Journal of Clinical and Investigative Surgery

https://doi.org/10.25083/2559-5555
https://proscholar.org/jcis/
ISSN: 2559-5555

The predictive role of monocyte-lymphocyte ratio and platelet-lymphocyte ratio in postmenopausal osteoporosis

Ibrahim Kale[1*]

[1]*Umraniye Training and Research Hospital Elmalikent Mahallesi Adem Yavuz Caddesi, Ümraniye, Istanbul, Turkey 34764*

ABSTRACT

Objective. To investigate the relationship between neutrophil to lymphocyte ratio (NEU/LY), monocyte to lymphocyte ratio (MO/LY), platelet to lymphocyte ratio (PLT/LY), mean platelet volume to lymphocyte ratio (MPV/LY), mean platelet volume to platelet ratio (MPV/PLT), plateletcrit to platelet ratio (PCT/PLT) and postmenopausal osteoporosis. *Materials and Methods*. The data of the patients who were admitted to Ümraniye Training and Research Hospital between January 2017 and July 2020 and had both bone mineral densitometry and hemogram tests on the same day were retrospectively scanned. A number of 177 patients who had been in natural menopause for at least one year and did not have any chronic disease nor used any medication were first divided into 3 groups: a number of 48 patients with osteoporosis, 103 with osteopenia and 26 patients included in the control group. Later on, 177 patients were divided into two groups: 151 patients with low bone mineral density and 26 patients were included in the control group. *Results*. There was no difference between the three groups in terms of NEU/LY, MPV/LY, MPV/PLT and PCT/PLT. The MO/LY ratio and PLT/LY ratio were statistically significantly higher in the osteoporosis group ($p = 0.002$, $p < 0.001$, respectively). The MO/LY ratio was significantly higher in the group with low bone mineral density compared to the control group ($p = 0.011$), while there was no statistical difference between the two groups in terms of PLT/LY ratio ($p = 0.281$). *Conclusions*. This study shows that MO/LY and PLT/LY are quite simple and cheap markers that can be used in the diagnosis of postmenopausal osteoporosis and MO/LY in the diagnosis of postmenopausal low bone mineral density.

Category: Original Research Paper

Received: May 16, 2021
Accepted: July 17, 2021
Published: November 15, 2021

Keywords:

monocyte-lymphocyte ratio, platelet-lymphocyte ratio, postmenopausal osteoporosis

***Corresponding author:**

Ibrahim Kale,

Umraniye Training and Research Hospital Elmalıkent Mahallesi Adem Yavuz Caddesi, Ümraniye, Istanbul, Turkey 34764

E-mail: dribakale@hotmail.com

Introduction

Osteoporosis is a chronic systemic disease characterized by increased bone fragility as a result of decreased bone density and deterioration in the microstructure of bone tissue [1]. While the production and resorption process in the bone tissue continues in a balanced way throughout life, bone resorption increases with the decrease in estrogen levels in the postmenopausal period. Osteoporotic fractures resulting from this are one of the most important causes of morbidity and mortality in the postmenopausal period.

In recent studies, it was found that inflammation plays an important role in the pathogenesis of postmenopausal osteoporosis; cytokines such as IL-1, IL-6 and TNF-α have been shown to be effective in osteoclast activation and bone resorption [2]. The frequent occurrence of postmenopausal osteoporosis, especially in chronic inflammatory diseases such as Systemic Lupus Erythematosus (SLE), Sjögren Syndrome and Rheumatiod Arthritis, also supports this relationship [3]. It is now known that neutrophils, monocytes, lymphocytes and platelets in the blood play an active role in systemic inflammation. In recent publications, the prognostic value of neutrophil lymphocyte ratio (NEU/LY), monocyte lymphocyte ratio (MO/LY) and platelet lymphocyte ratio (PLT/LY) has been investigated in cancer patients [4], autoimmune diseases [5], cardiovascular diseases [6] and even pulmonary embolism [7]. Again, the relationship between mean platelet volume [8] and the ratio between mean platelet volume and platelet count with cardiovascular diseases was investigated in various studies [9].

