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REVIEW ARTICLE

Demystifying the Risk Factors and Preventive Measures for Osteoporosis

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Abstract

Background Osteoporosis is a major health problem, globally. It is characterized by structural bone weakness leading to an increased risk of fragility fractures. These fractures commonly affect the spine, hip and wrist bones. Consequently, Osteoporosis related proximal femur and vertebral fractures represent a substantial, growing social and economic burden on healthcare systems worldwide. Indentification of the risk factors, clinical risk assessment, utilization of risk assessment tools and appropriate management that play a crucial role in reducing the burden of Osteoporosis by tackling modifiable risk factors.

Methods This chapter explores various risk factors that are associated with Osteoporosis and provides an overview of various clinical and diagnostic risk assessment tools with a particular emphasis on evidence-based strategies for their prevention.

Conclusion The role of emerging technologies such as Artificial Intelligence (AI) and perspectives such as newer diagnostic modalities, monitoring and surveillance approaches in prevention of risk factors in the pathogenesis of Osteoporosis is highlighted.

Keywords Osteoporosis · Fragility fracture · Spinal fractures · Fracture risk · Risk factors · Fracture risk assessment · Bone mineral density

Introduction

Osteoporosis (OP) is a multifactorial, metabolic bone disorder which is characterized by low bone mass, normal mineralization and abnormal bone micro-architecture with a consequent increased risk of bone fragility [1]. The World Health Organization (WHO) has defined OP as the bone mineral density (BMD) of 2.5 standard deviations (SD) below to that of patients at the time of peak bone mass (T-score) [2]. Worldwide, 200 million women are projected to get affected by OP, at a prevalence rate of 18.3 (95% CI 16.2–20.7). 1/3 females, and 1/5 male above the age of 50 are affected by OP [3, 4]. The prevalence of OP is higher in low–middle-income countries (LMIC) than in the high-income (HIC) countries. The clinical risk of OP is the development of fragility fractures (FF), which occur following a minor fall like falling from a standing height or even lesser. The International Osteoporosis Foundation (IOF) and National Institute of Health and Clinical Excellence (NICE) guidelines report fragility fractures being predominantly seen in the spine, proximal femur, and distal radius [5]. Though vertebral fractures are the most prevalent osteoporotic fractures, hip fractures necessitate hospitalization for surgical stabilization; both are associated with increased morbidity, and mortality [6]. The OP and associated FF are known to reduce health-related quality of life (HRQoL) to varying degrees in the population [7]. With increasing life expectancy and

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disparity in global health provision, OP-related fractures are a cause of concern due to their burden socially and economically [8, 9]. Consequently, it is crucial to identify patients at risk for OP and adopt strategies both to prevent FF in people at risk, and to prevent further fractures in patients identified with one or more FF. Bone mineral density (BMD) measurement by dual-energy X-ray absorptiometry (DXA) scans is currently used to diagnose OP, as per WHO guidelines. However, several risk assessment tools (RATs) are available to predict the probability of fracture risk, and consequently aid decision making algorithms to treat patients [10–13].

This chapter is focussed on the commonly associated Clinical Risk Factors (CRF) for the development of OP, role of RATs for evaluating the probability of FF risk in patients with suspected OP and prevention approaches that can be adopted to mitigate risks of OP. Future perspectives and role of emerging technologies is highlighted.

Risk Factors for the Development of Osteoporosis

Historically, OP is classified as primary and secondary types. Primary OP is linked with normal aging and decreased oestrogen levels, whereas secondary OP is associated with other factors like Type I diabetes mellitus, rheumatoid arthritis, cardiovascular disease, gastrointestinal disease and some malignancies [14]. These risk factors in the development of Osteoporosis are broadly classified as non-modifiable and modifiable one (Table 1).

Non-modifiable Risk Factors

These factors include those associated with genetic, race, gender, age, height, family history, and pregnancy and lactation status of a person.

