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A correlative studies between osteoporosis and blood cell composition
Implications for auxiliary diagnosis of osteoporosis

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Abstract

Osteoporosis is defined as a metabolic skeletal disease characterized by a decrease of the bone mass per unit volume, caused by a variety of reasons. Increasing evidence indicate that the host inflammatory response was correlated with the occurrence and development of osteoporosis, and it has been recognized that T lymphocytes and B lymphocytes play a critical role in pathogenesis of inflammatory bone disease. Between January 2018 and December 2018, retrospective analysis of 487 patients (exclusion of patients with recent infections and hematologic disorders whose leukocyte counts or classifications are markedly abnormal) who underwent bone mineral density (BMD) examinations in Huzhou Central Hospital. The patients were divided into normal bone density group, osteopenia group, and osteoporosis group according to the T score of BMD in the left femoral neck, respectively. Statistics of the lymphocyte ratio and the monocyte ratio in the blood routine examination results during the same period were performed so as to make a comparison of the differences among the groups. The correlation of the lymphocyte ratio and monocyte ratio with the T score of BMD in the left femoral neck was also analyzed. The difference between neutrocyte ratio lymphocyte ratio and the monocyte ratio was statistically significant in both males and females among the normal bone density group, osteopenia group and osteoporosis group ($P < .01$ or $P < .05$). Inflammation plays an important role in the progression of osteoporosis. By monitoring these three indicators in blood routine examination, early intervention for osteoporosis may become possible.

Abbreviation: BMD = bone mineral density.

Keywords: bone mineral density, lymphocyte ratio, monocyte ratio, osteoporosis, T score of BMD

1. Introduction

Osteoporosis is defined as a metabolic skeletal disease characterized by a decrease of the bone mass per unit volume, caused by a

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variety of reasons.[1] It increases the risk of fractures, and the most frequent complications are the "typical" osteoporotic fractures occurring at the hip, spine, distal forearm, and proximal humerus. The number of hip fractures, especially in the geriatric population, is continuously increasing with a cumulative mortality rate varying from 20% to 40%.[2] The incidence of major osteoporotic fractures increased in the latter part of the last century in both sexes and declined in the last decade.[3] There were still an estimated 2.7 million hip fractures worldwide in 2010, of which 1,364,717 were preventable with the avoidance of osteoporosis (264,162 in men and 1,100,555 in women).[4] Therefore, osteoporosis is a problem that needs to be paid attention to and worth solving.

Increasing evidence indicate that the host inflammatory response was correlated with the occurrence and development of osteoporosis,[5] and it has been recognized that T lymphocytes and B lymphocytes play a critical role in pathogenesis of inflammatory bone disease.[6] However, few studies regarded inflammatory cells as an independent correlation factor of osteoporosis. And there is few articles focus on the changes of components in the blood of patients with osteoporosis. Blood routine is a commonly used laboratory test for blood cell composition. Our aim was to investigate the changes of blood cell composition in osteoporosis patients, to explore the correlation between blood cell composition and osteoporosis, and to speculate a feasible index for the auxiliary diagnosis of osteoporosis.

2. Objects and methods

2.1. Research objects

A total of 487 patients (exclusion of patients with recent infections and hematologic disorders whose leukocyte counts or

classifications are markedly abnormal), including 165 males with an average age of 58.48 ± 15.06 years old and 322 females with an average age of 62.66 ± 11.47 years old, who underwent bone mineral density (BMD) examinations in Huzhou Central Hospital from January 2018 to December 2018 were selected. All cases were certified by the Medical Ethics Committee of Huzhou Central Hospital.

2.2. Methods

We collected the dual-energy X-ray BMD values of 487 patients and leukocyte count, lymphocyte ratio, and monocyte ratio in the blood routine examination results at the same time. According to the T score of BMD in the left femoral neck, all cases were divided into normal bone density group ($-1 < T \leq 1$), osteopenia group ($-2.5 < T \leq -1$) and osteoporosis group($T \leq -2.5$) based on the diagnostic criteria of the world health organization.[7]

2.3. Statistical analysis

All statistical analyses were performed using SPSS version 19.0. Measurement data are expressed as mean $\pm$ standard deviation and analyzed using analysis of variance. Enumeration data are expressed as percentages and analyzed using the χ^2 test. Linear regression analysis was used to make correlation analysis. $P < .05$ was considered to indicate statistical significance.