In our study, we aimed at investigating the relationship between NEU/LY, MO/LY, PLT/LY, MPV/LY, MPV/PLT, PCT/PLT and postmenopausal osteoporosis.

To cite this article: Ibrahim Kale. The predictive role of monocyte-lymphocyte ratio and platelet-lymphocyte ratio in postmenopausal osteoporosis. *J Clin Invest Surg*. 2021;6(2):141-147. doi: 10.25083/2559.5555/6.2.9

Materials and Methods

The data of the patients who were admitted to Ümraniye Training and Research Hospital between January 2017 and July 2020 and had both bone mineral densitometry and hemogram tests on the same day were retrospectively scanned from the hospital records. Patients with diabetes, adrenal, thyroid and parathyroid gland dysfunction, liver or kidney dysfunction, history of oncological, hematological disease, rheumatological, autoimmune or atherosclerotic coronary artery disease or hyperlipidemia and who had experienced surgical menopause or received medication for postmenopausal osteoporosis or postmenopausal hormone replacement therapy, history of trauma or acute infection within 6 months and history of pathological fracture or blood transfusion or steroid use within the last year and also smokers were excluded from the study. Out of the 514 patients, 177 patients who were in natural menopause for at least one year were included in the study.

The bone mineral density of the patients was measured in the supine position at the femur neck and L1-L4 vertebra with the Horizon DXA System Hologic device using the dual X-Ray absorptiometry (DXA) method. According to the criteria recommended by the World Health Organization, patients with femur neck or lumbar spine L1-L4 T score values of -2.5 or less were diagnosed with osteoporosis; patients with -1.0 to -2.5 osteopenia and more than -1.0 were diagnosed with normal bone density. On the same day, the hemogram results were obtained from the peripheral blood of the patients. A complete blood count was performed in an automated hematology analyzer Mindray BC6800 machine. Age, body mass index (BMI), duration of menopause, hemogram results, femur neck, femur total and lumbar spine L1-L4 T score, as well as bone mineral density (g/ cm2) were recorded.

NEU/LY was calculated by neutrophil count/ lymphocyte count, MO/LY was calculated by monocyte count/ lymphocyte count, PLT/LY was calculated by platelet count/ lymphocyte count, MPV/LY was calculated by mean platelet volume/ lymphocyte count, MPV/PLT was calculated by mean platelet volume/ platelet number, PCT/PLT was calculated by plateletcrit/ platelet count. The BMI of the patients was calculated by the following formula: Body Weight/ Height Square (kg / m2).

Results

The data were analyzed using the Spss 22.0 package program. Through the Kolmogorov Smirnov test, it was tested whether the distribution of the data revealed normal distribution. While evaluating the study data, in addition to descriptive statistical methods (mean, standard deviation, frequency), One Way Anova test for parametric data and Kruskal Wallis H test for non-parametric data were used for the comparison of more than 2 groups. For the comparison of 2 groups, the Independent Sample T test was used for parametric data and Man-Whitney U test was used for non-parametric data. The significance was evaluated at $p < 0.05$ levels for all the values. ROC analysis was used to calculate the sensitivity and specificity values in the study.

Firstly, a number of 177 patients were divided into three groups: 48 with osteoporosis, 103 with osteopenia and 26 with normal bone mineral density, as part of the control group.

While there was no statistically significant difference between the three groups in terms of mean age, the BMI was statistically significantly higher in the control group ($p = 0.001$), and the duration of menopause was shorter than the osteopenia and osteoporosis group ($p = 0.007$). the leukocyte count, neutrophil count, monocyte count, red blood cell count, mean corpuscular hemoglobin concentration (MCHC), platelet count, mean platelet volume (MPV), plateletcrit (Pct) and the platelet distribution width (PDW) were similar in all three groups. The lymphocyte count, hemoglobin level, hematocrit level, mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) levels were statistically significantly lower in the osteoporosis group (respectively, $p = 0.014$, $p = 0.02$, $p = 0.05$, $p = 0.022$, $p = 0.048$) (Table 1).

