A COMPREHENSIVE OVERVIEW OF OSTEOPOROSIS: AN ARTICLE REVIEW

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Abstract

Background: Osteoporosis is a common bone disease defined by decreased bone mineral density and increased fragility and fracture risk. A variety of factors, both genetic and environmental, contribute to the disease, which is frequently identified after a fracture occurs, especially in the hip, spine, and wrist, posing a significant health issue. This condition is observed more frequently in females and older adults. Diagnostic procedures typically involve assessments of bone mineral density using dual-energy X-ray absorptiometry. Treatment strategies encompass both non-pharmacological approaches and pharmacological interventions, especially for women undergoing menopause. Given its extensive impact on public health, strategies for preventive measures and therapeutic management are the keys to combating this prevalent disorder.

Aim: This article serves a crucial purpose in the field of osteoporosis research. It aims to comprehensively review basic science studies on osteoporosis and its risk factors, providing a deeper understanding of this prevalent bone disease.

Methods: Our review adheres to the preferred reporting items for review. We conducted an extensive literature search in the web databases PubMed, Research Gate, Google Scholar, and Scopus, covering original publications from 2011 to 2022 in the English language.

Conclusions: Osteoporosis is a pressing public health concern, particularly as the population ages. It is characterized by decreased bone mineral density and increased fragility and fracture risk. A multitude of factors contribute to its development. Diagnosis relies on assessing bone mineral density, and management strategies involve a combination of non-pharmacological and pharmacological interventions. However, a comprehensive understanding of osteoporosis is critical to effective prevention and management.

Keywords: Osteoporosis; Osteoporosis risk factors; Bone disease; Bone mineral density

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Introduction

Osteoporosis is a progressive bone disease marked by decreased bone mineral density, deterioration of bone microarchitecture, enhanced bone fragility, and increased risk of fractures (1-4). The World Health Organization's definition highlights the presence of low bone mass and associated fracture risks (2), while the National Institutes of Health points to a reduction in bone strength and a higher likelihood of fracture risk (3). Osteoporosis is a multifaceted disease with several types and causes. This condition classifies into primary osteoporosis, which divides further into type 1 (postmenopausal) and type 2 (senile), and secondary osteoporosis, which arises due to medical conditions or the use of certain medications (5).

Pathophysiology

Osteoporosis is a metabolic bone disorder stemming from a disruption in the balance between osteoclastic bone resorption and osteoblastic bone formation, leading to fragile bones (6). Traditional views on osteoporosis concentrated on endocrine mechanisms, but current studies emphasize the importance of the interactions between the bone and the immune system, the gut microbiome, and cellular aging (6). These findings have facilitated the creation of diverse medications for osteoporosis, such as antiresorptive agents and bone promote formation medications (6). Comprehending osteoporosis's underlying pathophysiology is essential for its prevention and management.

Epidemiology

Osteoporosis is a significant global health concern, particularly among the older population, with a prevalence of 21.7% in this population (7). This prevalence is even higher in Asia, at 24.3% (7). Women experience a higher incidence of this condition, with the most pronounced rates observed in Africa (7). Osteoporosis poses a significant health concern worldwide, particularly impacting women after menopause, leading to severe hip and spine fractures (8). Further, documentation shows the considerable economic burden associated with osteoporosis-related fractures, advocating for enhanced screening and management approaches to address this global health concern (9,10). These collective findings emphasize the dynamic nature of osteoporosis epidemiology and highlight the critical need for targeted public health strategies and personalized patient care.

Risk Factors

Age

Age is a well-recognized risk factor for osteoporosis. Research demonstrates that bone mass peaks in the third decade of life and then gradually declines, significantly accelerating after menopause in women and generally occurring at a slower but consistent pace in men (11,12). The decline in bone mineral density (BMD) with age is crucial, making older individuals susceptible to osteoporosis and related fractures. For instance, studies have shown that bone density measurements in various population samples decline with age, with a noted increase in osteoporosis risk correlating with older age (13). This age-related bone loss associated with changes in hormonal levels significantly reduced estrogen levels in women post-menopause and decreased testosterone levels in older men.

