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Research article

Comparative analysis of paraclinical parameters in the assessment of osteoporosis: an integrative approach

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Abstract: Osteoporosis is the most common metabolic bone disease with serious physical, psychosocial and economic consequences. It is a chronic, asymptomatic, progressive disease with multifactorial aetiology, characterized by reduced bone mineral density and microarchitectural deterioration of bone tissue; A retrospective study was conducted, which included an initial cohort of 243 patients hospitalized between January 2023 and December 2023 at the County Emergency Hospital of Sibiu, Clinical Endocrinology Department ; Study results suggest that assessment of bone mineral density (BMD) remains a primary standard in the diagnosis of osteoporosis, as measured by T and Z scores from DXA densitometry. However, biomarkers such as total calcium, ionic calcium, vitamin D, phosphorus, PTH and bone degradation markers (e.g. Beta Crosslaps) play a significant role in assessing bone metabolism and identifying fracture risk; The study highlights the importance of screening in postmenopausal women and the need for calcium and vitamin D supplementation in patients with osteoporosis or osteopenia.

Keywords: osteoporosis; biomarkers; screening; postmenopausal women

1. Introduction

Osteoporosis is the most common metabolic bone disease with serious physical, psychosocial and economic consequences. It is a chronic, asymptomatic, progressive disease with multifactorial aetiology, characterized by reduced bone mineral density and microarchitectural deterioration of bone tissue [1]. The disease is clinically silent for a long time, until a fracture occurs due to minimal trauma. Medical studies indicate it is a serious health problem worldwide, with an increasing incidence [2].

Osteoblasts, the bone-forming cells, create an unossified bone matrix in which calcium crystals are deposited, which give the bone its stiffness [3]. When there is an imbalance between these two interrelated processes, there is a decrease in bone

mineral density. It can therefore be said that osteoporosis occurs when the balance is broken, with bone resorption not being followed by adequate bone formation [4]. In general, people reach peak bone mass in the third decade of life, but the exact age varies depending on a number of factors such as gender or race. After peaking, both sexes experience a decrease in bone mass [5]. Due to lower peak bone mass and more rapid bone loss during menopause, women are at higher risk of osteoporosis than men [6,7].

In current practice, osteoporosis has been operationally defined on the basis of bone mineral density (BMD) assessment. According to World Health Organization (WHO) criteria, we can consider the diagnosis of osteoporosis when BMD is more than 2.5 x standard deviation below the mean value for young healthy women considered as control subjects (T score < -2.5 SD) [8]. Accordingly, the WHO defines osteoporosis as that situation where the T-score < -2.5 in postmenopausal women and men aged > 50 years. This definition, based on T-score value, does not apply to premenopausal women. Normal T-score > - 1, whereas osteopenia is characterized by T-score values between -1 and -2.5. In conclusion, the lower the T-score, the higher the risk of bone fractures. For premenopausal women, men under 50 and children, the Z-score is used. The Z-score is the difference between the bone mineral density and the average bone mineral density for healthy people of the same age, ethnicity and sex. In these cases, if the Z-score is less than -2, BMD is low, which may indicate the presence of osteoporosis caused by medication or other diseases and conditions [9,10,11,12]. Bone mineral density assessment is not the only tool used by physicians to determine osteoporosis [13].

Laboratory tests used in the diagnosis of osteoporosis include calcium, phosphorus, vitamin D, alkaline phosphatase (ALP) and alkaline phosphatase (ALP) as well as hormones such as parathormone (PTH), which plays a key role in regulating calcium and phosphorus levels in the body. These have a significant impact on bone metabolism [14].

Last but not least, bone degradation markers such as C-telopeptide or Beta Crosslaps [15] are used. Information from paraclinical investigations can lead to a better understanding of fracture risk and then guide treatment.

2. Results

2.1. Demographics. Of the 243 patients, 115 were chosen for the study. These patients were postmenopausal women with a primary or secondary diagnosis of osteoporosis (Table 1).

		Number of patients (N)	N %
Gen	Female	115	100.00%
Living environment	Rural	24	20.87%
	Urban	91	79.13%
Specific treatment	Yes	108	94.00%
	No	7	6.00%

The mean age of osteopenia patients enrolled was 64.8 ± 10.42 years, all patients were female. About 79% of the patients were from rural areas.

Only 6% of patients are at their first consultation and have not yet received supportive treatment.

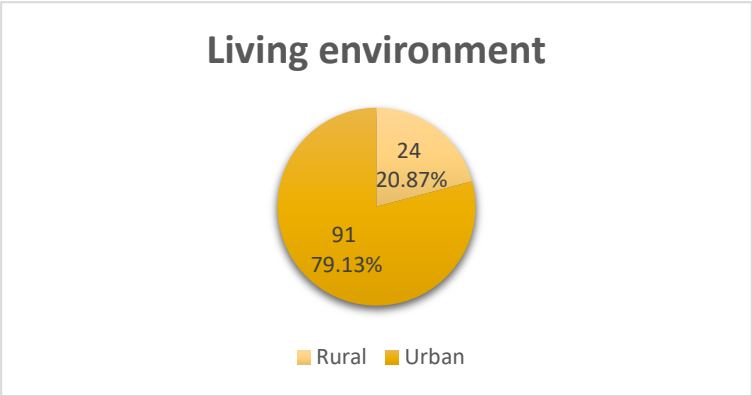

Figure 1. Distribution of patients by background

In this study, we utilized dual-energy X-ray absorptiometry (DXA) bone densitometry to assess the bone mineral density (BMD) of patients. The T-score helps to identify patients at increased risk of osteoporosis. A low T-score indicates a lower than normal bone mineral density, suggesting an increased predisposition to fractures. The Z score is particularly useful for identifying conditions that may influence bone metabolism (Table 2).

