (51). It is an indirect technique for BMD measurement (20, 54).

QUS has many advantages, for example: cheaper, smaller than DXA, no ionizing radiation, simplicity, and portability (49, 51).

1.2.8.6. Conventional skeletal radiography:

The conventional spinal radiographs have been used to detect vertebral fractures. However, the sensitivity and reliability of standard radiography to assess BMD are poor, because BMD must decrease by about 35% before it can be detected on radiographs (13, 42). On spinal radiograph, the general changes in patient with osteoporosis include:

1- The density of vertebral end plates and cortices increase, showing as a thin sharp line. Also there is resorption of transverse trabeculae.
2- Biconcavity of the vertebral bodies.
3- Anterior wedge fracture; vertebral flattening is rare (18, 25).

Spinal radiographs as the antero - posterior and lateral projections of both the thoracic and lumbar spines remain the best method for the initial assessment of spinal osteoporotic fractures. The lateral radiographs of the thoracic and lumbar spines are required for follow - up (39). In a recent study by Siminoski et al in 2005, found that there is a strong relation between the amount of height loss and the risk of a new vertebral fracture (56). So, spine radiographs should be taken to exclude the vertebral fractures in the postmenopausal women with kyphosis, back pain, historical height loss greater than 6 cm, or prospective height loss greater than 2 cm (39, 42).

1.2.8.7. Dental radiography:

1.2.8.7.A. Panoramic radiography:

Recent studies have shown that panoramic imaging may be one of the techniques that can be used to identify patients with low BMD, high bone turnover, or high risk of osteoporotic fracture at a low cost. The validity of such a diagnostic technique depends on two factors. Firstly, it is necessary that mandibular BMD relates significantly to that of other sites in the affected skeleton, mainly in individuals with osteoporosis. Secondly, the sensitivity and specificity of dental panoramic images in manifesting skeletal BMD must be high (30).

The panoramic image is a 2 D image for facial structures that includes both the maxillary and the mandible dental arches and their supporting structures. A panoramic x - ray machine is made up of an x - ray tube fixed on a horizontal arm and x - ray film fixed on another horizontal arm on the opposite side of the patient (57, 58, 59).

The patient's head is adjusted with chin, forehead and side rests for a sharper, clearer image. For proper mouth opening, the patient is asked to bite on a bite block (57). An x - ray

source and an image receptor move around a central point or plane in the same speed and in opposite direction. Objects in front of or behind of this plane are blurred. As the x - ray beam is directed through the patient into a film or a detector, the image is produced. The images can be obtained as hard film copies or as digital files that are stored electronically (57, 59).

The main advantages of the panoramic radiography include the following:

1- Suitability of the examination (57).
2- Can be used in the patient with restricted mouth opening (59).
3- Easy and painless.
4- The dose of radiation to the patient is fairly low.
5- Gives an image for a large region, including the facial bones and teeth (58, 59*)*.
6- Requires a short time to produce a single image (58, 59*)*.

The main disadvantages of the panoramic radiography are that:

1- Superimposition of anatomical landmarks.
2- The proximal surfaces of premolars are commonly overlapping (58, 59*)*.

Panoramic radiography is clinically indicated for:

1- Evaluation of trauma, location of third molars, extensive disease, known or suspected large lesions, tooth development (especially the mixed dentition), retained teeth or root tips (in edentulous patients), and developmental anomalies.
2- The initial evaluation image that can provide the required insight or assist in determining the need for other projections.
3- Patients who do not accept intraoral procedures well (59).
4- It can detect the deterioration of metabolic bone by cortical thickness measurement, as gonial thickness of less than 1 mm is a good descriptive metabolic bone deterioration index (60).
5- Some recent studies have shown that the panoramic radiography can be used for identify low BMD, high bone turnover, or high risk of osteoporotic fracture by the evaluation of mandibular inferior cortical shape and width (60, 61, 62).

Bone density can be assessed from dental radiographs by two main methods: By linear measurements (morphometric analysis) which is restricted to measurements of cortical

thickness at various sites by using various mandibular indices, or by measuring optical density of bone and comparing it with a reference step wedge (densitometric analysis).

There are many mandibular cortical indices that can be used to measure the mandibular bone mass and identify osteoporosis. The most common of these are: Mental Index (MI), Gonial Index (GI), Antegonial Index (AGI), Panoramic Mandibular Index (PMI), and Klemetti Index (KI) (30).

1.2.8.7. B. Cone Beam Computed Tomography (CBCT):

The inherent problems with 2D image lead to the need for 3D imaging, which can overcome the issue of superimposition and blurring, as these factors compromise measurement accuracy to a large extent. Simultaneously, the CBCT is a new technology that has been introduced in dental practice and dentists increasingly utilize CT scans (62). It provides cross - sectional and 3D imaging dedicated to the maxillofacial region at a low cost. And it reduces the radiation does significantly (63).

The use of the CBCT for scanning of the maxillofacial region can provide chances for dental practitioners to obtain multiplane imaging in the axial, coronal, sagittal and even the oblique or curved image planes.

The CBCT is made up of a 2D detector combined with a 3D x - ray beam. They synchronously move around the patient's head, which is stabilized with a head holder, and make a single 360° scan to produce projection images (" basis " images). Software programs use these images to produce a 3D volumetric data set, which help to provide in reconstruction images in three orthogonal planes (axial, sagittal and coronal).

The use of the CBCT technology has a number of potential advantages compared with conventional CT:

1- Minimizes the radiation dose by collimation of the primary x - ray beam to the area of interest (64).
2- Produce image with excellent quality and accuracy (65).
3- Decreased scan time (10 - 70 seconds).
4- It provides lower dose of radiation.
5- Reduced image artifact.
6- Low cost and less space requirements for scanning.

7- We can change the zoom or magnification and visual adjustments to narrow the range of displayed grey - scales (window) and contrast level within this window (63).

There are several disadvantages of the CBCT:

1- The cone beam projection geometry leads to irradiation of a large volume of tissue, resulting in a large amount of scattered radiation, which is recorded by the detector. As result, it does not show the actual attenuation of an object, and is termed as 'noise'.
2- The beam, when it comes across metal restorations in the mouth, is attenuated, producing information voids that result in streak artifacts in the images, obstructing the surrounding anatomy.
3- Patient's movement, causing image degradation artifact.
4- The CBCT images have poor soft tissue contrast (63).

Application of the CBCT imaging to clinical dental practice:

1- The capability to add annotation and cursor - driven measurement.
2- Imaging in implant planning.
3- Surgical assessment of pathology; pre - and postoperative.
4- TMJ assessment; pre - and postoperative.
5- Assessment of craniofacial fractures, growth and development (59, 64).
6- Measurement of bone loss even in the buccal and lingual / palatal aspects (65).

Density measurements are not valid in CBCT, the availability of different indices had to be tested on CT images as alternatives to the lack of accuracy in density measurements (62).

In addition, the coarseness of trabeculation of the alveolar bone on intraoral radiographs can be used to determine skeletal BMD better than densitometric measurements of the alveolar bone. Dense trabeculation means high BMD in the alveolar bone, whereas sparse /eculation may indicate to low BMD in the alveolar bone, as number and thickness of trabecular plates decrease in osteoporosis patient (66).

In summary, osteoporosis is a silent disease that is considered to be a serious public health concern for both elderly populations, and postmenopausal women. Early intervention may maximize bone mass retention and enhancement, thus reduce the risk of fracture, decrease the morbidity and mortality rates, and accordingly medical costs worldwide (67, 68, 69).

Osteoporosis is usually diagnosed by BMD measurements (70). Dental radiography may offer a screening tool for osteoporosis, as bone density in jaws can be assessed using panoramic radiographs, intraoral radiographs, QCT, and DXA. DXA is known as the most accurate clinical method for detecting those with low BMD (71, 72). Although BMD in the mandible is positively correlated with that in the lumbar spine and femoral neck (71). It is not practical to assess BMD in all postmenopausal women from the standpoint of cost - effectiveness and the limited number of facilities and trained personnel (73).

In the attempt to reduce the initial cost for the detection of osteoporosis with larger numbers of osteoporotic patients attending dental clinics; panoramic and / or CBCT images can be used for screening method in the diagnosis and predictor of osteoporosis, and evaluation of the bone changes (62). In this context, many studies have used different assessment indices such as: Bone Quality Index (BQI), Mandibular Cortical Width (MCW), Gonial Angle (GA), Mental Index (MI) or Computed Tomography Mental Index (CTMI), Klemetti Index (KI) (Computed Tomography Cortical Index [CTCI] or Mandibular Cortical Index [MCI]), Antegonial Index (AGI), Panoramic Mandibular Index (PMI) or Computed Tomography Mandibular Index Inferior (CTI"I"), Antegonial Depth (AD), Antegonial Angle (AGA), and Condylar Angle (CA). Those studies compared between normal and osteoporotic female groups by using these indices (61, 69, 74, 75, 76).

To the best of our knowledge in the literature, there are no previous studies comparing these radiological indices due to the lack of indication of acquiring both images from the same patient. The aim of this study is to compare the value of GA, MI, KI, AGI, PMI, AD, AGA, and CA in both panoramic and CBCT images of high risk osteoporotic female patients in relation to age.

2. MATERIALS AND METHODS

2.1. Patient sample:

The sample of the study is consisted of panoramic and CBCT images, which were prescribed for different indications (e.g. dental implant, oral surgery, tumor, impacted teeth, etc.), of the women, who presented to Yeditepe University, Faculty of Dentistry, Department of Dentomaxillofacial Radiology between 2011 and 2014.

Sixty - nine CBCT and panoramic images that were taken from each female patients, aged ranging between 44 - 80 years, were included in this study and were divided into two groups according to their age as 44 - < 60 and 60 - 80.

The exclusion criteria were as follows:

1. Subjects presented with systemic changes or metabolic bone diseases such as, diabetes, osteomalacia, thyrotoxicosis, hyperparathyroidism, hypoparathyroidism, Paget's disease, osteodystrophy, osteogenesis imperfect and renal disease.
2. Patient with fracture or pathology in the site of interest.

Bilateral measurement of all indices could not be made in all 69 images. Poor orientation of patient during CBCT images scanning prevented the measurement of GA and AGA in two images, whereas CA, AGI, and AD in one image. Poor visualization of inferior mandibular cortex at mental foramen prevented the measurement of KI on one panoramic image.

2.2. Radiographic image analysis:

The radiographic images were analyzed by one examiner. Measurements of all indices were bilaterally performed on CBCT and panoramic images by the same observer. This procedure was repeated for all the images in the sample with a two - week interval between two readings**.**

2.2.1. CBCT measurements:

The CBCT images were obtained using Iluma CBCT scanner (Imtec Corporation, Germany). Operating parameters were as follows: 120 kVp, 3.8 mA, and a voxel size of 0.2 mm, with an exposure time of 40 seconds. Image analyses and measurements were performed using Iluma Vision 3D (version 1.0.2.5, Imtec Image software), which provided axial, coronal, and sagittal views through multiplanar reconstructions (Figure 2.1). The contrast and the brightness of the images were adjusted using the image processing tools in software to ensure an optimal view.

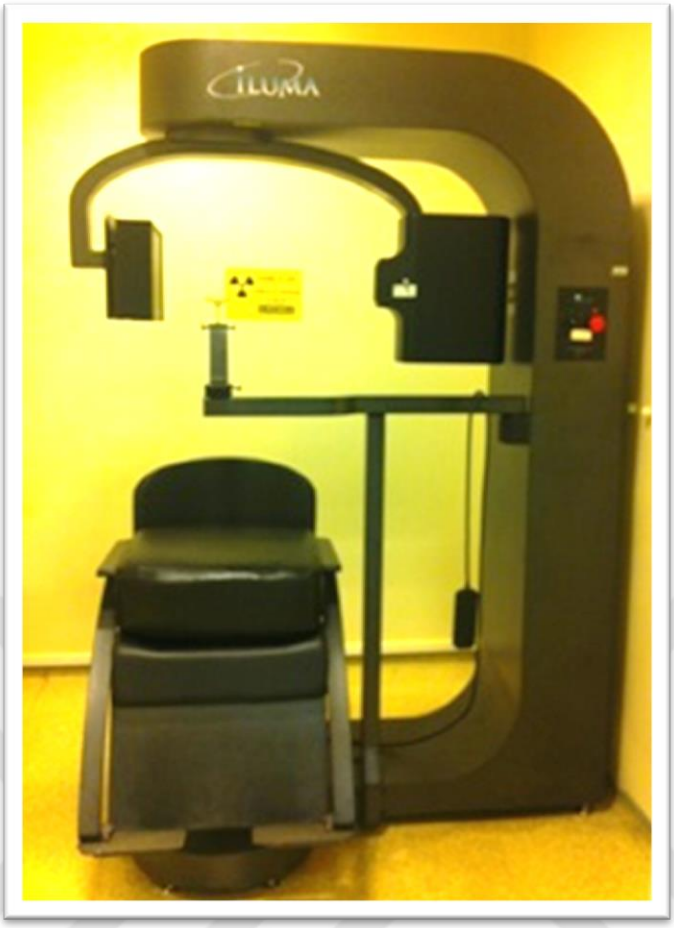

Figure 2.1: CBCT scanner.

Prior to the measurements, the images were oriented as follows:

1. In the sagittal plane, the orientation was performed according to Frankfort horizontal plane (a plane passing through the inferior margin of the orbit and the upper margin of each ear canal or external auditory meatus).
2. In the axial plane, the line extending horizontally at the tip of nose parallel to the line extending horizontally between the heads of the condyles.
3. In the frontal plane, the line extending horizontally between infraorbital foramens parallel to the line extending horizontally at inferior border of the mandible.

The mean axial, sagittal and coronal thickness were 1mm. The panoramic representations of the mandible were obtained from CBCT scans with 20 mm slice thickness, and cross - sectional slices were obtained from CBCT scans with 1 mm slice thickness.

MI, KI, PMI, and AGI were measured on cross - sections. GA, AD, AGA, and CA were measured using panoramic representations of the mandible on each side.

The following measurements were made:

1. GA: Assessed by tracing a line tangent to the lower border of the mandible and another line tangent to the posterior border of the ramus on each side. The intersection of these lines formed the mandibular angle (76) (Figure 2.2).
2. MI: Measured as the mandibular cortical width at mental foramen on each side (71) (Figure 2.3).
3. KI: The types of the inferior mandibular cortex were subjectively classified as follows on each side:

   Type 1: The cortical endosteal margin appears even and regular (CI 1).