Moreover, factors such as frailty, which increase with age, are significant independent risk factors for fractures, suggesting that the impact of age on bone health is multifaceted and extends beyond mere bone mineral density (14). Additionally, conditions like chronic obstructive pulmonary disease (COPD) and iron deficiency anemia are seen more commonly in older populations and have been independently associated with higher osteoporosis risks, illustrating the complex interplay of age-related health issues contributing to bone loss (15,16). Overall, while age is a significant risk factor, the development of osteoporosis is influenced by a variety of genetic, hormonal, environmental, and lifestyle factors, making it a complex disease with multiple contributing elements.

Gender

Osteoporosis is a condition that predominantly affects older adults, especially postmenopausal women (17, 18). Gender is a significant risk factor for osteoporosis; women face a higher risk of developing osteoporosis than men (19, 17). This higher risk is due to factors such as achieving a lower peak bone mass and experiencing faster bone loss in women (19). A study showed a 23.4% prevalence of primary osteoporosis in postmenopausal women based on lumbar vertebra T-scores, underscoring the high risk associated with gender-specific factors (20). Additional risk factors include age, genetic predisposition, hormonal imbalances, and various lifestyle and dietary habits (18). These findings collectively emphasize the critical impact of gender on osteoporosis risk, with notable variations across different demographics and geographical regions.

It is vital to tailor prevention and treatment plans to these gender-specific risk factors.

Race

Research highlighted that race and ethnicity do play significant roles in osteoporosis risk, with some studies identifying specific racial groups as having a higher risk compared to others. One study reviewed risk factors for osteoporosis in the Malaysian population, including race, over the decade, emphasizing the need to consider ethnic diversity in osteoporosis risk assessments (21). Similarly, another study noted that Chinese females had a higher risk of osteoporosis compared to their counterparts not using warfarin, indicating how racial differences can intersect with medical conditions to influence osteoporosis risk (22).

Moreover, studies such as "FRAX and ethnicity" and "Which fractures are most attributable to osteoporosis" discussed how clinical risk factors, including race/ethnicity, are essential in assessing osteoporosis risk and its contribution to fractures in diverse populations (23,24). Indicates a nuanced view where race not only contributes to the disease's prevalence but also affects the likelihood and severity of associated complications. This body of research underscores the complexity of osteoporosis as a multifactorial disease where race and ethnicity interplay with other demographic and clinical factors, influencing the disease's prevalence and severity. These findings advocate for personalized medical approaches that consider racial and ethnic backgrounds as part of comprehensive osteoporosis risk assessment and management strategies.

Family History

A person's family history can be crucial to determining their risk of getting the disease. Research suggests that genes determine as much as 90% of osteoporosis cases (25). For instance, a study noted that osteoporosis in close relatives, particularly mothers, is a non-preventable risk factor for the condition in postmenopausal women (26). Similarly, it found that the heritability of bone mineral density, a crucial indicator of osteoporosis, could be as high as 60%, with numerous genes implicated, indicating a substantial genetic component (27). Further research highlighted the potential of genetic markers for early diagnosis in high-risk families (28).

Additionally, specific genetic regulatory effects that influence osteoporosis risk identifying crucial genes and pathways, such as CCR5 and RIPK3, which could lead to new therapeutic strategies, have been characterized (29). The genetic foundations of osteoporosis, emphasizing the significant advances and challenges presented by genome-wide association studies, were also discussed (30). Additionally, the role of genetics in osteoporosis has examined how it has evolved, particularly concerning women's reproductive health and bone strength (31). Studies on ancient populations have also shed light on how osteoporosis has affected people historically (32). These findings collectively highlight the complex interplay between genetic predisposition and environmental factors in the development of osteoporosis. Understanding the role of genetics and family history is crucial for diagnosing osteoporosis and finding ways to treat or manage it.