Table 2. Disease stages according to T and Z scores (DXA)

Score	Reference values	Disease stage	Number of patients (N)	N %
T	T score ≥ -1.0	normal	6	5.22%
	-2.5<Scor T<-1.0	osteopenia	28	24.35%
	T score ≤ -2.5	osteoporosis	81	70.43%
Z	Z-score ≥ -2.5	normal	15	13.04%
	Z-score < -2.5	osteoporosis	100	86.96%

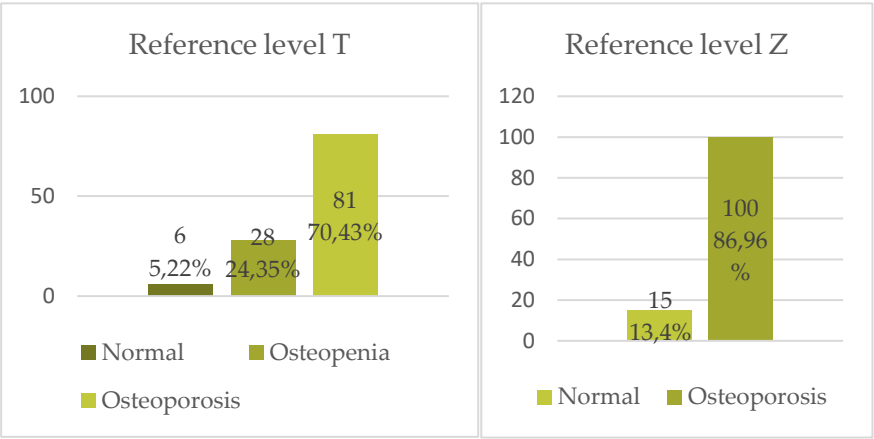

Figure 2. Distribution of patients according to T-score or Z-score values

Figure 2 shows, by T-score, that osteoporosis is the most common bone density disorder among the 115 patients followed by osteopenia. The number of results with normal bone density values being very low (5.22%). If we analyze according to Z-score values, it can be seen that osteoporosis is a very prevalent condition among the patients with almost 87%.

Among the most important markers chosen for this study are levels of total calcium, ionic calcium or calciuria, phosphorus, vitamin D and FAS (bone alkaline phosphatase) (Table 3).

Table 3. Description of values obtained for laboratory parameters

	Media	Standard Deviation	Minimum	Maximum
Density - lumbar collar	0,73	0,12	0,37	1,13
T - lumbar collar	-3,03	1,15	-6,70	-0,40
Z - lumbar collar	-1,31	1,28	-5,20	2,20
total calcium (mg/dl)	9,74	0,55	8,76	11,68
ionic calcium (mg/dl)	4,39	0,40	3,77	5,64
Calciuride (mg/24h)	129,52	93,82	2,00	477,40
TSH U/l	2,21	1,49	0,04	6,56
25-OH vit D (ng/ml)	28,33	10,55	7,88	54,00
PTH (pg/ml)	57,40	34,06	5,60	172,00
Phosphorus (mg/dl)	3,39	0,42	2,60	4,25
Beta-crosslaps (ng/ml)	0,47	0,21	0,10	1,05
FAS (U/L)	85,82	46,42	30,00	187,71
Magnesium (mg/dl)	1,94	0,23	1,57	2,27

The mean total calcium value is 9.74 mg/dl with a standard deviation of 0.55 mg/dl. The reference range is (8.8 - 10.2) mg/dl.

Ionic calcium shows an average value of 4.39±0.40 mg/dl. Reference values vary between 3.5 and 5.5 mg/dl.

Urinary calcium has a mean value of 129.52±93.82 mg/24h. The reference values of urinary calcium for a person with a normal diet and sufficient calcium intake are in the range of 100 - 300 mg/ 24h.

The mean value for vitamin D is 28.33±10.55 ng/ml, with a maximum value of 7.88 ng/ml and a maximum value of 54 ng/ml.

Another hormone of interest is PTH (parathyroid hormone), which regulates calcium and phosphorus levels in the body. The mean value is 57.40±34.06 pg/ml, with a maximum value of 172 pg/ml and 5.60 pg/ml.

The phosphorus assay gives a mean value of 3.39±0.42 mg/dl, with a maximum of 4.25 mg/dl and a minimum of 2.60 mg/dl. In this case, the reference range is (2.5-4.5) mg/dl.

FAS has widely varying values, from a maximum of 187.71 U/L to a minimum of 30.00 U/L. Normal values are < 104 U/L.

Finally, Beta Crosslaps is a marker of bone degradation that reflects osteoclast activity and helps to assess the rate of bone remodeling. For it an average value of 0.47±0.21ng/ml is obtained, with a minimum value of 0.10 ng/ml and a maximum value of 1.05 ng/ml.

If we analyze the distribution of values in terms of mean bone density, we obtain a bell-shaped curve, in which lumbar spine density values are symmetrically distributed around the mean, with most values clustering near the mean and fewer values occurring in tails (Figure 3).