3. Results

3.1. Analysis of the overall grouping situation of 487 patients

Among the 487 patients, osteoporosis patients accounted for 20.74%, and bone loss patients accounted for 43.74%. Female patients with osteoporosis accounted for 24.53% of the female group, male patients with osteoporosis accounted for 13.33% of the male group. The difference in prevalence rate between male and female was statistically significant ($\chi^2 = 8.33$, $P < .01$) (Table 1). In all cases, the difference between neutrocyte ratio, lymphocyte ratio, and the monocyte ratio was statistically significant among the normal bone density group, osteopenia group, and osteoporosis group ($P < .01$) (Table 2). Other components in the blood routine were not statistically significant among the three groups.

Table 1

Analysis of the overall grouping situation of 487 patients n (%).

Sex	Male (n = 165)	Female (n = 322)	Total
Bone density group	66 (40.00)	107 (33.23)	173 (35.52)
Osteopenia group	77 (46.67)	136 (42.24)	213 (43.74)
Osteoporosis group	22 (13.33)	79 (24.53)	101 (20.74)

3.2. Comparison of neutrocyte ratio, lymphocytes, and monocytes in female group

In female group, the difference among neutrocyte ratio, lymphocyte ratio, and the monocyte ratio was statistically significant among the normal bone density group, osteopenia group and osteoporosis group ($P < .05$) (Table 3).

3.3. Comparison of neutrocyte ratio, lymphocytes, and monocytes in male group

In male group, the difference among neutrocyte ratio, lymphocyte ratio, and the monocyte ratio was statistically significant among the normal bone density group, osteopenia group and osteoporosis group ($P < .01$) (Table 4).

3.4. Correlation analysis between neutrocyte ratio and T-score of bone density of left femoral neck

The T-score of bone density of the left femoral neck was negatively correlated with the neutrocyte ratio ($P < .01$) (Fig. 1).

3.5. Correlation analysis between lymphocyte ratio and T-score of bone density of left femoral neck

The T-score of bone density of the left femoral neck was positively correlated with the lymphocyte ratio ($P < .01$) (Fig. 2).

3.6. Correlation analysis between monocyte ratio and T-score of bone density of left femoral neck

The T-score of bone density of left femoral neck was negatively correlated with monocyte ratio ($P < .01$) (Fig. 3).

Table 2

Comparison of neutrocyte ratio, lymphocyte ratio, and monocyte ratio between groups in 487 patients ($\bar{x} \pm s$).

Group		Neutrocyte ratio	Lymphocyte ratio	Monocyte ratio	WBC counts
Normal	n = 173	56.79 ± 6.78	33.00 ± 6.53	6.21 ± 1.45	6.78 ± 1.01
Osteopenia	n = 213	64.24 ± 6.37	23.52 ± 6.07	8.23 ± 2.09	6.83 ± 0.99
Osteoporosis	n = 101	68.97 ± 4.53	17.90 ± 4.07	9.13 ± 2.30	6.80 ± 1.11
F		137.141	235.789	86.434	0.356
P		.000	.000	.000	.768

Table 3

Comparison of neutrocyte ratio, lymphocytes and monocytes in female group ($\bar{x} \pm s$).

Group		Neutrocyte ratio	Lymphocyte ratio	Monocyte ratio	WBC counts
Normal	n = 107	57.14 ± 6.73	32.84 ± 6.54	6.02 ± 1.44	6.73 ± 1.00
Osteopenia	n = 136	64.64 ± 6.47	23.44 ± 6.05	7.91 ± 2.11	6.80 ± 1.01
Osteoporosis	n = 79	69.80 ± 4.49	17.67 ± 4.20	8.53 ± 1.86	6.81 ± 1.12
F		101.247	163.776	49.886	0.346
P		.000	.000	.000	.772

Table 4

Comparison of neutrocyte ratio, lymphocytes and monocytes in male group ($\overline{x} \pm s$).