Lifestyle Factors

A range of lifestyle factors identified as risk factors for osteoporosis, several studies have emphasized the impact of lifestyle behaviors, such as the consumption of alcohol, smoking habits, and the level of physical activity, alongside the critical role of a nutritious diet and the use of dietary supplements in combating the disease, has been emphasized (33, 34). The importance of addressing modifiable risk factors, including a low body mass index (BMI), a sedentary lifestyle, and inadequate calcium and vitamin D intake, has been pointed out (35). Smoking and excessive alcohol intake are consistently associated with poor bone health. Quitting smoking and moderating alcohol consumption can significantly reduce osteoporosis risk (36). Regular weight-bearing and muscle-strengthening exercises are crucial; they help improve bone density and overall musculoskeletal health, reducing the risk of osteoporosis and fractures (37). Implementing measures to prevent falls is essential, especially in older people, as falls are a significant cause of fractures in individuals with osteoporosis (38). These studies collectively call for a comprehensive strategy for preventing and treating osteoporosis that incorporates lifestyle modifications and medical interventions.

Dietary Habits

Several dietary factors potentially contribute to the risk of developing osteoporosis. Adequate calcium and vitamin D intake remains a cornerstone in preventing osteoporosis. The role of balanced diets rich in these nutrients in mitigating bone loss has been emphasized (39). Proper calcium and vitamin D intake, along with regular engagement in weight-bearing exercises, play crucial roles in preventing osteoporosis (40). The significance of a balanced diet that includes sufficient calcium, vitamin D, potassium, magnesium, vitamins K and B12, and a wide variety of fruits, vegetables, and low-fat dairy has been stressed (41,42). A specific dietary regime

rich in milk, dairy, and green tea effectively lowers osteoporosis risk among postmenopausal Korean women has been identified (43). Conversely, diets high in soft drinks, fried foods, meats, and processed items, known as the "Meat/Western" pattern, were linked to an increased osteoporosis risk (41).

BMI

Several studies have elucidated the complex role of BMI in influencing osteoporosis risk. Obesity is associated with a diminished likelihood of osteoporosis, yet it does not mitigate the risk of osteopenia (44). An inverse association between BMI and bone mineral density in Indian women found that lower BMI is a risk factor for osteoporosis (45). In addition, individuals with a low body mass index (BMI), specifically below 18.5, exhibit an increased prevalence of osteoporosis (46). Factors such as muscle strength and lean body mass are crucial in determining osteoporosis risk, where reduced levels correlate with a greater risk of the condition (47). The notion that obesity offers a protective effect against osteoporosis remains contentious, with specific research indicating that obesity might elevate fracture risk at particular bone sites (48). A study highlighted that while a lower BMI increases the risk of hip and osteoporotic fractures, a higher BMI is a protective factor against most fragility fractures but increases the risk for upper arm fractures, underscoring BMI's multifaceted relationship with fracture risk (49). These studies collectively highlight the nuanced influence of body mass on bone health, indicating both protective and risk-enhancing effects of BMI on osteoporosis.

Medical Conditions

Various medical conditions and diseases can lead to osteoporosis, such as primary hyperparathyroidism, rheumatoid arthritis, type 2 diabetes, chronic kidney disease, and hematological diseases, including multiple myeloma, systemic mastocytosis, thalassemia, and hemophilia (50, 51).

Hormonal Imbalances

Hormonal fluctuations, especially those associated with the reproductive cycle, significantly develop osteoporosis and fracture susceptibility (52). An imbalance between osteoblasts and osteoclasts activities can result in excessive bone breakdown and insufficient bone formation (53). This disruption is often due to hormonal changes, notably the reduction of estrogen and testosterone levels (54). The critical role of estrogen depletion in the onset of postmenopausal osteoporosis is further highlighted (55). At the same time, the significant impact of estrogen deficiency on bone density during menopause is also pointed out (56). Together, these studies indicate that hormonal changes and significantly decreased estrogen levels are significant risk factors for developing osteoporosis. Consequently, conducting a comprehensive hormonal evaluation is critical to understanding bone loss and is instrumental in effectively managing osteoporosis (54). Employing hormonal contraceptives that contain estrogen and undergoing hormonal treatment can act as preventive measures, enhancing bone mineral density and safeguarding against the deterioration of bone tissue (52, 57).