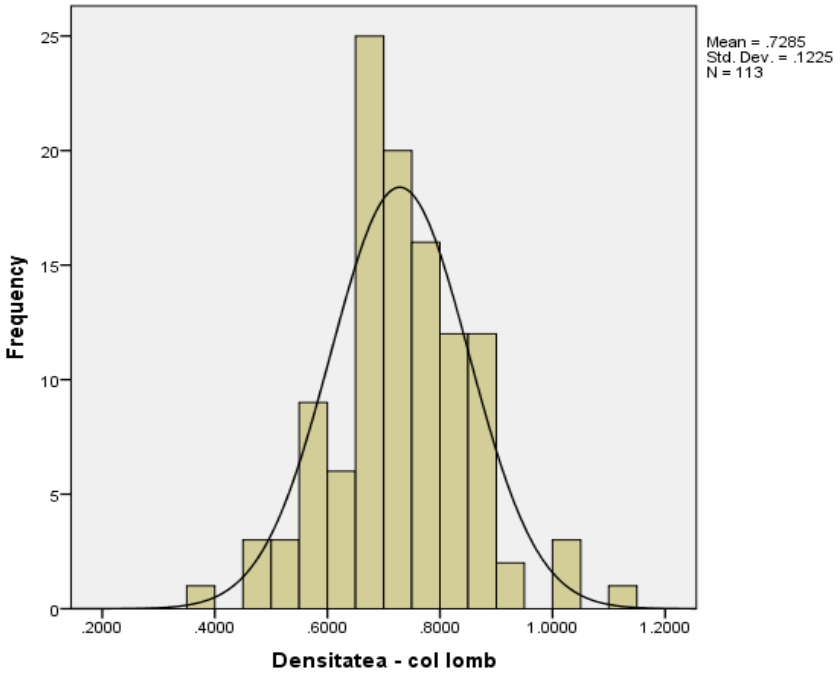

Figure 3. Lumbar spine density distribution in the 115 patients

The mean lumbar spine density for the 115 patients is approximately 0.73±0.12 g/cm^2 .

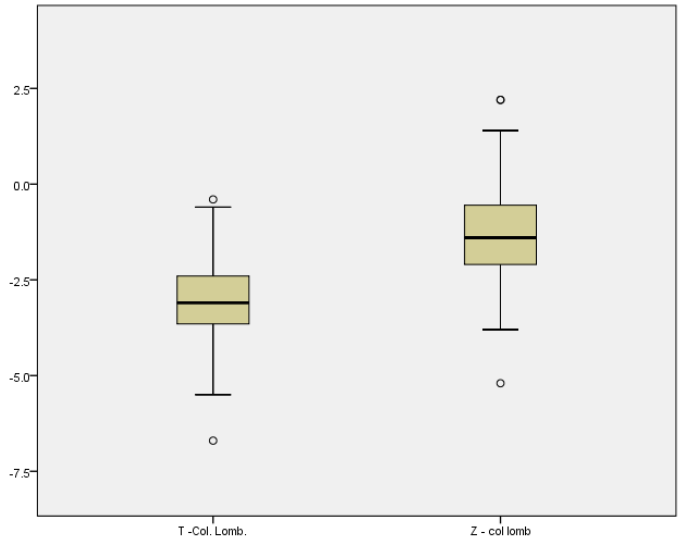

Figure 4. Distribution of T-score and Z-score values

The values for the T score are generally lower than those for the Z score. The mean value for T-score is -3.03, the minimum is -6.7 and the maximum is -0.40. The mean for the T-score falls in the osteoporosis zone, indicating a predominance of specific values.

The mean value for the Z-score is -1.31, with a minimum of -5.20 and a maximum of 2.20 2.20. The distance between lower and upper quartiles is similar for the T score and the Z score.

The correlation between DXA parameters and laboratory markers is shown in Table 4.

Table 4. Correlation between DXA values and laboratory parameters

		Densit.	T score	Z score
Density	r	1.000	0.773	0.650
	Sig.	-	0.000	0.000
T score	r	0.773	1.000	0.792
	Sig.	0.000	-	0.000
Z score	r	0.650	0.792	1.000
	Sig.	0.000	0.000	-
Total calcium (mg/dl)	r	0.174	0.329	0.277
	Sig.	0.120	0.003	0.012
Ionic calcium (mg/dl)	r	0.275	0.262	0.273
	Sig.	0.044	0.053	0.043
25-OHvit D (ng/ml)	r	-0.131	-0.223	-0.225
	Sig.	0.342	0.098	0.095
PTH (pg/ml)	r	0.044	-0.071	-0.106
	Sig.	0.708	0.545	0.365

Note: r- correlation coefficient
Sig. – level of significance

There was a minor positive relationship between bone density and total calcium with r=0.174, between bone density and ionic calcium with r=0.275, between T-score and ionic calcium with r=0.262, between Z-score and total calcium plus ionic calcium with r=0.277 and r=0.273 respectively (Figure 5).

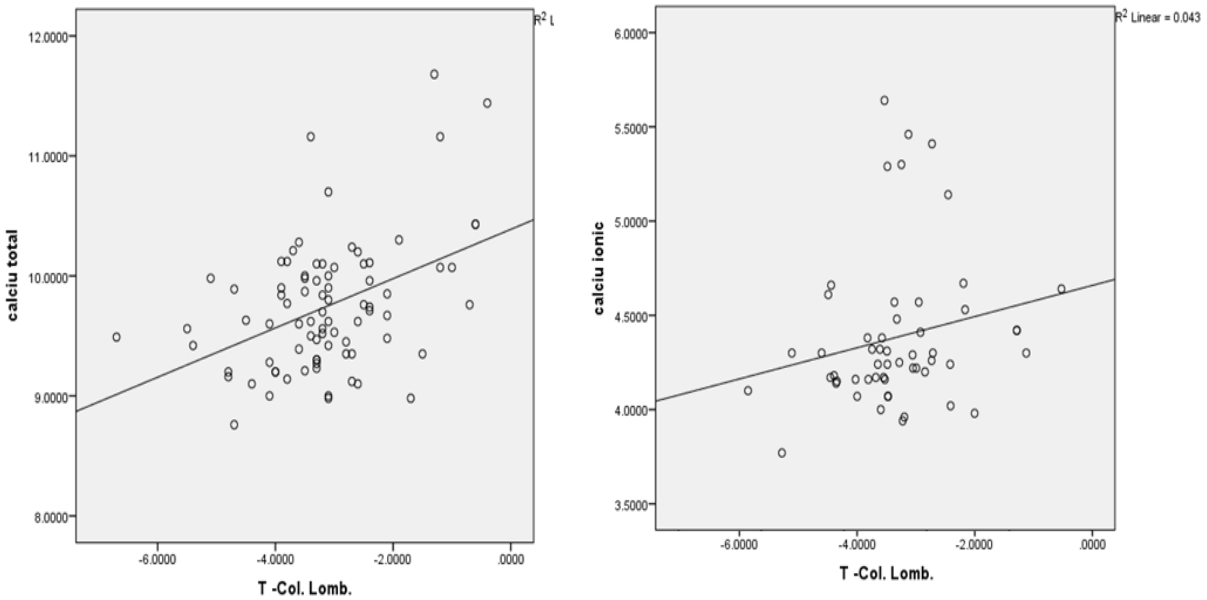

Figure 5. Correlation between T score and total and ionic calcium values

There was a moderate positive relationship between T score and total calcium with r=0.329.

