Relationship between body composition and bone mass in elderly Egyptian with primary osteoporosis

Thesis submitted for partial fulfillment of Master degree in Geriatric Medicine

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INTRODUCTION

Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, with consequent increase in bone fragility *(Ahmed and Elmantaser, 2009)*.

Osteoporosis is a systemic disease in which bone density is reduced leading to the weakening of the skeleton and increase vulnerability to fractures *(Wells, 2005).*

It is called silent disease since there are few associated symptoms; osteoporotic fracture is chief clinical feature with an enormous burden on the health related quality of life and mortality *(Bagnato, 2007).*

Osteoporosis can be classified as primary or secondary. Primary osteoporosis is simply the form seen in older persons and women past menopause in which bone loss is accelerated over that predicted for age and sex. (*Gallagher et al., 2000).*

Secondary osteoporosis results from a variety of causes, weakness, falls, functional limitations, immobility, and osteoprotic fractures may be linked to decline in musculoskeletal mass. It has been reported that loss of the skeletal muscle mass occurs with advancing age in elderly men and women, even in independently living healthy subject and that men lose significantly more leg skeletal muscle mass than women, furthermore, skeletal muscle mass loss in men is masked by weigh stability resulting from corresponding increase in fat mass (*Gallagher et al., 2000).*

Both cross sectional and longitudinal studies have shown age-dependent body composition changes, with increase in fat mass especially visceral fat and decrease muscle mass in both men and women *(Forbes, 2000).*

Studies have reported that in both sexes fat mass increases with age whereas there is a decline in bone mass (osteopenia) and muscle mass (sarcopenia) *(Baumgartner 1995; Nguyen et al., 1998).*

Despite the well established relationship between the body weight and bone mass, however, it

remains unclear which body mass compartment (i.e. fat versus lean mass) is truly correlated to bone mass reported that fat body mass (FBM) but not lean body mass (LBM) was important in determining bone mass *(Douchi et al., 1997).*

AIM OF THE WORK

To detect the relationship between body composition and primary osteoporosis in elderly Egyptian.

OSTEOPOROSIS IN ELDERLY

Definition of osteoporosis

Osteoporosis or "porous bone" is a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fractures, especially to hip, spine and wrist *(National osteoporosis foundation, 1998).*

Persons were considered to be osteoporotic if T score ≤-2.5 and normal BMD (bone mineral density) if T score ≥-1 and osteopenic ranging from -1.1 to -2.4 *(WHO, 2000).*

Physiology of bone formation

Being a primary structural framework of the body, bone undergoes dynamic microstructural remodeling throughout life to accommodate mechanical stress and calcium demand *(Sims and Gooi, 2008),* Bone remodeling is a coupled process of bone resorption and formation, and requires coordination of all three types of bone cells, namely osteocytes, osteoblasts and osteoclasts *(Sims and Gooi, 2008).*

Under mechanical stress, osteocytes act as mechanosensors to detect changes in the flow of bone fluid within bone canaliculi, and respond by transmitting signals to the osteoblasts via their syncytial processes. Osteoblasts later stimulate osteoclast differentiation and subsequent bone resorption. Normally, osteoblast-mediated bone formation takes place at the same site to fill up the resorption pit with new bone *(Sims and Gooi, 2008).*

Following bone resorption, osteoblast-mediated bone formation takes place to fill the resorption pits with newly mineralized bone. The type I collagen fibrils secreted by osteoblasts are arranged into the organic matrix osteoid, which is subsequently mineralized by calcium and phosphate in the presence of alkaline phosphatase, osteocalcin and osteopontin. Eventually, hydroxide ions are gradually added and mature hydroxyapatite crystals [Ca10(PO4)6(OH)2] are formed *(Sims and Gooi, 2008).*

Bone tissue undergoes constant remodeling. Under the physiologic conditions, bone formation and resorption are in a fair balance. After the third decade of life, bone resorption exceeds bone formation and

leads to osteopenia and, in severe situations, osteoporosis **(Kosmin and Diamond, *2011).***

Women lose 30-40% of their cortical bone and 50% of their trabecular bone over their lifetime, as opposed to men, who lose 15-20% of their cortical bone and 25-30% of trabecular bone **(Kosmin and Diamond, *2011).***

Basic mechanisms responsible for development of osteoporosis are poor bone mass acquisition during growth and development and accelerated bone loss in the period after peak bone mass is achieved. Both processes are modulated by environmental and genetic factors **(*Skugor, 2010).***

The main factor influencing peak bone mass is genotype. The genes implicated in osteoporosis include those for the estrogen receptor, transforming growth factor-β, and apo-lipoprotein E and collagen ***(Skugor, 2010).***

Bone loss, in contrast, appears to be mostly determined by environmental factors (nutritional., behavioral., and medications). However, genetic factors also play a role, mostly acting on a person's estrogen status ***(Skugor, 2010).***

Pathophysiology

The cells most involved in bone turnover are osteoclasts and osteoblasts. These cells have counter effects on bone. The former are the resorption cells; the latter are the formation cells. The balance between activation and apoptosis of cells is the key to maintaining bone mass. Formation of new bone goes through four steps: osteoclast activation, bone resorption, reversal with osteoclast inhibition and osteoblast activation, and finally bone formation. Therefore, everything starts by osteoclastogenesis. Osteoclasts are derived from the hematopoietic lineage and differentiate in order to degrade bone *(Boyle et al., 2003).*

Throughout aging, bone turnover unbalances in favor of bone resorption. Osteoporosis is a chronic bone disease characterized by a decreased bone mass leading to fragile bone and an increased risk for fractures, notably hip, vertebral., and forearm fractures, which are the source of a loss of autonomy and increased mortality in the elderly (*Compston , 2010).*

Suppression or control of bone resorption is therefore a major therapeutic strategy to prevent or

diminish bone loss. A critical signaling pathway with three major proteins, OPG (osteoprotegerin), RANK (Receptor activator of nuclear factor kappa-B), and RANKL (Receptor activator of nuclear factor kappa-B ligand), was discovered, thereby enlightening the cellular regulation of bone formation. OPG was the first protein of the pathway to be identified in 1997 *(Rogers and Eastell, 2005).*

OPG is a member of the TNF (tumor necrosis factor) receptor family but is atypical., as it is a secreted protein with no transmembrane domain. It contains four homologous domains for binding its target, RANKL. OPG is produced by many types of tissue, including osteoblasts, endothelial cells, vascular smooth muscle, and lymphoid cells, and other cell types, raising the question of the specificity of this protein in the bone mass regulation *(Khosla ,2001).*

RANKL is another new member of the TNF ligand family. It is produced by osteoblast lineage cells and activated T-cells. Macrophage colony-stimulating factor M-CSF (macrophage colony-stimulating factor) and RANKL have complementary activities. M-CSF increases the pool of osteoclast precursors, whereas RANKL binds to its receptor RANK expressed on