Medications

Osteoporosis is a multifactorial disease affected by various elements, including the use of certain medications known to cause bone deterioration and increased fracture risk, and poses a significant health issue (58, 59). Medications such as glucocorticoids, proton pump inhibitors, selective serotonin receptor inhibitors, thiazolidinediones, and anticonvulsants are among those implicated in affecting bone density (60, 61). The effects of antihypertensive drugs on bone health, noting that some may influence bone mineral density and the risk of fractures, have been pointed out (62). Furthermore, the connection between the use of antidepressants, particularly SSRIs and tricyclics, with a decrease in bone mineral density and a higher risk of fractures has been highlighted (63). Medical practitioners must recognize these risks and closely monitor patients' bone health during these treatments (59, 61). These findings underline the necessity of a comprehensive approach to osteoporosis management, which considers medication impacts alongside other risk factors.

Screening and Diagnosis

Epidemiological research on osteoporosis has highlighted significant trends and implications for diagnosis and treatment. For osteoporosis detection, Dual-energy X-ray absorptiometry (DEXA) is the benchmark, offering precise assessments of bone mineral density (BMD) and the ability to evaluate the risk of fractures (64, 65). According to the World Health Organization (WHO) criteria, a BMD 2.5 standard deviation (SD) or more below the average value for young, healthy females (T-score <−2.5 SD) indicates osteoporosis. Meanwhile, a T-score ranging from −1 to −2.5 SD signifies osteopenia. "Severe" or "established" osteoporosis refers to cases complicated by one or more fragility fractures (66). However, its broader adoption for screening has

some issues, such as the cost, the size of the machinery, and the risk associated with ionizing radiation (67). Despite these drawbacks, the DEXA scan is considered the most accurate technique for establishing an osteoporosis diagnosis after initial screenings using instruments like the osteoporosis self-assessment tool (OST) or quantitative ultrasound (QUS) devices (64, 67).

Fracture Risk Assessment

The significance of integrating bone density measurements with clinical risk indicators to enhance the forecasting of low-trauma fractures has been highlighted (68). Supporting this approach, the development of risk assessment models, including the Garvan Fracture Risk Calculator and FRAX, which offer tailored evaluation of fracture risk, has been elaborated (69). These researchers advocate for a holistic strategy considering bone health and other risk factors.

Prevention and Management

Non-Pharmacological Interventions

Non-pharmacological strategies play a crucial role in the management of osteoporosis, especially during its initial phases. Such strategies encompass lifestyle modifications like enhancing weight-bearing physical activities, securing sufficient amounts of calcium and vitamin D, minimizing alcohol and caffeine consumption, and abstaining from tobacco use (70). Furthermore, the significance of consuming adequate calcium and vitamin D, combined with sun exposure, in warding off osteoporosis has been highlighted (71). Nevertheless, it is essential to recognize that although these methods are advantageous, they might not be entirely adequate by themselves, and drug-based treatments could be required, particularly for individuals at elevated risk (72).

Pharmacological Interventions

The management of osteoporosis, especially in high-risk patients, is heavily reliant on pharmacological interventions (73). The treatment strategy is tailored according to the disease's intensity, aiming to prevent fragility fractures by combining pharmaceutical treatments, lifestyle adjustments, and nutritional supplementation (74).There exists a diverse spectrum of treatment options, including Bisphosphonates, Hormone Replacement Therapies, Selective Estrogen Receptor Modulators, Calcitonin, Denosumab, and Anabolic Medications like Teriparatide and Romosozumab (75). In addition, natural compounds, such as phytoestrogens and antioxidant agents, are also being explored as potential treatments (75). Researchers are also investigating the benefits of combining different therapies to enhance the reduction of fracture risk (76).