There was no statistically significant difference between the three groups in terms of neutrophil lymphocyte ratio, mean platelet volume lymphocyte ratio, mean platelet volume platelet count ratio and plateletcrit platelet count ratio. The monocyte-lymphocyte ratio and the thrombocyte-lymphocyte ratio were statistically significantly higher in the osteoporosis group ($p = 0.002$ and $p < 0.001$, respectively) (Table 2).

We accepted the osteopenia and osteoporosis group as the group of patients with low bone mineral density ($n = 151$) and compared with the control group with normal bone mineral density ($n = 26$). While there was no statistically significant difference between the two groups in terms of mean age, the body mass index was higher in the control group ($p = 0.001$) and the duration of menopause was shorter ($p = 0.005$). Leukocyte, neutrophil, monocyte, lymphocyte, red blood cell and platelet count and hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, mean platelet volume, plateletcrit, and platelet distribution width were similar in the two groups (Table 3).

While there was no statistically significant difference between the patient and the control groups in terms of neutrophil lymphocyte ratio, thrombocyte lymphocyte ratio, the mean thrombocyte volume lymphocyte ratio, the mean thrombocyte volume, the thrombocyte count ratio and the plateletcrit thrombocyte count ratio, the monocyte lymphocyte ratio was statistically significantly higher in the patient group ($p = 0.011$) (Table 4).

Table 1. Clinical and laboratory characteristics of the control, osteopenia and osteoporosis groups

	Control Group n=26	**Osteopenia Group n=103**	**Osteoporosis Group n=48**	**p value**
Age (years)	56,90 ± 6,238	58,92 ± 8,644	61,10 ± 7,957	0,095
BMI (kg/m2)	33,45 ± 4,58	30,15 ± 5,73	28,59 ± 5,05	**0,001**
Duration of menopause (year)	7,85 ± 7,71	12,27 ± 9,52	14,06 ± 8,59	**0,007**
Femur neck BMD (g/cm^2)	0,86 ± 0,08	0,71 ± 0,08	0,62 ± 0,09	**<0,001**
Femur total BMD (g/cm^2)	1,02 ± 0,09	0,87 ± 0,10	0,77 ± 0,11	**<0,001**
L1-L4 BMD (g/cm^2)	1,033 ± 0,07	0,884 ± 0,089	0,733 ± 0,109	**<0,001**
Leukocyte count	6757,69 ± 1852,38	6823,01 ± 1609,78	6645,83 ± 1766,99	0,860
Neutrophil count	3614,62 ± 1175,05	3827,09 ± 1344,47	3899,58 ± 1294,1	0,547
Monocyte count	392,69 ± 128,73	417,09 ± 129,29	432,92 ± 149,11	0,555
Lymphocyte count	2505 ± 692,78	2361,46 ± 520,02	2121,88 ± 562,95	**0,014**
RBC (10^6/mL)	4,52 ± 0,31	4,54 ± 0,31	4,53 ± 0,45	0,947
Hemoglobin (g/dl)	13,07 ± 1,2	13,29 ± 0,89	12,65 ± 1,13	**0,002**
Hematocrit (%)	39,39 ± 3,52	40,06 ± 2,55	38,42 ± 3,02	**0,005**
MCV (fL)	87,17 ± 4,16	88,38 ± 4,48	85,32 ± 6,77	**0,022**
MCH (pg)	28,94 ± 1,82	29,33 ± 1,72	28,13 ± 2,69	**0,048**
MCHC (g/dl)	33,18 ± 0,96	33,18 ± 0,86	32,93 ± 1,18	0,320
Platelet count	255884,62 ± 49705,8	252087,38 ± 54913,86	277854,17 ± 87840,76	0,317
MPV (fL)	9,63 ± 1,3	9,9 ± 1,41	9,8 ± 1,35	0,664
PCT (%)	0,24 ± 0,05	0,25 ± 0,06	0,27 ± 0,08	0,230
PDW (%)	16,4 ± 0,83	16,39 ± 0,81	16,42 ± 1	0,957