Table 1 Non-modifiable and modifiable risk factors for osteoporosis

Non-modifiable risk factors	Modifiable risk factors
Genetics	Physical inactivity
Ethnicity	Caffeine intake
Gender	Cigarette smoking
Age	Excess alcohol intake
Sex	Nutritional deficiencies
Height, Weight, and Obesity	Hormones
Previous fragility fractures	Medications
Family history of osteoporosis	Medical diseases
Pregnancy and Lactation	Underweight

Genetic Factors

The presence of FF in a first-degree relative of an osteoporotic patient is a strong indicator that genetic factors may contribute to the development of OP. It is well-established that both the peak bone mass and the ensuing bone loss are genetically predetermined. According to twin studies, the heritability of BMD ranges from 50% to 85%, with the axial skeleton showing the highest impact [15]. Despite being a polygenic condition with genetic, hormonal, metabolic and environmental risk factors, linked genes associated with OP are still mostly unknown. Multiple altered signalling pathways such as oestrogen pathway, osteocyte-derived sclerostin signalling and Wnt/β-catenin have been identified. Dys-regulation of these may be responsible for decrease in bone mass [16].

A heritable component which can contribute for risk of osteoporotic fracture includes geometry of femoral neck and hip axis length, ultrasound properties of bone, biochemical markers of bone turnover, body mass index (BMI), muscle strength, age at menarche and at menopause [17].

Ethnic Factors

There are variations in the occurrence of FF by ethnicity and race. Caucasians have the lowest bone mass amongst all races. A recent meta-analysis suggests that non-white persons are less likely to fracture than white people in age-adjusted hip fractures. Incidence rates are higher among Scandinavian residents [18]. High BMD and slower bone thinning rates are also common in Afro-American women [19]. There is a higher incidence of decreased bone mass, and significantly lower BMD in Indian women aged 40–60 years as compared to Western and other Asian counterparts [20].

Gender

Bone loss commences earlier in women as compared with men. Women are 2–4 times more likely than men to sustain hip and spine fractures due to osteoporosis. Such lower fracture incidence in men is due to differences in lean body mass percentage, bone size, width, and geometry, as well as men having protective effects of testosterone. Despite these differences the osteoporosis-related complications are seen more in men [4].

Age

Osteoporosis is one of many diseases for which ageing is a significant risk factor. Elderly people's quality of life is significantly impacted by osteoporotic fractures. It has been demonstrated that genetically driven bone loss starts to occur

around the age of 30 and occurs at a rate of between 0.5% and 1% every year [21].

Sex

Women experience this bone loss more than men do. The rate of loss in bone strength with subsequent osteoporosis and fractures in women continues to rise with the start of menopause following reduction in oestrogen release from ovaries. Oestrogen is crucial for skeletal homeostasis and regulates bone remodelling [22]. Another significant risk factor for osteoporosis is early menopause, i.e., before the age of 45 years.

Men's BMD is maintained in large part by testosterone. After the age of 60, men's testosterone levels also start to fall at the rate of 1% every year, which in turn causes a steady increase in fracture risk [23]. In American females (between 40 and 60 years), positive correlation between lumbar BMD and testosterone levels has been found.

With each additional decade of age after 60 years, the risk rises more in both genders. At 65 years, the risk ratio is increased by 2.94 in men and by 2.88 in women [24].

Height, Weight and Obesity

Being tall and obese with OP predisposes to an increased fracture risk. The Global Longitudinal Study of OP in women found an association between weight, Body Mass Index (BMI), and height and incidental clinical fracture. Taller females are at increased fracture risk, especially hip fractures, than the male counterparts [25].

Body weight and BMI are important determinants affecting BMD. A high BMI may increase the fracture risk regardless of gender. In addition, osteopenia and OP are more common in postmenopausal females with low BMI. The risk for future fractures is most marked for lean individuals especially post-menopausal females with a BMI of < 20 kg/m^2. The risk rises nearly twofold for individuals with a BMI of 25 kg/m^2 vs 20 kg/m^2 [26]. Overall, obesity increases the risk of fractures in women after menopause [27].

