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A SELECTION OF TEN CURRENT READINGS ON TOPICS RELATED TO OSTEOPOROSIS – 2019 UPDATE

Some available as free full-text and some requiring payment

Selection of readings made by A/Prof Goh Lee Gan

READING 1 – FRAGILITY FRACTURES IN OLDER PEOPLE IN JAPAN, THE COUNTRY WITH THE OLDEST POPULATION IN THE WORLD

Iihara N(1), Ohara E(1), Bando Y(2), Yoshida T(2), Ohara M(3), Kirino Y(1). Fragility Fractures in Older People in Japan Based on the National Health Insurance Claims Database. Biol Pharm Bull. 2019;42(5):778-785.

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ABSTRACT

Fragility fractures associated with age-related bone loss are of urgent concern worldwide because they reduce QOL and pose financial burdens for health care services. Currently, national data in Japan are limited. This study provides quantitative data for older patients throughout Japan who, although otherwise relatively healthy, sustained fragility fractures and were hospitalized for them.

The National Database of Health Insurance Claims and Specific Health Checkups of Japan was accessed to target patients aged 65 years or older who sustained fractures between May 2013 and September 2014 and were not hospitalized for at least 13 months prior to fracture. We investigated whether the first fracture sustained was fragility related at any of four locations (proximal humerus, distal radius, vertebra, or femoral neck) and whether it necessitated hospitalization.

Fragility fractures were identified in 490138 of 1188754 patients (41.2%, 345980 patients/year; 1: 4 male-to-female ratio). Regardless of gender, vertebral fractures were most common across the age cohorts studied (43286 males and 162767 females/year), and femoral neck fractures increased markedly with increased patient age. Approximately 80% of patients with femoral neck fractures were hospitalized (62.3% of males, 71.1% of females) compared with up to 10.4% of patients with other fragility fractures.

Data provided in this study can be used as a baseline for evaluating the health economy and establishing health policy in Japan.

READING 2 – ESTIMATED PREVALENCE OF OSTEOPOROSIS IN SINGAPORE USING OSTA

Wang P(1), Abdin E(1), Shafie S(1), Chong SA(1), Vaingankar JA(1), Subramaniam M(1). Estimation of Prevalence of Osteoporosis Using OSTA and Its Correlation with Sociodemographic Factors, Disability and Comorbidities. Int J Environ Res Public Health. 2019 Jul 2;16(13).

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ABSTRACT

Osteoporosis is a growing concern for an ageing society. The study aimed to estimate the prevalence of older adults who were at risk of osteoporosis and explore factors associated with osteoporosis. The relationship between the risk of osteoporosis, chronic conditions and disability was also explored. We hypothesized that respondents with high risk index of osteoporosis would be associated with greater disability.

Participants aged 60 years and above (N = 2565) who were representative of Singapore's multi-ethnic population were recruited. The Osteoporosis Self-Assessment Tool for Asians (OSTA) was used to classify the risk of osteoporosis. Information on sociodemographic details and chronic diseases were collected, while severity of disability was measured using the World Health Organization Disability Assessment Schedule 2.0.

The overall prevalence of the respondents who were at risk of osteoporosis was 52%. Those belonging to an older age, Chinese, female, never married or widowed, lower education and retired were associated with a higher risk of osteoporosis. A diagnosis of diabetes or hypertension was a protective factor against the risk of osteoporosis. High risk of osteoporosis was not associated with disability.

Our findings highlighted specific factors associated with the risk of osteoporosis that could be useful for the prevention of osteoporosis and fractures.

READING 3 – COMPARISON OF THREE TOOLS FOR PREDICTING PRIMARY OSTEOPOROSIS IN ELDERLY MALE POPULATION IN BEIJING

Zhang X(#)(1), Lin J(#)(1), Yang Y(1), Wu H(2), Li Y(3), Yang X(4), Fei Q(#)(1). Comparison of three tools for predicting primary osteoporosis in an elderly male population in Beijing: a cross-sectional study. Clin Interv Aging. 2018 Feb 2; 13:201-209.

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ABSTRACT

Purpose: In this cross-sectional study, three clinical tools, the Osteoporosis Self-Assessment Tool for Asians (OSTA), Fracture Risk Assessment Tool (FRAX) without bone mineral density (BMD), and body mass index (BMI), for predicting primary osteoporosis (OP) were compared and ideal thresholds for omission of screening BMD were proposed in a community-dwelling elderly Han Beijing male population.

