



## Assessment of the importance of physical activity and quality of life for patients diagnosed with osteoporosis during the COVID-19 pandemic

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### Abstract

**Introduction.** Osteoporosis is one of the most important ten diseases worldwide, still causing extreme suffering to patients and huge costs to the health system. The rapid increase of the population's aging was involved in many aspects of human health, and, among these ones, osteoporosis was one of the main public health issues.

**The aim** of the study was to assess the importance of physical activity and the quality of life in patients diagnosed with osteoporosis during the COVID-19 pandemic.

**Material and methods.** The study is longitudinal, it was conducted in an outpatient setting for a period of 1 year and it included 20 patients diagnosed with osteoporosis. The demographic variables (age, living environment, body mass index) were assessed, and as parameters: pain (VAS scale), fracture risk (FRAX score), quality of life (Qualeffo-41 questionnaire), bone mineral density at the spine and at the femur (DEXA). The patients received pharmacological treatment such as bisphosphonates and underwent physiotherapy for pains: low frequency currents (TENS), ultrasound and physical therapy.

**Results and discussions.** In all the studied cases, it was considered that the pain decreased following the use of the medicinal and physiotherapeutic treatment. This is an expected result given that other studies have shown this. Postmenopausal women in Romania with osteoporosis have a lower HRQoL than healthy controls, measured with the SF-36 instrument and the total QUALEFFO-41 score.

**Conclusions.** The obtained data point out the correlation between bone mineral density, fracture risks and exercises in patients diagnosed with osteoporosis. The FRAX score is useful to identify patients who need the combination of drug therapy and exercises to prevent vertebral and non-vertebral fractures in the next 10 years.

**Keywords:** *osteoporosis, physical activity, quality of life, COVID-19,*

### INTRODUCTION

Osteoporosis is one of the most important ten diseases worldwide, still causing extreme suffering to patients and huge costs to the health system [1]. The rapid increase of the population's aging was involved in many aspects of human health, and, among these ones, osteoporosis was one of the main public health issues [2]. Osteoporosis is a disease of the skeleton characterized by low bone mass or by diminished bone mineral density, by damage to the bones' micro-architecture and by increased fracture risks [3]. In this disease, the bones become so fragile that a simple fall or even common movements, such as bending or coughing, can cause a fracture [4]. In general, the incidence of osteoporosis is higher in women than in

men, with a male / female ratio of 1: 4 [5]. Different risk factors for the development of osteoporosis can be classified into unchangeable (female gender, old age, dementia, personal history of fracture, family background of fracture in a first degree relative) and potentially changeable risk factors: smoking [6], early menopause, low calcium intake, vitamin D deficiency and sedentary lifestyle [2].

The normal development of the bones depends on the percentage of calcium (having in view that 99% of the total calcium is found in the skeleton) [7] and magnesium (60% is found in the bones) [8], and it is necessary to know the intervals of normal reference for these ions.

Several diseases are associated with an increased risk of generalized osteoporosis in adults: hypogonadal conditions, endocrine disorders, nutritional and gastrointestinal disorders, hematological disorders, selected inherited disorders, certain drugs, immobilization and pregnancy [5]. The assessment of the bone density is usually made on women over the age of 50, it is quick and painless, and it can predict whether or not there will be bone issues. In addition, the doctor can prescribe an appropriate treatment based on the test results or can recommend a change of lifestyle.

There are several methods to measure the bone density: osteosonography, Dual-X-Ray-Absorptiometry osteodensitometry, QCT - quantitative tomography of the spine, pQCT - peripheral computed tomography or HRpQCT - high resolution peripheral computed tomography [9].

In Romania, only the first two methods are used to determine the bone density. In the National Program of Endocrine Diseases, in patients with osteoporosis, only the results of the DEXA diagnosis obtained after scanning the spine from L1 to L4 are used to validate the application of the program [10].