Group		Neutrocyte ratio	Lymphocyte ratio	Monocyte ratio	WBC counts
Normal	n=66	56.21±6.87	33.27±6.56	6.52±1.44	6.86±1.01
Osteopenia	n=77	63.55±6.17	23.67±6.14	8.79±1.95	6.88±0.96
Osteoporosis	n=22	65.97±3.26	18.74±3.53	11.30±2.48	6.87±0.99
F		33.508	67.622	61.878	0.321
P		.000	.000	.000	.792

4. Discussion

Bone diseases such as osteoporosis are the leading cause of fractures and have high morbidity and mortality worldwide. Skeletal pain and susceptibility to fracture are the main clinical manifestations of osteoporosis. With the explosion of the proportion of elderly and the serious social and economic burden[8] caused by osteoporosis fracture in many countries, osteoporosis is becoming an important global health concern. Immune dysfunction has been recognized as an important promoter of various bone diseases including osteoporosis,[9,10]

Huang and Li[5] have suggested that the increased level of neutrophil lymphocyte ratio (NLR) is associated with adverse outcomes inpatients with osteoporosis. Su et al[11] tested the hypothesis that the monocyte percentage among leukocytes could be a biomarker of osteoporosis in rheumatic diseases. However, there are few articles that clearly express the correlation between the blood cell composition and osteoporosis. How the cellular components of blood change in osteoporosis patients is a problem worth discussing. Meanwhile, there is no early, simple marker for osteoporosis, even the mild compression fracture itself reflects no clinical symptoms and the monitoring of inflammatory cytokines is complex for most laboratories.[11] Therefore, in this study, we analyzed the blood components of 487 patients with different bone densities to demonstrate the proportion change of inflammatory cells in blood of patients with osteoporosis.

The major findings of the present study are the following: The T-score of bone density was positively correlated with the lymphocyte ratio in both sexes, indicates that the lymphocyte ratio decreased with the increase of bone loss and the increased severity of osteoporosis. And the T-score of bone density was negatively correlated with monocyte ratio and neutrocyte ratio in both sexes, indicates that the monocyte ratio and neutrocyte ratio increased with the increase of bone loss and the increased severity of osteoporosis. We inferred that by continuous long-term monitoring lymphocyte ratio, monocyte ratio, and neutrocyte ratio, blood routine examination could be used for auxiliary diagnosis of osteoporosis.

Osteoporosis is closely related to inflammatory diseases such as rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, chronic obstructive pulmonary disease. In these
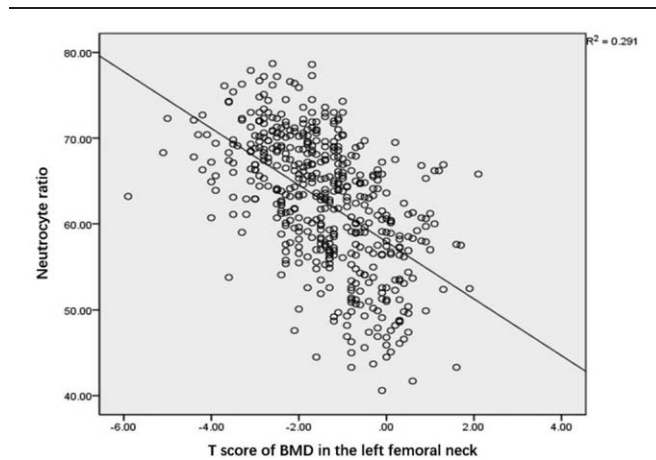

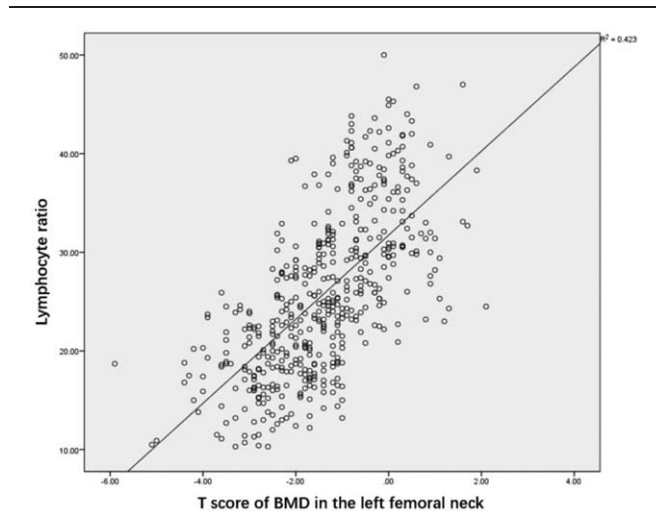Figure 1. Scatter diagram of neutrocyte ratios.