   Type 2: The endosteal margin shows semilunar defects or 1 to 2 layers of cortical endosteal residues (CI 2).

   Type 3: The cortical layer has numerous (≥3) endosteal residues and is clearly porous (CI 3) (71) (Figure 2.4).

4. AGI: Measurement of the cortical width in the region anterior to the gonion at a point identified by extending a "best fit" line along the anterior border from the ascending ramus down to the lower border of the mandible on each side (68) (Figure 2.5).
5. PMI: Measured as the ratio of the inferior cortical width to the distance from the inferior margin of the mental foramen to the inferior border of the mandible on each side (71) (Figure 2.6).

$$\text{PMI} = \frac{\text{inferior cortical width (MCW)}}{\text{distance from the inferior margin of the mental foramen to the inferior border of the mandible}}$$

6. AGA: Measured by tracing two lines parallel to the lower cortical border at the antegonial region and measuring the angle of their intersection at the deepest point of the antegonial notch on each side (76) (Figure 2.2).
7. AD: Measured as the distance along a perpendicular line from the deepest point of antegonial notch concavity to a line parallel to the inferior cortical border of the mandible on each side (76) (Figure 2.2).
8. CA: Assessed by tracing a line tangent to the border of the condylar neck and another line tangent to the border of the ramus on each side (76) (Figure 2.2).

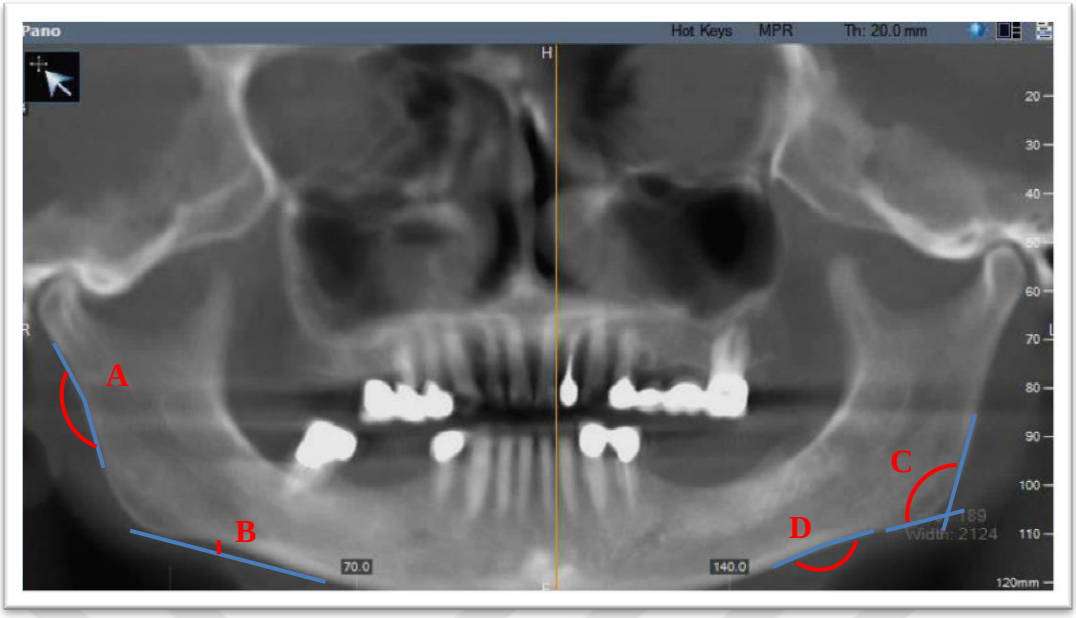

Figure 2.2: Measurements of Condylar Angle (A), Antegonial Depth (B), Gonial Angle (C), and Antegonial Angle (D) on CBCT image.

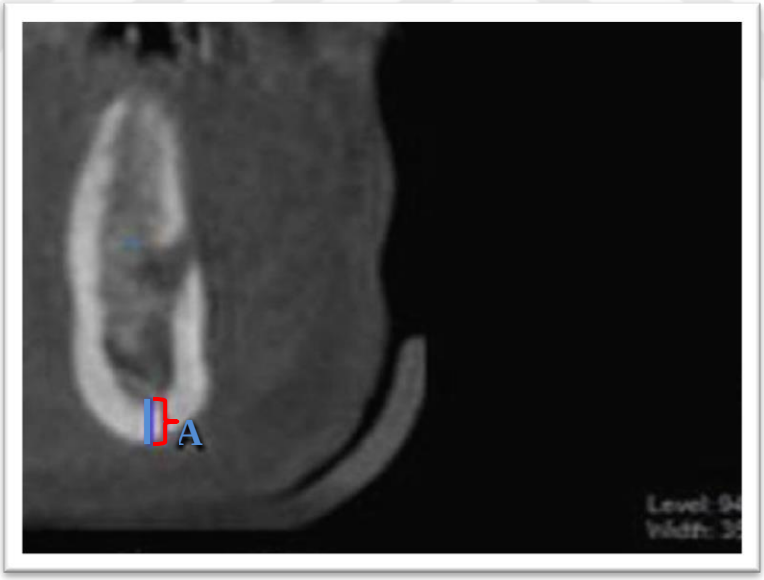

Figure 2.3: Measurement of Mental Index (A) on CBCT image.

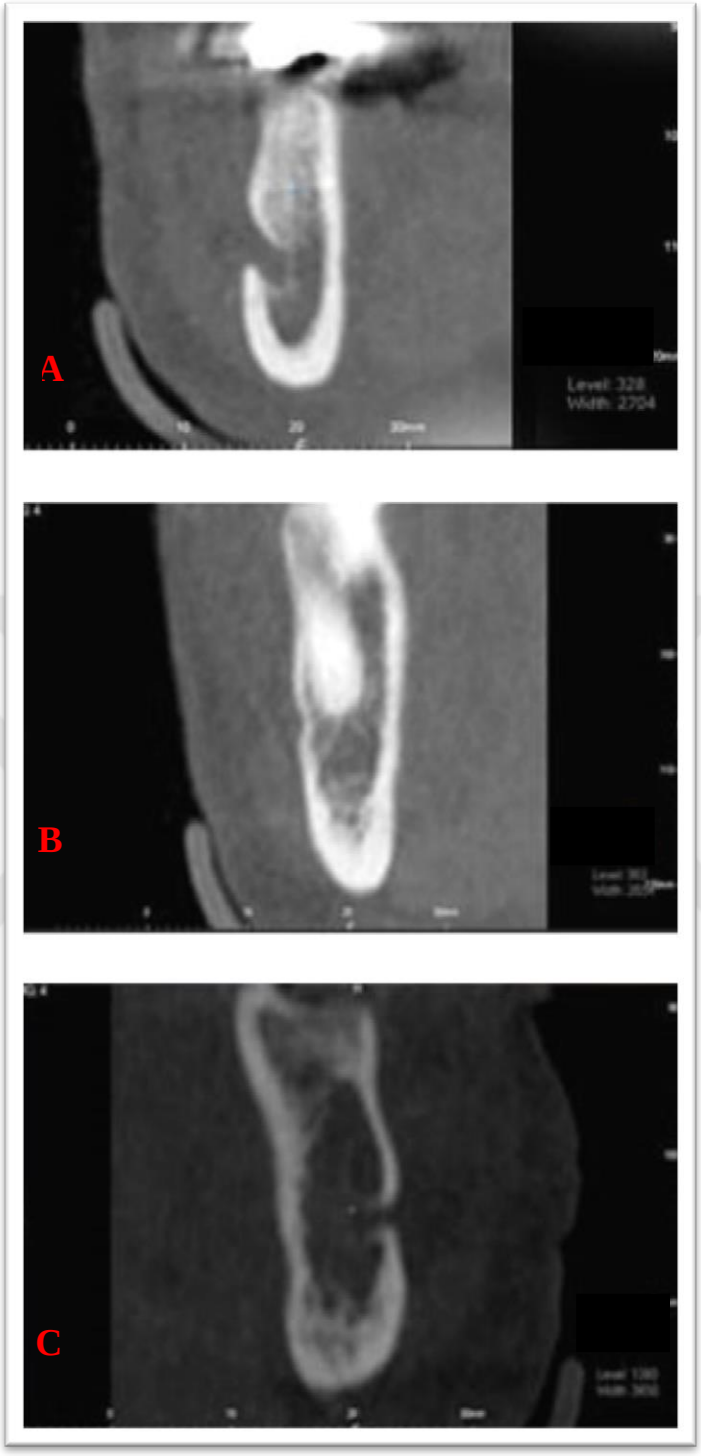

Figure 2.4: The types of the inferior mandibular cortex (A: CI 1, B: CI 2, and C: CI 3) on CBCT images.

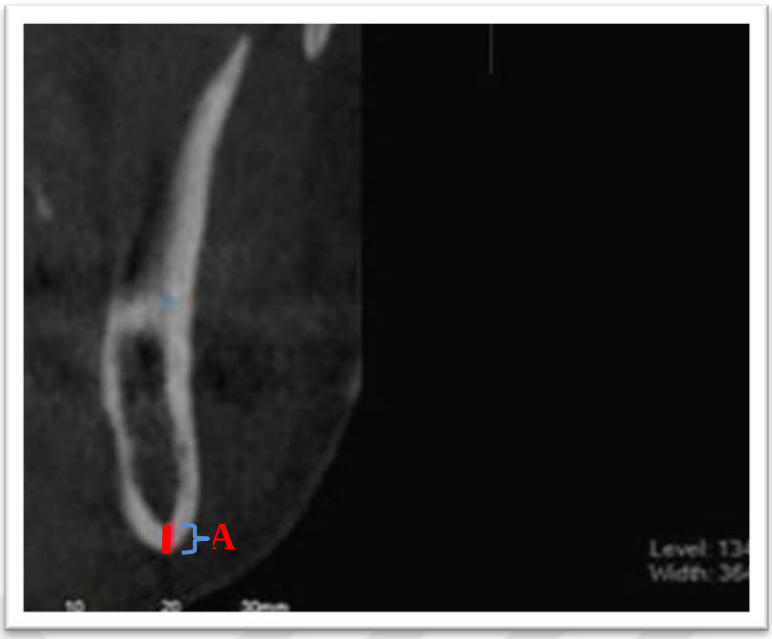

Figure 2.5: Measurement of Antegonial Index (A) on CBCT image.

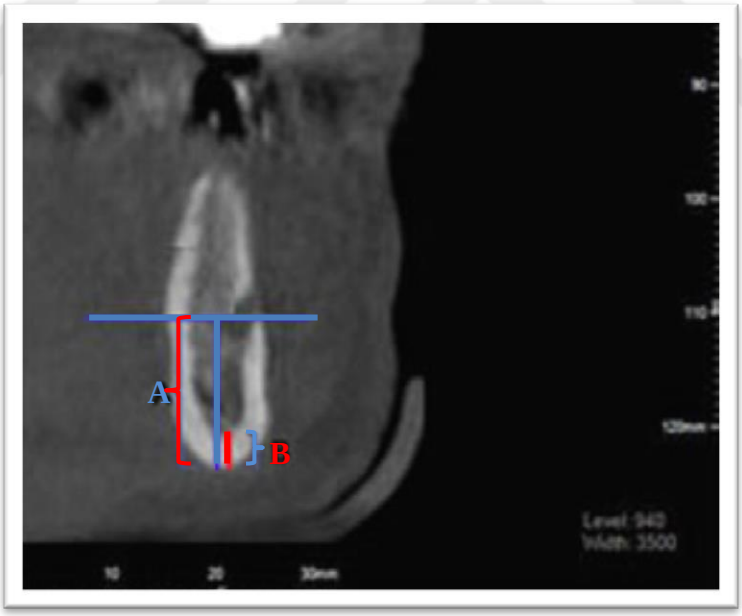

Figure 2.6: Measurement of Panoramic Mandibular Index (B/A) on CBCT image.

2.2.2. Panoramic radiography measurements:

The images were taken using Planmeca ProMax Digital Orthopantomograph (Planmeca, Helsinki, Finland). Linear and angular measurements were made using the ProMax software at 66 kVp, 8 mA and 16 seconds scan time (Figure 2.7).

Figure 2.7: Planmeca ProMax Dental Orthopantomograph.

Patients were positioned in the dental panoramic machine in such a way that the vertical line produced by the machine was aligned with the patient's sagittal plane, and the horizontal line (Frankfort plane) parallel to the floor.

The following radiomorphometric indices were measured bilaterally on each panoramic radiography:

1. GA: Assessed by tracing a line tangent to the lower border of the mandible and another line tangent to the posterior border of the ramus on each side. The intersection of these lines forms the mandibular angle on each side (68) (Figure 2.8).
2. MI: Measurement of the mandibular cortical width at the mental foramen region on each side (68) (Figure 2.9).
3. KI: The appearance of the inferior cortex of the mandible was classified as:
    i. Type 1: The cortical endosteal margin appears even and regular (CI 1).
    ii. Type 2: The endosteal margin shows semilunar defects or 1 to 2 layers of cortical endosteal residues (CI 2).
    iii. Type 3: The cortical layer has numerous ($\geq$3) endosteal residues and is clearly porous (CI 3) (68) (Figure 2.10).
4. AGI: Measurement of the mandibular cortical width in the region anterior to the gonion at a point identified by extending a "best fit" line along the anterior border from the ascending ramus down to the lower border of the mandible on each side (68) (Figure 2.9).
5. PMI: The ratio between mandibular cortical width and the distance between the lower margin of the mandible and the lower margin of the mental foramen on each side (normal value: $\geq$ 0.3) (61) (Figure 2.9).
6. AD: Measured as the distance along perpendicular line from the deepest point of antegonial notch concavity to a line parallel to the inferior cortical border of the mandible on each side (68) (Figure 2.8).
7. AGA: Measured by tracing two lines parallel to the lower cortical border at the antegonial region and measuring the angle of their intersection at the deepest point of the antegonial notch on each side (68) (Figure 2.9).
8. CA: Assessed by tracing a line tangent to the border of the condylar neck and another line tangent to the border of the ramus on each side (76) (Figure 2.8).