DEXA scanning is a widely accepted radiological instrument that can detect osteoporotic bone changes earlier and with greater accuracy than simple X-rays of the bone system. The DEXA radiological system is a device that uses two X-ray beams, each with a different energy level to determine their attenuation, namely by reducing the intensity of the X-ray beam as it passes through the patient's body. The use of two different X-ray energies enables the radiological installation to record different attenuation profiles. Attenuation is largely determined by the density and thickness of the tissue. For the low energy beam, the attenuation is higher in the bone than in the soft tissue. In the case of the high energy beam, the bone attenuation is similar to the one of the soft tissue. By using two different energies, two equations are created, the solution of which is the two unknown: the density of the bone and the one of the surrounding soft tissue [11]. Measuring bone density means estimating the total amount of the bone substance present in a given volume. The method called dual energy X-ray absorption (DEXA) actually measures the density of an area (g / cm<sup>2</sup>). Some indicators are used in measuring density by this method such as [1]:

The T-score: it is obtained when the bone mineral density is compared with the normal value (considered at the age of 30).

The Z-score: it is obtained by relating to normal values for the same age and sex

In the current practice, the T-score is the most used indicator [12]. If its value is less than -2.5, the diagnosis is osteoporosis. Osteopenia is characterized by a T-score value between -2.5 and -1.0 [13].

The WHO classification, according to the Z-score, is used in perimenopausal and postmenopausal women, but not in healthy premenopausal women, because the relationship between BMD and fracture risk is not well established in this category. The Z-score is used for clinical diagnosis in premenopausal women if they have fragility fractures or if low bone mineral density (determined by DXA) is associated with risk fracture factors. These risk fracture factors are: age, smoking, low body mass index (BMI), low calcium intake, vitamin D deficiency, sedentary lifestyle, early estrogen decrease, dementia, alcoholism, low visual acuity, history of falls, low bone mineral density. In order to improve health and to avoid complications caused by osteoporosis, medicine must find effective and accepted solutions to increase bone and muscle anabolism [14]. After a certain age, a lifestyle should be established to help improving the health and it should include the increase of the physical activity, quitting smoking, reducing alcohol consumption, reducing the risk of falling and providing an adequate diet, calcium and vitamin D [15,16].

Thus, physical exercise has been recommended by the WHO as physical therapy for the prevention and treatment of non-drug osteoporosis [16,17]. Exercises can prevent osteoporosis in the elderly as a preventive strategy without medication.

The interaction of mechanical loading, of hormones (estrogen, testosterone) or of cytokines, but also signaling pathways induced by effort, increase the bone remodeling and reduce the bone resorption [18]. The disorder of bone angiogenesis is associated with many bone diseases, including osteoporosis, whereas exercise improves bone angiogenesis by regulating key angiogenic mediators [2]. Throughout life, the bones are reshaped, which means that they are continuously resorbed by osteoclasts and replaced with new bones produced by osteoblasts. This process enables keeping mechanical strength and repairs.

The lack of balance in the remodeling activity where the resorption exceeds the formation can lead to physiopathological changes noted in osteoporosis [18]. Progress has been made in bone molecular biology and a protease called cathepsin K (CatK) has been identified, secreted by osteoclasts in the process of the bone resorption, resulting in the bone matrix degradation and the decomposition of the mineral components of the bone tissue. The parathyroid hormone also intervenes in the bone formation, by indirectly increasing the proliferation of osteoblasts and by regulating calcium homeostasis [19].

In the case of fractures, action is taken to control pain, for the early mobilization, to limit disability, to restore functions and to prevent further fractures.

There are several treatment options that include conventional analgesia, osteoporosis pain relievers, minimally invasive procedures, electrotherapy

modalities, external support devices and exercises [20]. In the case of physical exercises done by patients with osteoporosis, without the control of a specialist, it was found that there is insufficient cooperation between physiotherapists and specialists involved in the treatment, not being able to provide a constant follow-up of their frequency and correctness [21,22]. Ultrasound therapy is a commonly used way to treat pain syndrome in osteoporosis. However, its effects on osteoporosis are unclear, but therapeutic ultrasound will help reduce bone-related pains, it will improve exercise capacity, and it will reduce the risk of osteoporosis [23].

**The aim** of the study was to assess the importance of physical activity and the quality of life in patients diagnosed with osteoporosis during the COVID-19 pandemic.

**Material and methods**

The study is longitudinal, it was conducted in an outpatient setting for a period of 1 year and it included 20 patients diagnosed with osteoporosis.

