Original Article

The Association between Bone Mineral Density and Complete Blood Count in Postmenopausal Women: A Cross-Sectional Study

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Objective: To demonstrate the relationship between anemia and complete blood count (CBC) parameters with bone mineral density (BMD) in postmenopausal women.

Materials and Methods: A cross-sectional chart-review study was conducted between November 2017 and June 2019. Three hundred twenty-four postmenopausal women aged 50 years or older who had BMD and CBC results were included in the present study.

Results: The prevalence of osteopenia and osteoporosis diagnosed by T-score were 53.1% and 32.7%, respectively. Simple and multiple linear regression analyses showed that no association between CBC parameter with BMD except basophil count, which was negatively associated with BMD (p=0.011). There was no correlation between anemia and BMD status (p=0.168).

Conclusion: CBC parameters such as hemoglobin or white blood cell count were not statistically correlated with BMD. This is the first study demonstrating that basophil count may be an associated factor for deceased BMD.

Keywords: Postmenopausal women, Bone mineral density, Complete blood count, Basophil

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The association between hematologic diseases and the complete blood count (CBC) parameter on bone mineral density (BMD) is debatable[1]. Many studies have shown an association between hematologic diseases and BMD. Anemia is considered to be an associated factor with respect to osteoporotic fracture[2-5] and low BMD of the spine in postmenopausal women[6]. Thalassemia and sickle cell anemia have commonly been reported to affect BMD and fracture risk[7,8].

The previous study hypothesized that osteoblast dysfunction may cause stem cell dysfunction during hematopoiesis and inadequate bone formation. Loss of bone mass leads to a change of the micro-architecture of the bone marrow, and the marrow space is substituted with fat tissue instead of hematologic stem cells. However, the cause-and-effect relationship have not been identified[9].

Regarding the CBC parameters, hemoglobin and hematocrit levels have been revealed to have an association with BMD. Hemoglobin level has been shown to have a positive correlation with BMD in many previous reports[10-12]. Moreover, other parameters in CBC including total white blood cell (WBC) count, red blood cell (RBC) count, and platelet count have been demonstrated as having a positive correlation with BMD in postmenopausal women[9]. In addition, high neutrophil count and low monocyte count were found in men with lower hip BMD[13].

Many studies have shown the linkage between BMD and certain CBC parameters. One recent study could not show an association between BMD and the change in hemoglobin level either in men or women via T-score[14]. There was another report about an inverse association between hematocrit level and lumbar spine BMD in diabetic patients[15]. Therefore, the association between CBC parameters and BMD may need more elucidation. The present study aimed to reveal the association between CBC parameters and anemia with BMD in postmenopausal women. Types

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of WBC were also included in the analysis.

Materials and Methods

Study population

The present study was a cross-sectional study that enrolled postmenopausal women aged 50 years old or older who underwent BMD and CBC measurements at Bamrasnaradura Infectious Diseases Institute between November 2017 and June 2019. Dual-energy X-ray absorptiometry (DXA) was performed at two sites, the lumbar spine (L1 to L4) and the hip (femoral neck and total hip). All participants were performed by using the same DXA machine (Discovery Wi, Hologic, USA) with a professionally trained technician. For participants with more than one densitometry record, only the first measurement for that individual was included. Participants previously diagnosed or receiving treatment for osteoporosis, anemia, chronic infection, autoimmune diseases, or hyperthyroid disease were excluded. The study protocol was approved from the Institutional Review Board of Bamrasnaradura Infectious Diseases Institute (S024h/62_ExPD).

Data collection

Data collected included age, weight, height, body mass index (BMI), time since menopause, and BMD. The laboratory results including CBC parameters, creatinine, and estimated glomerular filtration rate (eGFR) were reviewed.

The CBC and creatinine data were collected from electronic medical records. The CBC data of the present study were collected from routine laboratory checks from underlying disease follow-ups. The CBC data recorded during acute illness conditions were excluded from analysis. The CBC data recorded during six months before the BMD measurement date and six months after the BMD measurement date were collected if there was more than one CBC value, and the value before BMD measurement date was collected for analysis. Hemoglobin level was used to diagnoses anemia according to the World Health Organization (WHO) criteria. Anemia in women was defined as a hemoglobin concentration less than 12 g/dL.

The lowest T-score among three values, the lumbar spine, femoral neck, and total hip, was defined as the T-score in the present analysis. The T-score interpretation used an Asian or Japanese matched value. Osteoporosis was diagnosed according to WHO criteria. The lowest T-score in femoral neck, total hip, or lumbar spine was used for classification. T-scores of −2.5 standard deviations (SD) or less below the reference mean were categorized as osteoporosis, T-scores between −1.0 and −2.5 SD as osteopenia, and T-scores −1.0 SD or greater as normal.