A positive correlation with high value (0.5<r<0.7) is realized between bone density and Z-score.

A very high positive correlation is realized between bone density and T score and between Z score and T score.

Weak and medium negative correlations are found between 25-OH vit D and all DXA parameters.

There is a minor positive correlation between PTH and bone density and is a minor negative correlation between PTW ant T-score and Z-score.

In the case of total calcium R^2 =0.185 indicates a positive, high correlation.

For ionic calcium, the R-value^2 may indicate a weak correlation (0.043), which means that factors other than lumbar spine density may play a significant role in determining ionic calcium levels.

Having the most positive correlations on Z-score, we study the stages of disease caused by decreased bone density from this perspective (Table 5).

Table 5. T-score classification of bone density deficiency stages

	Stages of bone density deficiency (T-score classification)					
	Normal		Osteopenia		Osteoporosis	
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
Density	0,91	0,16	0,82	0,09	0,68	0,10
T score	-0,65	0,20	-1,91	0,47	-3,60	0,77
Z score	0,78	1,52	-0,18	0,73	-1,86	0,97
Total calcium (mg/dl)	10,43	0,63	9,99	0,67	9,63	0,45
Ionic calcium (mg/dl)	4,43	0,17	4,40	0,35	4,38	0,44
Calciuria (mg/24h)	122,75	22,94	92,04	69,51	139,41	104,13
TSH U/l	1,85	0,66	2,16	1,46	2,25	1,58
25-OH vit D (ng/ml)	18,00		25,97	9,63	29,48	10,83
PTH (pg/ml)	36,80		46,72	36,02	61,47	33,06
Ph (mg/dl)	3,30	0,35	3,54	0,45	3,37	0,42
Beta-crosslaps (ng/ml)	.		0,45	0,07	0,47	0,25
FAS (U/L)	.		88,92	51,91	84,91	46,38
Mg (mg/dl)	1,57		.	.	2,00	0,18
Age (years)	69,50	11,74	66,86	8,74	68,32	8,18

The table helps to understand how these paraclinical parameters differ between people with normal bone density, osteopenia and osteoporosis.

By comparing mean values and standard deviations, trends and differences between categories can be identified.

For example it can be seen that people with osteoporosis have lower mean values for bone density parameters and higher standard deviations, indicating greater variability in their bone health.

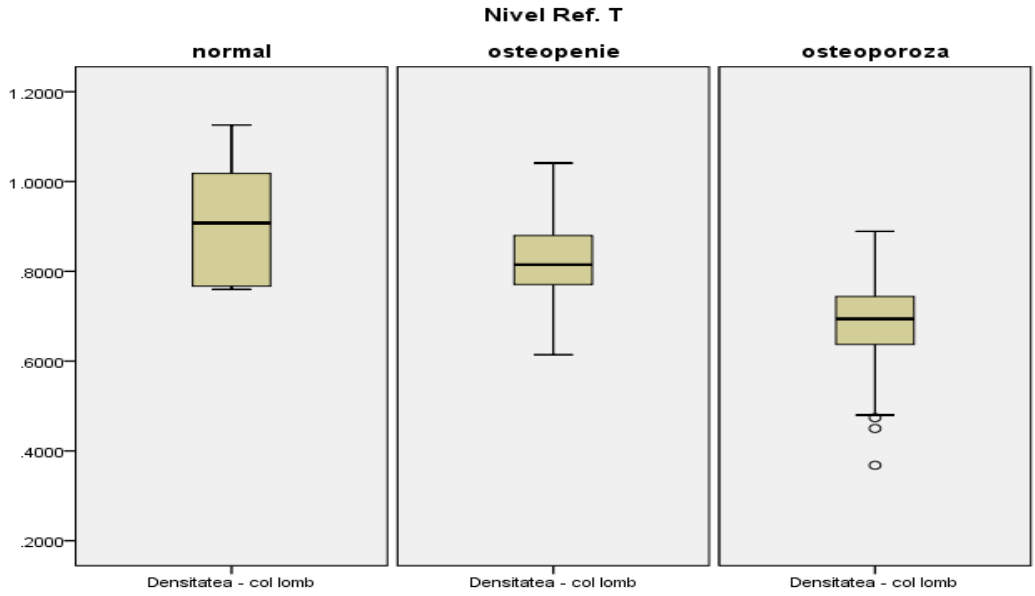

Figure 6. Bone density variation diagram for different disease stages

The box plot for the normal group shows a relatively narrow box with a median near the top of the range. This suggests that individuals with normal bone density tend to have higher values of bone density in the lumbar spine, with a smaller spread of values.

The plot for the osteopenia group is shifted lower on the y-axis compared to the normal group. The box is also slightly wider, indicating a wider spread of values. This suggests that people with osteopenia have lower values of bone density in the lumbar spine, with greater variability in bone density.