Conclusions

Osteoporosis is a pressing public health concern, particularly as the population ages. It is characterized by decreased bone mineral density and increased fragility and fracture risk. A multitude of factors contribute to its development. Diagnosis relies on assessing bone mineral density, and management strategies involve a combination of non-pharmacological and pharmacological interventions. However, a comprehensive understanding of osteoporosis is critical to effective prevention and management.

References

1. Knapp K. Dual energy X-ray absorptiometry: beyond bone mineral density. Imaging & Therapy Practice. 2015 Nov 1:5.
2. Hough S. The diagnosis of osteoporosis. Journal of Endocrinology, Metabolism and Diabetes in South Africa. 2012 Jan 1;17(2):67-8.
3. Shrivastava, Arvind Kumar, Alok Mukerjee, Pinaki Ranjan Gupta and Neha Srivastava. "OSTEOPOROSIS AND ITS MANAGEMENT: A TIMELY UPDATE." (2014).
4. Reid DM, Reid DM. Investigation and diagnosis. Handbook of Osteoporosis. 2011:33-47.
5. Das UN. Catechins and osteoporosis. Nutrition. 2013 Apr 1;29(4):697.
6. Föger-Samwald U, Dovjak P, Azizi-Semrad U, Kerschan-Schindl K, Pietschmann P. Osteoporosis: Pathophysiology and therapeutic options. EXCLI journal. 2020;19:1017.
7. Salari N, Ghasemi H, Mohammadi L, Behzadi MH, Rabieenia E, Shohaimi S, Mohammadi M. The global prevalence of osteoporosis in the world: a comprehensive systematic review and meta-analysis. J Orthop Surg Res. 2021;16:1-20.
8. Kehler T. Epidemiology of osteoporosis and osteoporotic fractures. Reumatizam. 2014;61(2):60-4.
9. Clynes MA, Harvey NC, Curtis EM, Fuggle NR, Dennison EM, Cooper C. The epidemiology of osteoporosis. Br Med Bull. 2020 Apr;133(1):105-17.
10. Hernlund E, Svedbom A, Ivergård M, Compston J, Cooper C, Stenmark J, McCloskey EV, Jönsson B, Kanis JA. Osteoporosis in the European Union: medical management, epidemiology and economic burden. Arch Osteoporos. 2013 Oct 11;8(1-2):136.