Inclusion criteria:

- Patients with a definite diagnosis of osteoporosis
- Age > 50 years
- Postmenopausal women
- Patients without decompensated chronic conditions

Exclusion criteria

- Patients < 50 years of age
- Non-cooperating patients
- Patients who did not want to participate in the study
- Patients with severe conditions contraindicating physiokinotherapy (heart failure, atrial fibrillation, myocardial infarction, stage II-III hypertension)

The assessment of the patients was done at the beginning of the physiotherapy treatment period, at the end and after 1 year. The demographic variables (age, living environment, body mass index) were assessed, and as parameters: pain (VAS scale), fracture risk (FRAX score), quality of life (Qualeffo-41 questionnaire), bone mineral density at the spine and at the femur (DEXA). The VAS scale is a method by which the patient assesses pain (0-absence of pain, 10-unbearable pain). The FRAX score enables the calculation of the probability that a patient may suffer a major osteoporotic fracture in the next 10 years. The Qualeffo-41 questionnaire assesses the quality of life in people with osteoporosis, it consists of 41 questions, marked from 0-4, grouped into 5 areas: pain (5 questions), physical function (17 questions), social function (7 questions), general perception of general health (3 questions) and mental function (9 questions).

DEXA is an absorption method with dual energy X-ray that determines the T- score and the Z - score. The patients received pharmacological treatment such as bisphosphonates and underwent physiotherapy for pains:

low frequency currents (TENS), ultrasound and physical therapy. TENS was applied for analgesic purposes, muscle relaxation and to improve the peripheral circulation, with the following parameters: the frequency of 50-100Hz, the intensity of 10-40 mA and a duration of 10 minutes. The ultrasounds were applied for analgesic, decontracting purposes, with the following parameters: pulsed shape, the frequency of 1 MHz, the power of 0.5W / cm2 with a duration of 5 minutes.

Physical therapy was made daily for 10 days and then 3 times/ week and it included active-passive mobilizations performed with low to medium intensity, in order to promote bone strengthening (dancing, walking), exercises for toning muscles (by using elastic bands) so as to increase flexibility, to keep the correct posture, balance exercises that improve coordination and prevent falls.

The pursued objectives were:

- Pain relief
- Keeping / increasing joint mobility, muscle tone
- Prevention of fracture risk
- Re-education of breathing
- Correction of vicious attitudes and posture

**Statistical analysis**

The obtained data at the initial, final and control assessment times were statistically processed by using Microsoft Excel 10.

The median, standard deviation were calculated whereas the t-student test was applied to confirm the working hypothesis. The chosen level of statistical significance was 5% and in this context p should be less than 0.05 (p < 0.05)

**Results**

Table no. 1. Demographic traits of the study group

Traits/ age group (years)		50-54	55-59	60-64	65-69	70-74	>75
Number		2	4	4	5	4	1
Environment	Urban	1	3	2	2	2	0
	Rural	1	1	2	3	2	1
<b>Status</b>							
Single		1	1		1	1	
Married			2	2	2		
Divorced		1		1			
Widow			1	1	2	2	1

The patients participating in the study had an average age of 64 (64 ± 6.71), and they were in equal numbers from urban and rural areas, whereas the average height was 167 cm (167.5±3.35). There is a decrease in the average weight of patients by 1,145 between moments M1 and M2, by 1.4% between moments M2 and M3 and by 2.52% between moments M1 and M3. The Body Mass Index registered a decrease of 0.22% between moments M1 and M2, of 1.23% between moments M2 and M3 and of 2.43% between moments M1 and M3.

As for the pain, it was assessed by using the VAS scale and it decreased by 28.57% between moments M1 and

M2, by 40% between moments M2 and M3 and by 57.74% between moments M1 and M3.

Table no. 2. Evolution of the parameters: weight, body mass index and pain

Parameters / Moments	M1 (M±STD DEV)	M2 (M±STD DEV)	M3 (M±STD DEV)
Body weight (Kg)	79.5±9.4	78.6±9.26	77.5±9.09
Body Mass Index (BMI)	27.99±2.96	27.65±2.96	27.31±2.91
VAS scale	7±0.71	5±0.49	3±0.79

For the T-score that assesses the mineral bone density the following data were obtained:

- For the spine, the T score at the moment M1 had values between -2.5 ÷ -2.9 in 13 patients (65%), values between -3 ÷ -3.4 in 4 patients (20%), between -3.5 ÷ -3.9 in a patient (5%) and over -4.5 in one patient (5%). At the end of M3, the T - score had values < -2.5 in 3 patients (15%), values between -2.5 ÷ -2.9 in 10 people (50%), between -3 ÷ -3.4 in 4 people (20%), values between -3.5 ÷ -3.9 for one person (5%), between -4 ÷ -4.5 for 2 people (10%) and over -4.5 for one person (5%).
- For the hip, at the initial moment M1, the T score had values < -2.5 in 16 patients (80%), and for 2 patients (10%) values between -2.5 ÷ -2.9 and > -3. At the end of M3, the T score had values < -2.5 in 17 patients (85%), between -2.5 ÷ 2.9 in 2 patients (10%) and > -3 in one patient (5%).

The values of the t-student test were statistically significant of 0.0007 for the spine between M1 and M3, and of 0.0036 at the hip.

Table no. 3. The average T-score at the level of the spine and of the hip

Parameters / Moments	M1 (M±STD DEV)	M3(M±STD DEV)
T -score in the spine	-2.85±0.63	-2.6±0.61
T-score in the hip	-1.6±0.99	-1.2±0.92

In order to assess the fracture risk, the FRAX score was calculated, which enabled showing the major risk of osteoporotic fracture for the first 10 years and the risk of initial fracture at the initial time M1 and at the control time M3.

Table no. 4. FRAX score: Fracture risk

Parameters / Moments	M1(M±STD DEV)	M3 (M±STD DEV)
Major risk of osteoporotic fracture for the first 10 years	7.25±2.31	7.2±2.47
Initial fracture risk	1±0.86	1±0.89

The quality of life of patients with osteoporosis was assessed by the questionnaire Qualeffo-41 and it recorded an increase of 44.16% between moments M1 and M2, of 41.7% between moments M2 and M3, and of 67.49% between moments M1 and M3.

Table no. 5. The assessment of the quality of life for patients in the group

Parameters / Moments	M1(M±ST DEV)	M2(M±ST DEV)	M3(M±ST DEV)
Quality of life	141.5±13.3	79±11.03	46±3.07

The values of the T-student test were statistically significant for the spine between M1 and M3 de 0.0007, whereas in the hip it was 0.0036.

#### Discussions

In all the studied cases, it was considered that the pain decreased following the use of the medicinal and physiotherapeutic treatment. This is an expected result given that other studies have shown this. For example, in Miyakoshi's study [24], the subscale scores of 36 items of the health survey in the short form (SF-36) for physical role, body pain, general health, and emotional role were all significantly lower in the osteoporosis group than in the volunteer group ( $p < 0.05$  each)

Postmenopausal women in Romania with osteoporosis have a lower HRQoL than healthy controls, measured with the SF-36 instrument and the total QUALEFFO-41 score [25]. There are also studies which show that osteoporosis may or may not cause any symptoms. About 60% of women with compression fractures do not realize they have had a fracture. Advanced cases suffer from deformities and changes in the mechanics of the spine and only in these cases is the pain noted [26]. It has been found that exercises and the application of recovery programs are effective in preventing falls or bone loss, having in view that over 90% of the hip fractures are due to falls [27, 28].

Following the comparative analysis between the results obtained for the T-score, in the final moment compared to the initial one, we can say that the pharmacological and physiotherapeutic treatment enabled the decrease of the T-score values in the spine, it decreased the number of patients diagnosed with osteoporosis but in 3 patients the diagnosis changed from osteoporosis to osteopenia. By studying the action mechanisms of the osteoporotic medication, it was noted that the maximum effect of treatment is obtained when their administration is combined with the physiotherapeutic treatment [29,30]. Another DXA test is recommended to patients undergoing treatment for osteoporosis, in which stagnation or improvement in the bone mineral density shows a favorable response to the treatment. Another DXA test is done when the results may influence clinical



management: one year after the commencement of the medication therapy, six months after the commencement of the corticosteroid therapy, or less frequently when testing does not bring new information [31]. In order to measure changes in the mineral bone density by using DXA, it is recommended to use the same device. Changes determined on different DXAs can only be quantified if a calibration is made between the two devices [32].

#### Conclusions

The obtained data point out the correlation between bone mineral density, fracture risks and exercises in patients diagnosed with osteoporosis. The FRAX score is useful to identify patients who need the combination of drug therapy and exercises to prevent vertebral and non-vertebral fractures in the next 10 years. Osteoporosis is considered a public health problem that affects the quality of life of patients with this diagnosis and also therapeutic, social and economic costs.