BMI: Body Mass İndex, BMD: Bone Mineral Density, RBC: Red Blood Cell, MCV: *Mean Corpuscular Volume, MCH:* Mean Corpuscular Hemoglobin, MCHC: Mean Corpuscular Hemoglobin Concentration, MPV: Mean Platelet Volüme, PCT: *Plateletkrit,* PDW: Platelet Distribution Width

Table 2. Comparison of the groups in terms of NEU/LY, MO/LY, PLT/LY, MPV/LYY, MPV/PLTLT, PCT/PLTLT.

	Control Group n=26	**Osteopenia Group n=103**	**Osteoporosis Group n=48**	**p value**
NEU/LY	1,47 ± 0,41	1,67 ± 0,63	1,91 ± 0,74	0,200
MO/LY	0,16 ± 0,03	0,18 ± 0,06	0,21 ± 0,07	**0,002**
PLT/LY	107,94 ± 29,52	110,66 ± 29,8	132,83 ± 29,4	**<0,001**
MPV/LY	0,0041 ± 0,0013	0,0044 ± 0,0012	0,005 ± 0,0015	0,200
MPV/PLT	0,0000397 ± 0,000013	0,0000414 ± 0,000012	0,0000383 ± ,000011	0,375
PCT/ PLT	0,0000010 ± 0,00000013	0,0000010 ± 0,00000014	0,0000010 ± 0,00000014	0,703

NEU / LY: neutrophil lymphocyte ratio, MO / LY: monocyte lymphocyte ratio, PLT / LY: platelet lymphocyte ratio, MPV / LY: mean platelet volume lymphocyte ratio, MPV / PLT: mean platelet volume platelet count ratio, PCT / PLT: plateletcrit platelet ratio

Table 3. Clinical and laboratory characteristics of the control and patient group

	Control Group n=26	Patient Group (osteopenia + osteoporosis) n=151	p value
Age (years)	56,9 ± 6,238	59,61 ± 8,467	0,077
BMI (kg/m2)	33,45 ± 4,58	29,65 ± 5,553	**0,001**
Duration of menopause (year)	7,85 ± 7,71	12,84 ± 9,24	**0,005**
Femur neck BMD (g/cm2)	0,86 ± 0,084	0,68 ± 0,093	**<0,001**
Femur total BMD (g/cm2)	1,02 ± 0,092	0,84 ± 0,113	**<0,001**
L1-L4 BMD (g/cm2)	1,03 ± 0,07	0,84 ± 0,119	**<0,001**
Leukocyte count	6757,69 ± 1852,383	6766,69 ± 1657,506	0,916
Neutrophil count	3614,62 ± 1175,051	3850,13 ± 1324,786	0,401
Monocyte count	392,69 ± 128,734	422,12 ± 135,605	0,351
Lymphocyte count	2505 ± 692,776	2285,3 ± 543,793	0,255
RBC (106/mL)	4,52 ± 0,313	4,54 ± 0,361	0,800
Hemoglobin (g/dl)	13,07 ± 1,203	13,09 ± 1,012	0,845
Hematocrit (%)	39,39 ± 3,523	39,54 ± 2,803	0,957
MCV (fL)	87,17 ± 4,157	87,41 ± 5,48	0,559
MCH (pg)	28,94 ± 1,816	28,95 ± 2,145	0,815
MCHC (g/dl)	33,18 ± 0,962	33,1 ± 0,974	0,722
Platelet count	255884,62 ± 49705,796	260278,15 ± 67920,263	9,865
MPV (fL)	9,63 ± 1,298	9,87 ± 1,39	0,418
PCT (%)	0,24 ± 0,045	0,26 ± 0,065	0,523
PDW (%)	16,4 ± 0,83	16,4 ± 0,874	0,85

BMI: Body Mass Index, BMD: Bone Mineral Density, RBC: Red Blood Cell, MCV: Mean Corpuscular Volume, MCH: Mean Corpuscular Hemoglobin, MCHC: Mean Corpuscular Hemoglobin Concentration, MPV: Mean Platelet Volume, PCT: Plateletcrit, PDW: Platelet Distribution Width

Table 4. Comparison of the groups in terms of NEU/LY, MO/LY, PLT/LY, MPV/LYY, MPV/PLTLT, PCT/PLTLT.