11. Minn Y, Suk S, Do S. Osteoporosis as an independent risk factor for silent brain infarction and white matter changes in men and women: the PRESENT project. Osteoporos Int. 2014 Jul 11;25(8):2079-2094.
12. Aluoch AO, Jessee RC, Habal H, Garcia-Rosell M, Shah R, Reed G, Carbone L. Heart Failure as a Risk Factor for Osteoporosis and Fractures. Curr Osteoporos Rep. 2012 Aug 23;10(4):258-269.
13. Hendrickx G, Boudin E, Van Hul W. A look behind the scenes: the risk and pathogenesis of primary osteoporosis. Nat Rev Rheumatol. 2015 Aug;11(8):462-474.
14. Kennedy C, Ioannidis G, Rockwood K, Thabane L, Adachi J, Kirkland S, Pickard L, Papaioannou A. A Frailty Index predicts 10-year fracture risk in adults age 25 years and older: results from the Canadian Multicentre Osteoporosis Study (CaMos). Osteoporos Int. 2014 Aug 8;25(12):2825-2832.
15. Adas-Okuma MG, Maeda SS, Gazzotti M, Roco CM, Pradella CO, Nascimento OA, Porto E, Vieira J, Jardim J, Lazaretti-Castro M. COPD as an independent risk factor for osteoporosis and fractures. Osteoporos Int. 2019 Dec 6;30(12):2489-2499.
16. Pan ML, Chen LR, Tsao HM, Chen KH. Iron Deficiency Anemia as a Risk Factor for Osteoporosis in Taiwan: A Nationwide Population-Based Study. Nutrients. 2017 Jun 1;9(6):616.
17. Akid I, Doberman DJ. Bone Health. Clinics in geriatric medicine. 2021 Aug 23;37(4):683-96.
18. Reshma H, Mohanraj KG, VishnuPriya V. Association between osteoporosis and gender, age, hypothyroidism, sex hormones among the middle-aged and old-aged population - A survey-based analysis. Int J Res Pharm Sci. 2020.
19. Alswat KA. Gender disparities in osteoporosis. Journal of clinical medicine research. 2017 May;9(5):382.
20. Hemmati E, Mirghafourvand M, Mobasseri M, Shakouri S, Mikaeli P, Farshbaf-Khalili A. Prevalence of primary osteoporosis and low bone mass in postmenopausal women and related risk factors. J Educ Health Promot. 2021;10:184.
21. Ahmad MS, Mohamed IN, Mokhtar SA, Shuid AN. Review of the risk factor of osteoporosis in the Malaysian population. RUMes. 2014;3:77-82.
22. Abdulameer Alhashimi AH, Abdulrazzaq Al-Ani HA, Talib Al-Ani IN, Syed Sulaiman SA, Hussein HH. The Differences in Predictors of Osteoporosis between Genders Using Warfarin. Circ Cardiovasc Qual Outcomes. 2016;9(Suppl 2):A256-A256.
23. Kanis JA, Oden A, Johnell O, Johansson H, De Laet C, Brown J, et al. FRAX and ethnicity. Osteoporos Int. 2020 Sep 4;31(10):1911-1919.
24. Warriner AH, Patkar NM, Curtis JR, Delzell E, Gary L, Kilgore M, Saag K. Which fractures are most attributable to osteoporosis? J Clin Epidemiol. 2011;64(1):46-53.
25. Urano T, Inoue S. Genetics of osteoporosis. Biochem Biophys Res Commun. 2014;452(2):287-93.
26. Bijelić R, Milićević S, Balaban J. The Influence of Non-preventable Risk Factors on the Development of Osteoporosis in Postmenopausal Women. Med Sci Monit. 2019;31:62-65.
27. Wu S, Liu Y-j, Zhang L, Han Y, Lin Y, Deng H. Genome-wide approaches for identifying genetic risk factors for osteoporosis. Genome Med. 2013 May;5(5):44.
28. Pouresmaeili F, Kamalidehghan B, Kamarehei M, Goh Y. A comprehensive overview on osteoporosis and its risk factors. Ther Clin Risk Manag. 2018;14:2029-2049
29. Mullin BH, Tickner J, Zhu K, Kenny J, Mullin S, Brown S, et al. Characterisation of genetic regulatory effects for osteoporosis risk variants in human osteoclasts. Genome Biol. 2020 Mar;21(1):100.
30. Richards JB, Zheng H, Spector TD. Genetics of osteoporosis from genome-wide association studies: advances and challenges. Nat Rev Genet. 2012 Aug;13(8):576-588.
31. Madimenos FC. An evolutionary and life-history perspective on osteoporosis. Annu Rev Anthropol. 2015;44:189-206.
32. Curate F. Osteoporosis and paleopathology: a review. J Anthropol Sci. 2014;92:119-46.
33. Wu A, C Johnson J, Schauer Z, A Mardon A, Wu T, A Johnson P. Risk Factors and Therapeutic Interventions for Osteoporosis. Canadian Journal of Medicine. 2021 Apr 1;3(2):99-104.
34. Tański W, Kosiorowska J, Szymańska-Chabowska A. Osteoporosis-risk factors, pharmaceutical and non-pharmaceutical treatment. European Review for Medical & Pharmacological Sciences. 2021 May 1;25(9).
35. Ahmad, M.S., Mohamed, I.N., Mokhtar, S.A., & Shuid, A.N. (2015). Review of the Risk Factor of Osteoporosis in the Malaysian Population.
36. Nawrat-Szołtysik A, Miodońska Z, Zarzeczny R, Zając-Gawlak I, Opara J, Grzesińska A, Matyja B, Polak A. Osteoporosis in Polish Older Women: Risk Factors and Osteoporotic Fractures: A Cross–Sectional Study. Int J

