Assessment of Physical Performance in Postmenopausal Women and its Relation to Bone Mineral Density

Thesis

Submitted in partial fulfillment for the master degree in Rheumatology and Rehabilitation

By

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Abstract

Objective: To assess the relationship between bone mineral density (BMD) and physical performance in postmenopausal women.

Methods: Forty postmenopausal women (age range 48 – 69; mean 57.6±6.1 years) with a duration of menopause of 1.0-31.0; mean 10.0±7.2 years were included. Twelve women (30.0%) had diabetes and 23 (57.5%) had hypertension. BMD of the distal radius, lumbar spine and femoral neck was assessed by dual energy Xray absorptiometry. Physical performance measures included normal and brisk eight meter gait speed, normal step length (NSL), brisk step length (BSL), timed one-leg stance (OLS), five repetitions timed sit-to-stand (STS) and grip strength.

Results: Mean BMD of the lumbar spine was 1.04 ±0.17,at the femoral neck0.93 ± 0.11 and at the distal forearm 0.76± 0.10 g/cm^2. Surprisingly, BMD of the lumbar spine was positively correlated with STS[r=0.367, p= 0.020] and negatively correlated with normal gait speed [r=-0.578, p=0.0001], brisk gait speed [r=-0.554, p=0.0001] and BSL [r=-0.416, p=0.008]. There were no significant correlations between BMD of the femoral neck or distal forearm and any of the physical performance measures. Diabetic patients had lower grip strength, shorter NSL, shorter BSL, yet higher femoral BMD than non-diabetics (p=0.03, 0.0001, 0.016, 0.011, respectively) while hypertensive subjects had higher BMD of the femoral neck and distal radius (p= 0.029 and 0.043, respectively). In multivariate regression models, diabetes and hypertension were independently correlated with BMD of the femoral neck [B=0.139, p=0.003; B=0.089, p=0.041, respectively].

Conclusions: There was no relation between higher BMD and better physical performance.

Key words: Bone mineral density – Physicalperformance- osteoporosis.

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List of Abbreviations

- **ABONE:** Age, BOdy size, No Estrogenscore.
- **BMD**: Bone Mineral Density.
- **BMI:** Body mass index.
- **BSL:**brisk step length.
- **CaSR:** calcium-sensing receptor.
- **CORE:** 4-year Continuing Outcomes Relevant to Evista.
- **CRFs:** clinicalrisk factors.
- **CTSK:** Cathepsin K
- **CTX:** Serum C –telopeptidescross links of type I collagen.
- **D.M.:** Diabetes mellitus.
- **DEXA:** Dual Energy X-ray Absorbitometry.
- **EphB4:** Ephrin B4
- **8 FTW:** 8-feet timed walk.
- **FIT:** Fracture Intervention Trial.
- **5 TSTS:**five-Times-Sit-to-Stand test.
- **FN BMD:**femoral neck bone mineral density.
- **FRAX**: Fracture Risk Assessment Tool for 10 years.
- **GH:** growth hormone.
- **H.T.N:** hypertension.
- **HAQ:** Health Assessment Questionnaire.
- **HAQ-DI:**health assessment questionnaire disability index.
- **HORIZON:** HealthOutcomes and Reduced Incidence with ZoledronateONceyearly study.
- **HRT:** Hormone Replacement Therapy.
- **HS:** Highly significant.
- **IGF:**insulin-like growth factor.

- **ILs**: Interleukins.
- **IOM:** Institute of Medicine.
- **IQR:**Interquartile range.
- **IU:** international units.
- **M-CSF:** macrophage colony-stimulating factor.
- **MHR:** maximum heart rate.
- **MOBILE:** Monthly Oral iBandronate In LadiEs.
- **MORE:** MultipleOutcomes of Raloxifene Evaluation.
- **MRS:**maximum rising strength.
- **NICE:**National Institute for health and Clinical Excellence.
- **NOF:** National Osteoporosis Foundation.
- **NS:**Non significant.
- **NSL:** normal step length.
- **NTX:** Serum N - telopeptidescross links of type I collagen.
- **OA:**osteoarthritis.
- **OC:** osteocalcin.
- **OLS:**One-leg stand.
- **OPG:** osteoprotegerin.
- **ORAI:**Osteoporosis Risk Assessment Instrument.
- **OSIRIS:** Osteoporosis Index of RISk.
- **OST:** Osteoporosis Self-assessment Tool.
- **OTC Vitamins:** Over-The-Counter Vitamins.
- **PBM**: Peak bone mass.
- **pDEXA:** Peripheral DEXA.
- **PEARL:** PostmenopausalEvaluation and Risk Reduction with Lasofoxifene.
- **PTH:** parathormone.
- **QUS:** quantitative ultrasound.
- **RA:** rheumatoid arthritis.

