UPDATE IN OSTEOPOROSIS

Essay

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List of Abbreviations

ADLs ..... Activities of Daily Living
ADRB 2 .. Adrenergic Receptors Beta2
AP ..... Alkaline Phosphatase
APC ..... Adenomatous Poliposis Coli
Bad ..... BCL2 Antagonist of cell death
BHRT ..... Bio- identical Hormone Therapy
BMC ..... Bone Mineral Component
BMD ..... Bone Mineral Density
BMPs ..... Bone Morphogenic Proteins
BMU ..... Bone Multi-cellular Unite
BRC ..... Bone Remodeling Compartment
BSAP ..... Bone Specific Alkaline Phosphatase
BUA ..... Broad band Ultrasound Attenuation
CAMP ..... Cyclic Adenosine Mono Phosphate
CEE ..... Conjugated Equal Estrogen
COX 2 ..... Cyclo oxygenase 2
CREM ..... CAMP Responsive Element Modulator
CRTAP ... Cartilage Associated Protein
CTX ..... C – Telopeptides
DHEA ..... Dehydropiandrosterone
DKK ..... Dikkopf
DKK 1 ..... Dickkopf homolog 1
DMP 1 ..... Dentin Matrix Protein 1
DPA ..... Dual Photo Absorptiometry
DPD ..... Deoxy Pyridine Oliate
DXA ..... Dual energy X-ray Absorptiometry
ECM ..... Extra Cellular Matrix
Eph B4 .... EPH receptor B4
EPT ..... Estrogen and Progestin Therapy
ERR ..... Estrogen receptor Related Receptor

ERs ..... Estrogen Receptors
FDA ..... Food and Drug Administration
FDPS ..... Farmesyl Diphosphate System
FGF2 ..... Fibroblast Growth Factor 2
FIT ..... Fracture Intervention Trial
Fzl ..... Receptor Frizzled
GSK 3B ... Glycogen Synthesae Kinase 3 B
GnRH ..... Gonadotropen Releasing Hormone
HIP..... Hip Intervention Program
HOPE ..... Health Osteoporosis Progestin / Estrogen study
HORIZONE ..... Health Outcome and Reduced Incidence with oledranic acid One yearly
HRMRI ... High Resolution MRI
HRPQCT High Resolution Peripheral Quantitative C T
HRT ..... Hormone Replacement Therapy
ICV ..... Intra CerebroVentrecular
IGF ..... Insulin – like Growth Factor
IL 1 ..... Interleukin 1
IOM ..... Institute Of Medicine
ISCD ..... International Society for Clinical Denstiometry
ITAM ..... Immune receptor Tyrosine based Activated Motif
Lef 1 ..... Lymphocyte enhancing factor 1
LepR ..... Leptin Receptor
LRP ..... Low density lipoprotein Related Protein
M CSF .... Macrophage Colony Stimulating Factor
MORE .... Multiple Outcome of Raloxifene Evaluation study
MPA ..... Medroxyprogesterone
NCOR ..... Nuclear Receptor Co – Receptor
NIH ..... National Institute of Health
NFAT ..... Nuclear Factor of Activated T cell
NTX ..... N Telopeptide
OC N ..... Osteocalcin
OHP..... Hydroxyproline

OI ..... Osteogenesis Inperfecta
ONJ ..... Osteonecrosis of the Jaw
OPG ..... Osteoporotogeren
OST ..... Osteoporosis Self assessment Tool
PEPI ..... Postmenopausal Estrogen /Progestin Intervention trial
PFT ..... Pevotal Fracture Trial
PGE2 ..... Prostaglandin E 2
PROOF ... Prevent Recurrence Of Osteoporotic Fracture study
PSF ..... Point Spread Function
PTH ..... Para Thyroid Hormone
PTHrp ..... Para Thyroid Hormone related protein
QCT ..... Quantitative Computed Tomography
QUI ..... Quantitative Ultrasound Index
QUS ..... Quantitative Ultrasound
RANK ..... Receptor Activator of NF – KB
RANKL .. Receptor Activator of NF – KB Ligand
RCT ..... Randomized Controlled Trial
RGD ..... ARG- Glycen – Aspartate Amino acid sequence
ROS ..... Reactive Oxygen Species
RR ..... Relative Risk
Rumx 2 ... Runt related Transcription factor 2
SAXS ..... Small Angle X ray Scattering
S D ..... Standard Deviation
SEQCT ... Single Energy Quantitative Computed Tomography
SERM ..... Selective Estrogen Receptor Modulators
SFRP 1 .... Secreted Frizzled – Related Protein 1
S 1 P ..... Sphingosine 1 Phosphate
SMRT ..... Silencing Mediator For Retinoid And Thyroid hormone Receptors
SNPs ..... Single Neocleotide Polymorphisms
SOS ..... Speed Of Sound
SPA ..... Single Photon Absorpiometry
STAR ..... Study of Tamoxefen and Raloxefen trial
TGF – B .. Transforming Growth Factor – Beta

TNF ..... Tumor Necrotizing Factor
TRAP ..... Tartarate Resistant Acid Phosphatase
T 2 ..... Relaxation Time
uCT ..... Micro Computed Tomography
VDR ..... Vitamin D Receptor
VEGF ..... Vascular Endothelial Growth Factor
VERT ..... Vertebral Efficacy with Risedronate Therapy
VOS ..... Velocity Of Sound
WHI ..... Women Health Institute
WHO ..... World Health Organization
Wnt ..... Wingless –type MMTV integration site family