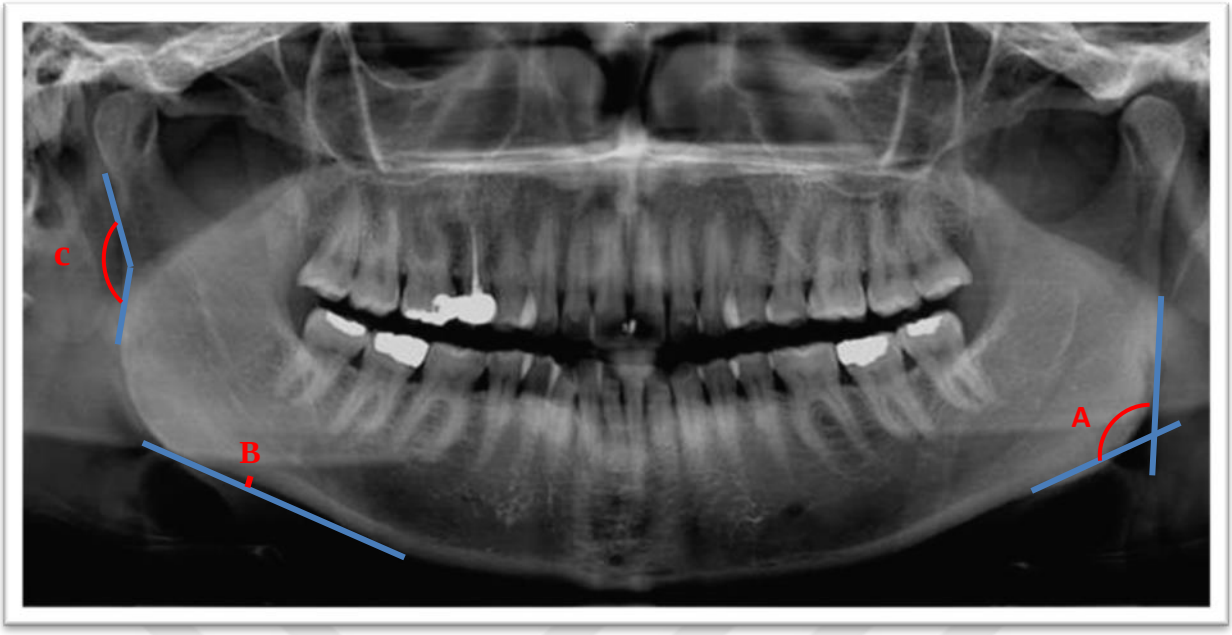

Figure 2.8: Measurement of Gonial Angle (A), Antegonial Depth (B), and Condylar Angle (C) on panoramic radiography images.

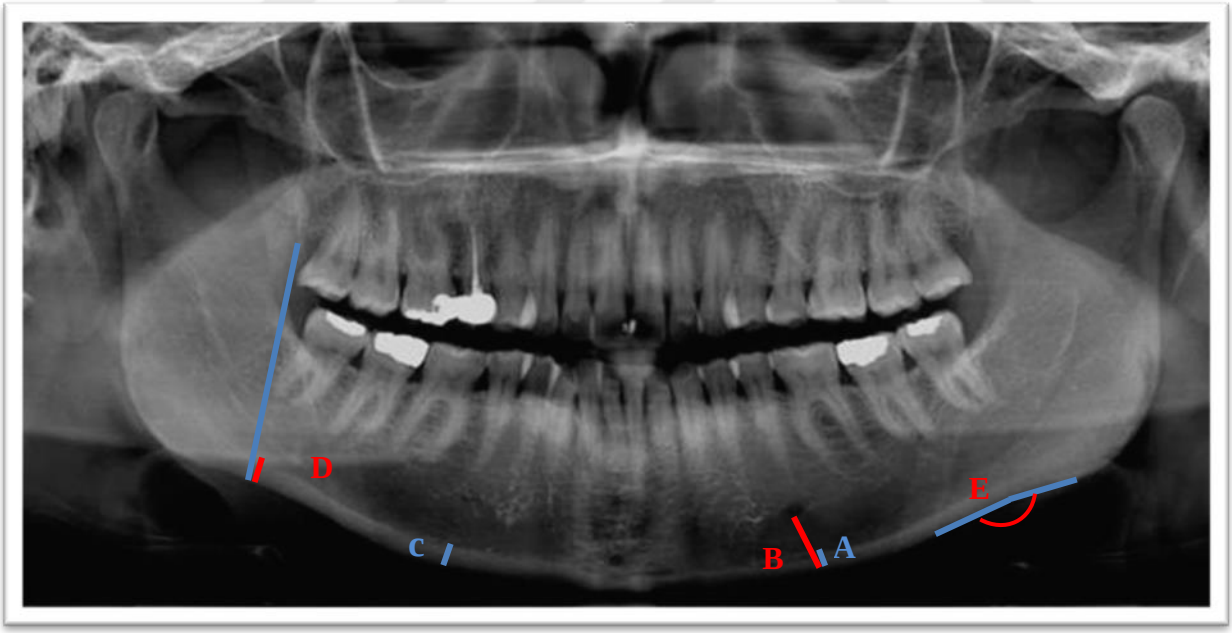

Figure 2.9: Measurement of Panoramic Mandibular Index (A/B), Mental Index (C) Antegonial Index (D), and Antegonial Angle (E) on panoramic radiography images.

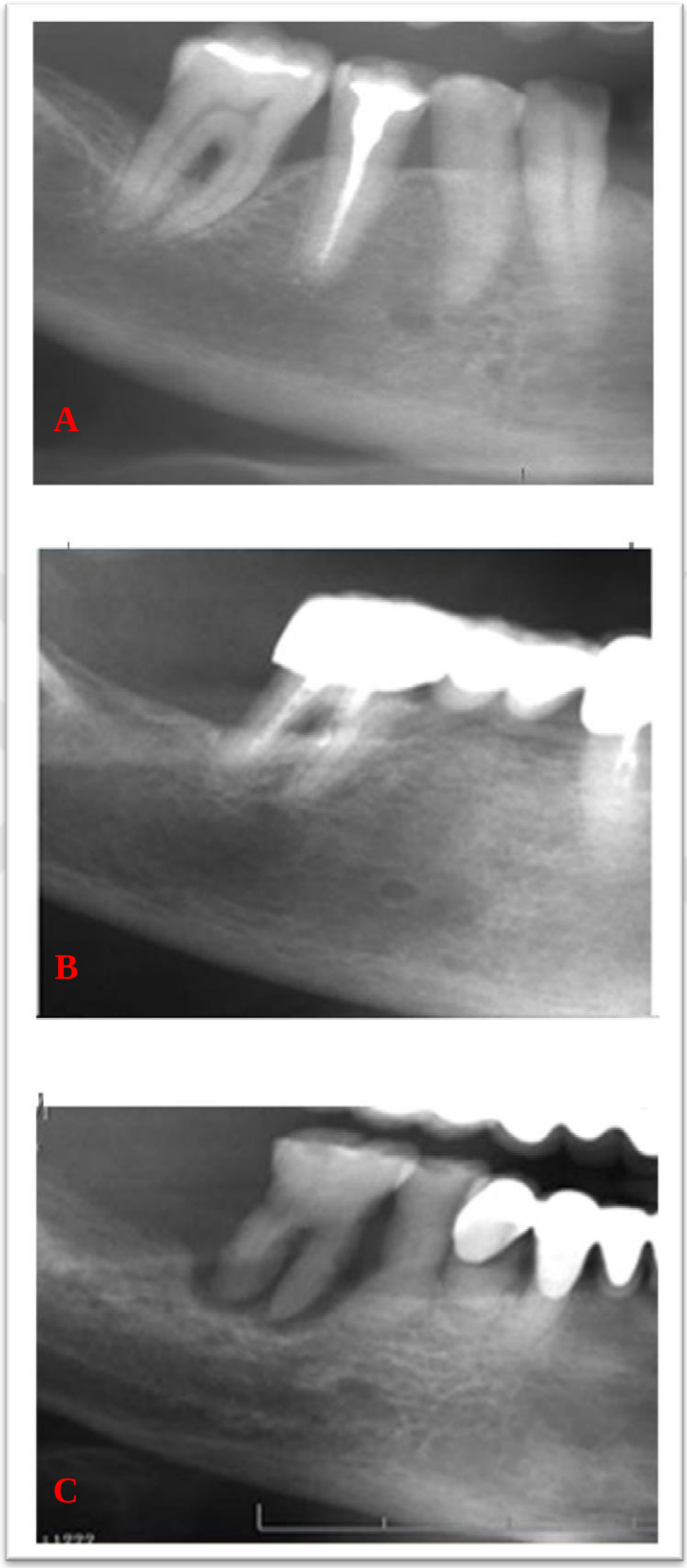

Figure 2.10: The types of the inferior mandibular cortex (A: CI 1, B: CI 2, and C: CI 3) on panoramic radiography images.

2.3. Statistical analysis:

Statistical analysis was performed using SPSS for Windows (SPSS 22, Chicago, IL, USA). Mean and standard deviation were used as descriptive statistics. Kolmogorov - Smirnov test was used to evaluate if the measurements were normally distributed or not.

Intraclass Correlation Coefficient (ICC) test was used to evaluate the agreement between the first and the second measurement readings. The correlation between the right and the left sides for GA, MI, AGI, PMI, AGA, AD, and CA was examined by using Pearson's Correlation Coefficient test. The correlation between the right and the left sides for KI was examined by using Contingency Coefficient test.

The two independent sample t - test was used to compare the mean difference of GA, MI, AGI, PMI, AGA, AD, and CA between two groups. Chi - Square test was used to compare KI classification between two groups. P value less than 0.05 was considered statistically significant.

5. RESULTS

Kolmogorov - Smirnov test was used to evaluate if the measurements were normally distributed or not. We found that our date were normal distributed ($p > 0.05$).

The degree of the agreement between the first and the second CBCT and panoramic radiography measurements on the right and the left sides was tested by ICC test. There was an agreement between the first and the second CBCT (ranging between 0.71 - 0.98 and 0.84 - 1 for the right and left, respectively) and panoramic radiography (ranging between 0.75 - 0.98 and 0.63 - 0.98 for the right and left), respectively measurements on both the right and the left sides for all indices.

Table 3.1 shows the degree of the correlation of CBCT measurements between right and left sides for all indices. There was a significant correlation between right and left sides for all the indices measured on CBCT ($p < 0.05$), except in the GA ($p > 0.05$).

Table 3.2 shows the degree of the correlation of panoramic radiography measurements between right and left sides for all indices. There was a significant correlation between the right and the left sides for all these indices measured on panoramic images ($p < 0.05$).

Table 3.3 and Table 3.4 show a comparison between the mean values of all indices measured on the panoramic images and the mean values of same indices measured on the CBCT on both sides. There were no significant differences between the two groups in all indices measured on both sides ($p > 0.05$), except in left GA ($p < 0.05$).

Table 3.5 and Table 3.6 show a comparison between the two age groups in terms of different indices measured on CBCT. There were no significant differences between the two age groups in all indices measured on both sides ($p > 0.05$).

Table 3.7 and Table 3.8 show a comparison between the two age groups in terms of different indices measured on panoramic images. There were no significant differences between the two age groups in all the indices measured on both sides ($p > 0.05$).

Table 3.1: The correlation of CBCT measurements between right and left sides by using Pearson Correlation Coefficient (r) test.

Indices		RPMI	RMI	RKI	RGA	RAGA	RAD	RCA	LAGI
LPMI	r	0.55	0.46	0.10	0.12	0.09	0.14	0.17	0.27
	P	*	0.00	0.40	0.30	0.43	0.22	0.15	0.02
	n	69	69	69	67	67	68	68	68
LMI	r	0.40	0.55	0.05	0.03	0.12	0.17	0.02	0.14
	P	0.00	*	0.67	0.78	0.30	0.15	0.83	0.22
	n	69	69	69	67	67	68	68	68
LKI	r	0.22	0.19	**	0.08	0.03	0.17	0.19	0.04
	P	0.05	0.11	*	0.50	0.77	0.15	0.10	0.70
	n	69	69	69	67	67	68	68	68
LGA	r	0.01	0.00	0.08	0.10	0.02	0.17	0.21	0.23
	P	0.90	0.94	0.50	0.41	0.81	0.16	0.08	0.05
	n	67	67	67	67	67	67	67	67
LAGA	r	0.14	0.14	0.03	0.00	0.43	0.46	0.26	0.25
	P	0.25	0.25	0.78	0.98	*	0.00	0.03	0.04
	n	67	67	67	67	67	67	67	67
LAD	r	0.00	0.02	0.05	0.08	0.64	0.76	0.30	0.13
	P	0.99	0.82	0.63	0.51	0.00	*	0,01	0.26
	n	68	68	68	67	67	68	67	68
LCA	r	0.05	0.15	0.10	0.03	0.38	0.39	0.42	0.18
	p	0.64	0.21	0.38	0.78	0.00	0.00	*	0.14
	n	68	68	68	67	67	67	68	67
LAGI	r	0.16	0.25	0.08	0.15	0.07	0.12	0.11	0.76
	p	0.18	0.03	0.49	0.20	0.52	0.31	0.37	*
	n	68	68	68	67	67	68	67	68

**The correlation between right and left sides for KI measured on CBCT was tested by using Contingency Coefficient test. * Significant correlation.

Table 3.2: The correlation of panoramic radiography measurements between the right and the left sides by using Pearson Correlation Coefficient (r) test.

Indices		LPMI	LMI	LKI	LGA	LAGA	LAD	LCA	LAGI
LPMI	r	0.66	0.47	0.00	0.07	0.23	0.12	0.16	0.08
	p	*	0.00	0.94	0.52	0.05	0.30	0.17	0.50
	n	69	69	68	69	69	69	69	69
LMI	r	0.40	0.54	0.04	0,02	0.18	0.11	0.11	0.00
	p	0.00	*	0.71	0.87	0.13	0.32	0.34	0.95
	n	69	69	68	69	69	69	69	69
LKI	r	0.01	0.03	**	0.02	0.13	0.00	0.04	0.19
	p	0.89	0.77	*	0.81	0.25	0.96	0.72	0.10
	n	69	69	68	69	69	69	69	69
LGA	r	0.01	0.15	0.15	0.29	0.10	0.04	0.17	0.27
	p	0.89	0.19	0.196	*	0.40	0.70	0.14	0.02
	n	69	69	68	69	69	69	69	69
LAGA	r	0,116	0.13	0.07	0.00	0.46	0.43	0.10	0.41
	p	0.34	0.26	0.54	0.96	*	0.00	0.39	0.00
	n	69	69	68	69	69	69	69	69
LAD	r	0.04	0.03	0.19	0.00	0.56	0.64	0.13	0.26
	p	0.69	0.75	0.11	0.96	0.00	*	0.28	0.02
	n	69	69	68	69	69	69	69	69
LCA	r	0.05	0.18	0.13	0.19	0.35	0.48	0.33	0.40
	p	0.64	0.12	0.26	0.10	0.00	0.00	*	0.00
	n	69	69	68	69	69	69	69	69
LAGI	r	0.09	0.03	0.08	0.08	0.24	0.24	0.24	0.54
	p	0.44	0.79	0.48	0.48	0.04	0.03	0.04	*
	n	69	69	68	69	69	69	69	69

** The correlation between right and left sides for KI measured on panoramic radiographies was tested by using Contingency Coefficient test. * Significant correlation.