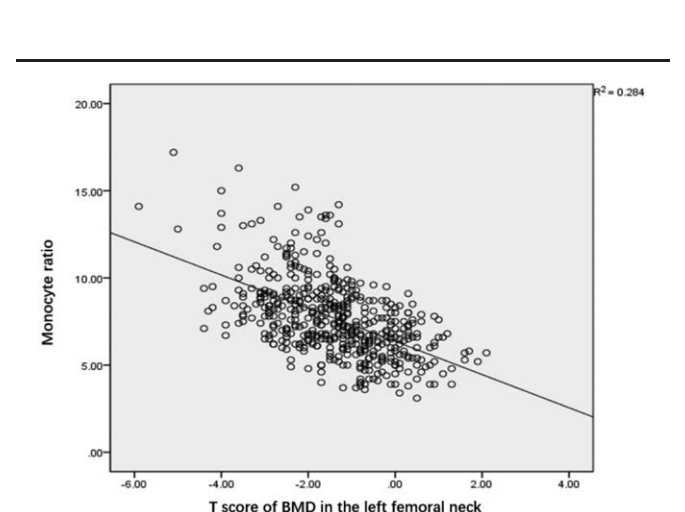
Figure 2. Scatter diagram of lymphocyte ratios.

Figure 3. Scatter diagram of monocyte ratios.

diseases, inflammation on the one hand led to the generation of the primary disease,[12,13] on the other hand, could affect the skeletal system and disrupt the balance of skeletal metabolism. In vitro and animal experiments found that there was a significant correlation between BMD and inflammatory cytokines, such as IL-1, IL-6, IL-17, IL-32, CRP, and TNF-α.[14–16] The effect of inflammatory cytokines on bone metabolism is mainly through the RANK/RANKL/OPG signaling pathway.[17–19]

Inflammatory markers play a modulating role through osteoclast activation by surrounding cytokines in bone formation and destruction.[20] Eghbali-Fatourechi et al[21] has reported increased RANKL production by both B- and T-cells in postmenopausal women and excessive activation of T lymphocytes and B lymphocytes has been considered an important cause of bone loss.[22] As in our study, we found lymphocyte ratio decreased with the increase of bone loss. Similar to our study, Valderrabano et al's[23] found that high BMD loss was associated with decreased lymphocyte counts. Some evidence[24–26] indicate that monocytes are also involved in bone changes associated with different diseases, such as thyroid toxic osteodystrophy, metastatic cancer, and ankylosing spondylitis. In this study, we found monocyte ratio increased with the increase of bone loss. Su et al[11] found that higher monocyte percentages could be an independent risk factor for osteoporosis in Chinese men. When the association of neutrocyte ratio with BMD was examined, neutrocyte ratio was significantly higher in the low BMD group and BMD values and neutrocyte ratio were found to be correlated. But contrary to our study, Valderrabano et al[23] showed that high BMD loss was associated with decreased monocyte counts in American older men, he suggested the increase in neutrophils may be related to the chronic inflammation that occurs with aging regardless of general health or co-morbidities. Chakravar et al[27] describes the neutrophil as a cell that acquires roles beyond that of a prototypic inflammatory cell, directly capable of activating osteoclasts through the RANKL signaling pathway and, consequently, abnormal bone erosions.

However, the results of this investigation also should be kept within the context of its limitations. First, the factor of race was not considered. The variation of ethnic groups in this study might, at least in part, originate from this diversity. Secondly, the sample size of this study is limited, the information of patient is incomplete and the data are inevitably biased, comprehensive statistical analysis with larger sample size, and more in-depth research are warranted to draw a firm conclusion of the true value of these two indicators in the clinical diagnosis of osteoporosis.

5. Conclusion

The proportion of inflammatory cells in peripheral blood may changes with the progression of osteoporosis in both sexes. Older Chinese people with BMD loss had low lymphocyte ratio, high monocyte ratio or high neutrophil ratio. By continuous long-term monitoring these three indicators in blood routine examination, early intervention for osteoporosis may become possible. Blood routine examination could be used for auxiliary diagnosis of osteoporosis.

Author contributions

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