Previous Fragility Fractures

The likelihood of suffering another fracture independent of BMD, increases when one has a significant past history of a FF. This is perhaps, individual who have already suffered a fracture are more likely to fall due to medications and get more fractures than those who do not have. The pre-existing risk factors also contribute to future fracture risk. The study conducted using a Swedish database showed an increased incidence of subsequent fractures within 12 months with 7.1%, increasing to 12.0% at 24 months. The study also observed the highest risk of subsequent fractures following a clinical vertebral fracture [28]. The greatest increase in risk was for subsequent fractures seen in the axial skeleton, with a 12.6-fold increase in vertebral fractures and a 2.3-fold increase in hip fractures [29].

Family History of Osteoporosis

According to recent studies, having a parent with osteoporosis, especially mothers, adversely affects sibling bone density and greatly raises the risk of fractures. The latter occurs irrespective of bone density measurements [30].

Pregnancy and Lactation

A loss in bone mass of up to 5% is estimated to occur during pregnancy and lactation. The lactation increases the chances of OP due to secretion of calcium from the milk, bed rest, medications, etc. Although it can happen at any point during pregnancy, vertebral fractures typically develop during the first pregnancy. Fractures during pregnancy and lactation typically have more levels than postmenopausal osteoporotic fractures [31].

Modifiable Risk Factors for Osteoporosis

The most significant modifiable risk factors for OP are low body weight, low BMI, excessive coffee intake, physical inactivity, uncontrolled weight loss, and daily high alcohol consumption [32]. When several of these risk factors are present in combination, the bone loss and fragility is higher than when only one risk factor is present.

Physical Inactivity

Physical inactivity is a vital risk factor for OP. Lack of activity and a sedentary lifestyle promote bone mass loss. Increasing physical activity at any stage of life has a good impact on bone health. Bones-related doles of physical activity continue from adolescence to adulthood and from adulthood to middle age and so forth. Regular exercise, such as weight-bearing endurance exercises three to five times per week, enhanced BMD as well as bone size and strength, which reduced the incidence of FF [33]. It has been shown that exercise benefits by decreasing bone resorption biomarkers, such as amino-terminal cross-linked Telopeptide of type 1 collagen [34].

After immobilisation, bone loss always outpaces recovery at whatever age. The recovery of bone mass occurs over an almost years following a few weeks or months of immobilization. Conditions like neurologic injuries to the spine and cerebrovascular accidents, paraplegia from any cause, cast immobilisation of the extremities after a fracture,

etc. can all result in rapid bone loss after immobilisation. A sizable portion of patients with distal radius fractures develop hand osteopenia at 6 weeks after conservative or operative treatment [35, 36].

Caffeine Intake

It is debated that caffeine is a risk factor for Osteoporosis. Cortical bone loss is predisposed by high caffeine, as it promotes urine and faecal calcium loss. The effect may be more people who drink coffee without milk. The effect of caffeine on bone loss may be genetically determined [37, 38].

Cigarette Smoking

According to meta-analyses, [39, 40] cigarette smoking (CS) and active smoking are associated with a lower BMD and hence higher fracture risk. Women who smoke had a 13% higher lifetime risk than men (32% higher) of experiencing a vertebral fracture. According to estimates, smoking increases men's and women's lifetime fracture risk at the hip by 31% and 40%, respectively. Long-term smoking imbalance of bone turnover reduces bone mass, bone length and impairs muscular function. CS affects bone metabolism indirectly through change in weight, hormones (inhibit vitamin D-parathyroid hormone axis and oestrogen secretion) and oxidative stress levels. It also induces Osteoporosis through direct action on bone by affecting the RANKL–RANK–OPG and other signalling pathways [41].

Excess Alcohol Intake

Excessive alcohol use has negative effects on bone health, increased risk of FF and bone healing. It is dependent on the amount of intake. The use of chronic alcohol intake and subsequent poor bone health is due to lower calcium absorption, malnutrition, liver damage and low oestrogen levels. Drinking more than three standard drinks a day has been reported to increase the risk of fracture and four drinks a day increased the risk of fracture. However, the role of alcohol at lower doses is unclear as light drinkers have even higher lumbar and femur neck BMD than abstainers do [42]. An alcohol drink of about 0–22 g/d is related to a lower risk of osteoporotic and hip fractures as modest level of intake increases the oestradiol concentration and, therefore, with higher bone density. According to the NOREPOS study the risk of hip fracture is high among men under 60 who consume alcohol frequently and heavier than other group age and gender [43, 44].