Table 3.3: Comparison of CBCT and panoramic radiography in terms of PMI, MI, GA, AGA, AD, CA, and AGI by using t - test.

Indices	CBCT	Panoramic radiography	p
	Mean ± SD	Mean ± SD	
RPMI	0.36 ± 0.06	0.39 ± 0.12	0.13
RMI	4.72 ± 0.87	4.47 ± 1.03	0.13
RGA	147.77 ± 8.10	145.59 ± 6.99	0.09
RAGA	160.57 ± 8.64	159.9 5 ± 7.24	0. 65
RAD	2.15 ± 1.02	2.26 ± 1.24	0.58
RCA	159.59 ± 6.58	160.60 ± 4.44	0.29
RAGI	3.55 ± 0.98	3.26 ± 1.10	0.10
LPMI	0.37 ± 0.07	0.38 ± 0.10	0.62
LMI	4.52 ± 0.89	4.55 ± 0.94	0.84
LGA	151.248 ± 5.76	148.98 ± 4.98	0.01*
LAGA	161.58 ± 9.30	161.18 ± 9.74	0.80
LAD	1.91 ± 1.09	1.88 ± 1.27	0.89
LCA	161.36 ± 4.46	161.81 ± 4.17	0.54
LAGI	3.53 ± 0.94	3.37 ± 0.98	0.34

* Significant difference.

Table 3.4: Comparison of CBCT and panoramic radiography in terms of different types of inferior mandibular cortex by using Chi - Square test.

Indices		CBCT	Panoramic radiography	Total	p
RKI	CI 1	48 (69.6%)	46 (67.6%)	94 (68.6%)	0.21
	CI 2	15 (21.7%)	10 (14.7%)	25 (18.2%)	
	Cl 3	6 (8.7%)	12 (17.6%)	18 (13.1%)	
Total		69 (100%)	68 (100%)	137 (100%)	
LKI	CI 1	50 (72.5%)	49 (71.0%)	99 (71.7%)	0.43
	CI 2	15 (21.7%)	12 (17.4%)	27 (19.6%)	
	Cl 3	4 (5.8%)	8 (11.6%)	12 (8.7%)	
Total		69 (100%)	69 (100%)	138 (100 %)	

Table 3.5: Comparison of the age groups in terms of PMI, MI, GA, AGA, AD, CA, and AGI measured on CBCT by using t - test.

Indices	44 - < 60	60 - 80	p
	Mean ± SD	Mean ± SD	
RPMI	0.37 ± 0.05	0.35 ± 0.08	0.23
RMI	4.95 ± 0.72	4.60 ± 0.97	0.09
RGA	146.61 ± 7.49	149.72 ± 8.86	1.14
RAGA	161.24 ± 6.07	159.45 ± 11.84	0.48
RAD	2.08 ± 0.95	2.26 ± 1.152	0.51
RCA	158.72 ± 6.71	161 ± 6.25	0.16
RAGI	3.59 ± 0.87	3.49 ± 1.17	0.70
LPMI	0.37 ± 0.06	0.36 ± 0.076	0.44
LMI	4.70 ± 0.84	4.48 ± 0.93	0.32
LGA	151.76 ± 5.77	150.38 ± 5.77	0.34
LAGA	161.98 ± 8.11	160.91 ± 11.17	0.65
LAD	1.87 ± 1.01	1.96 ± 1.24	0.75
LCA	160.77 ± 4.26	162.31 ± 4.68	0.16
LAGI	3.56 ± 0.83	3.47 ± 1.12	0.69

Table 3.6: Comparison of age groups in terms of different types of inferior mandibular cortex observed on CBCT by using Chi - Square test.

Indices		Age groups		Total	p
		44 - < 60	**60 - 80**		
RKI	**CI 1**	32 (74.4%)	16 (61.5%)	48 (69.6%)	0.27
	CI 2	9 (20.9%)	6 (23.1%)	15 (21.7%)	
	CI 3	2 (4.7%)	4 (15.4%)	6 (8.7%)	
Total		43 (100%)	26 (100)	69 (100%)	
LKI	**CI 1**	34 (79.1%)	16 (61.5%)	50 (72.5%)	0.28
	CI 2	7 (16.3%)	8 (30.8%)	15 (21.7%)	
	CI 3	2(4.7%)	2 (7.7%)	4 (5.8%)	
Total		43 (100%)	26 (100%)	69 (100%)	

Table 3.7: Comparison of age groups in terms of PMI, MI, GA, AGA, AD, CA, and AGI measured in panoramic radiographies by using t - test.

Indices	44 - < 60	60 - 80	P
	Mean ± SD	Mean ± SD	
RPMI	0.39 ± 0.11	0.39 ± 0.15	0.86
RMI	4. 32± 0.96	4.50 ± 1.63	0.62
RGA	145.60 ± 6.25	145.57 ± 8.19	0.98
RAGA	160.18 ± 6.88	159.57 ± 7.92	0.73
RAD	2.09 ± 1.06	2.53 ± 1.47	0.18
RCA	160.95 ± 4.56	160.03 ± 4.28	0.41
RAGI	3.41 ± 1.02	3.00 ± 1.20	0.12
LPMI	0.37 ± 0.09	0.39 ± 0.12	0.37
LMI	4.23 ± 0.81	4.26 ± 0.91	0.86
LGA	149.25 ± 4.69	148.53 ± 5.48	0.56
LAGA	161.65 ± 9.14	160.42 ± 10.81	0.61
LAD	1.83 ± 1.06	1.96 ± 1.58	0.69
LCA	161.86 ± 4.06	161.73 ± 4.42	0.90
LAGI	3.44 ± 0.88	3.26 ± 1.15	0.48

Table 3.8: Comparison of age groups in terms of different types of inferior mandibular cortex observed on panoramic radiographies by using t - test.

Indices		Age groups		Total	p
		44 - < 60	60 - 80		
RKI	CI 1	34 (70. 8%)	14 (29.2%)	48 (100.0%)	0.13
	CI 2	5 (45.5%)	6 (54.5%)	11 (100%)	
	CI 3	4 (44.4%)	5 (55.6%)	9 (100%))	
Total		43 (%63.2)	25 (36.8%)	68 (100%)	
LKI	CI 1	34 (79.1%)	15 (57.7%)	49(71%)	0.05
	CI 2	7 (16.3%)	5 (19.2%)	12(17.4%)	
	CI 3	2 (4.7%)	6 (23.1%)	8 (11.6%)	
Total		43 (100%)	26 (100 %)	69 (100%)	

4. DISCUSSION

Bone loss occurs with age (age - related osteoporosis) in men and women, but in the latter the rate of loss increases at menopause (postmenopausal osteoporosis) (77). The rate of bone loss has been reported to vary from 0.5 to 1% per year, and the decline in estrogen levels during menopause is considered as the major cause of bone loss. However, there are other risk factors associated with osteoporosis, such as age, heredity, alcohol drinking, tobacco smoking, physical inactivity, low - calcium intake, and high - sodium intake. Although menopause puts women at greater risk of osteoporosis, it might not be detected until symptoms or fractures occur. Early detection of the disease is important to maximize bone mass retention, reduce the risk of fracture, and avoid subsequent pain of patients (62, 78).

Osteoporotic bone loss affects various parts of the body, including the jaws. Various studies have demonstrated the correlation between the BMD in the mandible and that in the hip and spine (62). The decrease in BMD of skeletal bone affects the morphometric, densitometric and architectural characteristics of the mandibular bone (71, 77, 79, 80).

Since the disease is preventable, diagnostic techniques are of major importance. A considerable effort has been made to identify methods of detecting individuals with osteoporosis at an early stage to limit the disease process (77).

BMD testing by DXA is the ‘‘gold standard’’ method of osteoporosis diagnosis, but BMD testing of all postmenopausal women by DXA is difficult, because it requires extensive facilities and high costs, it requires the time of both patient and medical personnel, and it is limited in many countries. Therefore, there is a need for less expensive alternative methods for assessing the skeletal status (74).

Dental radiology is a useful imaging technique, by which the dentist can evaluate the teeth and jaws in general dental practice. The dental radiographies are relatively inexpensive (71,81, 82, 83, 84), easy (85), and rather non - invasive technique for identifying individuals with low bone mass (71, 82, 86). They are already used in a large part of the adult population. The incidental findings detected on dental images like CBCT and panoramic images may be used as a screening tool for osteoporosis as well as for identifying women, who have no awareness of their low BMD and would benefit from BMD testing and help decrease the mortality and morbidity associated with osteoporosis (81, 82, 83, 84, 85, 86).

One of the most useful bony landmarks to use as an indicator for the analysis of bone metabolism is the mandibular angular cortex; the inferior cortex of the mandible is dense, wide, and appears as a very radiopaque strip of bone along the inferior border of the

mandible. Most researchers only involve mandibular measurements in their analysis and consider the area of the mandible posterior to the mental foramen as the standard measurement site for jaw bone analysis, because it has the lowest inter - and intra - individual variations in anatomical size, shape, bone structure, and function (86).

In women, the thickness of the inferior cortex of the mandible will become thinner over time, and cortical changes of the mandibular angular area are observed in women, who are more than 20 years of age. Mandibular inferior cortical measurements, cortical width, and cortical shape detected on dental radiographs are useful for identifying postmenopausal women with low skeletal BMD or osteoporosis. Therefore, a thin or eroded cortex of the mandible detected on dental radiographs is associated with low vertebral BMD or osteoporosis (68, 71, 74, 75, 82, 86, 87, 88, 89, 90, 91, 92, 93).

Clinicians have started to focus on dental radiomorphometric indices such as GA, MI, KI, AGI, PMI or CTI"I", AGA, AD, and CA to assess mandibular cortical shape and width, to evaluate bone quality, to observe signs of resorption on panoramic radiographs and CBCT (68, 94), to identify patients with low skeletal BMD (93), and to identify elderly individuals, who should undergo BMD assessment (77, 75, 82, 84).

Although some researches have suggested that dental radiomorphometric indices on dental radiographs should not be used to assess a patient's osteoporotic status, others believe that they are reliable tools in the screening for osteoporosis (77, 82, 84, 95). Dentists may be able to refer postmenopausal women younger than 65 years for bone densitometry on the basis of incidental findings on dental radiographs (81, 90).

CBCT examination is being increasingly requested by dentists, mainly for the assessment of bony structures in patients, who will undergo insertion of dental implants. The CBCT examination allows the visualization of the structures without superimposition, magnification, or distortion, besides a great 3D visualization of bone volume and architecture. However, by CBCT, the density measurement is not reliable, and accordingly an alternative approaches for this image modality are required. So, computed tomography indices on CBCT images are used in the visualization of the mandibular cortex to assess osteoporotic women (62). It is unclear whether the index values obtained by CBCT evaluation are equivalent or superior to panoramic images for visualization of bone structures with high levels of detected porosity. Unlike other studies, the present study makes comparisons between a qualitative and quantitative index sets that take into account the appearance of the mandibular cortex in the panoramic and CBCT images in regards to age.

4.1. Gonial Angle (GA):

The angle formed by the lower margin of the body and the posterior margin of the ramus of the mandible is called the Goinal Angle (GA) (96). GA could be used as an indicator of the age and the gender (97). Also, it could be used as a tool in near age assessment in extreme situations like mass disaster, remains of human dead exhumed and murderous mutilations, and missing individuals (97).

A previous study evaluated the angle of the mandible between normal and osteoporotic bones. It concluded that the GA showed a significant difference among two groups, hence the decrease in the angle of mandible could be conveniently used for the early detection of osteoporosis (98). However, other studies revealed no association between GA and BMD of bone skeletal status, and this index could not be useful for osteoporosis prediction (68, 92, 99).

The correlation between the right and the left GA has been evaluated by number of researchs, their results were variable and inconsistent. Shahabi et al. (100), Gungor et al. (101), and Dutra et al. (102) evaluated the right and the left GA on the panoramic radiographs. They found small differences in GA between left and right sides, and the variability was relatively small and statistically non - significant. In regards to GA measurements, our results gathered with panoramic radiography were in agreement with these studies, whereas there were no agreement with CBCT results.

In contrast, Chole and Cakur (96) and Raustia and Salone (103) measured the right and the left GA on panoramic radiographs. Also, Tozoglu et al. (76) measured the right and the left GA on CBCT. They found that the right GA was statistically significantly smaller than the left one. Our results strongly support these findings when we used CBCT for measuring the GA, but not when we measured it on panoramic radiographs. This difference between right and left sides can be due to the increased function on a preferred chewing side. It can also be due to the random asymmetry of the facial skeleton (102).

There have been studies carried out on factors that could affect the GA which concluded that the postural and functional interrelationships of the cheek, lips and tongue in edentulous individuals can alter the GA. Also, the consecutive atrophy of the masticatory muscles in elderly edentulous people, after many years of increased function, leads to changes in the region of the mandibular angle. Resorption of the bone at the posterior or inferior border of this region, the area of the masseter muscle insertion, leads to increasing obtuseness of the mandibular angle. Accordingly, after loss of all teeth, non - denture wearers have wider GA

than denture wearers (97). Also, the muscular activity associated with mastication preserves the angle from any changes. Electromyography studies have shown strong masseter and anterior temporal muscle activity to be associated with a small GA. Those subjects with strong maximum masticatory force have small GA. These facts may explain the findings that the edentulous women had greater GA than the dentulous women (104).

In our results, there was no statistically significant difference between panoramic radiography and CBCT in regarding to the right GA measurement. However, there was statistically significant difference between panoramic radiography and CBCT in regarding to the left GA measurement. This may be attribute to the potential sources of variability included errors in patient positioning in the radiographic machine, inaccuracies in the accurate location of the mandibular measurement site in the dental panoramic radiographs, or measurement error in the software detection of the bone margins (105).

Various research studies have described a number of changes that take place in the morphology of the human mandible with advancing age. Although one of the prominent changes suggested is the change in the gonial angle, their results were variable and inconsistent.

Upadhyay et al. (97) and Ohm and Silness (106), who evaluated the GA on the cephalograms, found statistically non - significant positive association between GA and age. As well in previous studies performed on the panoramic radiographs, there was no significant association between the GA and the age (96, 102, 103, 106, 107). As regarding our results, the difference between the mean value of GA in both age groups was not statistically significant on CBCT or panoramic radiography.