	Control Group n=26	Patient Group (osteopenia + osteoporosis) n=151	p value
NEU/LY	1,47 ± 0,415	1,75 ± 0,675	0,055
MO/LY	0,16 ± 0,031	0,19 ± 0,063	**0,011**
PLT/LY	107,94 ± 29,517	117,71 ± 31,339	0,281
MPV/LY	0,00413 ± 0,00129	0,00458 ± 0,00134	0,13
MPV/PLT	0,00004 ± 0,000013	0,00004 ± 0,000012	0,352
PCT/PLT	0,000001 ± 0,00000013	0,000001 ± 0,00000014	0,269

NEU / LY: neutrophil lymphocyte ratio, MO / LY: monocyte lymphocyte ratio, PLT / LY: platelet lymphocyte ratio, MPV / LY: mean platelet volume lymphocyte ratio, MPV / PLT: mean platelet volume platelet count ratio, Pct / PLT: plateletcrit platelet ratio

We performed ROC curve analysis to determine the diagnostic value of monocyte lymphocyte ratio in postmenopausal low bone mineral density. According to the ROC curve analysis, the area under the curve was 0.656 (95% confidence interval [CI]: 0.565-0.747) and the optimal cutoff value was 0.161 (65% sensitivity and 65% specificity) for the monocyte lymphocyte ratio (Figure 1).

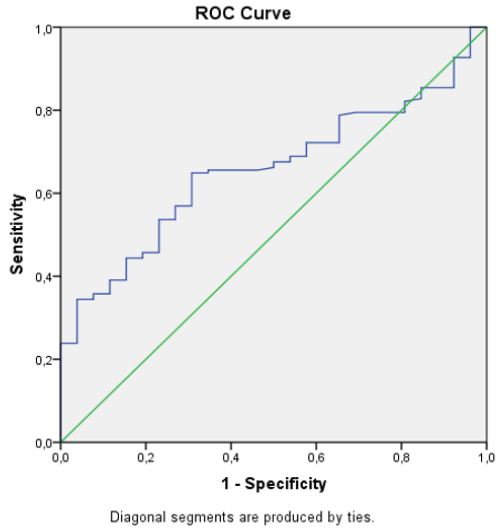

Figure 1. ROC curve showing the diagnostic value of monocyte lymphocyte ratio in detecting postmenopausal low bone mineral density.

Discussions

In current practice, the measurement of bone mineral density with dual X-ray absorptiometry is accepted as the gold standard in the diagnosis of postmenopausal osteoporosis, but it has been stated that methods such as quantitative computed tomography, high resolution peripheral quantitative tomography or ultrasonography can be used in the diagnosis of postmenopausal osteoporosis [1]. As an alternative to these complicated and expensive diagnostic methods, in this study, we investigated the role of the parameters in the hemogram examination in the diagnosis of postmenopausal osteoporosis.

In a study published by Huang et al. it was stated that the neurtophil lymphocyte ratio could be an important marker in the diagnosis of osteoporosis in postmenopausal women without diabetes [10]. In addition, Yu et al. found that the high neutrophil lymphocyte ratio was associated with arterial stiffness in women with postmenopausal osteoporosis [11]. In another paper published in 2017, the relationship between low bone mineral density and neutrophil lymphocyte ratio and platelet lymphocyte ratio was studied in postmenopausal women. While the thrombocyte lymphocyte ratio was found to be statistically significantly higher in the group with low bone mineral density compared to the group with normal bone mineral density ($p = 0.008$), such a relationship was not shown in the neutrophil lymphocyte ratio [12-14].