Nutritional Deficiencies

Various minerals (calcium, phosphorus), vitamins (D, C, K, B12), proteins and essential fatty acids maintain bone health. The deficiency of any of these has detrimental effects on bones. Vitamin D is essential for bone homeostasis by bone growth and remodelling and also promotes the calcium absorption from the gut. Deficiency of Vitamin D accelerates bone turnover, bone loss, and osteoporotic fractures [45]. In addition, a key mediator in bone metabolism, vitamin C deficiency can also result in pathological fractures, osteolysis, and bone loss. The incidence of hip fracture, OP, and BMD loss is negatively correlated with dietary vitamin C oriented food, according to a recent meta-analysis [46, 47].

Vitamin K is crucial for bone health, because it participates in the carboxylation of numerous proteins connected to bones, controls the genetic transcription of osteoblastic signals, and bone reabsorption. Any deficiency brought on by a poor diet or by taking oral anticoagulants such as Vitamin K antagonists is associated with an increased fracture risk and a reduced BMD [48].

Low B-vitamin concentration (Vitamin B12 and B6) may also be responsible for decreased bone density. High homocysteine levels, which some studies have found to be strongly and independently connected with an increased fracture risk in older women and men [49, 50].

Hormones

Hormonal abnormality can be risk factors for Osteoporosis directly or through other risk factors influenced by them. For women, an early menopause and for men insufficient testosterone due to hypogonadism can lead to Osteoporosis. Low serum oestradiol, insulin like growth factor, dehydroepiandrosterone, and high PTH, cortisol follicular stimulating hormones (FSH) are attributed to an increased fracture risk in the elderly and postmenopausal women [51].

Medications

Glucocorticoid (GCs) over usage results in OP. There is a dose-dependent association between chronic glucocorticoid usage and fracture risk, with high dosages (prednisolone 7.5 mg/day or more) having the highest risk. Steroids cause bone demineralization, which affects the bone's spatial heterogeneities significantly at the microscale and raises the possibility of fracture. Excessive GCs harm bone cells, including osteoblasts, osteoclasts, and osteocytes, at the cellular level, impairing bone resorption and production [52]. At the molecular level, it blocks the generation of Wnt protein, increases PPAR-2 production, overexpression of Dickkopf-1 (DKK1), and disrupts the BMP pathway, causing

development towards adipocytes rather than osteoblasts [53]. Other medications related to risk of secondary OP include proton pump inhibitors (PPI), anticonvulsants, selective serotonin receptor inhibitors, chemotherapeutic agents, aromatase inhibitors, medroxyprogesterone acetate etc.

Medical Disease

Several medical diseases such as rheumatoid arthritis (RA), diabetes, ankylosing spondylitis, inflammatory bowel diseases, renal disease, mal-absorption syndrome, tuberculosis (TB), thyroid disorders, hypogonadism etc. can cause OP. Patients with rheumatoid arthritis, in particular, have disease-specific risk factors for OP, such as persistent exposure to chronic systemic inflammation and pathologic autoantibodies. Smoking, a lack of calcium and vitamin D, hypogonadism, and long-term glucocorticoid exposure are additional risk factors [54]. The OP and osteoporotic fractures, especially hip fractures, are independently linked to Tuberculosis (TB) incidence. According to a study, compared to matched controls, patients with TB had an OP incidence of 6.1 cases per 1000 person-years [55].

Underweight

Being severely underweight (< 16.50 kg/m^2) increases the risk factor for developing vertebral fractures. Both increased height and weight loss beyond f 50 years in women predispose them to hip fractures, while weight gain lowers it. Furthermore, in older white men, the risk of hip fracture increases with weight loss (10% or more) starting at age 50, while weight gain (10% or more) reduces that risk [56].

The BMD is impacted by attempts to lose weight by surgical procedures, exercise, or caloric restriction-induced weight loss. In various studies, it has been found that dietary inadequacies, such as poor calcium absorption, cause the BMD to decline dramatically over time after bariatric surgery [57, 58].