4.2. Mental Index (MI):

A considerable attention has been paid to low skeletal bone mass screening based on MCW measurements at the mental foramen area. Many studies found that MI was significantly smaller in individuals with low bone mass, and they noticed an increased risk of osteoporosis with corresponding decrease in the MI at the mental region (108).

Most authors have suggested that patients with the thin mandibular cortices at the mental foramen ($\leq$ 3 mm) should be referred for further osteoporosis investigation, because this group has the highest likelihood of osteoporosis (109, 110, 111). However, other studies have failed to prove that a significant difference in MI exists between osteoporotic and control subjects (71, 99, 112). This conflict may be attributed to the difference in the age groups and referral criteria in their studies.

Kingsmill and Boyde (113) studied the variability in the anatomy of mandibles of differing ages. They studied the cross sectional slices of the dry mandibles and measured MCW from the radiographs of those slices. They concluded that unlike other bones, the mandible may show an increase in apparent density with age, implying that the mandible may not be suitable for evaluating osteoporotic status and they found no relationship between radiographic MCW and age.

The correlation between the right and left MI has been evaluated by many studies and their result variable and inconsistent. Our results are in consistent with result of earlier studies conducted on the panoramic radiographs when they reported that the correlation between the right and the left sides was high for MI with no significant differences demonstrated (78, 93, 94, 114, 115, 116). In contrast, the result of studies conducted by Khayam et al. (82) and Papamanthos et al. (117) on the panoramic radiographs demonstrated a significant difference between the two sides. Such differences could be due to the increased function on the preferred chewing side, or the random asymmetry of the facial skeleton. This result is neither in agreement with our result nor with other result (82).

In our study, there were no significant differences between the mean value of MI recorded in CBCT and panoramic images on both sides.

Several authors have studied changes in MI of the mandible throughout ageing on the panoramic radiographs. Hajipour et al. (99) conducted a study on women over 45 years of age and found that the value of MI measured on panoramic radiographs was 12.72mm. It is important to highlight that the mean value reported for MI in Hajipour et al. (99) study was much higher than the mean value obtained in the current study. Differences reported in studies may be due to different age range of women, sample size, and ethnic differences related to nutrition and climate. On the contrary, Taguchi et al. (90) evaluated MI on panoramic radiographs of postmenopausal women younger than 65 years and found that MI in all cases was less than 3mm. In a study conducted by Ledgerton et al. (114), in a population of British women aged between 25 -74 years, this value was reported to be 4.46 mm. Also, this value was reported to be 4.73mm by Devlin et al. (109). The values reported for MI in the above - mentioned studies were not much different from the mean value obtained in the current study.

Many studies found that MI showed a negative correlation with age i.e. decreasing mean values of MI with increasing age (77, 78, 79, 114, 118). Dhandapani and Mariamichael (108) evaluated the panoramic radiographs of the South Indian female patients; with age ranging between 48 and 86 years. They found that there was a negative correlation between the MI

and age, and a statistically significant difference in the MI between subjects aged greater than 60 years and subjects aged lesser than 60 years ($p < 0.05$). As well Ledgerton et al. (119) and Alonso et al. (93) found significant differences in MI measured on panoramic radiographs among different age groups.

In addition, previous studies evaluated the relationship of MI with age on panoramic radiographs. They found that the measured MI between different age group of the patients was significantly different (78, 82, 118). The smaller values of such index in the old females were already expected, owing to the bone loss of women after the fourth decade of life. Nevertheless, these are in disagreement with our result when we used panoramic radiography or CBCT for measuring MI as the mean values in both age groups showed statistically non - significant differences.

In contrast , our results are in agreement with the results reported by previous studies when they evaluated the relationship of MI with age on panoramic radiographs. Their results revealed that the measured MI in different age group of the patients was non significantly different (115, 120).

4.3. Klemetti Index (KI):

One of the most established techniques for the diagnosis and evaluation of bone changes and as a predictor of osteoporosis is the Mandibular Cortical Index (MCI), also known as Klemetti Index (KI), which is the qualitative assessment of the appearance of the inferior cortex of the mandible on dental radiographs (80, 81).

In order to evaluate the MCI of the mandible, the morphology of mandibular inferior cortex was visually examined distally from the mental foramen bilaterally using Klemetti's classification (87, 121, 122) which are :

CI 1: The endosteal margin of the inferior cortex is smooth on both ends.
CI 2: The endosteal margin shows semilunar defects or appears to form endosteal cortical residues.
CI 3: The cortex is obviously porous with dense endosteal residues.

Previous studies showed that the mean BMD assessed by DXA had a non - significant relationship with the KI scale. So, it could not be utilized as a tool for perdition of osteoporosis (72, 84, 112, 123, 124).

On the other hand, others studies showed that the mean BMD assessed by DXA had significant relationship with the KI (110, 120, 122, 123, 125, 126, 127). So, it could be

utilized as a tool to identify the patient with low mineral bone density, to identify the risk for bone mass loss and appropriately refer the patient for assessment by bone densitometry, but not for diagnostic purposes. These can assist in the prevention of the disease development (71, 99, 108, 118, 122, 125, 126, 128).

Mandibles classified as CI 3 have the lowest bone density (129). The BMD in CI 1 is significantly higher than that in CI 2 (99). The risk of osteoporosis in CI 3 category is 12.6 times more than CI 2, the risk of osteoporosis in CI 2 category is 12 times more than CI1 and the risk of osteoporosis in CI 3 category is 142.8 times more than CI 1 with 95% confidence interval (67, 75, 80, 90, 114, 130, 131, 132, 133, 134).

Various research performed to assess the correlation between right and left sides for KI on the panoramic radiographs as they reported that the correlation between the right and the left sides was high for KI with no significant differences demonstrated in both sides (68, 75). Our results are in consistent with result of these studies, but are not in agreement with result of study conducted on panoramic radiographs by Mudda et al. (118) as it found significant differences between two sides.

Furthermore, in our result; there was no statically significant difference between the proportions of KI measured by CBCT and panoramic radiography on both sides. This may attribute to that KI involves no measurements; it is a subjective index of porosity for which minor magnification differences between two machines should have no effect (74).

Gomes et al. (62) compared the KI obtained from panoramic and cross sectional images constricted from 44 CBCT images of postmenopausal female subjects aged more than 45 years. The results of Gomes agree with our results in which there were no statistically significant differences between panoramic and cross sectional images. The KI assigned in tomographic images is comparable to that obtained in panoramic images, indicating a valid use of this index in CBCT images, which can lead to the identification of patients with bone mass loss and a premature referral to further management.

According to Gomes's study, the classification of KI during evaluations of bone structures in CBCT slices in three - dimensional views can be applied, being more suitable for bone assessments than panoramic radiography. Moreover, their intraclass results demonstrated better reproducibility of the evaluation in cross sectional images and a higher agreement between the professionals assessing the images. However, it is worth mentioning that a CBCT exam must not be requested just for this purpose, yet an incorporation of KI evaluation should be done in the routine tomographic appraisal of the practitioners (62).

The age factor is significantly associated with KI; by aging human bones decrease in density and increase in porosity (114, 135). Also, as the age increases, the likelihood of being in the CI 3 category increases presumably reflecting age - related bone loss. These age related changes are in agreement with our result in which the proportions of KI changed with age (increased in the proportions of CI 2 and CI 3 and decreased in proportion of CI 1). But they reached to non - significant difference between age groups when we used panoramic radiography or CBCT for evaluate the relation between the age and the KI.

Gulsahi et al. (129) assessed how the age affected in KI on panoramic radiographs of the Turkish population by dividing them into three age groups: 20 - 49 years old group, 50 - 69 years old group, and the over 70 years old group. The results showed that both CI 1 (46%), and CI 2 (49%) were the most observed KI categories and CI 3 (5%) was the least observed KI category. Compared with patients aged 20 - 49 years, the likelihood of being in the CI 3 category for patients over 70 years of age was 79.14 times higher and for patients aged 50 – 69 years was 9.17 times higher. So, the age factor was significantly associated with KI. The result of this study was in agreement with the results of Mudda et al. (118) as they found that CI 3 category was seen only in postmenopausal group after 54 years of age.

In a study conducted by Ledgerton et al. (114), 500 British female Patients were grouped according to age into ten 5 - year age groups. The youngest age group was 25 ± 29 years and the oldest 70 ± 74 years. KI showed an age - related distribution. The majority (52%) was demonstrated type CI 2 cortices whilst the remainder was divided between types CI 1 (22%) and CI 3 (26%). The relative proportions of the three KI classes in (45 ± 54 years) age group were similar to those reported by Klemetti et al. (122) in their study of 355 Finnish women (48 ± 56 years). However, Taguchi et al. (125) identified a far greater proportion of CI 1 cortices in their study of 124 Japanese women in a broad age band (33 ± 68 years).

Concurrently, age related changes were in agreement with the results of Knezovic et al. (120) and Yüzügüllü et al. (94) who evaluate KI on panoramic radiographs of female patients. The results revealed that only two categories (CI 2 and CI 3) of KI were recognized in the sample and non of the patients had category CI 1 of KI. This may be attributable to the fact that the group of selected patients was relatively older, in comparison to the age of 30, when the first signs of bone loss start to manifest. Mild erosions on the endosteal margin of the mandible (CI 2) were more frequently seen in age groups of ≤ 60, and severe erosions on the endosteal margin of the mandible (CI 3) were more frequently seen in age groups of > 60 in women ($P < 0.05$). The number of patients with category CI 3 increased significantly, indicating a decrease in bone quality with age.

In contrast, Hajipour et al. (99) assessed KI on panoramic radiographs of 70 women aged over 45 years. They found that the morphology of the inferior cortex was in CI 1, CI 2 forms (62.9% and 37.1%). CI 3 was not seen in women over 45.

Dhandapani and Mariamichael (108) and Pal et al. (79) tried to extract information about KI from dental panoramic radiographs and to identify its age related changes among the Indian population (age ranged between 30 - 80 years). They found that KI was negatively correlated with age, and statistically significant difference in the appearance of cortex among women in various age groups ($p = 0.013 < 0.05$). Our results disagree with the result of these study because we found non - statically significant difference between the age groups when we used CBCT or panoramic radiography for KI evaluation.

In a study conducted by Dalili and Qujeq (136) in 2003 on healthy women; age ranged between 20 - 75 years, the CI 1, CI 2 and CI 3 forms were seen in 20.9%, 71.3%, and 7.8% of the subjects, respectively. Moreover, in a study conducted by Imani et al. (137): CI 1, CI 2 and CI 3 forms were seen in 29.9%, 65.7%, and 4.4% of the subjects, respectively (137).

In addition, Hastar et al. (61) evaluated KI in female patients of an age group ranging from 60 to 88 years: 28.6%, 68.5%, and 2.8% of the women had eroded mandibular cortex; CI 1, CI 2, and CI 3 respectively.

Differences reported in studies may be due to different age range of women, sample size, and ethnic differences related to nutrition and climate. Moreover, difference in the observer's vision and a difference in the interpretation of the definitions of the KI groups may also affect these results. If the latter is the case, then there could be significant problems with repeatability of assessments in different centers (99).

4.4. Antegonial (AGI) :

Measurement of the MCW in the region anterior to the gonion at a point identified by extending a "best fit" line along the anterior border from the ascending ramus down to the lower border of the mandible is called Antegonial Index (AGI) (68). Several studies have evaluated the relation between MCW measured on this region (normal value: ≥ 3.2 mm) and BMD, and they have concluded that AGI values are significantly smaller in individuals with low bone mass ($P < 0.05$). So, the AGI reliably reflects the systemic condition associated with bone as osteoporosis (72, 75, 92, 114). However, other study has revealed no association between AGI and BMD of bone skeletal, and this index cannot be useful for the prediction of osteoporosis (99).

In previous studies conducted on panoramic radiographs (82, 120, 138), there was a statistically significant difference between the left and the right AGI, and it had a significantly greater value on the left side of the mandible than that of the right one. This could be due to increased function on a preferred chewing side or random asymmetry of the facial skeleton (120). The results of these studies disagree with our result when we used CBCT and panoramic radiography for measuring AGI, but we agree with the result of other studies conducted on panoramic radiographs in which the means of AGI measured on the right and the left sides of the mandible were non - significantly different (75, 79, 114, 115). In additional, in our result; the mean values of AGI recorded in both types of images were non - significant difference.

A number of studies have conducted to evaluate changes in AGI measured on panoramic radiographs throughout aging. The result reveled that AGI showed negative correlation with age and there was a significant difference in AGI between age groups ($p < 0.05$) (79, 82, 115, 120, 138). These results are not consistent with our study, because we found a non - statistically significant difference between the age groups when using CBCT or panoramic radiography for measuring AGI. The reasons for this inconsistency may be due to the fact that many factors, such as food regimen, lifestyle, the time that a person has had no teeth, and environmental stress can influence the results and bias the findings.

4.5. Panoramic Mandibular Index (PMI):

PMI is a radiomorphometric method presented in 1991 by Benson et. al. (139). It was partly based on Wical and Scoope study (140) where they suggested that despite of the alveolar bone resorption above the foramen, the distance from the foramen to the inferior border of the mandible remains relatively constant throughout life. The distance below the foramen in a non - resorbed mandible is approximately one third of the total height of the mandible in that region (140). Thus, the PMI provides a measure of mandibular cortical thickness for normal mandibular size and it could be used for the evaluation of local bone loss in dental practice (141).

Many studies evaluated the relationship between PMI and BMD, and they found that the PMI was significantly related to BMD measured by DXA; the lower the BMD the more decreased the PMI. The BMD in other skeletal areas was in concordance with the mandibular density, and therefore could be used as diagnostic indicators of mandibular BMD and played a significant role in the screening for osteoporosis (61, 72, 75, 123 , 134, 142, 143, 144, 145,

146). Other studies found that PMI was not significantly correlated with BMD, and accordingly it was not useful for screening of osteoporosis (77, 80, 99, 122, 123, 147).

It is possible to make a direct comparison of absolute values of PMI with other published studies. The mean value of PMI in Ledgerton et al. (114) study was 0.31 (range: 0.24 ± 0.36), and it was very similar to that shown by Benson et al. (139) for white females (0.26 - 0.35), but it differed from the mean value quoted by Klemetti et al. (148) for postmenopausal Finnish females (0.38). These values were higher than the mean value recorded by Yüzügüllü et al. (94) (0.23 - 0.24). These differences may not only be due to ethnic origins, but also may arise due to the inclusion of partially edentulous patients as well as completely edentulous individuals.