#### Declaration of conflict of interests

There is no conflict of interest for any of the authors regarding this paper.

#### Accordance to ethics standards

The study complies with the rules of ethics and deontology according to the legislation in force.

#### Author contribution

The authors of this article have equal contribution and equal rights over it.

#### References

1. Bartl R, Bartl C. *Das Osteoporose Manual*. Springer, Biologie, Diagnostik, Prævention und Therapie, Springer. 2021, Berlin, Heidelberg
2. Daly RM, Dalla Via J, Duckham RL, Fraser SF, Helge EW. Exercise for the prevention of osteoporosis in postmenopausal women: an evidence-based guide to the optimal prescription. *Brazilian journal of physical therapy*. 2019, 23(2), 170-180
3. Link TM, Kazakia G. Update on imaging-based measurement of bone mineral density and quality. *Current rheumatology reports*. 2020, 22(5), 1-11.
4. van de Loo I, Harbeck B. Knochen und Kalziumstoffwechsel. In *In Facharztwissen Endokrinologie und Diabetologie*. 2020, pg 105-133, Springer, Berlin, Heidelberg
5. Zaman M, Aliya SHAH, Singal R, Kirmani A, Abdul Rashid BHAT, & Singal RP. Role of dual energy X-ray absorptiometry (DEXA) scan in the diagnosis of chronic low back pain—A Prospective Randomized Controlled Study in Osteoporotic Patients Hospitalized in a Tertiary Care Institute. *Maedica*. 2018;13(2), 120.
6. Akkawi I, Zmerly H. Osteoporosis: current concepts. *Joints*. 2018, 6(02), 122-127.
7. Antonescu E, Totan M, Boitor GC, Szakacs J, Silisteanu SC, Fleaca SR, Cernusca Mitariu S, Serb BH. The Reference Intervals Used in Pediatric Medical Analysis Laboratories to Interpret the Results Analysis for Total Serum Calcium, *Rev.Chim. (Bucharest)*. 2017,68 (2),
8. Antonescu E, Bota G, Serb B, Atasie D, Dahm Tataru C, Totan M, Duica L, Silisteanu SC, Szakacs J, Arghir OC, Oswald I, Manea MM. Study of the Total Serum Concentration of Serum Ionized Magnesium in Copii și adolescenți din zona Sibiu, *Revista de Chimie*. 2018, Volumul 69(12), 3389-3392
9. Sinaki M. Osteoporosis. In *Braddom's Physical Medicine and Rehabilitation*; Elsevier, 2021, pp. 690-714.
10. <http://www.casan.ro/page/programul-national-de-boli-endocrine.html>
11. Jones A, Goh M, Milat F, Ebeling PR, Vincent A. Dual Energy X-ray Absorptiometry Reports Fail to Adhere to International Guidelines. *Journal of Clinical Densitometry*. 2021, 24(3), 453-459
12. Kanis JA, Melton LJ, Christiansen C, Johnston CC, Khaltaev N. The diagnosis of osteoporosis. *J Bone Miner Res*. 1994; 9(8):1137-1141.
13. Stanciu LE, Ionescu EV, Oprea C, Almasan ER, Vrajitoru AB, Iliescu MG. Rehabilitation in Osteoporosis-therapeutic challenge? *Balneo Research Journal*, Vol.11 (4), December 2020 p: 501-506 DOI: <http://dx.doi.org/10.12680/balneo.2020.388>
14. Kanis J.A, Cooper C, Rizzoli R, Reginster J.Y. Executive summary of European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Aging clinical and experimental research*. 2019,31(1), 15-17.
15. Compston J, Cooper A, Cooper C, Gittoes N, Gregson C, Harvey N, Vine N. UK clinical guideline for the prevention and treatment of osteoporosis. *Archives of osteoporosis*. 2017, 12(1), 43
16. Marcu FM, Lazăr L, Cioară F, Nemeth S, Bungău S, Bănică F. Clinical STUDY regarding the rehabilitation treatment of osteoporotic patients. *Farmacia*. 2021, 69(1), 123-128.
17. Koevska V, Nikolikj-Dimitrova E, Mitrevska B, Gjeracarska-Savevska C, Gocevska M, Kalcovska B. Effect of exercises on quality of life in patients with postmenopausal osteoporosis—randomized trial. Open access