Patients and methods: A total of 1,349 community-dwelling elderly Han Beijing males aged ≥50 years were enrolled in this study. All subjects completed a questionnaire and measured BMD by dual-energy X-ray absorptiometry (DXA). Osteoporosis was defined as a T-score of -2.5 SD or lower than that of the average young adult in different diagnostic criteria (lumbar spine [L1-L4], femoral neck, total hip, worst hip, and World Health Organization [WHO]). FRAX without BMD, OSTA, and BMI were assessed for predicting OP by receiver operating characteristic (ROC) curves. Sensitivity, specificity, and areas under the ROC curves (AUCs) were determined. Ideal thresholds for omission of screening BMD were proposed.

Results: The prevalence of OP ranged from 1.8% to 12.8% according to different diagnostic criteria. This study showed that the BMI has highest discriminating ability. The AUC of FRAX without BMD ranged from 0.536 to 0.630, which suggested limiting predictive value for identifying OP in elderly Beijing male.

The AUCs of BMI (0.801-0.880) were slightly better than OSTA (0.722-0.874) in predicting OP at all sites. The AUC of BMI to identify OP in worst hip was 0.824, yielding a sensitivity of 84.8% and a specificity of 64.4%. 40% of participants on BMD measurements saved only 0.1%-2.7% missed OP.

Compared to OSTA and FRAX without BMD, the BMI got the best predictive value for OP.

Conclusion: BMI may be a simple and effective tool for identifying OP in the elderly male population in Beijing to omit BMD screening reasonably.

READING 4 – INDIVIDUALISED FRACTURE RISK ASSESSMENT – STATE-OF-THE-ART IN 2018

Nguyen TV (1)(2)(3). Individualized fracture risk assessment: State-of-the-art and room for improvement. Osteoporos Sarcopenia. 2018 Mar;4(1):2-10.

PMID: 30775534 [Free Full Text].
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ABSTRACT

Fragility fracture is a serious clinical event, because it is associated with increased risk of mortality and reduced quality of life. The risk of fracture is determined by multiple risk factors, and their effects may be interactional.

Over the past 10 years, a number of predictive models (e.g., FRAX, Garvan Fracture Risk Calculator, and Qfracture) have been developed for individualized assessment of fracture risk.

These models use different risk profiles to estimate the probability of fracture over 5- and 10-year period. The ability of these models to discriminate between those individuals who will and will not have a fracture (i.e., area under the receiver operating characteristic curve [AUC]) is generally acceptable-to-good (AUC, 0.6 to 0.8), and is highly variable between populations. The calibration of existing models is poor, particularly in Asian populations. There is a strong need for the development and validation of new prediction models based on Asian data for Asian populations.

We propose approaches to improve the accuracy of existing predictive models by incorporating new markers such as genetic factors, bone turnover markers, trabecular bone score, and time-variant factors.

New and more refined models for individualized fracture risk assessment will help identify those most likely to sustain a fracture, those most likely to benefit from treatment, and encouraging them to modify their risk profile to decrease risk.

READING 5 – DIAGNOSIS AND MANAGEMENT OF BONE FRAGILITY IN DIABETES MELLITUS

Ferrari SL(1), Abrahamsen B(2)(3), Napoli N(4)(5), Akesson K(6), Chandran M(7), Eastell R(8), El-Hajj Fuleihan G(9), Josse R(10)(11), Kendler DL(12), Kraenzlin M(13), Suzuki A(14), Pierroz DD(15), Schwartz AV(16), Leslie WD(17); Bone and Diabetes Working Group of IOF. Diagnosis and management of bone fragility in diabetes: an emerging challenge. Osteoporos Int. 2018 Dec;29(12):2585-2596.

PMID: 30066131 [Free Full Text].
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ABSTRACT

Fragility fractures are increasingly recognized as a complication of both type 1 and type 2 diabetes, with fracture risk that increases with disease duration and poor glycaemic control. Yet the identification and management of fracture risk in these patients remain challenging. This review explores the clinical characteristics of bone fragility in adults with diabetes and highlights recent studies that have evaluated bone mineral density (BMD), bone microstructure and material properties, biochemical markers, and fracture prediction algorithms (i.e., FRAX) in these patients. It further reviews the impact of diabetes drugs on bone as well as the efficacy of osteoporosis treatments in this population. We finally propose an algorithm for the identification and management of diabetic patients at increased fracture risk.

READING 6 – REVIEW OF OSTEOPOROSIS TREATMENT OPTIONS IN 2018

Tu KN, Lie JD, Wan CKV, Cameron M, Austel AG, Nguyen JK, Van K, Hyun D. Osteoporosis: A Review of Treatment Options. P T. 2018 Feb;43(2):92-104.