The box plot for the osteoporosis group is shifted further down the y-axis compared to the osteopenia group. The box is also wider, indicating an even wider spread of values. This suggests that people with osteoporosis have significantly lower bone density values in the lumbar spine, with a high degree of variability in bone density. Figure 7 shows the variation of total calcium for different stages of the disease

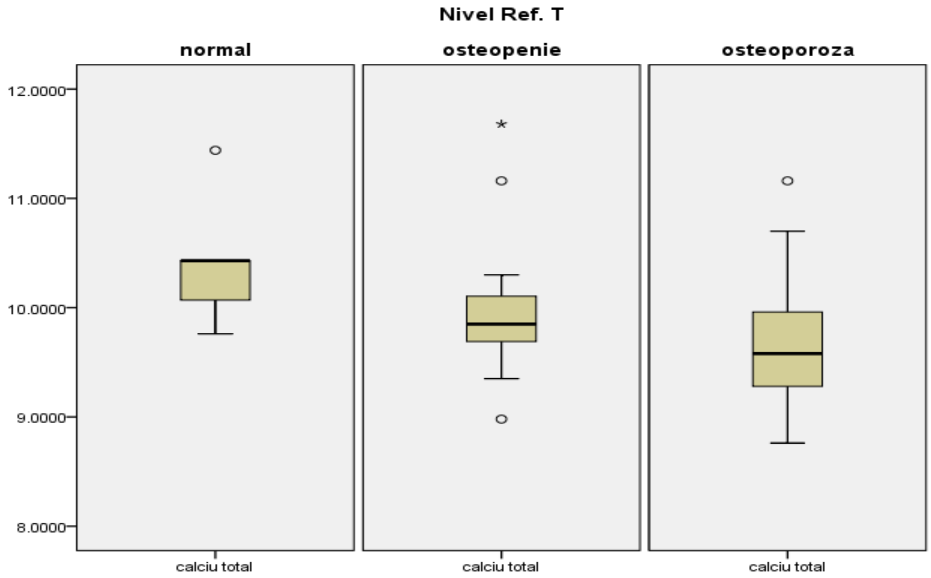

Figure 7. Diagram of total calcium variation for different stages of the disease

The plot for the normal group shows a relatively narrow box with a median near the middle of the range. This suggests that individuals with normal bone density tend to have total calcium levels in a relatively narrow range.

The box plot for the osteopenia group is shifted slightly lower on the y-axis compared to the normal group. The box is also slightly wider, indicating a wider spread of values. This suggests that people with osteopenia have slightly lower total calcium levels compared to those with normal bone density, with greater variability in their calcium levels.

The plot for the osteoporosis group is shifted further down the y-axis compared to the osteopenia group. The box is also wider, indicating an even wider spread of values. This suggests that people with osteoporosis have significantly lower total calcium levels compared to those with osteopenia or normal, with a high degree of variability in their calcium levels.

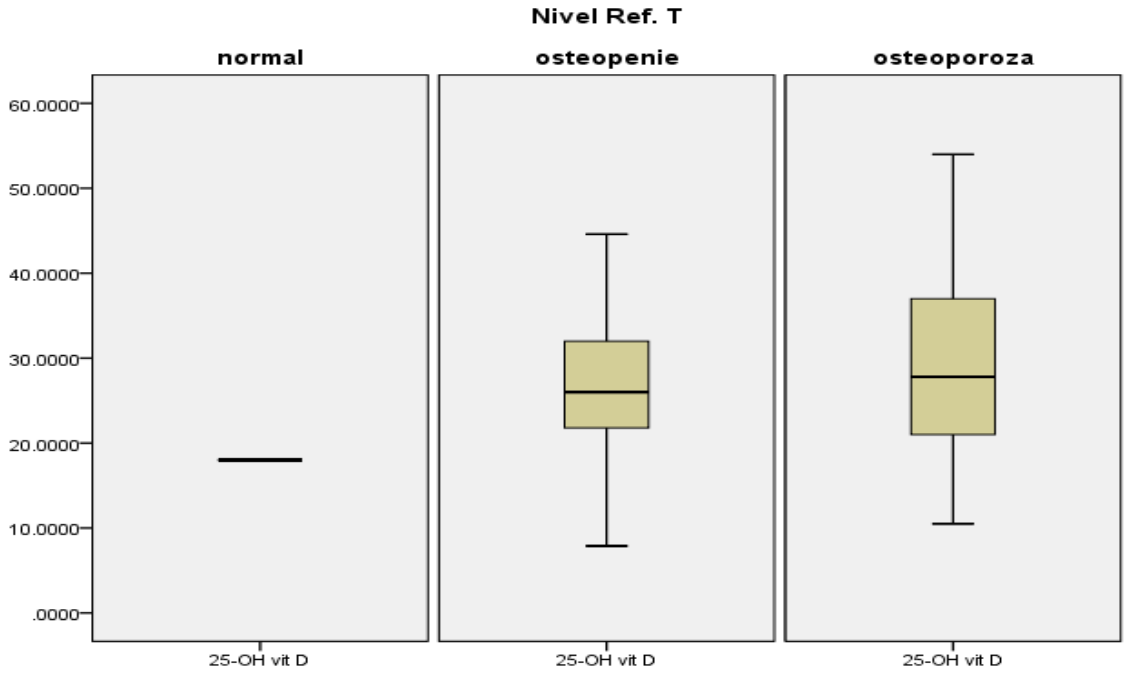

Figure 8. Diagram of variation of 25-OH vit D for different stages of the disease

Figure 8 shows the variation of total calcium for different stages of the disease

The plot for the normal group shows a single line at the bottom of the y-axis without a box. This suggests that vitamin D levels for people with normal bone density are very low, with little variability.

The box plot for the osteopenia group shows a box with a median near the middle of the range. The whiskers extend slightly out of the box, indicating some variability in vitamin D levels.

The plot for the osteoporosis group is similar to the osteopenia group, with a median close to the middle of the range and some variability in vitamin D levels.

3. Discussion

Although osteoporosis is a health problem affecting both sexes, most research has focused on the female gender, as women are more likely than men to develop osteoporosis and subsequent fractures [16].

Osteoporosis is classified into two categories, primary and secondary. Primary osteoporosis is seen in postmenopausal women and in women and men over the age

of 70, and is due to the normal aging process. Secondary osteoporosis is caused by various systemic diseases, endocrine diseases or malignant neoplasms, treatments, lifestyle, habits and major depressions, etc. [17,18].