Environ Res Public Health. 2020 May;17(10):3725.
37. Lee K. Evidence-based management for osteoporosis. J Korean Med Assoc. 2011 Mar;54(3):294-302.
38. Griffin SC. Primary prevention of osteoporosis. Ther Adv Musculoskelet Dis. 2013 Mar;5(2):77-86.
39. Kangalgil M, Canbolat E, Çakıroğlu F. A Research on the Incidence of Risk Factors of Osteoporosis in Women. Ankara Med J. 2018;18(3):478-487.
40. Zhu K, Prince RL. Lifestyle and osteoporosis. Current osteoporosis reports. 2015 Feb;13:52-9.
41. Naldini G, Fabiani R, Chiavarini M. The Role of Diet in Osteoporotic Fracture Risk. JOURNAL OF FOOD NUTRITION AND METABOLISM. 2020;3(1):2-6.
42. Higgs J, Derbyshire E, Styles K. Nutrition and osteoporosis prevention for the orthopaedic surgeon: A wholefoods approach. EFORT open reviews. 2017 Jun 23;2(6):300-8.
43. Park SJ, Joo SE, Min H, Park JK, Kim Y, Kim SS, Ahn Y. Dietary patterns and osteoporosis risk in postmenopausal Korean women. Osong public health and research perspectives. 2012 Dec 1;3(4):199-205.
44. Andreoli A, Bazzocchi A, Celi M, Lauro D, Sorge R, Tarantino U, Guglielmi G. Relationship between body composition, body mass index and bone mineral density in a large population of normal, osteopenic and osteoporotic women. Radiol Med. 2011;116(7):1115-23.
45. Mishra AK, Gajjar K, Patel K. Association between body mass index and bone mineral density among healthy women in India. Int J Med Res Health Sci. 2016;5(4):156-60.
46. Cui R, Zhou L, Li Z, Li Q, Qi Z, Zhang J. Assessment risk of osteoporosis in Chinese people: relationship among body mass index, serum lipid profiles, blood glucose, and bone mineral density. Clin Interv Aging. 2016:887-95.
47. Rikkonen T, Sirola J, Salovaara K, Tuppurainen M, Jurvelin JS, Honkanen R, Kröger H. Muscle strength and body composition are clinical indicators of osteoporosis. Calcif Tissue Int. 2012;91:131-8.
48. Mpalaris V, Anagnostis P, Goulis DG, Iakovou I. Complex association between body weight and fracture risk in postmenopausal women. Obes Rev. 2015;16(3):225-33.
49. Johansson H, Kanis JA, Odén A, McCloskey E, Chapurlat R, Christiansen C, et al. A Meta-Analysis of the Association of Fracture Risk and Body Mass Index in Women. J Bone Miner Res. 2014;29(1):223-33.
50. Yamaguchi T. [Osteoporosis secondary to various disorders]. Clin Calcium. 2012;22(6):813-8.
51. Gaudio A, Xourafa A, Rapisarda R, Zanoli L, Signorelli SS, Castellino P. Hematological diseases and osteoporosis. International Journal of Molecular Sciences. 2020 May 16;21(10):3538.
52. Randolph Jr JF, Karvonen-Gutierrez C. Reproductive and hormonal factors and the risk for osteoporosis. InMarcus and Feldman's Osteoporosis 2021 Jan 1 (pp. 545-573). Academic Press.
53. Oleson CV, Oleson CV, Morina AB. Causes and risk factors of osteoporosis. Osteoporosis Rehabilitation: A Practical Approach. 2017:5-14.
54. Cannarella R, Barbagallo F, Condorelli RA, Aversa A, La Vignera S, Calogero AE. Osteoporosis from an endocrine perspective: the role of hormonal changes in the elderly. Journal of clinical medicine. 2019 Oct 1;8(10):1564.
55. Eastell R, O'Neill TW, Hofbauer LC, Langdahl B, Reid IR, Gold DT, Cummings SR. Postmenopausal osteoporosis. Nature reviews Disease primers. 2016 Sep 29;2(1):1-6.
56. Beadini A, Beadini S, Bexheti S, Beadini N. Menopause, hormonal changes and osteoporosis among women in region of the western Macedonia. International Journal of Biology. 2019 Jul 10;11(4):9-15.
57. Horst-Sikorska W, Wawrzyniak A. The role of hormonal therapy in osteoporosis. Endokrynologia Polska. 2011;62(II):19-22.
58. Taqui M, Swamivelmanickam M, Billah MA. Adverse drug reactions associated with drugs inducing osteoporosis. National Journal of Physiology, Pharmacy and Pharmacology. 2021;11(4):356-9.
59. Panday K, Gona A, Humphrey MB. Medication-induced osteoporosis: screening and treatment strategies. Therapeutic advances in musculoskeletal disease. 2014 Oct;6(5):185-202.
60. Byreddy DV, Bouchonville II MF, Lewiecki EM. Drug-induced osteoporosis: from Fuller Albright to aromatase inhibitors. Climacteric. 2015 Dec 18;18(sup2):39-46.
61. Nguyen KD, Bagheri B, Bagheri H. Drug-induced bone loss: a major safety concern in Europe. Expert opinion on drug safety. 2018 Oct 3;17(10):1005-14.
62. Ghosh M, Majumdar SR. Antihypertensive medications, bone mineral density, and fractures: a review of old cardiac drugs that

