



Correlation between capillaroscopic findings and bone mineral density results in the systemic lupus erythematosus patients

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Abstract

Introduction: Systemic lupus erythematosus (SLE) is an autoimmune disorder that can cause vascular involvement. The vascular changes can be seen in the bed of the nails. It was observed that SLE has a relationship with bone mineral density (BMD) changes.

Objectives: This study aimed to investigate the frequency and types of capillaroscopic change in SLE and its relationship between capillaroscopic changes with BMD in SLE.

Patients and Methods: Thirty-three patients with SLE who were referred to Resalat hospital (Tehran, Iran) underwent nailfold capillaroscopy (NFC). In addition, these patients were evaluated for BMD from spine and hip. Moreover, the correlation of these data was assessed.

Result: Scleroderma pattern was seen in 12.12% of patients, non-scleroderma pattern (NSP) in 27.3% patients and normal pattern in 60.6% based on NFC. There was no relationship between gender and NFC. The mean age was 43.30 years and 78.8% of patients were female. Dimension and morphological abnormalities had a relationship with scleroderma pattern ($P=0.033$ and $P=0.014$ respectively). There was a relationship between spine BMD and morphological abnormality too ($P=0.013$).

Conclusion: NFC is a good method for evaluating vascular change in patients with SLE and in this method, abnormal morphology and dimension have higher prevalence than other abnormalities in patients with SLE. Additionally, a relationship between abnormal morphology in NFC and spinal osteoporosis in SLE patients was detected.

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disorder with various clinical and immunological symptoms, including vascular involvement (1-3). The clinical manifestation of SLE, results from its complicated immunopathology, including autoantibodies formation and immune complex vasculitis with endothelial cell destruction (4). Chronic systemic inflammation causes vascular endothelial damage, which leads to blood vessel destruction (5,6). Microvascular involvement in rheumatic disorders has been investigated employing nailfold capillaroscopy (NFC), a non-invasive method. There are some different prevalence rates of the SLE's capillary abnormalities (7-11). Few SLE studies have shown a varied incidence of periungual capillary abnormalities, with typical NFC alterations occurring in 40%–90%

Key point

To investigate the capillaroscopic change in systemic lupus erythematosus (SLE) and its relationship with bone mineral density (BMD), 33 patients with SLE were evaluated. In these patients, 12.12% had scleroderma pattern and 27.3% had non-scleroderma pattern (NSP). The dimension and morphological abnormalities had a relationship with scleroderma pattern. There was a relationship between spine BMD and morphological abnormality.

of patients; consequently, others reporting only non-specific abnormalities (12-14). The presence of particular autoantibodies and the capillaroscopic alterations in the nailfolds appear to be seen (15).

Patients with SLE are at risk for osteopenia with a decrease in bone mineral density (BMD) (16-19). Patients with SLE are at high risk for decreased BMD because they



are female, usually use corticosteroids and may be of menopause age. Accordingly, these factors predispose patients with SLE to decrease BMD (20-22).

Objectives

There are few studies of the correlation between BMD and NFC in patients with SLE. The present study aimed to investigate the type and frequency of capillaroscopic findings in patients with SLE and the correlation between BMD and NFC in patients with SLE.

Patients and Methods

Study design

This prospective-descriptive study was conducted from 2016 January to 2020 January on 33 patients with SLE [diagnosis based on 1997 ACR (American College of Rheumatology) criteria], referred to Resalat hospital in Tehran. Inclusion criteria were SLE involvement, age greater than 18 years. Exclusion criteria were any other rheumatologic disorders involvement, age lower than 18 years, the reluctance of the patient to participate in the study. After obtaining informed consent from patients to participate in this study, patient demographic data, including age, gender, spine BMD, including value and its result, hip BMD, including value and its result and nail capillaroscopy data (dimension abnormality, microhemorrhage, capillary density changes and morphological abnormality) were recorded. Nail capillaroscopy was conducted and recorded by a rheumatologist.

Statistical analysis

After recording data, all data were analyzed using SPSS version 25. Quantitative data were described through the mean and standard deviation, and qualitative data were displayed with frequency and percentage. Independent t-test, chi-square and Fisher's exact test were used to compare study quantities based on capillaroscopic findings and compare BMD based on capillaroscopic pathology. Significance level was considered 5% for statistical tests. SPSS software version 25 was used for data analysis.

Results

Thirty-three patients with SLE were studied in this study. The mean age of patients was 43.30 years with a standard deviation of 12.97 years. The youngest and oldest patients were 16 and 72 years old, respectively. Twenty-

three patients (69.7%) were less than 50 years old and 10 (30.3%) were more than 50 years old. Seven (21.2%) were male and 26 (78.8%) were female. Two patients (6.1%) had underlying disorders and 31 patients (93.9) had recently detected SLE. According to the capillaroscopic findings, four patients had a scleroderma pattern. The prevalence of capillaroscopic findings for scleroderma pattern was 12.12% with a confidence interval (3.96%-29.14%). Capillaroscopy findings were normal in 20 patients (60.6%) and non-scleroderma pattern (NSP) in nine patients (27.3%).

The mean age of patients with typical capillaroscopy patterns was 47.05 ± 12.05 years, in NSP was 37.00 ± 12.09 years and in scleroderma pattern was 38.75 ± 15.65 years. There was no statistically significant difference between the ages of these three groups ($P=0.116$). Among patients under 50 years old, three patients (10%) and over 50 years old, three patients (13%) had a scleroderma pattern. In addition, according to capillaroscopic findings, four (15.4%) women had a scleroderma pattern, while none of the men had a scleroderma pattern. The proportion of patients with scleroderma patterns was not significantly different in terms of age ($P=0.999$) and gender ($P=0.555$).