Demographic analysis of patients showed a higher distribution of osteoporosis among urban (79%) compared to rural (20%) women. This may reflect differences in lifestyle, physical activity, sun exposure and access to calcium and vitamin D supplements. Previous studies have shown an association between urbanization and increased incidence of osteoporosis due to dietary changes and reduced physical activity [19.20].

Study results suggest that assessment of bone mineral density (BMD) remains a primary standard in the diagnosis of osteoporosis, as measured by T and Z scores from DXA densitometry. However, biomarkers such as total calcium, ionic calcium, vitamin D, phosphorus, PTH and bone degradation markers (e.g. Beta Crosslaps) play a significant role in assessing bone metabolism and identifying fracture risk [21,22].

Calcium is essential for maintaining bone structure and more than 1/3 of the phosphate in the body is found in the bones, where it acts synergistically with calcium to form hydroxyapatite, the main mineral in bone tissue. This is why deficiencies can lead to impaired bone mineralization [23,24].

Vitamin D deficiency impairs calcium absorption, contributing to the development of osteoporosis [24].

Magnesium plays a crucial role in regulating calcium metabolism and the activity of osteoblasts, the cells responsible for bone formation.

The analysis of thyroid hormones, such as TSH (thyroid stimulating hormone), also plays a crucial role, having a significant impact on bone metabolism.

Another hormone of interest is PTH (parathyroid hormone), which regulates calcium and phosphorus levels in the body. An imbalance in its secretion may indicate problems in bone metabolism and may contribute to the risk of osteoporosis [25].

Finally, Beta Crosslaps is a marker of bone degradation that reflects osteoclast activity and helps to assess the rate of bone remodeling. Analysis of these markers allows clinicians to gain a detailed understanding of the patient's osteologic status and identify risks associated with osteoporosis [26].

The moderate correlations identified between total calcium, ionic calcium and DXA values (T and Z scores) emphasize the importance of these parameters in monitoring calcium homeostasis. In the literature, it has been observed that calcium levels play a crucial role in bone health, and abnormalities may indicate imbalances in bone resorption and bone formation [27].

Although values for vitamin D and PTH showed weak and moderate negative correlations with DXA, these results are in line with other studies that have observed that vitamin D deficiency and secondary hyperparathyroidism are common in patients with osteoporosis and contribute to decreased bone density [28].

In our study, the box plots suggest that individuals with normal bone density tend to have very low levels of vitamin D, whereas those with osteopenia or osteoporosis have a wider range of vitamin D levels. However, it is important to note that the reference range for vitamin D levels is not provided, so it is difficult to determine whether the observed levels are within the normal range. This somewhat unexpected result is obtained because most of the patients are under treatment with old records of osteoporosis in the database [29].

Study results show that T-score is essential in the assessment of osteoporosis in postmenopausal women [30,31].

Approximately 70% of patients studied had T-scores indicating osteoporosis, confirming that this population group is prone to rapid bone loss. Z-scores, although less commonly used in this age group, provided additional information on impaired bone metabolism [32].

Another important aspect of the analysis is that 87% of the patients had Z-score values indicating osteoporosis, which emphasizes the extent of the disease in this group. Also, the strong correlation between T and Z scores suggests a good concordance between these two indicators in assessing the severity of osteoporosis [33].

In correlation analysis, it was found that biochemical parameters such as total calcium and ionic calcium had positive correlations with bone density, suggesting that a good mineral status contributes to the maintenance of BMD. Bone density variability was higher in the osteopenia and osteoporosis groups compared to the normal group. This suggests that individuals with these conditions have a wider range of bone density values, indicating a more heterogeneous population [34].

Also, alkaline phosphatase (ALP), a marker of bone formation, showed significant variations, being an important indicator in the assessment of bone remodeling activity [35].

The bone degradation marker Beta Crosslaps had mean values indicating moderate osteoclastic activity, which corresponds to an accelerated resorption process in patients with osteoporosis. This may correlate with the literature, which suggests that increased levels of bone resorption markers are associated with a higher risk of fractures.

In Diba, S.F.'s study analyzing the correlation between Beta-CrossLaps (β-CTx) and trabecular structural parameters of postmenopausal women using CBCT found no significant positive correlation of to bone volume fraction (bone density equivalent) [35].

Some people don't realize they have osteoporosis until a habitual movement or walking causes a bone fracture. That's why laboratory tests along with DEXA scans are effective tools to prevent the disease and stop this pandemic that causes extreme suffering to patients and huge costs to the health care system. In addition, specialists are seeking to identify effective methods to relieve patient suffering and prevent the disease [36,37].

3.1.Study limitations

A major limitation of the study is the retrospective selection of patients and the absence of a control group of patients with no problems of decreased bone density. The study also did not include patients with DXA for bone locations other than the lumbar spine, which limits the generalizability of the results. Another problem that marks the marker variation analysis is that the patients are in different phases of treatment, which does not allow us to correctly stage the disease. This does not prevent the correlation of DXA values with the results of laboratory analysis.

4. Materials and Methods

A retrospective study was conducted, which included an initial cohort of 243 patients hospitalized between January 2023 and December 2023 at the County Emergency Hospital of Sibiu, Clinical Endocrinology Department.

4.1.Aim of the study**.** This study aims to perform a comparative analysis of the main paraclinical investigations used in the evaluation of osteoporosis.

4.2. The objectives we will pursue are:

- **To identify and analyze relevant biomarkers** and assess the importance of each laboratory test in the diagnosis of osteoporosis.
- **Correlation of laboratory tests with DXA test results** by investigating the relationships between paraclinical markers and bone densitometry (DXA) results to assess the consistency and relevance of these tests in determining the severity of osteoporosis.
- To examine the relationships between paraclinical markers and the severity of osteoporosis.

The values for the biochemical parameters studied and for the results of osteodensitometry DXA were retrieved from the Hospital archive (ATLAS - Integrated Computerized Information System for Electronic Document Management).