- **RANKL**: receptor activator of nuclear factor-kB ligand.
- **RAS:**renin-angiotensin system.
- **RPE:**Rating ofPerceived Exertion.
- **S:**Significant.
- **SCORE:** the Simple Calculated Osteoporosis Risk Estimation.
- **sCT:**salmon calcitonin.
- **SDs:** Standard Deviations.
- **SERMs:** Selective estrogen-receptor modulators.
- **SI:** stiffness index.
- **SOTI:** SpinalOsteoporosis Therapeutic Intervention.
- **STS:** sit to stand.
- **TGF-b:** transforming growth factor beta.
- **TGUGT:** timed get-up-and-go test.
- **TNF:**tumor necrosis factor.
- **TROPOS:** Treatment ofPeripheral Osteoporosis.
- **UL:** upper level.
- **VEGF:**vascular endothelial growthfactor.
- **VIP:** Västerbotten Intervention Project.

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INTODUCTION

Osteoporosis is the major cause of fractures in the elderly that may increase mortality rate, reduce independence, and limit walking ability and activities of daily living, thus seriously affecting quality of life in the later years **[Fink et al, 2003].**

Osteoporosis is classified into primary and secondary types. Postmenopausal osteoporosis is type I of primary osteoporosis. Osteoporosis can be diagnosed using dual-energy x-ray absorptiometry (DEXA) which is used to assess bone mineral density at the lumbar spine, distal forearm, and proximal femur **[Lane and Leboff, 2005].**

Multiple factors, in addition to low bone mineral density (BMD) and poor nutrition, have been identified as risks for fractures, including reduced levels of physical activity, general frailty, poor balance, and slowed gait speed **[Dargent-Molina et al, 1999].**

There are many risk factors affecting BMD and physical performance measures: age, age at onset of menarche, duration of menopause, number of children, body mass index and total daily calcium intake **[Lindsey et al, 2005].**

Physical activity increases bone mass during childhood and adolescence, and is necessary to achieve the highest peak bone mass. It is clear that physical activity is vital in adults because it reduces the rate of bone loss during the peri-menopausal period, and decelerates bone loss associated with aging **[Dionyssiotis et al, 2010].** It was found that there is a higher prevalence of osteopenia and osteoporosis in people with disability than in the general young adult population **[Smith et al, 2009].** The Health Assessment Questionnaire (HAQ) disability index is widely used for assessment of disability in activities of daily living including dressing,

grooming, rising, eating, walking, hygiene, reach and grip and **[Bruce and Fries, 2003].**

Physical performance measures are independent predictors of change in health status, and decline in function in a primary care clinical environment. Performance measures have the potential to be incorporated into clinical practice as convenient global markers or "vital signs" for health-related risk in older adults **[Studenski et al, 2003].** Epidemiologic evidence suggests that being active can nearly halve the incidence of hip fractures in the older population. **[Rutherford, 1999]** Walking and physical activity levels have been positively associated with femoral BMD **[Brownbill et al, 2003].** Diminished physical performance is associated with increased fall risk in samples of frail elders and can be quantified using simple measures, such as gait speed, step length, one-leg stance (OLS) time, sit-to-stand (STS) time and grip strength **[Lindsey et al, 2005].**

The purpose of the present study was to evaluate the relationship between BMD at various skeletal sites, self-reported disability using the HAQ and simple measures of physical performance in postmenopausal women aiming to identify postmenopausal women at greater risk of osteoporosis. These measures are: eight-meter normal and brisk gait speed, normal and brisk step length, one leg stance time, five repetition STS time, and grip strength.

Chapter I

OSTEOPOROSIS

Introduction

Osteoporosis is defined as a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture. Bone strength primarily reflects the integration of bone density and bone quality **[NIH, 2001].**

Bone density is expressed as grams of mineral per area or volume, and in any given individual is determined by peak bone mass and amount of bone loss**[Lane and Leboff, 2005].**

Bone quality refers to architecture, turnover, damage accumulation (e.g.microfractures) and mineralization. Osteoporosis is characterized by reduced bone mass while osteomalacia encompasses disorders in which there is decreased mineralization of bony matrix **[Pande, 2010].**

