Exercise, Smoking, and Calcium Intake as Determinants of Peak Bone Mass

Thesis

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Internal Medicine

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ABSTRACT

Evidences emerging to suggest that osteoporosis is a glo0bal epidemic increasing worldwide. Lifestyle risk factors as the amount of calcium intake, exercise, smoking & caffeine consumption are important in determining BMD. We studied 1001 subjects, 726 were females & 275 were males between 20-70 years, for all subjects weight, height, Self assessment questionnaire & peripheral radial DXA were done. BMD is strongly related to age, sex, menopausal status, amount of calcium intake, the smoking state performance of exercise high caffeine consumption.

Key word: BMD, T-score, DXA, BMI

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List of Abbreviations

ANOVA	:	Analysis of variance test
BA	:	Bone area
BMAD	:	Bone mineral apparent density
BMC	:	Bone mineral content
BMD	:	Bone mineral density
BMI	:	Body mass index
BMP-2	:	Bone morphogenetic protein-2
CEE	:	Conjugated equine estrogens
CSF	:	Colony-stimulating factor
DNA	:	Deoxyribonucleic acid
DXA	:	Dual-energy X-ray absorptiometry
FDA	:	Food and Drug Administration
FRAX	:	Fracture Risk Assessment Tool
FSH	:	Follicle stimulating hormone
GI	:	Gastrointestinal
GM-CSF	:	granulocyte monocyte-colony stimulating factor
GnRH	:	gonadotropin-releasing hormone
IGF	:	insulin-like growth factor
IGFBP	:	IGF-binding-protein
IL	:	interleukin
ISCD	:	International Society for Clinical Densitometry
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LDL	:	Low-density-lipoprotein
LRP-5	:	Receptor related protein 5
LSC	:	Least significant change
M-CSF	:	macrophage-colony stimulating factor
MPA	:	Medroxyprogesterone acetate
mRNA	:	Messenger Ribonucleic acid
N	:	SAMPLE SIZE
NHANES	:	National Health and Nutrition Examination Survey
NOF	:	National Osteoporosis Foundation
NSAIDs	:	non-steroidal antiinflammatory drugs

PBM	:	Peak bone mass
PBM	:	Peak bone mass
PTH	:	parathyroid hormone
PTHrP	:	PTH-related protein
qCT	:	Quantitative computerized tomography
QCT	:	Quantitative computed tomography
r	:	Correlation coefficient
RANKL	:	Receptor activator of nuclear factor kappa-B ligand
ROI	:	Regions of interest
SD	:	Standard deviations
SERM	:	Selective estrogen receptor modulator
SNP	:	Single nucleotide polymorphism
TGF	:	transforming growth factor
TGF-beta	:	Transforming growth factor-beta
TNF-α	:	Tumor necrosis factor-alpha
VFA	:	Vertebral fracture assessment
VFA	:	Vertebral fracture assessment
VFs	:	Vertebral fractures
WHI	:	Women's Health Initiative
WHO	:	World Health Organization

LIST OF FIGURES

LIST OF TABLES

CONTENTS

INTRODUCTION

Peak bone mass in young adults is a major determinant of bone mass later in life. Thus even though most osteoporotic fractures occur in elderly people, the risk of osteoporosis may be profoundly affected by events in early life. Genetic factors play a major part in the determination of peak bone mass, accounting for up to 80% of the variance **(Ralston et al 2001)**, but 20% or more may be due to environmental factors, including exercise, smoking and calcium intake.

To date, the role of calcium intake in achieving peak bone mass has been most convincingly supported by prospective interventional studies **(Dawson-Hughes et al., 2005)** and that of exercise in a cross sectional study of children aged 5-14 **(Wolff I et al., 1999)**. The effect of smoking has not been studied in Egyptian adults groups.

Over the part 15 years, much has been learned about the epidemiology of osteoporosis in white women, particularly those aged 65 years and older. The study of osteoporotic fractures (SOF) in the United States and the EPIDOS study in France have been particularly useful in defining risk factors for fractures and characterizing the relationship between bone mineral density (BMD) and fracture risk.

In recent years, there has been increasing interest in osteoporosis among Egyptian women. Calcium intake is generally very the low among Egyptians. Larger and longer-term studies are needed to test whether calcium supplementation can help increase bone mass (and possibly later bone strength) in geographic regions with low dietary calcium intake.

AIM OF WORK

To evaluate the contribution of exercise, smoking and calcium intake on BMD in Egyptian adults. Peripheral DXA scan will be used as an easy, cheap and accurate way of measurement of BMD.

CHAPTER I

Pathogenesis of Osteoporosis

Osteoporosis is a skeletal disorder characterized by low bone mass with microarchitectural disruption and fragility, resulting in an increased risk of fracture (table 1) **(CDC, 1993; Raisz, et al 2005)**.

Category	Bone mass
Normal	A value for bone mineral density (BMD) within one standard deviation of the young adult female reference mean (T-score greater than or equal to -1 SD).
Low bone mass (osteopenia)	A value for BMD more than one but less than 2.5 standard deviations below the young adult female reference mean (T-score less than -1 and greater than -2.5 SD).
Osteoporosis	A value for BMD 2.5 or more standard deviations below the young adult female reference mean (T-score less than or equal to -2.5).
Severe (established) osteoporosis	A value for BMD more than 2.5 standard deviations below the young adult female reference mean in the presence of one or more fragility fractures.

Diagnostic categories for osteopenia and osteoporosis based upon bone mass measurements (Scientific Group. 2007; WHO, Geneva).