In an article published by Eroğlu et al., the relationship between postmenopausal osteoporosis and neutrophil lymphocyte ratio, monocyte lymphocyte ratio and thrombocyte lymphocyte ratio was studied. Out of these three parameters, only the thrombocyte lymphocyte ratio was found to be statistically significantly higher in patients with postmenopausal osteoporosis ($p = 0.02$) [15]. In another study published in 2019, the role of neutrophil lymphocyte ratio, monocyte lymphocyte ratio and platelet lymphocyte ratio in the diagnosis of osteoporosis in both men and women was investigated. All three parameters were found to be statistically significantly higher in patients with osteoporosis compared to the control group ($p <0.001$, $p <0.001$, $p = 0.001$, respectively). According to the ROC curve analysis, the diagnostic power of the monocyte lymphocyte ratio was higher than the ratio of neutrophil lymphocyte and thrombocyte lymphocyte (respectively AUC: 0.75 [95% CI: 0.698-0.808], AUC: 0.70 [95% CI: 0.556- 0.682], AUC: 0.619 [95% CI: 0.556-0.682) [16]. In our study, we found that the monocyte-lymphocyte ratio and the thrombocyte-lymphocyte ratio were statistically significantly higher in patients with postmenopausal osteoporosis compared to the control and osteopenia groups (respectively $p = 0.02$ and $p <0.001$). When we consider the osteopenia and osteoporosis group as the patient group with low bone mineral density and compare it with the control group, the monocyte-lymphocyte ratio was significantly higher in the patient group with low bone mineral density ($p = 0.11$). However, there was no significant difference between the two groups in terms of platelet-lymphocyte ratio. In our study, according to the ROC curve analysis, we found the optimal cuttoff value of 0.16 with 65% sensitivity and 65% specificity in detecting postmenopausal low bone mineral density of monocyte lymphocyte ratio (AUC: 0.656 [95% CI: 0.565-0.747).

In a study including 338 postmenopausal women, examining the relationship between the number of peripheral blood cells (erythrocyte, leukocyte and platelet) and bone mineral density, it has been reported that there is a positive relationship between the number of peripheral blood cells and bone mineral density. In women with osteoporosis and osteopenia, the number of all peripheral blood cells was found to be statistically significantly lower than in women with normal bone mineral density [17]. In another article published in 2020, the relationship between platelet count and bone mineral density was examined. In this study, which included 2,877 postmenopausal women and 2,304 male patients over the age of 50, it was stated that high platelet count was statistically significantly associated with osteopenia and osteoporosis, and cutoff values were given as 217 × 103 / μL for osteopenia and 269 × 103 / μL for osteoporosis [18]. Li et al. investigated the relationship between the mean platelet volume and bone

mineral density in postmenopausal women. A statistically significantly higher mean platelet volume was found in patients with postmenopausal osteoporosis compared to the control and osteopenia groups ($p < 0.001$), and it was suggested that increased platelet volume was associated with low bone mineral density [19]. The fact that patients with diabetes and hypertension, as well as patients using anti-platelet drugs and statins were included in this study, has been criticized as it may affect the results of the study. In a study published by Akbal et al. in 2014, the mean platelet volume and the platelet distribution width were found to be statistically significantly lower in patients with osteoporosis compared to the control and osteopenia groups ($p = 0.004$, $p = 0.034$, respectively) [20]. Unlike the four studies above, we also looked at the number of erythrocytes, leukocytes and platelets, mean platelet volume, platelet distribution width, mean platelet volume-lymphocyte ratio, mean platelet volume-platelet count ratio and plateletcrit-platelet count ratio in our own study and we did not find a statistically significant relationship with postmenopausal osteoporosis in any of them.

In the literature, different results were obtained in many studies examining the relationship between hemogram parameters and osteoporosis [21,22]. We think that the heterogeneity of the groups included in the study (gender, surgical or natural menopause status, etc.), chronic diseases or the drugs used by the patients caused differences in the results. The limitations of our study are that our study was single-centered and retrospective, the number of our patients was low, and the calcium and vitamin D levels of the patients were not known.