Epidemiologyof osteoporosis

Osteoporosis is the most common metabolic bone disease and the most common cause of fractures in older adults in the United States. Ten million people in the United States have osteoporosis, and an additional 33 million people have low bone mass (osteopenia) and are at increased risk for fractures. More than 2 million fractures occur each year as a result of osteoporosis or osteopenia, including 300,000 hip fractures, 547,000 vertebral fractures, and 135,000 pelvic fractures. Postmenopausal white women have a 40% life time risk of at least one osteoporotic fracture **[Favus, 2010].**

In Bahrain, a sample of 170 postmenopausal Bahraini women was recruited and bone density was measured using ultrasound. It was observed that only 21.7% of the women who participated in the study had normal bone density: 51.2% had osteopenia and 27.1% had osteoporosis**[El-Hajj Fuleihan et al, 2011].**

In Iran, 11% of 245 randomly selected postmenopausal women with a mean age of 57.7 ± 7 years were found to be osteoporotic in the femoral neck and 25.3% were osteoporotic in the lumbar spine**[Hosseinapanah et al, 2008].**

In Egypt, it has beencalculated that 53.9% of postmenopausal women haveosteopenia and 28.4% have osteoporosis and in men, 26%have osteopenia and 21.9% have osteoporosis**[El-Hajj Fuleihan et al, 2011].**

Several studies have been conducted in the Middle East, in an effort to evaluate Bone Mineral Density (BMD) and adjust the means to those of Western populations. Indeed, reference ranges have been suggested for Lebanon, Saudi Arabia, Kuwait, Qatar and Iran. All these studies, conducted mainly on female populations, found lower BMD than the standard established for the US/European reference data, except the Kuwait study, where the BMD reference range was similar**[Maalouf et al, 2007].**

Pathophysiology of osteoporosis

The structural components of bone consist of extracellular matrix (largely mineralized), collagen and cells. The collagen fibers are of type I, comprise 90% of the total protein in bone and are oriented in a preferential direction giving lamellar bone its structure.
Spindle- or plate-shaped crystals of hydroxyapatite [$3Ca_3(PO_4)_2(OH)_2$] are found on the collagen fibers, within them, and in the ground substance. The ground substance is primarily composed of glycoproteins and proteoglycans. These highly anionic complexes have a high ion-binding capacity and are thought to play an important role in the calcification process. Numerous non-collagenous proteins have been identified in bone matrix, such as osteocalcin synthesized by the osteoblasts**[Rey et al, 2009].**
The principal cells in bone are the osteoclasts and osteoblasts (including bone-lining cells and osteocytes). Normally, bone turnover is tightly coupled with osteoclast mediated bone resorption followed by

osteoblast-stimulated bone formation; this delicate balance in bone remodeling results in no net change in skeletal mass. Osteoblasts synthesize osteoid, bone that subsequently undergoes mineralization and becomes mature bone matrix. The skeleton contains approximately 80 percent cortical bone, which is concentrated in the appendicular skeleton and femoral neck and 20 percent more metabolically active trabecular bone, which is located in the spine, epiphyses, and pelvis **[Lane and Leboff, 2005].**

The process of bone remodeling is based upon the coupled action of bone resorbing cells (osteoclasts) and bone-forming cells (osteoblasts). Osteoblasts, as well as many other cell types such as adipocytes, chondrocytes, fibroblasts and myoblasts, differentiate from mesenchymal stem cells.Osteoclasts, on the contrary, are derived from the hematopoietic mononuclear lineage.Two cytokines, which are mainly produced by bone marrow stromal cells and osteoblasts, are essential for osteoclastogenesis: macrophage colony-stimulating factor (M-CSF) and receptor activator of nuclear factor-kB ligand (RANKL), which belongs to the tumor necrosis factor (TNF) superfamily **[Sipos et al, 2009].**

RANKL interacts with its cognate receptor (RANK) that osteoclasts and their precursors express. The binding between RANK and its ligand stimulates osteoclast differentiation and activation and prevents osteoclast cell death **[Roodman, 2006].**Concurrently,a decoy receptor known as osteoprotegerin, which the osteoblasts produce and inhibits RANK–RANKL signaling, regulates this process. Many factors stimulate RANKL expression, including parathormone (PTH), vitamin D, cytokines, interleukins (ILs), prostaglandins, and thiazolidinediones. Conversely, estrogen,transforming growth factor beta (TGF-b), and mechanical force inhibit RANKL expression. More recently, signaling by ephrin has been thought to play an important role in osteoclast–osteoblast coupling. This cellular communication is bidirectional and involves a transmembrane ligand known as ephrinB2, which osteoclasts express, and its receptor EphB4, which osteoblasts express **[Figure**