provides new insights into osteoporosis. Endocrine. 2014 Aug;46(3):397-405.
63. Rizzoli R, Cooper C, Reginster JY, Abrahamsen B, Adachi JD, Brandi ML, Bruyère O, Compston J, Ducy P, Ferrari S, Harvey NC. Antidepressant medications and osteoporosis. Bone. 2012 Sep 1;51(3):606-13.
64. Subramaniam S, Ima-Nirwana S, Chin KY. Performance of osteoporosis self-assessment tool (OST) in predicting osteoporosis – a review. Int J Environ Res Public Health. 2018;15(7):1445.
65. Punda M, Grazio S. Bone densitometry--the gold standard for diagnosis of osteoporosis. Reumatizam. 2014;61(2):70-4.
66. Sözen T, Özışık L, Başaran NÇ. An overview and management of osteoporosis. European journal of rheumatology. 2017 Mar;4(1):46.
67. Pisani P, Renna MD, Conversano F, Casciaro E, Muratore M, Quarta E, Casciaro S. Screening and early diagnosis of osteoporosis through X-ray and ultrasound based techniques. World J Radiol. 2013;5(11):398.
68. Baim S. Assessment of fracture risk. Rheumatic Disease Clinics. 2011 Aug 1;37(3):453-70.
69. Nguyen TV, Eisman JA. Fracture risk assessment: from population to individual. Journal of Clinical Densitometry. 2017 Jul 1;20(3):368-78.
70. Ragucci KR, Shrader SP. Osteoporosis treatment: an evidence-based approach. J Gerontol Nurs. 2011;37(7):17-22.
71. Ito M, Tanaka S. Bone disorder and nutrition. Clin Calcium. 2016;26(3):375-83.
72. Reginster J, Neuprez A, Lecart MP, Sarlet N, Distèche S, Bruyère O. Treatment of post-menopausal osteoporosis: what's new in 2014? Rev Med Liege. 2014;69(7-8):441-53.
73. Riek AE, Towler DA. The pharmacological management of osteoporosis. Mo Med. 2011;108(2):118-23.
74. Pavone V, Testa G, Giardina SM, Vescio A, Restivo DA, Sessa G. Pharmacological therapy of osteoporosis: a systematic current review of literature. Frontiers in pharmacology. 2017 Nov 7;8:803
75. Martiniakova M, Babikova M, Omelka R. Pharmacological agents and natural compounds: available treatments for osteoporosis. J Physiol Pharmacol. 2020;71(3).
76. Mitlak BH, Burr DB, Allen MR. Pharmaceutical treatments of osteoporosis. In: Basic and applied bone biology. Academic Press; 2014. p. 345-63.