Conclusions

In conclusion, in our study, we found that the monocyte-lymphocyte ratio and the thrombocyte-lymphocyte ratio were statistically significantly higher in women with osteoporosis who had been in natural menopause for at least one year and did not have any chronic disease or drug use, compared to the osteopenia and control groups. We also found that the monocyte-lymphocyte ratio is a useful marker that can be used to detect low bone mineral density in the postmenopausal period. We believe that the monocyte-lymphocyte ratio and the thrombocyte-lymphocyte ratio will be an easy and cheap marker for routine use in the diagnosis of postmenopausal osteoporosis with studies to be conducted on a larger number of patients.

Abbreviations

RBC: red blood cell, MCHC: Mean Corpuscular Hemoglobin Concentration, MCV: Mean Corpuscular Volume, MCH: Mean Corpuscular Hemoglobin, MPV: Mean Platelet Volume, Pct: Plateletcrit, PDW: Platelet Distribution Width, NEU/LY: neutrophil to lymphocyte ratio, MO/LY: monocyte to lymphocyte ratio, PLT/LY: platelet to lymphocyte ratio, MPV/LY: mean platelet volume to lymphocyte ratio, MPV/PLT: mean platelet volume to platelet ratio, PCT/PLT: plateletcrit to platelet ratio, DXA: dual X-Ray absorptiometry, BMI: body mass index

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

Compliance with ethical standards

The ethical approval of the study was obtained from the local Institutional Ethics Committee (B.10.1.TKH.4.34.H.GP.0.01 / 216) and the study was conducted in accordance with the Declaration of Helsinki.

References

1. Schultz K, Wolf JM. Emerging Technologies in Osteoporosis Diagnosis. *J Hand Surg Am*. 2019 Mar; 44(3):240-243. doi: 10.1016/j.jhsa.2018.07.006.
2. Lorenzo J, Horowitz M, Choi Y. Osteoimmunology: interactions of the bone and immune system. *Endocr Rev*. 2008 Jun;29(4):403-40. doi: 10.1210/er.2007-0038
3. Adami G, Fassio A, Rossini M, Caimmi C, Giollo A, Orsolini G, Viapiana O, Gatti D. Osteoporosis in Rheumatic Diseases. *Int J Mol Sci*. 2019 Nov 22; 20(23):5867. doi: 10.3390/ijms20235867
4. Ethier JL, Desautels D, Templeton A, Shah PS, Amir E. Prognostic role of neutrophil-to-lymphocyte ratio in breast cancer: a systematic review and meta-analysis. *Breast Cancer Res*. 2017;19(1):2. doi: 10.1186/s13058-016-0794-1
5. Erre GL, Paliogiannis P, Castagna F, Mangoni AA, Carru C, Passiu G, Zinellu A. Meta-analysis of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio in rheumatoid arthritis. *Eur J Clin Invest*. 2019 Jan;49(1):e13037. doi: 10.1111/eci.13037
6. Yu S, Arima H, Bertmar C, Clarke S, Herkes G, Krause M. Neutrophil to lymphocyte ratio and early clinical outcomes in patients with acute ischemic stroke. *J Neurol Sci*. 2018 Apr 15;387:115-118. doi: 10.1016/j.jns.2018.02.002
7. Ma Y, Mao Y, He X, Sun Y, Huang S, Qiu J. The values of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in predicting 30 day mortality in patients with acute pulmonary embolism. *BMC Cardiovasc Disord*. 2016 Jun 4;16:123. doi: 10.1186/s12872-016-0304-5