Statistical analysis

Descriptive analysis such as mean values with SD or median with the twenty-fifth to the seventy-fifth percentile ranges was performed. Simple and multiple linear regression analyses were used to estimate the association between variables of interest, including CBC parameters and T-scores. Sample size calculation was performed by using G*Power 3.1 software (University of Dusseldorf, Dusseldorf, Germany) determined a minimum of 175 participants were required for the effect size 0.15, for a statistical power greater than or equal to 90, for an α level of p-value less than or equal to 0.05 and for 16 predictors. Simple linear regression analysis was analyzed between variables and the T-score. Variables with p-values less than 0.25 in simple linear regression analysis or other variables of known clinical relevance were included for further multiple linear regression analysis[16]. Incidence rates of anemia and bone density status using the chi-square test were revealed. All data were analyzed using the IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). A p-value of less than 0.05 was considered statistically significant.

Results

One thousand one hundred one participants with a DXA result were included in the present study. There were 318 participants excluded because they took osteoporosis treatment, and 459 participants were also excluded because of the lack of CBC values. The remaining 324 women with a median age of 73.0 (67.0, 79.0) years were included in the analysis. The median T-score was –2.10 (–2.70, –1.50). The prevalence of osteopenia and osteoporosis diagnosed by the T-score was 53.1% (n=172) and 32.7% (n=106), respectively. Characteristics of the present study population are shown in Table 1.

The prevalence values of anemia in the normal bone density, osteopenia, and osteoporosis status group were 39.1%, 37.8%, and 49.0%, respectively. There were no significant differences in the prevalence of anemia among the three bone density status groups (p=0.168) (Figure 1).

The simple linear regression analyses showed the association of age, weight, height, body mass index, and basophil count with T-score (all $p<0.05$) (Table 2).

Table 1. Clinical characteristics of the study population

Clinical characteristics	Total (n=324); median (P25, P75)	Normal (n=46); median (P25, P75)	Osteopenia (n=172); median (P25, P75)	Osteoporosis (n=106); median (P25, P75)
Age (years)	73.0 (67.0, 79.0)	71.5 (66.0, 77.0)	72.0 (67.0, 78.0)	74.5 (69.0, 83.3)
Weight (kg)	58.0 (51.0, 65.0)	65.5 (56.5, 72.0)	59.5 (52.0, 66.0)	52.4 (48.0, 61.0)
Height (cm)	152.0 (150.0, 156.0)	152.5 (150.0, 158.0)	153.0 (150.0, 157.0)	150.0 (148.0, 155.0)
Body mass index (kg/m^2)	24.79 (22.01, 27.95)	27.62 (24.14, 31.05)	25.16 (22.66, 28.40)	22.79 (21.33, 26.45)
Time since menopause (years)	23.0 (18.0, 30.0)	22.0 (17.0, 26.0)	22.0 (17.0, 29.0)	22.5 (19.0, 35.5)
Laboratory parameters				
Creatinine (mg/dL)	0.81 (0.68, 1.00)	0.88 (0.73, 1.04)	0.78 (0.66, 1.01)	0.81 (0.70, 0.98)
eGFR	73.20 (54.68, 87.12)	67.25 (50.65, 83.14)	75.24 (54.47, 88.16)	71.77 (55.59, 85.69)
White blood cell (×10^3/mm^3)	6.40 (5.60, 7.60)	6.35 (5.68, 7.90)	6.40 (5.43, 7.38)	6.55 (5.60, 7.60)
Red blood cell (×10^6/mm^3); mean±SD	4.31±0.55	4.31±0.59	4.34±0.51	4.25±0.60
Platelet (×10^3/mm^3)	243.00 (208.25, 288.00)	249.50 (215.50, 307.25)	246.50 (210.25, 289.00)	234.00 (201.75, 277.00)
Hemoglobin (g/mm^3)	12.20 (11.30, 12.80)	12.20 (11.10, 12.90)	12.30 (11.43, 12.90)	12.00 (11.08, 12.70)
Hematocrit (%)	37.0 (35.0, 39.0)	37.0 (34.0, 39.25)	38.0 (35.0, 40.0)	37.0 (34.0, 39.0)
Neutrophil count (cell/mm^3)	3,677.0 (2,940.0, 4,658.3)	3,927.0 (3,104.3, 5,185.0)	3,609.0 (2,785.5, 4,389.0)	3,832.5 (3,105.5, 4,819.5)
Lymphocyte count (cell/mm^3)	1,986.0 (1,617.0, 2,400.0)	2,018.0 (1,557.5, 2,341.8)	2,019.5 (1,647.8, 2,455.3)	1,934.5 (1,548.0, 2,364.0)
Monocyte count (cell/mm^3)	455.0 (364.0, 579.0)	459.0 (348.3, 600.5)	444.5 (364.0, 565.3)	457.0 (374.0, 588.5)
Eosinophil count (cell/mm^3)	166.5 (92.5, 259.5)	190.0 (85.0, 313.5)	172.0 (94.0, 264.0)	150.0 (86.5, 234.0)
Basophil count (cell/mm^3)	44.5 (0.0, 64.0)	0.0 (0.0, 50.5)	48.5 (0.0, 64.0)	48.5 (0.0, 66.5)
Bone mineral density				
Lumbar spine T-score	−1.40 (−2.20, −0.30)	0.35 (−0.03, 1.03)	−1.30 (−1.80, −0.50)	−2.60 (−3.08, −1.73)
Femoral neck T-score	−1.90 (−2.50, −1.30)	−0.20 (−0.70, 0.20)	−1.70 (−2.08, −1.40)	−2.80 (−3.30, −2.50)
Total hip T-score	−0.70 (−1.40, −0.10)	0.80 (0.38, 1.40)	−0.60 (−1.00, −0.20)	−1.70 (−2.50, −1.30)
T-score	−2.10 (−2.70, −1.50)	−0.25 (−0.80, 0.13)	−1.90 (−2.20, −1.50)	−3.00 (−3.43, −2.70)