Risk Assessment Tools (RAT)

The Need of RAT

Though there are several treatments available for OP, BMD measurement with DXA imaging does not capture Clinical Risk Factors (CRF) or non-skeletal factors of FF risk. A number of CRF can contribute to the increased FF risk above and beyond that provided by the BMD. The combination of CRF and BMD provide higher diagnostic accuracy than either alone in managing patients at risk of OP [59]. To predict fracture incidence over a period of time, several RATs have been developed [11, 12]. These help in decision making, evaluating the probability of FF risk in patients with suspected OP and initiating preventative measures. In certain situations, frailty may pose a challenge in the diagnosis and management. In such a scenario a clinical decision along with the use of clinical prediction tools are helpful in directing the appropriate treatment of OP [60].

The RAT can also help better categorise individuals into low, medium and high-risk groups. This in turn can focus management strategies in the form of either initiating monitoring or commencement of targeted treatment.

Risk Assessment Tools (RAT)

The commonly used RATs are highlighted in Table 2.

Clinical Risk Factors (CRF) Variables

The CRF used in the FRAX® algorithm are: age, sex, height, weight, previous and parenteral hip fractures, glucocorticoids use, current smoking, alcohol intake

Table 2 Commonly used risk assessment tools for evaluating the probability of fragility fracture risk in patients with suspected osteoporosis [12]

Risk assessment tools	Integration	Use in clinical practice
FRAX® risk assessment tool	Integrates CRF With or without BMD as required	Calculates the 10-year probability of a major osteoporotic fracture
QFracture® risk assessment score	Integrates various CRF History of falls History of hip fracture in the parents Hormone replacement therapy in women No provision is made for BMD	Provides a risk prediction algorithm
The Garvan tool	History of falls Number of previous FF Does not include all FRAX® CRF variables	
Trabecular bone score (TBS)	Measures bone microarchitecture	TBS provides microarchitectural information
Dual-energy X-ray absorptiometry (DXA) bone mineral density (BMD)	BMD at the femoral neck provides the reference site Bone microarchitecture is not assessed	Gold standard in OP diagnosis

(≥ 3units/day), RA, and secondary OP. The additional CRF are: history of falls, hormone replacement therapy (HRT).

FRAX® Risk Assessment Tool

The FRAX® tool was developed in 2008 by the University of Sheffield (UK). It is a fracture risk calculator for estimating an individual's 10-year probability of developing a major osteoporotic fracture [61]. The FRAX® tool algorithm integrates CRF (with or without femoral neck BMD) for its calculation. It is applicable to people middle aged and older people (40–90 years) and is particularly useful in situations, such as:

- Men (> 50 years), with or without fracture, but with a BMI < 19 kg/m^2 or a WHO risk factor.
- Postmenopausal women with a WHO risk factor or a BMI < 19 kg/m, but without a fracture.

With its universal availability and validation in over more than 11 prospective population-based cohorts, it supports Clinicians' judgment in the decision-making process to initiate treatment of monitor patients [62].

QFracture® Risk Assessment Score

The QFracture tool developed in 2009 after large primary populations-based studies in the UK. It is a validated tool to estimate an individual's 10-year risk of developing a major osteoporotic fracture, without measuring the BMD. It integrates various CRF used in the FRAX® tool but also uses additional CRF, such as history of falls, history of hip fracture in the parents, and HRT in women [63].

The Garvan Tool

The Garvan tool was developed by the Garvan Institute of Medical Research differs from the FRAX® tool in that it does include history of falls and number of previous FF reporting the risk of a larger number of fracture sites, such as distal femur, tibia and hands and feet [64].

Trabecular Bone Score (TBS)

The TBS measures bone microarchitecture and provides complementary skeletal information. Thus, it is a useful clinical adjunct to improve patient OP management [65].