8. Erdem K, Ayhan S, Ozturk S, Bugra O, Bozoglan O, Dursin H, Yazici M, Daglar B. Usefulness of the mean platelet volume for predicting new-onset atrial fibrillation after isolated coronary artery bypass grafting. *Platelets*. 2014;25(1):23-6. doi: 10.3109/09537104.2013.767443
9. Azab B, Torbey E, Singh J, Akerman M, Khoueiry G, McGinn JT, Widmann WD, Lafferty J. Mean platelet volume/platelet count ratio as a predictor of long-term mortality after non-ST-elevation myocardial infarction. *Platelets*. 2011;22(8):557-66. doi: 10.3109/09537104.2011.584086
10. Huang C, Li S. Association of blood neutrophil lymphocyte ratio in the patients with postmenopausal osteoporosis. *Pak J Med Sci*. 2016;32(3):762-765. doi: 10.12669/pjms.323.10292
11. Yu XY, Li XS, Li Y, Liu T, Wang RT. Neutrophil-lymphocyte ratio is associated with arterial stiffness in postmenopausal women with osteoporosis. *Arch Gerontol Geriatr*. 2015 Jul-Aug;61(1):76-80. doi: 10.1016/j.archger.2015.03.011
12. Koseoglu SB. Bone loss & platelet-to-lymphocyte ratio. *Biomark Med*. 2017 Jan;11(1):5-10. doi: 10.2217/bmm-2016-0188
13. Miulescu RD, Guja L, Ochiana LC, Ungurianu A, Șeremet OC, Ștefănescu E. Serum markers of bone fragility in type-2 diabetes mellitus. *J Mind Med Sci*. 2019; 6(1): 78-85. doi: 10.22543/7674.61.P7885
14. Andrei CA, Scăunașu RV, Simionescu AA, Burcoș T, Lupușoru MD, Lica G. The incidence of haemorrhagic and thrombo-embolic events after breast cancer surgery in patients treated with pharmacological thrombo-prophylaxis. *J Clin Invest Surg*. 2019; 4(1): 10-18. doi: 10.25083/2559.5555/4.1/10.18
15. Eroglu S, Karatas G. Platelet/lymphocyte ratio is an independent predictor for osteoporosis. *Saudi Med J*. 2019;40(4):360-366. doi: 10.15537/smj.2019.4.24009
16. Gao K, Zhu W, Liu W, Ma D, Li H, Yu W, Li Q, Cao Y. The predictive role of monocyte-to-lymphocyte ratio in osteoporosis patient. *Medicine (Baltimore)*. 2019;98(34):e16793. doi: 10.1097/MD.0000000000016793
17. Kim HL, Cho HY, Park IY, Choi JM, Kim M, Jang HJ, Hwang SM. The positive association between peripheral blood cell counts and bone mineral density in postmenopausal women. *Yonsei Med J*. 2011 Sep;52(5):739-45. doi: 10.3349/ymj.2011.52.5.739
18. Kim J, Kim HS, Lee HS, Kwon YJ. The relationship between platelet count and bone mineral density: results from two independent population-based studies. *Arch Osteoporos*. 2020 Mar 12;15(1):43. doi: 10.1007/s11657-020-0700-4
19. Li XS, Zhang JR, Meng SY, Li Y, Wang RT. Mean platelet volume is negatively associated with bone mineral density in postmenopausal women. *J Bone Miner Metab*. 2012 Nov;30(6):660-5. doi: 10.1007/s00774-012-0362-4
20. Akbal A, Gökmen F, Gencer M, Inceer BS, Kömürcü E. Mean platelet volume and platelet distribution width can be related to bone mineralization. *Osteoporos Int*. 2014;25(9):2291-5. doi: 10.1007/s00198-014-2764-8
21. Gavrilă MT, Cristea S, Antoneac E. Study on the arthroscopic repair of the rotator cuff tear. *J Clin Invest Surg*. 2019;4(1):38-41. doi: 10.25083/2559.5555/4.1/38.41
22. Tudorachi NB, Eva I, Dascalu CG, AL-Hiary R, Barbieru B, Paunica M, Motofei C, Moraru AC. The influence of serum calcium and magnesium levels in the radiological evolution of knee osteoarthritis. *J Mind Med Sci*. 2020;7(2):217-226. doi: 10.22543/7674.72.P217226