SD=standard deviation; P25=25th percentile; P75=75th percentile; eGFR=estimated glomerular filtration rate

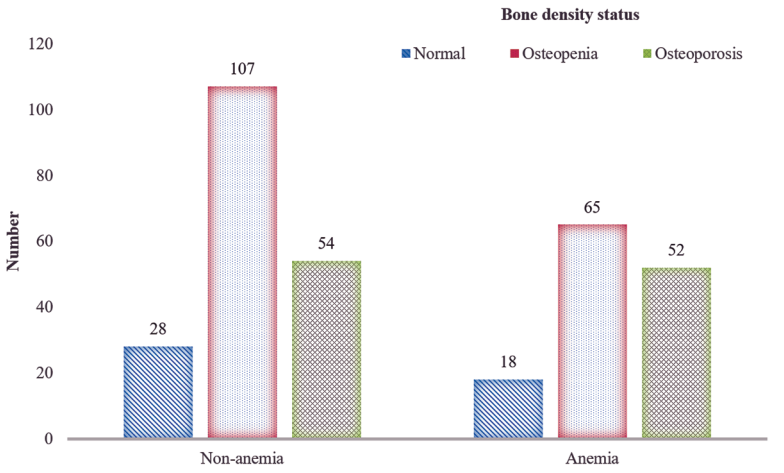

Figure 1. Prevalence of postmenopausal women according to bone density status and anemia status (p=0.168).

Age, weight, height, BMI, WBC counts, hemoglobin, hematocrit, neutrophil count, and basophil count were defined as significant independent factors in the simple linear regression models, which were corrected for the multiple linear regression analysis. Platelet count, lymphocyte count, monocyte

Table 2. Simple linear regression analyses of the relationship between variables and T-score

Variable	β (SE)	t	p-value	R^2
Age	–0.207 (0.007)	–3.788	<0.001	0.043
Weight	0.441 (0.005)	8.829	<0.001	0.195
Height	0.210 (0.010)	3.846	<0.001	0.044
Body mass index	0.227 (0.006)	4.173	<0.001	0.051
Creatinine	–0.003 (0.136)	–0.047	0.962	0.000
eGFR	0.002 (0.003)	0.027	0.978	0.000
White blood cell count	0.065 (0.035)	1.163	0.246	0.004
Red blood cell count	0.063 (0.107)	1.125	0.261	0.004
Platelet count	0.039 (0.001)	0.697	0.486	0.002
Hemoglobin	0.080 (0.050)	1.443	0.150	0.006
Hematocrit	0.098 (0.016)	1.766	0.078	0.010
Neutrophil count	0.072 (0.000)	1.300	0.195	0.005
Lymphocyte count	0.002 (0.000)	0.040	0.968	0.000
Monocyte count	0.048 (0.000)	0.868	0.386	0.002
Eosinophil count	0.038 (0.000)	0.691	0.490	0.001
Basophil count	–0.135 (0.001)	–2.441	0.015	0.018

B=standardized coefficient; SE=standard error; t=corresponding t values; R^2=percent variance explained by each variable; eGFR=estimated glomerular filtration rate