PMID 29386866 [Free Full Text]

ABSTRACT

Approximately 10 million men and women in the U.S. have osteoporosis[1], a metabolic bone disease characterized by low bone density and deterioration of bone architecture that increase the risk of fractures.[2] Osteoporosis-related fractures can increase pain, disability, nursing home placement, total health care costs, and mortality.[3] The diagnosis of osteoporosis is primarily determined by measuring bone mineral density (BMD) using non-invasive dual-energy x-ray absorptiometry.

Osteoporosis medications include bisphosphonates, receptor activator of nuclear factor kappa-B ligand inhibitors, estrogen agonists/antagonists, parathyroid hormone analogues, and calcitonin.[3-6]

Emerging therapies utilizing novel mechanisms include a cathepsin K inhibitor and a monoclonal antibody against sclerostin.[7,8]

While professional organizations have compiled recommendations for the management of osteoporosis in various populations, a consensus has yet to develop as to which is the gold standard; therefore, economic evaluations have been increasingly important to help guide decision-makers. A review of cost-effectiveness literature on the efficacy of oral bisphosphonates has shown alendronate and risedronate to be most cost-effective in women with low BMD without previous fractures.[9]

Guidelines are inconsistent as to the place in therapy of denosumab (Prolia, Amgen). In economic analyses evaluating treatment of postmenopausal women, denosumab outperformed risedronate and ibandronate; its efficacy was comparable to generic alendronate, but it cost more.[10]

With regard to older men with osteoporosis, denosumab was also found to be cost-effective when compared with bisphosphonates and teriparatide (Forteo, Lilly).[11]

READING 7 – CHALLENGES OF DIAGNOSING OSTEOPOROSIS

Choksi P (1), Jepsen KJ (2), Clines GA (1)(3). The challenges of diagnosing osteoporosis and the limitations of currently available tools. Clin Diabetes Endocrinol. 2018 May 29; 4:12.

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ABSTRACT

Dual-energy X-ray absorptiometry (DXA) was the first imaging tool widely utilized by clinicians to assess fracture risk, especially in postmenopausal women. The development of DXA nearly coincided with the availability of effective osteoporosis medications.

Although osteoporosis in adults is diagnosed based on a T-score equal to or below - 2.5 SD, most individuals who sustain fragility fractures are above this arbitrary cut-off. This incongruity poses a challenge to clinicians to identify patients who may benefit from osteoporosis treatments.

DXA scanners generate 2-dimensional images of complex 3-dimensional structures, and report bone density as the quotient of the bone mineral content divided by the bone area. An obvious pitfall of this method is that a larger bone will convey superior strength, but may in fact have the same bone density as a smaller bone. Other imaging modalities are available such as peripheral quantitative CT, but are largely research tools.

Current osteoporosis medications increase bone density and reduce fracture risk but the mechanisms of these actions vary. Anti-resorptive medications (bisphosphonates and denosumab) primarily increase endocortical bone by bolstering mineralization of endosteal resorption pits and thereby increase cortical thickness and reduce cortical porosity. Anabolic medications (teriparatide and abaloparatide) increase the periosteal and endosteal perimeters without large changes in cortical thickness resulting in a larger more structurally sound bone.

Because of the differences in the mechanisms of the various drugs, there are likely benefits of selecting a treatment based on a patient's unique bone structure and pattern of bone loss.

This review retreats to basic principles in order to advance clinical management of fragility fractures by examining how skeletal biomechanics, size, shape, and ultra-structural properties are the ultimate predictors of bone strength.

Accurate measurement of these skeletal parameters through the development of better imaging scanners is critical to advancing fracture risk assessment and informing clinicians on the best treatment strategy. With this information, a "treat to target" approach could be employed to tailor current and future therapies to each patient's unique skeletal characteristics.

READING 8 – PREVENTION AND TREATMENT OF GLUCOCORTICOID INDUCED OSTEOPOROSIS (GIOP)

Park SY(1), Gong HS(2), Kim KM(3), Kim D(4), Kim HY(5), Jeon CH(6), Ju JH(7), Lee SS(8), Park DA(9), Sung YK(10), Kim SW(11). Korean Guideline for the Prevention and Treatment of Glucocorticoid-induced Osteoporosis. J Bone Metab. 2018 Nov;25(4):195-211.

PMID: 30574464 [Free Full Text].
doi: 10.11005/jbm.2018.25.4.195.