Dual-Energy X-Ray Absorptiometry (DXA)

DXA is the most commonly used investigation in the diagnosis of OP, It measures the BMD; and the WHO has defined OP as a BMD of 2.5 SD below that of healthy individuals of the same sex at their peak bone mass and is measured as T-score. The Z-score on the other hand allows comparison with the bone density of people of the same age and sex as the patient. A negative Z-score of 2.5 SD below should raise concerns about secondary causes of OP. Severe OP (established OP) means OP in the presence of one or more FF.

Prevention Strategies—to Decrease the Risk due to Osteoporosis and Fragility fractures

The OP is a major and growing public health problem and organisations across the world have suggested preventative strategies to reduce the risk of OP and associated FF [66–68]. Preventative strategies for the OP are broadly classified as:

Primary Prevention

Primary prevention refers to resourceful identification, e.g., during routine hospital visits of patients (postmenopausal women) for some other clinical reason, who are at risk of osteoporotic FF and who could benefit from drug treatment [69].

Secondary Prevention

Secondary prevention refers to treatments for secondary prevention of FF in postmenopausal women who have established OP and who have sustained a clinically apparent osteoporotic FF [70].

General Strategies to Reduce Risk due to Osteoporosis and Fragility Fractures

i. *Assessment of CRF*: the application of BMD measurement in the diagnosis of Osteoporosis can be enhanced by concomitant assessment of CRF (Table 3) to initiate interventions and preventative measures.
ii. Lifestyle measures

- Recommendation of a healthy, nutrient well-balanced diet
- Avoidance of smoking
- Moderation of alcohol consumption (to ≤ 2–3 units/day)
- Adequate sunlight exposure
- Regular weight-bearing and muscle strengthening exercises
- Falls prevention regime or programmes.
- Frailty assessment and management.

Table 3 Clinical risk factors (CRF) for osteoporosis and fragility fractures

Skeletal	Extra-skeletal risk factors including secondary causes of osteoporosis	
Low BMI (≤ 18.5–19 kg/m^2) (BMI)	General	Increasing age Female gender Early menopause Caucasians race Dementia Poor coordination/risk of falls
Reduced bone mineral density (BMD)	Social	Smoking Excessive alcohol intake Recreational drug overuse
Reduced bone turnover	Diet and nutrition	Low protein intake Low calcium intake Vitamin D deficiency
Previous fragility fractures (spine, hip, wrist)	Medications	Recent glucocorticoid treatment (during 3 months or more) Anticonvulsant or antidepressant use
Prolonged immobility	Hormone	Untreated hypogonadism in men and women Endocrine disorders
Parental history of hip fractures	Others	Metabolic disorders, e.g., Diabetes mellitus (especially Type I) Rheumatoid arthritis and Inflammatory arthropathies Malignancy Organ transplantation Chronic kidney/lung/liver disease

iii. *Prevention services*: fracture liaison service
- Access and provision of multidisciplinary, coordinator-based Fracture Liaison Service (FLS).

iv. *Blood tests*: appropriate blood tests to evaluate bone health and rule out risks due to secondary causes of OP.

Specific Measures and Interventions to Reduce the Risk due to OP and FF

i. *Use of RATs*: proactive steps to use a fracture risk assessment tool such as FRAX® tool in people with a CRF for FF (Table 2).
ii. *BMD* evaluation in people with intermediate and high fracture risk by FRAX® to detect 10-year probability of fragility risk factors, baseline and medication choice.
iii. *Investigation of OP and FF*: diagnostic assessment of patients with diseases mimicking OP.
iv. *Pharmacological treatment options*: these are broadly classified as below following Fracture risk assessment, patient suitability, availability, cost and guideline recommendations in combination with calcium and/or vitamin D supplementation as an adjunct.

- Antiresorptive drug treatment:
  - Bisphosphonates: (a) Oral (alendronate, risedronate, ibandronate) or (b) Intravenous (zoledronate, ibandronate) as the first line agents.
  - Alternative options include denosumab, HRT, raloxifene and strontium ranelate.