Elements that distinguish it from other causes of low bone mass, such as hyperparathyroidism and osteomalacia, include normal serum calcium and phosphorus and microarchitectural disruption without an increase in unmineralized osteoid. (figure 1).

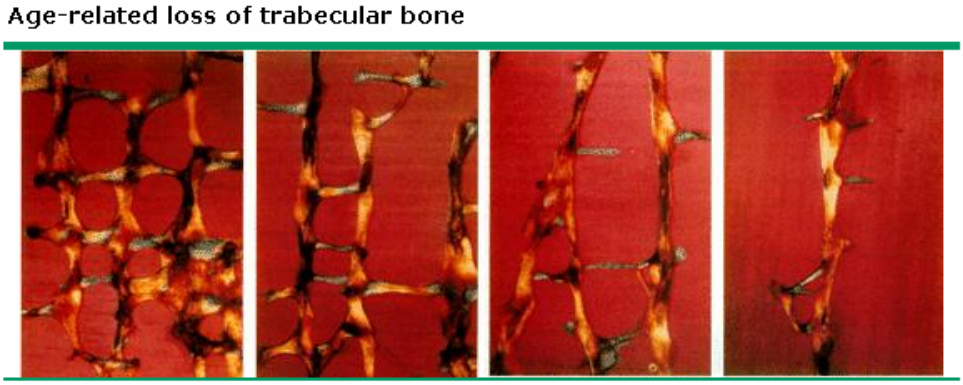

Fig. (1): The figure shows normal bone in panel A, and progressively more osteoporotic bone in panels B, C and D

The bone that is present is normally mineralized, which distinguishes osteoporosis from osteomalacia. There is disruption of the normal architecture, as illustrated in the figure, panel D (figure 1). There are fewer bony spicules in osteoporotic bone and they are thinner than normal; in addition, there are disrupted horizontal "struts" that do not join up to any other structure, and thereby provide no structural support.

This microarchitectural disruption undermines the structural integrity of the bone, and leads to the major clinical features of osteoporosis: skeletal fragility and an increase in fracture risk [1]**((CDC, 1993)** .

The mechanisms of the microarchitectural disruption are not clear. Increased remodeling itself may cause structural weakening, which may account for the independent association of high bone turnover with fracture risk **(Garnero, et al 1996)**. Other possible factors include: Microfractures and fatigue damage The development of perforations and discontinuities in trabecular bone, as well as a relatively excessive loss of horizontal trabeculae (show figure 1) "Macroarchitecture" may play a role; as an example, increased length of the femoral neck appears to increase the risk of hip fracture Posture, muscle strength and the frequency and type of falls affect fracture frequency and site.

Decreased bone mass can occur because peak bone mass is low, bone resorption is excessive, or bone formation during remodeling is decreased. All three processes are likely to contribute, in varying degrees, to osteoporosis in individual patients. Their relative contribution to fracture risk is not known, but it seems likely that increased bone resorption has the greatest impact **(Melton, et al 1997; Garnero, et al 1996)**.

Age- and menopause-related bone loss are clearly important pathogenetic factors, but their expression must vary because there are wide variations in the amount of bone and the amount of "porosity" of bone in older persons of the same age (figure 1) (**Feik, et al 1997)**.

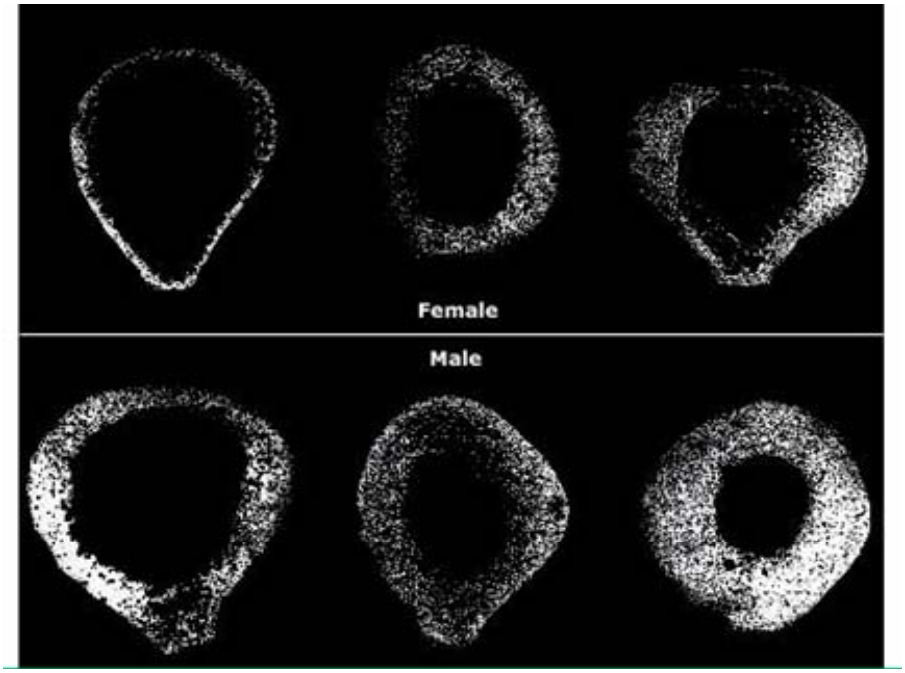

Fig. (2): Variations in bone mass in the femur.

Mid-shaft of the femur from three women and three men over the age of 80. Despite the fact that all subjects were the same age and all of the women were postmenopausal and estrogen deficient, there is marked variability in cortical thickness and porosity. The reasons for these differences are not known.