The correlation between the right and left sides regarding to PMI measuring was evaluated by several studies. Parlani et al. (116) and Ledgerton et al (114) agreed with result of Dhandapani and Mariamichael (108), who found that there was no significant difference between PMI measured on panoramic radiographs on the right and the left sides. Also these results are in agreement with our results when we use the CBCT or panoramic radiography to assess the correlation between the right and left sides regarding to PMI measuring.

One major advantage of PMI over MI is that its method of calculation takes account of differences in magnification associated with different equipments (114). In our result, the mean values of PMI recorded in panoramic and CBCT images were non - significantly different.

PMI calculation includes a degree of subjectivism, mainly because of the amount of time it requires to establish the optimum visual distance, which is determined by the individual visual acuity and affects the perception of small details. There are also other difficulties in identifying the borders of the mental hole caused by what appears to be several mental holes, by the porous aspect of the mandibular body or the dense trabecular pattern, or occasionally by technical conditions (116, 146).

The relation between the age and PMI was evaluated in many studies; Mudda et al. (118), who assessed PMI on panoramic radiographs of 60 Indian women, found that PMI was positively correlated with age. However, after dividing the sample based on age, a sub-group with age more than 60 years showed a negative correlation with age, and these results were consistent with the results of Taguchi et al. (149), who found that the PMI demonstrated a gradual increased until the sixth decade and then it decreased. These pattern of change in mean PMI demonstrated throughout the age range differed from the result of previous studies

when they evaluated the relation of the age with PMI measured on panoramic radiographs, PMI demonstrated a very gradual reduction with age (79, 114, 120, 150).

In addition, a number of studies revealed that with advancing age the bone mass decreased, but PMI demonstrated no significant difference between age groups ($p > 0.05$) (94, 120, 150). these are in consistent with the results of our study, but were in disagreement with the result of other studies who revealed a statistically significant difference for the PMI measured on panoramic radiographs ($p < 0.05$) between subjects of various decade age groups (108, 114, 139, 149, 151).

These differences in the values of the index reported by different authors are attributed to the racial or ethnic differences which exist in various populations of the world for any morphometric measurements. Besides that, non - uniformity of the sample size could also be a contributory factor (151).

In females, the mean values of PMI showed a decrease with increasing age. This trend is attributed to the onset of postmenopausal osteoporosis. The onset of menopause (45 years onwards) leads to deficiency of estrogen hormone which augments osteoclastic activity leading to the bone resorption (151).

4.6. Antegonial Angle and Antegonial Depth (AGI & AD):

The upward curving of the inferior border of the mandible anterior to the angular process (gonion) is known as antegonial notching. It lies at the junction of body and the ramus (152).

A previous study evaluated the relation of BMD of the skeletal bone and AD and AGA of the mandible by comparing normal and osteoporotic subjects. Their results concluded that the AGA was significantly smaller in individuals with low bone mass ($P < 0.05$), and the AD was significantly greater in osteoporotic individuals ($P < 0.05$). According to their results, individuals with smaller angles (less than 163 degrees) were 6.0 and 6.9 times more likely to be osteoporotic, and subjects with AD greater than 1.6 mm were 4.4 times more likely to have osteoporosis (92). However, others studies revealed no association between AGA, AD, and BMD of the bone skeleton, and these indices could not be useful for osteoporosis prediction (68, 99).

Many studies evaluated the correlation between the right and left sides for AGA and AD. Their results were variable and inconsistent. Dutra et al. (153) evaluated the correlation between the right and the left sides for AGA and AD on panoramic radiographs. They found that small differences were observed between the left and the right sides for AD, and the variability was relatively small. These results are in agreement with our results. Nevertheless,

they are inconsistent with our results because they found a statistical difference between the left and the right AGA. The AGA had significantly greater values on the left side of the mandible than on the right side.

In addition, our result is in agreement with the result of Tozoğlu and Cakur (76), who assessed the AGA and AD on 50 CBCT. Values of AGA and AD in the left and the right sides were measured. The result revealed that there were no significant differences between the right and the left sides.

The result of study conducted by Ghosh et al. (152) was in agreement with result of study conducted by Chole et al. (96) on panoramic images, in which a significant difference was found for AGA and AD between the right and the left sides of the mandible. Also, Preston et al. (154) who reported that the mean dimension of the right mandibular antegonial notches was significantly greater than the corresponding mean dimension recorded for the left antegonial notches, where they suggested that the differences between the right side and the left side antegonial region contributed to the resorption of the right antegonial region occurred more as compared to the left antegonial region, and that can be due to the increased function on a preferred chewing side, or random asymmetry of the facial skeleton (152, 153). These results are in disagreement with our results when we used the panoramic radiography or CBCT to measured AGA and AD on both sides.

Several authors have studied changes in angles of the mandible in ageing patients, and their alterations throughout ageing. Their results were variable and inconsistent, even using similar methodologies. Ghosh et al. (152) and Dutra et al. (153) evaluated the changes in the AGA and AD on panoramic radiographs of patients in different age periods. They found that there was no significant correlation between AGA and AD with age ($p > 0.05$) even when there was an observed trend of decrease in the AGA and increase in AD with age. This is as a result of bone deposition that takes place throughout the inferior border except in the antegonial region, where a resorptive pattern is found. This resorptive pattern might be accentuated by bone deposition that probably takes place anterior to this region which would decrease the AGA and increase the AD (153). Our results do not support these findings while measuring AD and AGA by CBCT or panoramic radiography. Also, we found no statistically significant difference between the mean value of AD and AGA recorded in panoramic and CBCT images on both sides.

The changes in the antegonial region are not the same as in the gonial region. The antegonial region undergoes resorption in the edentulous individuals, perhaps due to the reduced muscle function in this region in comparison with that of the gonial angle. Muscle

function tends to preserve bone at its point of insertion; therefore the structure of the gonial region will be maintained by the insertion of the medial pterygoid and masseter muscles (97, 152).

4.7. Condylar Angle (CA):

In our result, the mean values of CA recorded on panoramic and CBCT images were not statistically - significantly different. Also, there were no significant differences between the right and the left CA either when we used the panoramic radiography or CBCT to assess the correlation between both sides. This is in agreement with the result of Tozoğlu and Cakur (76), who assessed the CA on 50 CBCT. Panoramic representations of the mandible with superimposed axial slices and cross - sectional slices were constricted from the CBCT scans. Values of the condylar angle in the left and the right sides were measured. The result revealed that there were no significant differences between the right and the left sides. In addition, in our result; there were no significant difference between the age groups when we used the panoramic radiography or CBCT to evaluation the relation between CA and age on both sides.

5. CONCLUSION

In many phases of dentistry, healthy bone with a normal regenerative capacity is essential for a successful outcome.

This is the first study to determine whether the index values obtained by CBCT evaluation are equivalent or superior to panoramic images for visualization of bone structures of female high risk osteoporotic patients in relation to age.

It can be concluded from our study that:

- There was significant correlation between right and left measurements of CBCT and panoramic radiography in all indices except in GA measured in CBCT.
- There were no significant differences between two independent samples (CBCT and panoramic radiography) in all indices except in left GA.
- There were no significant differences between two age groups in all indices measured by CBCT or panoramic radiography on both sides . The present study supports that there was no much of age - related changes in mandibular radiomorphometric indices.

Although CBCT imaging is rather expensive, have high radiation dose, and limited availability, it does not magnify or overlap neighboring structures. However; it is worthwhile to look for alternative diagnostic techniques for osteoporosis. Panoramic radiography can be used for evaluation of bone changes instead of CBCT images. Moreover the panoramic radiography allows images to be acquired using a low dose of radiation, shorter patient examination time, and lower costs than CBCT. Panoramic radiographs constitute an integral part of almost every routine oral and maxillofacial procedures. For this reason, we think that the panoramic radiography is a good tool to measure mandibular indices and dentists may be able to refer postmenopausal women with undetected low skeletal BMD or osteoporosis to medical professionals for further examination on the basis of incidental findings on dental panoramic radiographs.

It should be noted that, in this study, there were no osteoporotic women included. furthermore, the number of subjects was relatively small for safe conclusions to be drawn. These data will be useful as standards for further comparison studies conducted in larger populations between the panoramic radiography and CBCT. Thus, further investigations of age - related changes in mandibular radiomorphometric indices may be required.

6. REFFERENCE

1- Steven R, Cummings. Bone Biology, Epidemiology, and General Principles. 2002.

2- Clarke B. Normal Bone Anatomy and Physiology. *Clin J Am Soc Nephrol* 2008;3 S3:S131-9. Doi: 10.2215/CJN.04151206.

3- McNamara L. Perspective on postmenopausal osteoporosis: establishing an interdisciplinary understanding of the sequence of events from the molecular level to whole bone fractures. *Interface* 2010;7:353-372. Doi:10.1098/rsif.2009.0282.

4- McCreadie BR, Morris MD, Chen TC, Sudhaker RD, Finney WF, Widjaja E, et al. Bone tissue compositional differences in women with and without osteoporotic fracture. *Bone* 2006;39(6):1190-5.

5- McNamara LM, Van der Linden JC, Weinans H, Prendergast PJ. Stress concentrating effect of resorption lacunae in trabecular bone. *J Biomech* 2006;39(4):734-41.

6- Doventas A, Bolayirli IM, Incir S, Yavuzer H, Civelek S, Erdincler DS. Interrelationships between obesity and bone markers in postmenopausal women with either obesity or osteoporosis. *European Geriatric Medicine* 2015;6:15-20.

7- Chen H, Zhou X, Fujita H, Onozuka M, Kubo KY. Age - related changes in trabecular and cortical bone microstructure. *Int J Endocrinol* 2013;2013:213234-9. Doi : 10.1155/2013/ 213234 .

8- Leng H, Reyes MJ, Dong XN, Wang X. Effect of age on mechanical properties of the collagen phase in different orientations of human cortical bone. *Bone* 2013;55(2):288-91. Doi: 10.1016/j.

9- Andersena S, Laurbergb P. Age impact on clinical risk factors does not justify the age relatedchange in referral pattern for osteoporosis assessment. *Maturitas* 2015;80:302-307.

10- Epstein S. Is Cortical Bone Hip? What determines Cortical Bone Properties?. *Bone* 2007; 41:S3-S8.

11- Caputo EL, Costa M Z. Influence of physical activity on quality of life in postmenopausal women with osteoporosis. *Rev Bras Reumatol* 2014;54(6):467-73. Doi: 10.1016/j.rbr.2014.02.008.

12- Kósa JP, Balla B, Speer G, Kiss J, Borsy A, Podani J, et al. Effect of menopause on gene expression pattern in bone tissue of non - osteoporotic women. *Menopause* 2009;16(2):367-77. Doi: 10.1097/gme. 0b013e318188b260.

13- Jacques P, Robert G. Clinical practice guidelines for the diagnosis and management ofosteoporosis in Canada. *CMAJ* 2002;167 suppl 10:S1-34.

14- National Institutes of Health. Consensus Development Conference Statement (NIH). Osteoporosis Prevention, Diagnosis, and Therapy. 2000;17(1):1-36.

15- Nikander R, Sievänen H, Heinonen A, Daly R M, Uusi-Rasi K, Kannus P. Targeted exercise against osteoporosis: A systematic review and meta - analysis for optimising bone strength throughout life. *BMC Med* 2010;8-47. Doi: 10.1186/1741-7015-8-47. http://www.biomedcentral.com/1741-7015/8/47.

16- World Health Organization. WHO Scientific group on the assessment of osteoporosis at primary health care level . Summary Meeting Report Brussels, Belgium, 5-7 May 2004.

17- Brunader R, Shelton DK. Radiologic bone assessment in the evaluation of osteoporosis. *Am Fam Physician* 2002;1;65(7):1357-64.

18- Hough S, Ascott - Evans B, Brown S, Cassim B, DeViliers T, Lipschitz S, et al. NOFSA guideline for diagnosis and management of osteoporosis. *Endocrinology, Metabolism and Diabetes of South Africa* 2010;15(3)supple1:1608-9677.

19- National Medicines Information Centre. Update on osteoporosis. 2013;19 (2):1-9.

20- National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. *BONE* 2010.www.nofstore.org.

21- Watts NB, Bilezikian JP, Camacho PM, Greenspan SL, Harris ST, Hodgson SF, et al. American Association of Clinical Endocrinologists Medical Guidelines for clinical practice for the diagnosis and treatment of postmenopausal osteoporosis. *Endocr Pract* 2010;16 Suppl 3:1-37.

22- Orthopedic specialists north Carolina. Classification of osteoporosis. 2014. http://www.orthonc.com.

23- Riggs BL, Khosla S, Melton LJ. A unitary model for involutional osteoporosis: estrogen deficiency causes both type I and type II osteoporosis in postmenopausal women and contributes to bone loss in aging men. *J Bone Miner Res*1998;13(5):763-73.

24- Ra'ed A1-Sadhan. Detecting postmenopausal osteoporosis by using pixel intensity of digital panoramic images. the University of Connecticut - Saudia, Masters Theses 2002.

25- Michael P. Diagnosis and management of involutional osteoporosis. *Can Fam Physician* 1979;25:467-472.

26- Mauck KF, Clarke BL. Diagnosis, screening, prevention, and treatment of osteoporosi. *Mayo Clin Proc* 2006;81(5):662-672.

27- Watanabe PC, De Faria M L, Issa JP, Monteiro SA, Tiossi R. Morphodigital study of the mandibular trabecular bone in panoramic radiographs. *Int. J. Morphol* 2007*; 25(4)*:875-880.

28- Tuzun S, Eskiyurt N, Akarirmak U, Saridogan M, Senocak M, Johansson H. Incidence of hip fracture and prevalence of osteoporosis in Turkey: the FRACTURK study**.** *OsteoporosInt* 2012;23(3):949-55. Doi: 10.1007/s00198-011-1655-5.

29- Zhu X, Luo J, Chen X, Wang J, Wang G, Li H, et al. Expression characteristic and significance of interleukin - 6, nuclear factor kappa beta, and bone formation markers in rat models of osteoporosis. *Translational Research* 2008;152:18-23.

30- Emel D, Oral implications of osteoporosis. *Oral Surg Oral Med Oral Pathol Oral RadiolEndod* 2005;100:349-56.

31- Hirai T, Ishijima T, Hashikawa Y, Yajima T. Osteoporosis and reduction of residual ridge in edentulous patient. *J Prosthet Dent* 1993;69(1):49.