Patients were selected who had the diagnosis of postmenopausal osteoporosis with pathologic fracture, multiple localizations, unspecified vitamin D deficiency, unspecified vitamin D deficiency, vertebral fatigue fracture, multiple localizations in the spine in the inpatient, principal, secondary or discharge diagnosis.

The study was approved by the Ethics Commission of the Sibiu County Emergency Hospital.

4.3. The criteria for including patients in this study were: postmenopausal women with a diagnosis of osteoporosis or osteopenia who had DXA measurements of the lumbar spine.

Exclusion criteria were the following: women in the fertile period, men, lack of complete information about the DXA value or about the value of the results of medical tests. Patients with DXA measurements for femoral neck or calf were also eliminated.

4.4. Statistical Analysis

Microsoft Excel and SPSS version 22 were used for statistical analysis. Pearson linear correlation was evaluated. The Kolmogorov-Smirnov test was used to check the normality of data distribution. The significance threshold for all tests was 0.05.

5. Conclusions

The results of this study emphasize the importance of an integrative diagnosis in osteoporosis, combining both imaging (DXA) and biochemical analysis to assess fracture risk and guide therapeutic treatments. The study also highlights the importance of screening in postmenopausal women and the need for calcium and vitamin D supplementation in patients with osteoporosis or osteopenia

Author Contributions: For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Conceptualization, O.R.A, A.C.V. and E.N.N.; methodology, O.R.A., S.C.S., E.N.N.; software, A.C.V., I.E.A.; validation, O.R.A., A.C.V., and E.N.N.; formal analysis, I.E.A., M.R., S.C.S.; investigation, O.R.A., A.C.V., I.E.A.; resources, S.C.S., E.N.N.; data curation, O.R.A., S.C.S., E.N.N.; writing—original draft preparation, O.R.A., A.C.V., E.N.N.; writing—review and editing, S.C.S, M.R., A.C.V.; visualization, O.R.A., A.C.V., E.N.N.; supervision, S.C.S., I.E.A.; project administration, O.R.A., E.N.N.; funding acquisition, M.R. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board (or Ethics Committee) of Clinical County Emergency Hospital Sibiu (3028/10.02.2023) for studies involving humans.

Informed Consent Statement: Not applicable

Data Availability Statement: Not applicable here

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References

1. Curate, F. Osteoporosis and Paleopathology: A Review, Journal of Anthropological Sciences 2014, 92.
2. Silisteanu, S.C.; Silisteanu, A.E. Interrelation of risk factors and occurrence of a possible fracture in patients with osteoporosis. Balneo Research Journal 2018, 9(3), 240 –244
3. Rinaldo, N.; Pasini, A.; Donati, R.; Giovanna, B.M.; Gualdi-Russo, E. Quantitative Ultrasonometry for the Diagnosis of Osteoporosis in Human Skeletal Remains: New Methods and Standards, J Archaeol Sci 2018, 99
4. Balanuca, D.; Silișteanu, S.C.; Costea, A.I. Changes in nutritional status and their influence on bone mass. Romanian Journal of Oral Rehabilitation 2024, 16(1)
5. Vizitiu, E.; Costea, A.I.; Silișteanu, S.C. Prevalence of osteoporosis and risk factors in different age categories in adult women. Balneo and PRM Research Journal 2023, 14(4)
6. Alswat, K.A. Gender Disparities in Osteoporosis, J Clin Med Res 2017, 7(9)
7. Chin, K.Y.; Ng, B.N.; Rostam, M.K.I.; Muhammad Fadzil, N.F.D.; Raman, V.; Mohamed Yunus, F.; Syed Hashim, S.A.; Ekeuku, S.O. A Mini Review on Osteoporosis: From Biology to Pharmacological Management of Bone Loss, J Clin Med 2022, 11
8. Faisal-Cury, A.; Zacchello, K.P. Osteoporosis: Prevalence and Risk Factors among > 49 YearOld Women in Private Practice Environment, Acta Ortop Bras 2007, 15
9. Nazia Fathima, S. M.;Tamilselvi, R.; Parisa Beham, M.A Survey on Osteoporosis Detection Methods with a Focus on X-ray and DEXA Images, IETE Journal of Research 2022, 68(6), 46404664.
10. Bisaccia, M.; Rinonapoli, G.; Meccariello, L.; Ripani, U.; Pace, V.; Rollo, G.; De Masi De Luca, A. Osteoporosis in male patients: epidemiology, clinical aspects and DEXA Scan assessment. Clinical Cases in Mineral & Bone Metabolism 2019, 16(1).
11. Holubiac, I.Ș.; Leuciuc, F.V.; Crăciun, D.M; Dobrescu, T. Effect of strength training protocol on bone mineral density for postmenopausal women with osteopenia/osteoporosis assessed by dual-energy X-ray absorptiometry (DEXA), Sensors 2022, 22(5), 1904.
12. Strugariu, G.; Pomirleanu, C.; Bran, C.; Costea, A.I.; Vicovan, A.; Tatarciuc, D.; Esanu, I.; Ancuta, E.; Chirieac, R.; Ancuta, C. The prevalence of atopy in biolocically treated spondyloarthropathies: A retrospective study of 200 patients. J.Clin.Med 2022, 11(1),55
13. Wheater, G.; Elshahaly, M.; Tuck, S.P.; Datta, H.K.; van Laar, J.M. The clinical utility of bone marker measurements in osteoporosis. Journal of translational medicine, 2013, 11, 1-14.
14. Garnero, P. Bone markers in osteoporosis, Current osteoporosis reports, 2009, 7(3), 84-90
15. Nielsen, B. R.; Andersen, H.E.; Hovind, P.; Jørgensen, N.R.; Schwarz, P.; Kristensen, S.H.; Suetta, C. Sarcopenia and self-reported markers of physical frailty in patients with osteoporosis, Archives of Osteoporosis 2024, 19(1), 1-8
16. Shaikhomar, O.A.; Abdelghnay, A.H.; Qutob, H.M.H. Diagnosis of Low Bone Mass Density: Serological versus Radiological Methods, Int J Gen Med 2022, 15
17. Silisteanu, S.C.; Silisteanu, A.E. 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 2018, 9(2), 64 –68.
18. Salari, N.; Ghasemi, H.; Mohammadi, L.; Behzadi, M. hasan; 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.
19. Marcucci, G.; Brandi, M.L. Rare Causes of Osteoporosis, Clinical Cases in Mineral and Bone Metabolism 2015, 12.
20. Askari, M.; Lotfi, M. Hassan; Owlia, M. bagher; Fallahzadeh, H.; Mohammadi, M. Survey of Osteoporosis Risk Factors. Review Article, Journal of Sabzevar University of Medical Sciences, 2019, 25.