- Anabolic drug treatment: teriparatide (a PTH derivative)

xxii. The National Osteoporosis Guideline Group (NOGG) in association with various sister organisations have proposed revised guidelines for the assessment and management of OP and the prevention of FF. The following specific updates including the new concept of 'very high fracture risk' is proposed [66, 71]:

- Focus on the detection of vertebral fractures
- Consideration for the use of parenteral anti-OP therapy (e.g., Zoledronic acid)
- Use of anabolic agents
- Urgent treatment of patients with FF to reduce refracture risk and to follow these closely for checking the tolerance and adherence
- Concerns regarding cessation of denosumab
- Intervention thresholds for cases who are too frail to undergo BMD scanning [64, 69].

Newer Technologies to Detect and Quantify Risk of Osteoporosis

With significant advances made in the treatment modalities for OP, the focus has shifted to the development of more specific technologies and RATs [12, 13].

The purpose of RAT is to evaluate the probability of FF risk in patients with suspected OP. The diagnosis of OP currently depends on the quantitative assessment of BMD by DXA [72]. However, BMD analysis with DXA has its own limitations. It is unable to measure bone the quality of bone (i.e., trabecular microarchitecture) and this has led to further research in complementary technologies to improve diagnostic accuracy and target early treatment in patients with suspected OP [73]. These include DXA-based Trabecular Bone Score (TBS), Spectral Detector CT, a 3-D volumetric assessment of BMD with QCT, MRI of bone microarchitecture and Quantitative ultrasound (QUS) assessment of bone [74–76].

Newer Interventions

Osteoporosis has been treated using calcium, vitamin D, and other medications (e.g., bisphosphonates, teriparatide, denosumab etc.) based on a variety of factors. Recently, the USFDA approved the use of a monoclonal anti-sclerostin antibody which is both bone-forming and antiresorptive (Romosozumab) for the treatment of patients with multiple FF, patients with high fracture risk, and those who cannot tolerate or have not responded to conventional OP treatments. Although it is a good alternative for the patients mentioned earlier, people with a recent history of myocardial infarction or stroke should use it with caution [77, 78].

Novel Diagnostics

Despite bone densitometry (DXA) being the gold standard, quantitative computed tomography (QCT) scans are becoming increasingly frequently used because of their sensitivity in providing a more precise evaluation of bone density. In addition, quantitative ultrasonography QUS might be utilised as a screening device for Osteoporosis [79, 80].

Monitoring Response to Treatment

After a year or two of starting OP medication, DXA is used to assess BMD to track the treatment's effectiveness. It has to be noted that patients who are adherent to antiresorptive medications the frequent need of monitoring with DXA is not required. Blood or urine tests such as procollagen type 1 N-terminal pro-peptide, and C-terminal collagen telopeptide (CTX) might be used for monitoring [81].

Gene Therapy

It is possible for adults with severe idiopathic OP to have 10% of harmful WNT1 mutations. As the OP has a genetic connection in its pathogenesis and genetic factors influence the response to the OP treatment the role of gene therapy has been explored. Recently, Adeno-Associated Virus (AAV)-mediated gene therapy has been proposed as a cure for OP. In addition, it has been reported that the VDR gene may be used in personalised OP medication [82–84].

Newer Technologies in the Role of Detection and Prevention of Osteoporosis

Applications based on artificial intelligence (AI) models can offer practical answers at every point of managing OP, including prognosis assessment, therapeutic management, diagnostic evaluation, and screening. Extreme gradient boosting (XGBoost) model to identify early OP risk has been created using bioinformatics and machine learning. It enhances elderly men's and women's DXA OP categorization identification [85, 86]. In post-operative follow-ups, mechatronic learning has also been utilised to identify new vertebral fractures following vertebroplasty [87].

Conclusion

Osteoporosis is influenced by several risk factors, which may be non-modifiable or modifiable. Identification of risk factors is important for an early diagnosis and prevention. Various risk assessment tools are now available which are proving to be reliable. Prevention strategies are crucial in diminishing the risks due to Osteoporosis and Fragility fractures. These strategies include identifying the clinical risk factors and implementing effective measures and interventions. Several newer technologies have come to foray for detection, treatment, and monitoring of Osteoporosis. Gene therapy and the use of Artificial Intelligence seems promising for Osteoporosis prevention and management in the near future.

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Declarations

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Informed Consent For this type of study, informed consent is not required.

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