32- Kuo LC, Polson AM, Kang T. Associations between periodontal diseases and systemic diseases: A review of the inter - relationships and interactions with diabetes, respiratory diseases, cardiovascular diseases and Osteoporosis. *Public Health* 2008;122(4):417-33.

33- Tezal M, Wactawski-Wende J, Grossi SG, Ho AW, Dunford R, GencoRJ. The relationship between bone mineral density and periodontitis in postmenopausal women. J *Periodontol* 2000;71(9):1492-8.

34- Sato M, Vietri J, Flynn JA, Fujiwara S. Treatment for Osteoporosis among women in Japan: Associations with patient characteristics and patient - reported outcomes in the 2008-2011 Japan National Health and Wellness Surveys. *J Osteoporos* 2014;2014:909153. Doi: 10.1155/2014/909153.

35- Stein EM, Liu XS, Nickolas TL, Cohen A, Thomas V, McMahon DJ. Abnormal microarchitecture and reduced stiffness at the radius and tibia in postmenopausal women with fractures. *J Bone Miner Res* 2010;25(12):2572-81. Doi: 10.1002/jbmr.152.

36- Hasegawa K, Takahashi H, Koga Y, Kawashima T, Hara T, Tanabe Y, et al. Failure characteristics of osteoporotic vertebral bodies monitored by acoustic emission. *Spine* 1993;18(15):2314-20.

37- Li B, Aspden RM. Material properties of bone from the femoral neck and calcar femorale of patients Trabecular bone architecture in the pathogenesis and prevention of fracture. *Am J Med* 1987;82(1B):68-72.

38- Parfitt AM. Trabecular bone architecture in the pathogenesis and prevention of fracture. *Am J Med* 1987;82(1B):68-72.

39- Brown JP, Fortier M, Frame H, Lalonde A, Papaioannou A, SenikasV. Canadian consensus conference on osteoporosis. *J Obstet Gynaecol Can* 2006;28(Suppl 1):S95-112.

40- Bauer DC, Browner WS, Cauley JA, Orwoll ES, Scott JC, Black DM. Factors associated with appendicular bone mass in older women. The study of osteoporotic fractures research group. *Ann Intern Med* 1993;118(9):657-65.

41- Orwoll ES, Bauer DC, Vogt TM, Fox KM. Axial bone mass in older women. Study of osteoporotic fractures research group. *Ann Intern Med* 1996;124(2):187-96.

42- Hodgson SF, Watts NB, Bilezikian JP, Clarke BL, Gray TK, Harris DW. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the prevention and treatment of postmenopausal osteoporosis: 2001edition, with selected updates for 2003. *Endoc rPract* 2003;9(6):544-64.

43- Torgerson DJ, Campbell MK, Thomas RE, Reid DM. Prediction of perimenopausal fractures by bone mineral density and other risk factors. *J Bone Miner Res*1996;11(2):293-7.

44- Siminoski K, Jiang G, Adachi JD, Hanley DA, Cline G, Ioannidis G. A ccuracy of height loss during prospective monitoring for detection of incident vertebral fractures. *Osteoporos Int* 2005;16(4):403-10.

45- Cummings SR, Nevitt MC, Browner WS, Stone K, Fox KM, Ensrud KE, et al. Risk factors for hip fracture in white women. Study of osteoporotic fractures research group. *N Engl J Med* 1995 23;332(12):767-73.

46- Doventas A, BolayirliIM, Incir S, Yavuzer H, Civelek S, Erdincler DS, et al. Interrelationships between obesity and bone markers in postmenopausal women with either obesity or osteoporosis. *European Geriatric Medicine* (2015);6:15-20.

47- Marshall D, Johnell O, Wedel H. Meta - analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. *BMJ* 1996;312(7041):1254-9.

48- Molina DP, Schott AM, Hans D, Favier F, Grandjean H, Baudoin C, et al. Separate and combined value of bone mass and gait speed measurements in screening for hip fracture risk: results from the EPIDO study. *Osteoporos In* 1999;9(2):188-92.

49- Zhen D, Liu L, Guan C, Zhao N, Tang X. High prevalence of vitamin D deficiency among middle - aged and elderly individuals in north western China: Its relationship to osteoporosis and life style factors. *Bone* 2015;71:1-6. Doi: 10.1016/j.

50- Schousboe JT, Shepherd JA, Bilezikian JP, Baim S. International Society for Clinical Densitometry 2013. *JCD* 2013;16(4):455-467.

51- Genant HK, Njeh CE. Update on the diagnosis of osteoporosis. *Current Orthopaedics* 1999;13:144-155.

52- Celenk C, Celenk P. Bone density measurement using computed tomography, computed tomography. *ISBN* 2012;978-953-307-378.

53- Ishii K, Taguchi A, Nakamoto T, Ohtsuka M, Sutthiprapaporn P, Tsuda M, et al. Diagnostic efficacy of alveolar bone loss of the mandible for identifying postmenopausal women with femoral osteoporosis. *Dentomaxillofacial Radiology* 2007;36, 28-33 .

54- Blake GM, Fogelman I. The role of DXA bone density scans in the diagnosis and treatment of osteoporosis. *Postgrad Med J* 2007; 83(982): 509 517.doi: 10.1136/pgmj.2007.057505 .

55- Liu XS, Stein EM, Zhou B, Zhang CA, Nickolas TL, Cohen A. Individual Trabecula Segmentation (ITS) - based morphological analyses and microfinite element analysis of HR - p QCT images discriminate postmenopausal fragility fractures independent of DXA measurements. *Journal of Bone and Mineral Research* 2012;27:263-272.DOI: 10.1002/jbmr.

56- Siminoski K, Jiang G, Adachi JD, Hanley DA, Cline G, Ioannidis G, et al. Accuracy of height loss during prospective monitoring for detection of incident vertebral fractures. *Osteoporos Int* 2005;16(4):403-10.

57- Radiological Society of North America. Panoramic dental x-ray. *radiology info org*. 2014. http://www.radiologyinfo.org/.

58- Martin J. Panoramic radiography for the general practitioner. *Oral Rad* 2000-02-01. http://www.oralhealthgroup.com/features/panorami-radiography-for-the general practitioner/.

59- Stuart CW, Michael JP. Oral radiology, principles and interpretation. 5 th ed. St. Louis: Mosby;2004.

60- Ardakani F, Owlia MB, Hesami S, Hosseini P. Digital panoramic radiography as a useful tool for detection of bone loss: a comparative study. *Acta MedIran* 2013; 51(2):94-100.

61- Hastar E, Huseyin Y, Orhan H. Evaluation of mental index, mandibular cortical index and panoramic mandibular index on dental panoramic radiographs in the elderly. *Eur J Dent 2011*;5:60-67.

62- Gomes CC, de Rezende Barbosa GL, Bello RP, Bóscolo FN, de Almeida SM. A comparison of the mandibular index on panoramic and cross - sectional images from CBCT exams from osteoporosis risk group. *Osteoporos Int* 2014;25(7):1885-90. Doi: 10.1007/s00198-014-2696-3.

63- Sheikhi M, Ghorbanizadeh S, Abdinian M, Goroohi H, Badrian H. Accuracy of linear measurements of galileos cone beam computed tomography in normal and different head positions. *Int J Den* 2012;2012:214954. Doi: 10.1155/2012/214954.

64- Scarfe WC, Farman AG, Sukovic P. Clinical applications of cone beam computed tomography in dental practice. *J Can Dent Assoc* 2006; 72(1):75-80.

65- Takeshita WM, Vessoni LC, Da Silva MC, Tonin RH. Evaluation of diagnostic accuracy of conventional and digital periapical radiography, panoramic radiography, and cone beam computed tomography in the assessment of alveolar bone loss. *Contemp Clin Dent* 2014;5(3):318-23. Doi: 10.4103/0976-237X.137930.

66- Jonasson G, Bankvall G, Kiliaridis S. Estimation of skeletal bone mineral density by means of the trabecular pattern of the alveolar bone, its interdental thickness, and the bone mass of the mandible. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001;92(3):346-52.

67- Nakamoto T, Taguchi A, Ohtsuka M, Suei Y, Fujita M, Tanimoto K. Dental panoramic radiograph as a tool to detect postmenopausal women with low bone mineral density: untrained general dental practitioners' diagnostic performance. *Osteoporos Int* 2003; 14:659-64. Doi: 10.1007/s00198-003-1419-y.

68- Leinte AF, Figueiredo PT, Guia CM, Melo NS, de Paula AP. Correlations between seven panoramic radiomorphometric indices and bone mineral density in postmenopausal women. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2010;109(3):449-56. Doi: 10.1016/j.

69- Dutra V, Devlin H, Susin C, Yang J, Horner K, Fernandes AR. Mandibular morphological changes in low bone mass edentulous females: evaluation of pano ramic radiographs. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006;102(5):663-8.

70- Verheij JG, Geraets WG, Vander S PF, Horner K, Lindh C, Nicopoulou - Karayianni K. Prediction of osteoporosis with dental radiographs and age. *Dentomaxillofacial Radiology* 2009;38:431-437.

71- Koh KJ, Kim KA. Utility of the computed tomography indices on cone beam computed tomography images in the diagnosis of osteoporosis in women. *Imaging Sci Dent* 2011;41(3):101-6. Doi: 10.5624/isd.2011.41.3.101.

72- Dagistan S, Bilge OM. Comparison of antegonial index, mental index, panoramic mandibular index and mandibular cortical index values in the panoramic radiographs of normal males and male patients with osteoporosis. *DentomaxillofacRadiol* 2010;39(5):290-4. Doi: 10.1259/dmfr/46589325.

73- Nakamoto T, Taguchi A, Ohtsuka M, Suei Y, Fujita M, Tsuda M.A computeraided diagnosis system to screen for osteoporosis using dental panoramic radio graphs. *Dentomaxillofac Radiol*. 2008;37(5):274-81. Doi: 10.1259/dmfr/68621207.

74- Horner K, Karayianni K, Mitsea A, Berkas L, Mastoris M, Jacobs R. The mandibular cortex mandibular cortex on radiographs as a tool for osteoporosis risk assessment: the OSTEODENT Project. *J ClinDensitom* 2007;10(2):138-46.

75- Mahl CRW, Licks R, Fontanella VRC. Comparison of morphometric indices obtained from dental panoramic radiography for identifying individuals with osteoporosis/osteopenia. *Radiol Bras* 2008;41(3):183-187.

76- Tozoğlu U, Cakur B. Evaluation of the morphological changes in the mandible for dentate and totally edentate elderly population using cone beam computed tomography. *Surg Radiol Anat*2014;36(7):643-9. Doi: 10.1007/s00276-013-1241-y.

77- Marandi S, Bagherpour A, Imanimoghaddam M, Hatef M, Haghighi A. Panoramic - based mandibular indices and bone mineral density of femoral neck and lumbar vertebrae in women. *J Dent (Tehran)*2010;7(2):98-106.

78- Dutra V, Yang J, Devlin H, Susin C. Radiomorphometric indices and their relation to gender, age, and dentalstatus. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2005;99(4):479-84.

79- Pal S. Evaluation of panoramic radiomorphometric indices in Indian population. *Cumhuriyet Dent J* 2013;16(4):273-281. Doi:10.7126/cdj.

80- Yaşar F, Akgünlü F. The differences in panoramic mandibular indices and fractal dimension between patients with and without spinal osteoporosis. *Dentomaxillofac Radiol* 2006;35(1):1-9.

81- Taguchi1 A, Suei1 Y, Sanada M, Ohtsuka M, NakamotoT, Sumida H. Validation of dental panoramic radiography measures for identifying postmenopausal women with spinal osteoporosis. *AJR Am J Roentgenol* 2004;183(6):1755-60.

82- Khayam E, Tavakoli MA, Varshosaz M, Moeini M, Razavi SH, Tavakoli NA. Evaluation of the correlation between antegonial and mental indices with age, gender, and dental status. *J Am Sci* 2012;8(7):617-620.

83- Vlasiadis KZ, Skouteris CA, Velegrakis GA, Fragouli I, Neratzoulakis JM, Damilakis J. Mandibular radiomorphometric measurements as indicators of possible osteoporosis in postmenopausal women. *Maturitas* 2007;58(3):226-35.

84- Cakur B, Dagistan S, Sahin A, Harorli A, Yilmaz A. Reliability of mandibular cortical index and mandibular bone mineral density in the detection of osteoporotic women. *Dentomaxillofac Radiol*2009;38(5):255-61. Doi: 10.1259/dmfr/22559806.

85- Verheij JG, Geraets WG, van der Stelt PF, Horner K, Lindh C, Nicopoulou - Karayianni K. Prediction of osteoporosis with dental radiographs and age. *Dentomaxillofac Radiol* 2009; 38(7):431-7. Doi:10.1259/dmfr/55502190.

86- Khojastehpour L, Mogharrabi S, Dabbaghmanesh MH, Iraji NN. Comparison of the mandibular bone densitometry measurement between normal, osteopenic and osteoporotic postmenopausal women. *J Dent (Tehran)*2013;10(3):203-9.

87- Imre MM, Preoteasa E. Mandibular panoramic indexes predictors of skeletal osteoporosis for implant therapy. *Current Health Sciences* 2009; 35(4).

88- Taguchi A, Ohtsuka M, Tsuda M, Nakamoto T, Kodama I, Inagaki K. Risk of vertebral osteoporosis in postmenopausal women with alterations of the mandible. *Dentomaxillofac Radiol* 2007;36(3):143-8.

89-Taguchi A, Asano A, Ohtsuka M, Nakamoto T, Suei Y, Tsuda M. Observer performance in diagnosing osteoporosis by dental panoramic radiographs: results from the osteoporosis screening project in dentistry (OSPD). *Bone* 2008;43(1):209-13. Doi: 10.1016/j.

90- Taguchi A, Tsuda M, Ohtsuka M, Kodama I, Sanada M, Nakamoto T. Use of dental panoramic radiographs in identifying younger postmenopausal women with osteoporosis. *Osteoporos Int* 2006;17(3):387-94.

91- Taguchi A, Sanada M, Krall E, Nakamoto T, Ohtsuka M, Suei Y. Relationship between dental panoramic radiographic findings and biochemical markers of bone turnover. *J Bone Miner Res* 2003;18(9):1689-94.

92- Dutra V, Devlin H, Susin C, Yang J, Horner K, Fernandes A. Mandibular morphological changes in low bone mass edentulous females: evaluation of panoramic radiographs. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006;102(5):663-8.