Table 3. Multiple linear regression analyses of the relationship between variables and T-score

Variable	β (SE)	t	p-value	VIF
Age	–0.238 (0.009)	–3.762	<0.001	1.391
BMI	0.196 (0.006)	3.512	0.001	1.084
eGFR	–0.124 (0.003)	–1.876	0.062	1.529
Platelet count	0.014 (0.001)	0.248	0.804	1.090
Hemoglobin	0.052 (0.052)	0.889	0.375	1.215
Neutrophil count	0.036 (0.000)	0.564	0.573	1.405
Lymphocyte count	–0.046 (0.000)	–0.805	0.421	1.160
Monocyte count	0.016 (0.000)	0.244	0.808	1.522
Eosinophil count	0.025 (0.000)	0.712	0.477	1.097
Basophil count	–0.140 (0.001)	–2.552	0.011	1.055

R square: 0.122, Adjusted R square: 0.09

B=standardized coefficient; SE=standard error; t=corresponding t values; VIF=variance inflation factor; BMI=body mass index

count, eosinophil count, and eGFR were analyzed in the model because of their clinical relevance to BMD[9,17-20]. The authors excluded weight, height, RBC count, WBC count, and hematocrit from the present study model due to multicollinearity problems. The basophil count was significantly associated with T-score (p=0.011) (Table 3).

Discussion

The study on the association between hematologic diseases and CBC parameters with BMD is inconclusive. The present study demonstrated no correlation between anemia and BMD, nor between CBC parameters and BMD except for basophil count. The study about the types of WBC and BMD was limited. A novel significant negative correlation between BMD and basophil count was found. The physiologic role of basophils remains unknown, although they are thought to play a role in host defense and allergic responses. There have been few reports about the relationship between basophil count and bone diseases. One study shows basophil count has been defined as a predicting factor of the inferior outcome of patients with primary myelofibrosis[21]. However, further study may be needed to determine the pathogenesis of this association.

One previous study showed that men who have BMD loss had a high neutrophil count and low lymphocyte count[13]. In the present study, total WBC count and other types of WBC were within the clinically normal range. Furthermore, the present study did not demonstrate any relationship between neutrophil and lymphocyte counts with BMD in postmenopausal women. Gender may be an important factor in determining the association between types of WBC and BMD.

The controversial relationship between CBC parameters and BMD may depend on age group, gender, or individual BMD site in each study. One previous study reported a positive correlation between CBC parameters and BMD[9]. The characteristics of the population between the previous study and the present study were different. The median age in the present study was higher than the previous report at 73.0 versus 61.2 years. Therefore, the median T-score was lower at –2.10 versus –0.98, and the prevalence of osteoporosis was higher in the present study compared to the former study at 33.3% versus 5%. There may be other confounding factors influencing this relationship[12]. The correlation between CBC parameters and BMD may be changed during life-time period. A larger sample size with age-subgroup analysis may be needed to elucidate the relationship between CBC parameters and BMD.

Another previous study demonstrated no association between BMD and a change in hemoglobin level either in men or women via T-score[14]. One previous report showed that anemia was not related to BMD loss[12]. Similarly, the present study found no correlation between hemoglobin level and T-score,

nor one between bone density status and anemia. The present study supports the idea that hemoglobin and anemia are not significantly associated with BMD. These findings suggest that a single hemoglobin measurement would not be a useful marker of low BMD in postmenopausal women.

The present study had many limitations. Firstly, sample size was limited to only women with complete data, such as the CBC result. Secondly, the CBC result was selected at a single time, which was close to the date of BMD measurement. Changes in the CBC data over a period of time may affect the study's results. Thirdly, the present study did not explore the cause of anemia, especially thalassemia, which has a high prevalence in Thailand and may affect BMD[22]. Fourthly, the present report did not study the consequences of low BMD, such as fracture and using lowest T-score rather than individual site T-score. Moreover, bone mineral content was not used in the analysis. Future studies should be conducted on different age groups and genders, as well as on the relationship between blood count changes and fracture rate or bone mineral content. Finally, because the present study was a retrospective study, some data such as vitamin D level and parathyroid hormone were missing and were not included in the analysis.

Conclusion

In conclusion, the present study reported no association between CBC parameters and anemia with BMD, except basophil count that may have a negative relationship with BMD.

What is already known on this topic?

The association between hematologic diseases and the CBC parameter on BMD is debatable and need more elucidation. Moreover, there has been no study about type of WBC and BMD.

What this study adds?

This study could not demonstrate the correlation between anemia and other CBC parameters with BMD. From the authors' literature review, this is the first study that demonstrates that basophil count is negatively associated with BMD in postmenopausal women.

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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