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ABSTRACT

Background: To develop guidelines and recommendations to prevent and treat glucocorticoid (GC)-induced osteoporosis (GIOP) in Korea.

Methods: The Korean Society for Bone and Mineral Research and the Korean College of Rheumatology have developed this guideline based on Guidance for the Development of Clinical Practice Guidelines ver. 1.0 established by the National Evidence-Based Healthcare Collaborating Agency.

This guideline was developed by adapting previously published guidelines, and a systematic review and quality assessment were performed.

Results: This guideline applies to adults aged ≥19 years who are using or plan to use GCs. It does not include children and adolescents.

An initial assessment of fracture risk should be performed within 6 months of initial GC use. Fracture risk should be estimated using the fracture-risk assessment tool (FRAX) after adjustments for GC dose, history of osteoporotic fractures, and bone mineral density (BMD) results.

All patients administered with prednisolone or an equivalent medication at a dose ≥2.5 mg/day for ≥3 months are recommended to use adequate calcium and vitamin D during treatment.

Patients showing a moderate-to-high fracture risk should be treated with additional medication for osteoporosis. All patients continuing GC therapy should undergo annual BMD testing, vertebral X-ray, and fracture risk assessment using FRAX.

When treatment failure is suspected, switching to another drug should be considered.

Conclusions: This guideline is intended to guide clinicians in the prevention and treatment of GIOP.

READING 9 – UPDATE ON MANAGEMENT OF OSTEOPOROSIS OF POSTMENOPAUSAL WOMEN

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PMID: 29654947 [Free Full Text].
doi: 10.1016/j.jbspin.2018.02.009.

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ABSTRACT

OBJECTIVES: To update the 2012 recommendations on pharmacotherapy for postmenopausal osteoporosis, under the aegis of the Bone Task Force of the French Society for Rheumatology (SFR) and of the Osteoporosis Research and Information Group (GRIO), in collaboration with scientific societies (Collège national des généralistes enseignants, Collège national des gynécologues et obstétriciens français, Fédération nationale des collèges de gynécologie médicale, Groupe d'étude de la ménopause et du vieillissement hormonal, Société française de chirurgie orthopédique, Société française d'endocrinologie, and Société française de gériatrie et de gérontologie).

METHODS: Updated recommendations were developed by a task force whose members represented the medical specialties involved in the management of postmenopausal osteoporosis. The update was based on a literature review and developed using the method advocated by the French National Authority for Health (HAS).

DISCUSSION AND CONCLUSION: The updated recommendations place strong emphasis on the treatment of women with severe fractures, in whom the use of osteoporosis medications is recommended. All the available osteoporosis medications are suitable in patients with severe fractures; zoledronic acid deserves preference as the fist-line drug after a hip fracture.

In patients with or without non-severe fractures, the decision to use osteoporosis medications is based on bone mineral density values and in challenging cases, on probabilities supplied by prediction tools such as FRAX®. All osteoporosis medications are suitable; raloxifene should be reserved for patients at low risk for peripheral fractures.

The fracture risk should be re-evaluated every 2 to 3 years to decide on the best follow-up treatment. These updated recommendations discuss the selection of first-line osteoporosis medications and treatment sequences.

READING 10 – OPTIMISING SEQUENTIAL AND COMBINED ANABOLIC AND ANTIRESORPTIVE OSTEOPOROSIS THERAPY

Leder BZ (1)(2). Optimizing Sequential and Combined Anabolic and Antiresorptive Osteoporosis Therapy. JBMR Plus. 2018 Feb 27;2(2):62-68.

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doi: 10.1002/jbm4.10041.

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ABSTRACT

As osteoporosis therapy options have expanded, and clinical guidelines have begun to embrace the concept of limited treatment courses and "drug holidays," the choices that physicians must make when initiating, electing to continue, or switching therapies have become more complex.

As a result, one of the fundamental issues that must be carefully considered is whether, when, and in what sequence anabolic therapies should be utilized.

This review evaluates the current evidence supporting the optimal sequence for the use of anabolic and antiresorptive drugs and assesses the expanding number of clinical trials favouring the initial use of anabolic therapy followed by an antiresorptive agent.

This review also explores the evidence suggesting that the effectiveness of anabolic medications is diminished when used in patients that have been previously treated with specific antiresorptive drugs for prolonged periods.

Finally, the recent advances in designing combination antiresorptive/anabolic treatment approaches are detailed, with a focus on combined denosumab/teriparatide regimens, which appear to provide the most substantial and clinically relevant skeletal benefits to patients with established osteoporosis.