93- Alonso MB, Cortes AR, Camargo AJ, Arita ES, Haiter - Neto F, Watanabe PC. Assessment of panoramic radiomorphometric indices of the mandible in a brazilian population. *ISRN Rheumatol* 2011;2011:854287. Doi: 10.5402/2011/854287.

94- Yüzügüllü B, Gulsahi A, Imirzalioglu P. Radiomorphometric indices and their relation to alveolar bone loss in completely edentulous Turkish patients: are retrospective study. *J Prosthet Dent* 2009;101(3):160-5. Doi: 10.1016/S0022-3913 (09)60021-4.

95- Vlasiadis KZ, Damilakis J, Velegrakis GA, Skouteris CA, Fragouli I, Goumenou A. Relationship between BMD, dental panoramic radiographic findings and biochemical

markers of bone turnover in diagnosis of osteoporosis. *Maturitas* 2008 20;59(3):226-33. Doi: 10.1016/j.

96- Chole RH, Patil RN, Balsaraf CS, Gondivkar S, Gadbail AR, Yuwanati MB. Association of mandible anatomy with age, gender, and dental status: a radiographic study. *ISRN Radiol* 2013 18; 2013:453763. Doi: 10.5402/2013/453763.

97- Upadhyay RB, Upadhyay J, Agrawal P, Rao NN. Analysis of gonial angle in relation to age, gender, and dentition status by radiological and anthropometric methods. *J Forensic Dent Sci* 2012;4(1):29-33. Doi: 10.4103/0975-1475.99160.

98- Rehman DE, Sarwath S, Nigar S. Association between changes in the angle of mandible and reduced bone mineral density.*J Coll Physicians Surg Pak* 2015;25(2):87-90. Doi: 02.2015/JCPSP.8790.

99- Hajipour M , Safi Y, Kadkhodazadeh M, Mirakhori M, Amid R, Dehghan A. Validity of panoramic indices to evaluate the association of bone mineral density with morphology of the mandible in osteoporotic patients. *Beheshti Univ Dent J* 2015; 32(4): 217-224.

100- Shahabi M, Ramazanzadeh B, Mokhber N. Comparison between the external gonial angle in panoramic radiographs and lateral cephalograms of adult patients with class Imalocclusion. *Journal of Oral Science* 2009;51(3):425-429.

101- Gungor K, Sagir M, Ozer I. Evaluation of the gonial angle in the anatolian populations: from past to present. *Collegium Antropologicum* 2007;31:375-378.

102- Dutra V, Yang J, Devlin H, Susin C. Mandibular bone remodelling in adults: evaluation of panoramic radiographs. *Dentomaxillofacial Radiology* 2004;33:323-328.

103- Raustia AM, Salonen MA. Gonial angles and condylar and ramus height of the mandible in complete denture wearers - a panoramic radiograph study. *J Oral Rehabil* 1997;24(7):512-6.

104- Xie QF, Ainamo A. Correlation of gonial angle size with cortical thickness, height of the mandibular residual body, and duration of edentulism. *J Prosthet Dent* 2004:91(5):477-82.

105- Roberts M, Yuan J, Graham J, Jacobs R, Devlin H. Changes in mandibular cortical width measurements with age in men and women. *Osteoporos Int* 2011; 22(6):1915-25. Doi: 10.1007/s00198-010-1410-3.

106- Ohm E, Silness J. Size of the mandibular jaw angle related to age, tooth retention and gender. *J Oral Rehabil* 1999; 26:883-91.

107- Osato S, Kuroyama I, Nakajima S, Ogawa T, Misaki K. Differences in 5 anatomic parameters of mandibular body morphology by gonial angle size in dentulous Japanese subjects. *Ann Anat* 2012;194(5):446-51. Doi: 10.1016/j.aanat.2012.01.005.

108- Dhandapani K , Mariamichael A. Influence of age and gender on mandible among South Indian population. *Biological Sciences* 2015;15(1):23.29.

109- Devlin H, Horner K. Mandibular radiomorphometric indices in the diagnosis of reduced skeletal bone mineral density. *Osteoporos Int* 2002;13(5):373-8.

110- Devlin H, Karayianni K, Mitsea A, Jacobs R, Lindh C, van der Stelt P, et al. Diagnosing osteoporosis by using dental panoramic radiographs: the OSTEODENT project. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007;104(6):821-8.

111- Horner K, Devlin H, Harvey L. Detecting patients with low skeletal bone mass. *J Dent* 2002;30(4):171-5.

112- Gulsahi A, Paksoy CS, Ozden S, Kucuk NO, Cebeci AR, Genc Y. Assessment of bone mineral density in the jaws and its relationship to radiomorphometric indices. *Dentomaxillofac Radiol* 2010;39(5):284-9. Doi: 10.1259/dmfr/20522657.

113- Kingsmill VJ, Boyde A. Variation in the apparent density of human mandibular bone with age and dental status. *J Anat* 1998;192:233-244.

114 -Ledgerton D, Horner K, Devlin H, Worthington H. Radiomorphometric indices of the mandible in a British female population. *Dentomaxillofac Radiol* 1999; 28:173-181.

115- Musa I, Zlataric DK, Celebic A, Boπnjak A. The influence of gender and age on the values of linear radiomorphometric indices measured on the lower border of the mandible, *Acta Stomat Croat* 2002;199-202.

116- Knezovic ZD, Celebic A, Lazic B, Baucic I, Komar D, Stipetic OJ, et al. Influence of age and gender on radiomorphometric indices of the mandible in removable denture wearers. *CollAntropol* 2002;26:259-66.

117- Papamanthos M, Varitimidis S, Dailiana Zh, Kogia E, Malizos K. Computer-assisted evaluation of Mandibular Cortical Width (MCW) index as an indicator of osteoporosis. *Hippokratia* 2014;18(3):251-7.

118- Mudda JA, Bajaj M, Patil VA. A radiographic comparison of mandibular bone quality in pre - and postmenopausal women in Indian population. *J Indian Soc Periodontol* 2010;14(2):121-5. Doi: 10.4103/0972-124X.70833.

119- Ledgerton D, Horner K, Devlin H, Worthington H. Panoramic mandibular index as a radiomorphometric tool: An assessment of precision. *Dentomaxillofac Radiol* 1997;26(2):95-100.

120- Parlani S, Preeti Nair, Surender Agrawal, Rajkiran Chitumalla, Gaurav Beohar, Utkarsh Katar. Role of Panoramic radiographs in the detection of osteoporosis. *Oral Hyg Health* 2014;2:121. Doi: 10.4172/2332-0702.1000121.

121- Roberts WE, Simmons KE, Garetto LP, DeCastro RA. Bone physiology and metabolism in dental implantology: risk factors for osteoporosis and other metabolic bone diseases. *Implant Dent*1992;1(1):11-21.

122- Klemetti E, Kolmakov S, Kröger H. Pantomography in assessment of the osteoporosis risk group. *Scan J Dent Res* 1994;102(1):68-72.

123- Drozdzowska B, Pluskiewicz W, Tarnawska B. Panoramic - based mandibular indices in relation to mandibular bone mineral density and skeletal status assessed by dual energy x - ray absorptiometry and quantitative ultrasound. *Dentomaxillofac Radiol* 2002;31(6):361-7.

124- Amorim MA, Takayama L, Jorgetti V, Pereira RM. Comparative study of axial and femoral bone mineral density and parameters of mandibular bone quality in patients receiving dental implants. *Osteoporos Int* 2006;17:1494-1500.

125- Taguchi A, Suei Y, Ohtsuka M, Otani K, Tanimoto K, Ohtaki M. Usefulness of panoramic radiography in the diagnosis of postmenopausal osteoporosis in women. Width and morphology of inferior cortex of the mandible. *Dentomaxillofac Radiol* 1996;25(5):263-7

126- Horner K, Devlin H. The relationships between two indices mandibular bone quality and bone mineral density measured by dual energy x-ray absorptiometry. *Dentomaxillofac Radiol*1998;27(1):17-21.

127- Jowitt N, MacFarlane T, Devlin H, Klemetti E, Horner K. The reproducibility of the mandibular cortical index. *DentomaxillofacRadiol* 1999;28:141–144.

128- Ardakani FE, Niafar N. Evaluation of changes in the mandibular angular cortex using panoramic images. *J Contemp Dent Pract* 2004;5:1–5.

129- Gulsahi A, Yüzügüllü B, Imirzalioglu P, Genç Y. Assessment of panoramic radiomorphometric indices in Turkish patients of different age groups, gender and dentalstatus. *Dentomaxillofac Radiol* 2008;37(5):288-92. Doi: 10.1259/dmfr/19491030.

130- Klemetti E, Kolmakow S. Morphology of the mandibular cortex on panoramic radiographs as an indicator of bone quality. *DentomaxillofacRadiol* 1997; 26: 22-25.

131- Mansour S, AlGhamdi AS, Javed F, Marzouk H, Khan EA. Panoramic radio-morphometric indices as reliable parameters in predicting osteoporosis. *Am J Med Sci* 2013; 346:473-478.

132- Bollen AM, Taguchi A, Hujoel PP, Hollender LG. Case-control study on self reported osteoporotic fractures and mandibular cortical bone. *Oral Surg Oral Med Oral Pathol Oral RadiolEndod* 2000;90:518-524.38.

133- White SC, Taguchi A, Kao D, Wul S, Service SK, Yoon D, et al. Clinical and panoramic predictors of femur bone mineral density. *Osteoporos Int* 2005;16:339-346.

134- Halling A, Persson R, Berglund J, Johansson O, Renvert S. Comparison between the klemetti index and heel DXA BMD measurements in the diagnosis of reduced skeletal bone mineral density in the elderly. *Osteoporos Int* 2005;16: 999-1003.

135- Wowern VN. Microradiographic and histomorphometric indices of mandibles for diagnosis of osteopenia**.** *Scand J Dent Res*b1982;90(1):47-63.

136- Dalili Z, Qujeq MA. An investigation on mandibular radiometric indices I normal female population referred to maxillofacial radiology centers in Rasht. *JDM* 2003;16:14-21.

137- Imani M, Bagherpour A, Hatef MR, Ebrahimzadeh S. Evaluation of the relationship between skeletal status and radiomorphometric indices of the mandible observed in panoramic radiography in women. *Journal of Mashhad Dental School* 2006;29:145-152.

138- Dutra V, Yang J, Devlin H, Susin C. Radiomorphometric indices and their relation to gender, age, and dental status. *Oral Surg Ora lMed Oral Pathol Oral Radiol Endod* 2005;99:479-846 .

139- Benson BW, Prihoda TJ, Glass BJ. Variations in adult cortical bone mass as measured by a panoramic mandibular index. *Oral Surg Oral Med Oral Pathol* 1991;71(3):349-56.

140- Wical KE, Swoope CC. Studies of residual ridge resorption: Part 1: Use of panoramic radiographs for evaluation and classification of mandibular resorption. *J Prosthet Dent* 1974;32:7-12.

141- Gungor K, Akarslan ZZ, Akdevelioglu M, Erten H, Semiz M. The precision of the panoramic mandibular index. *DentomaxillofacRadiol* 2006;35:442-6.

142- Khojastehpour L, Shahidi SH, Barghan S, Aflaki EL. Efficacy of panoramic mandibular index in diagnosing osteoporosis in women. *Journal of Dentistry* 2009;6(1).

143- Horner K, Devlin H. The relationship between mandibular bone mineral density and panoramic radiographic measurements. *J Dent* 1998;26:337-343.

144- Kribbs PJ. Comparison of mandibular bone in normal and osteoporotic women. J *Prosthet Dent* 1990;63(2):218-22.

145- Othman HI, Ouda SA. Mandibular radiomorphometric measurements as indicators of possible osteoporosis in celiac patients. *Med. Sci* 2010;17(2):21-35.

146- Ioana D, Angela P, Carmen E. The relationship between osteoporosis and the panoramic mandibular index. *International Journal of the Bioflux Society* 2013;5. http://www.hvm.bioflux.com.ro/.

147- Watson EL, Katz RV, Adelezzi R, Gift HC, Dunn SM. The measurement of mandibular cortical bone height in osteoporotic vs. non - osteoporotic postmenopausal women. *Spec Care Dentist*1995;15(3):124-8.

148- Klemetti E, Kolmakov S, Heiskanen P, Vainio P, Lassila V. Panoramic mandibular index and bone mineral densities in postmenopausal women. *Oral Surg Oral Med Oral Pathol* 1993;75(6):774-9.

149- Taguchi A, Tanimoto K, Suei Y. The estimation of the radiomorphometric indices of the mandible using panoramic radiography. *Dent Radiol* 1993;33:309-16.

150- Rao GS, Chatra L, Shenai P. Evaluation of adult cortical bone mass as measured by panoramic mandibular index - a radiological study. *Webmed Central radiology* 2011;2(1):WMC001447. Doi: 10.9754/journal.wmc.2011.001447.

151- *Bathla S, Srivastava SK, Sharma RK, Chhabra S.* Panoramic mandibular index: Effect of age and gender related variations in the North - Indian population. *IJMDS* 2015;4(2).

152- Ghosh S, Vengal M, Pai KM, Abhishek K. Remodeling of the antegonial angle region in the human mandible: a panoramic radiographic cross - sectional study. *Med Oral Patol Oral Cir Bucal* 2010;15(5):e802-7.

153- Dutra V, Yang J, Devlin H, Susin C. Mandibularbone remodelling in adults: evaluation of panoramicradiographs. *Dentomaxillofac Radiol* 2004;33(5):323-8.

154- Preston B, Al-Sehaibany F, Salem O. The morphology of the mandibular antegonial notches and facial symmetry. *J ClinPediatr Dent* 2002;26:155-60.

7. CURRICULUM VITAE

I was born in Benghazi - Libya on December the 29 th 1982. I completed my secondary education in Al – Fatah Center For Distinguished Students School - Benghazi - Libya in 2000. I joined Benghazi University, Faculty of Dentistry in 2001 - 2002. Then, I was awarded the degree of B.D.S in 2005. I completed one year of compulsory internship rotation work in all clinical departments of Dentistry in Benghazi University from September 2005 till June 2006. Then, I was posted as a postgraduate student in the same faculty, and I have more than seven years of experience instructing and teaching undergraduate students. And I was awarded a scholarship for a master degree in 2009. As regarding language skills, I attended many English courses (TOFEL [537] - IELTS [5.5]). I also attended Turkish language courses at Tömer Center - Ankara University (TEMEL 4). As regarding computer skills, I was certified an ICDL license (International Computer Driving License) in 2008. On 2014, I got an accepted in a master degree program in Dentomaxillofacial Radiology in Yeditepe University Istanbul - Turkey.