- Macedonian journal of medical sciences. 2019, 7(7), 1160.
18. Tu KN, Lie JD, Wan CKV, Cameron M, Austel AG, Nguyen JK, Hyun D. Osteoporosis: a review of treatment options. *Pharmacy and Therapeutics*. 2018, 43(2), 92.
  19. Das S, Crockett J. Osteoporosis—a current view of pharmacological prevention and treatment. *Drug Des Devel Ther*. 2013; 7:435–448.
  20. Ong T, Sahota O. (2020). Osteoporotic thoracolumbar fractures: My preferred method of nonoperative treatment. In *Surgical and Medical Treatment of Osteoporosis*. 2020, p. 305-314. CRC Press
  21. Lange U, Müller-Ladner U, Teichmann J. Physiotherapy in outpatients with osteoporosis. Insufficient evidence for therapy success. *Zeitschrift für Rheumatologie*. 2012, 71(4), 319-325.
  22. Nava T. Physiotherapy rehabilitation in patients with osteoporosis. *Journal of Advanced Health Care*. 2020, 2(II); <https://doi.org/10.36017/jahc2003-007>
  23. Yadollahpour A, Rashidi S. Therapeutic applications of low-intensity pulsed ultrasound in osteoporosis. *Asian J Pharm*; 2017, 11, S1-S6.
  24. Miyakoshi N, Kudo D, Hongo M, Kasukawa Y, Ishikawa Y, Shimada Y. Comparison of spinal alignment, muscular strength, and quality of life between women with postmenopausal osteoporosis and healthy volunteers. *Osteoporosis International*. 2017, 28(11), 3153-3160.
  25. Ciubean AD, Ungur RA, Irsay L, Ciortea VM, Borda IM, Onac I, Vesa SC, Buzoianu A D. Health-related quality of life in Romanian postmenopausal women with osteoporosis and fragility fractures. *Clinical interventions in aging*. 2018, 13, 2465–2472. <https://doi.org/10.2147/CIA.S190440>
  26. Zaman M, Shah A, Singal R, Kirmani A, Bhat AR, Singal RP. Role of Dual Energy X-ray Absorptiometry (DEXA) Scan in the Diagnosis of Chronic Low Back Pain – a Prospective Randomized Controlled Study in Osteoporotic Patients Hospitalized in a Tertiary Care Institute, *Maedica (Bucur)*. 2018 Jun; 13(2): 120–124.
  27. Abe S, Narra N, Nikander R, Hyttinen J, Kouhia R, Sievänen H, Exercise loading history and femoral neck strength in a sideways fall: A three-dimensional finite element modeling study, *Bone*. 2016 Nov; 92:9-17.
  28. Silisteanu SC, Silisteanu AE. The importance of physical exercise-bone mass density correlation in reducing the risk of vertebral and non-vertebral fracture in patients with osteoporosis. *Balneo Research Journal* DOI: <http://dx.doi.org/10.12680/balneo.2018.174> Vol.9, No.2, May 2018 p: 64 –68
  29. van der Burgh AC, de Keyser CE, Zillikens MC, Stricker BH. The Effects of Osteoporotic and Non-osteoporotic Medications on Fracture Risk and Bone Mineral Density. *Drugs*. 2021, 81(16), 1831–1858. <https://doi.org/10.1007/s40265-021-01625-8>
  30. Silisteanu SC, Silisteanu AE. Interrelation of risk factors and occurrence of a possible fracture in patients with osteoporosis. *Balneo Research Journal* DOI: <http://dx.doi.org/10.12680/balneo.2018.187> Vol.9, No.3, September 2018 p: 240 –244
  31. Sözen T, Özışık L, Başaran NÇ. An overview and management of osteoporosis. *European journal of rheumatology*. 2017,4(1), 46–56. <https://doi.org/10.5152/eurjrheum.2016.048>
  32. Mir FR, Nazir I, Naseed M. Comparison of Radiographic Singh Index with Dual-Energy X-Ray Absorptiometry Scan in Diagnosing Osteoporosis. *Matrix Science Medica*. 2021, 5(1), 17].