Introduction

Definition

The World Health Organization (WHO) established a classification of bone mineral density (BMD) according to the standard deviation (SD) difference between a patient's BMD and that of a young-adult reference population. This value is now commonly expressed as a "T-score." A T-score that is equal to or less than -2.5 is consistent with a diagnosis of osteoporosis; a T-score between -1.0 and -2.5 is classified as low bone mass (osteopenia); and a T-score of -1.0 or higher is normal. **(Kor et al., 2008).**

Osteoporosis now is defined as an impairment in bone strength due to an abnormal quantity or quality of bone, or both. Quantity is measured from BMD. Quality is affected by many factors, including the degree of mineralization, the connectivity of the bony trabeculae, the quality of the collagen fibres, and the health of the bone cells. **(Rowe et al., 2009).**

This definition was concluded in 2001 by National Institutes of Health (NIH). It takes into consideration that there are other factors that influence bone quality such as the microarchitecture, remodeling rate (bone turnover), damage accumulation, and mineralization. The problem with this definition is that strength cannot be measured in vivo, thus requiring surrogates that somehow quantify parameters that determine bone quality and therefore strength. **(Felix, 2007)**.

Health impact

The most significant complication of osteoporosis is a fracture, and while fractures may occur at many sites, they most

commonly occur in the hip, spine, and wrist. Associated clinical complications include pain, disability, deformity, postural changes associated with vertebral compression fractures, and deconditioning secondary to physical inactivity. In the United States alone, osteoporosis is responsible for over 1.5 million fractures annually, including 300,000 hip fractures and 250,000 wrist fractures. **(Sybold et al., 2008).**

Osteoporosis remains a major public health problem through its association with fragility fractures. Despite the availability of preventative therapeutic agents, the incidence and its associated costs continue to rise globally. Understanding osteoporosis epidemiology is essential to developing strategies to reduce the burden of osteoporotic fracture in the population**. (Cole et al., 2008).**

Survival depends greatly on the fracture types, age, gender, and race. Deaths are predominately due to co-morbidities, but may also be attributed to the fracture event itself, either directly or indirectly. The goal of osteoporosis care is prevention of fractures and ultimately reduction in morbidity and mortality. Large observational cohort studies over considerable time are needed to determine whether improving osteoporosis quality of care will improve mortality rates.**(Teng et al., 2008).**

Vertebral fractures account for the majority of osteoporotic fractures at 700,000, while fractures at other sites total more than 300,000. Simple activities such as bending over to pick up a piece of paper or sneezing can cause a fracture in a patient with osteoporosis. Fractures associated with osteoporosis have a high predilection in females and are compounded by the patient's age. While vertebral fracture is the most common type of osteoporotic fracture, hip fractures have a particularly high morbidity and mortality rate. They are more

common in females than the combined risk of breast, uterine, and cervical cancer. **(Sybold et al., 2008).**

Application of the WHO fracture prediction algorithm in conjunction with an updated US economic analysis indicates that osteoporosis treatment is cost effective in patients with fragility fractures or osteoporosis, in older individuals at average risk, and in younger persons with additional clinical risk factors for fracture, supporting existing practice recommendations. **(Dawsqn- Hughe et al., 2008).**

Fracturing a hip is a major concern in many older people, in that it makes it difficult for the individual to perform necessary activities of day living (ADLs) and limits independence, and secondary complications may even lead to death. Hip fractures may occur at any age but are more common in the aging population. Aging results in loss of bone density, increasing the risk of fracture related to osteoporosis. Hospitalizations associated with hip fractures tend to occur in patients over 65 years of age. Surgical repair of hip fractures is almost always recommended, and is usually very effective; however, recovery requires patience and time. The future health of the patient often directly correlates with the postoperative outcome and mobility. **(Sybold et al., 2008).**

It is estimated that one-fifth of the number of women suffering a hip fracture are likely to die within one year as a result of secondary postoperative complications (such as pulmonary embolism). While the incidence of hip fractures is more common in women, the one-year mortality rate is about twice as high in men. Two-thirds of patients suffering a hip fracture cannot return to their previous level of function. Basic activities of daily living (ADLs) become a challenge, forcing more than 50% of patients suffering a hip fracture to need long-term nursing care. This dependent care is usually provided to

patients in the form of home health care, or in a nursing facility with a skilled nursing or assisted-living level of care. **(Sybold et al., 2008).**

The number of hip fractures will increase enormously in the decades to come as will the cost of treatment of these patients do. In the USA the annual cost has estimated to be nearly $10 billion. Hip fractures, therefore, represent an enormous socio-economic and medical problem and challenge orthopaedic surgeons and anaesthetists to find the cheapest and most effective way to treat them. At the same time the search for preventive measures should be continued. Bisphosphonates and hip protectors seem to be able to decrease the risk of suffering a hip fracture with 50%. **(Raavmakers, 2006).**

Vertebral compression fractures are a significant source of morbidity and mortality for patients with osteoporosis. Such fractures are not a problem confined to just the elderly. It is estimated that over 700,000 fractures occur annually in the Unites States alone. Vertebral compression fractures occur in 25% of women over 50 years of age and 40% of those aged 80–85 years. Approximately 60% of these fractures are clinically silent. The majority of clinically apparent vertebral compression fractures are secondary to relatively minor trauma applied to an already compromised spinal structure. Often, patients may not recall any specific inciting event at all but merely present to the practitioner with a sudden increase in back pain. Other times, patients can identify a specific date and time when their back pain became severe. **(Sybold et al., 2008)**.

Vertebral compression fractures in elderly osteoporotic patients are primarily the result of low-energy flexion injuries, and are therefore typically stable injuries. This does not mean, however, that they are not a cause of significant pain and morbidity. This designation merely implies that catastrophic