21. Kruger, M.C.; Kruger, I.M.; Wentzel-Viljoen, E.; Kruger, A. Urbanization of black South African women may increase risk of low bone mass due to low vitamin D status, low calcium intake, and high bone turnover, Nutrition Research 2011, 31(10), 748-758.
22. Hurjui, L.L.; Hurjui, I.; Delianu, C.; Tărniceriu, C.C.; Mârțu, A.M.; Balcoș, C.; Grădinaru, I. Biological markers importance in the diagnosis of osteoporosis. Romanian Journal of Oral Rehabilitation 2020, 12(4), 181-189.
23. Chew, C.K.; Clarke, B. L. Biochemical testing relevant to bone, Endocrinology and Metabolism Clinics 2017, 46(3), 649-667.
24. Aibar-Almazán, A.; Voltes-Martínez, A.; Castellote-Caballero, Y.; Afanador-Restrepo, D.F.; Carcelén-Fraile, M.D.C.; López-Ruiz, E. Current status of the diagnosis and management of osteoporosis, International Journal of molecular Sciences 2022, 23(16), 9465.
25. Kalia, R. B.; Ansari, S.; Regmi, A. The Interpretation of Biochemical Investigations in the Management of Metabolic Bone Disorders, Journal of Cardio-diabetes and metabolic disorders 2022, 2(1), 1-8.
26. Aslan, M.; Çöğendez, E.; Eken, M.; Arıoglu, P.; Eren, S. Serum beta crosslapses as a predictor for osteoporosis in postmenopausal women. Journal of Istanbul Faculty of Medicine 2015, 78(2), 36-40.
27. Bergmann, P.; Body, J.J.; Boonen, S.; Boutsen, Y.; Devogelaer, J.P.; Goemaere, S. & Advisory Board on Bone Markers. Evidence-based guidelines for the use of biochemical markers of bone turnover in the selection and monitoring of bisphosphonate treatment in osteoporosis: a consensus document of the Belgian Bone Club, International journal of clinical practice 2009, 63(1), 19-26
28. Voulgaridou, G.; Papadopoulou, S.K.; Detopoulou, P.; Tsoumana, D.; Giaginis, C.; Kondyli, F.S.; Lymperaki, E.; Pritsa, A. Vitamin D and Calcium in Osteoporosis, and the Role of Bone Turnover Markers: A Narrative Review of Recent Data from RCTs, Diseases 2023, 11, 29.
29. Wheater, G.; Elshahaly, M.; Tuck, S.P.; Datta, H.K.; van Laar, J.M. The clinical utility of bone marker measurements in osteoporosis, Journal of translational medicine 2023, 11, 1-14.
30. Panchagnula, R.; Amarnath, S.S. Osteoporosis: Investigations and monitoring, Indian Journal of Orthopaedics 2023, 57(Suppl 1), 70-81.
31. Bagur, A.; Vega, E.; Mautalen, C. Discrimination of total body bone mineral density measured by dexa in vertebral osteoporosis, Calcified tissue international 1995, 56, 263-267.
32. Al-Bogami, M.M.; Alkhorayef, M.; Sulieman, A.; Bradley, D.; Jawad, A.S., Mageed, R.A. The clinical assessment of changes in bone density in Rheumatoid Arthritis patients': Role of DEXA scan and bone turnover biomarkers, Applied Radiation and Isotopes 2024, 111373.
33. Anish, R. J.; Soumya, N.P.P.; Nair, A.; Rauf, A.A. Standardization Of Sprague-Dawley Rats As A Post-Menopausal Osteoporotic Model Through Biochemical Marker Evaluation And Dexa Scan, Exploratory Animal & Medical Research 2023, 13(1).
34. Lorentzon, M.; Branco, J.; Brandi, M.L.; Bruyère, O.; Chapurlat, R.; Cooper, C.; Cavalier, E. Algorithm for the use of bio-chemical markers of bone turnover in the diagnosis, assessment and follow-up of treatment for osteoporosis, Advances in therapy 2019, 36, 2811-2824.
35. Garnero, P. New developments in biological markers of bone metabolism in osteoporosis, Bone 2014, 66, 46-55.
36. Diba, S. F.; Pramanik, F.; Tjahajawati, S. Analysis of Beta-Crosslaps (B-Ctx) and mandible trabecular parameters in menopausal women using cone beam computed tomography (CBCT), J Int Dent Med Res 2020, 13(1), 189-93
37. Silisteanu, S.C.; Vizitiu, E.; Filip, F; Antonescu, E.; et al. Changes Induced by Physical Exercise and Therapeutic Swimming on the Health Status of Menopausal and Postmenopausal Women with Osteoporosis. Romanian Journal of Oral Reha-bilitation, 2024, 16(2)
38. Antonescu, O.R.; Silisteanu, A.E.; Racheriu, M.; Mihalache, C. Assessment of the importance of physical activity and quality of life for patients diagnosed with osteoporosis during the COVID-19 pandemic. Balneo and PRM Research Journal, 2021, 12 (4), 386-391.