Regarding BMD, five patients (15.2%) had osteopenia in the spine and eight patients (24.2%) in the hip. Scleroderma pattern was observed in two (7.1%) patients with normal BMD in the spine and two (40%) patients with osteopenia. The proportion of patients with scleroderma pattern who had spine osteopenia, was significantly higher than patients with hip osteopenia ($P=0.038$). Twelve percent of patients with normal BMD in the hip had a scleroderma pattern on the capillaroscopic findings, which was not statistically significant ($P=0.999$). The results are presented in [Table 1](#).

Based on capillaroscopic findings, abnormal morphology among 15 (45.5%) patients, bleeding of one (3%), dimension abnormality among six (18.2%), capillary density changes of two (6.1%) patients were seen. The proportion of patients with scleroderma patterns was zero among patients with normal morphology and 26.7% with abnormal morphology ($P=0.033$). Additionally, the proportion of patients with scleroderma patterns was 9.4% among normal and 100% abnormal bleeding in NFC. These results did not have a statistically significant difference based on Fisher's exact test ($P=0.121$). Besides, the proportion of patients with scleroderma patterns was

Table 1. Assessing capillaroscopy result of patients according to BMD level

Area	Level	Total	Capillaroscopy results		P value
			Scleroderma pattern	Normal NSP	
Spine BMD	Normal	28 (84.8)	2 (7.1)	26 (92.9)	0.038
	Osteopenia	5 (15.2)	2 (40)	3 (60)	
Hip BMD	Normal	25 (75.8)	3 (12)	22 (88)	0.999
	Osteopenia	8 (24.2)	1 (12.5)	7 (87.5)	

BMD, bone mineral density; NSP: non-scleroderma pattern.

normal (3.7%) and abnormal (50%) between dimensions of NFC results, which this difference was statistically significant ($P=0.014$) based on Fisher's exact test. The proportion of patients with scleroderma patterns was 9.7% among patients with normal and 50% with abnormal NFC results that were not significantly different ($P=0.231$). The proportion of patients with scleroderma pattern was 3.7% between patients with normal dimension capillary NFC results and 50% between abnormal dimension capillary NFC results, and there was no statistically significant difference ($P=0.014$) based on Fisher's exact test. The proportion of patients with scleroderma pattern with normal density was 9.7%, and abnormal in the 50% of patients who did not have a statistically significant difference ($P=0.231$; Table 2).

According to the BMD of the spine, none of the patients with normal morphology had osteopenia. However, 33.3% of patients with abnormal morphology had osteopenia. There is a statistically significant difference between patients with normal and abnormal morphological findings ($P=0.013$). There was no statistically significant difference between osteopenia based on the BMD of the spine and the pathological findings of capillary bleeding ($P=0.999$), dimension abnormality ($P=0.999$), and capillary density changes ($P=0.999$; Table 3).

Based on the BMD of the hip, 16.7% of patients with normal morphology and 33.3% with abnormal morphology

had osteopenia, which did not have a statistically significant difference between patients with normal and abnormal morphological findings ($P=0.418$). Moreover, 21.9% of patients with normal bleeding and 0% with abnormal bleeding in NFC results had osteopenia. Thus, there was no statistically significant difference between these two types of results ($P=0.242$). The proportion of patients diagnosed with osteopenia was 25.9% in the normal and 16.7% in the abnormal dimension results, which were not statistically significant ($P=0.999$).

In the patients who had osteopenia, 22.6% had normal capillary density changes and 50% had abnormal capillary density changes which showed no significant difference between capillary density changes in patients with hip osteopenia ($P=0.432$; Table 4).

Discussion

This study was conducted on 33 patients with SLE, referred to the hospital for BMD. NFC was taken from all patients. The mean age was 43 years, and approximately 70% of patients were lower than 50 years. Twelve percent of patients had a scleroderma pattern, 27% had an NSP, and the rest had a normal pattern. In the study by Lambova et al, "non-specific changes" in 30%, a normal pattern in 6.6%, and a scleroderma pattern in 13.3% of patients with SLE were seen. These two studies were similar regarding the rate of scleroderma and NSP in NFC of patients with

Table 2. Assessing capillaroscopy results of patients according to the type of pathology

Capillaroscopy pathology results		Total	Capillaroscopy results		P value
			Scleroderma pattern	Normal NSP	
Morphological ab ^b	Abnormal	15 (45.5)	4 (26.7)	11 (73.3)	0.033
	Normal	18 (54.5)	0 (0)	18 (100)	
Microhemorrhage	Abnormal	1 (3)	1 (100)	0 (0)	0.121
	Normal	32 (97.0)	3 (9.4)	29 (90.6)	
Dimension ab ^a	Abnormal	6 (18.2)	3 (50)	3 (50)	0.014
	Normal	27 (81.8)	1 (3.7)	26 (96.3)	
Capillary density changes	Abnormal	2 (6.1)	1 (50)	1 (50)	0.231
	Normal	31 (93.9)	3 (9.7)	28 (90.3)	

NSP: non-scleroderma pattern.

^a Enlarged loops and mega capillary.

^b Angiogenesis and architectural derangement.

Table 3. Assessing spine BMD level according to capillaroscopy pathologic results

Capillaroscopy pathology results		Spine BMD		P value
		Normal	Osteopenia	
Morphological ab ^b	Abnormal	18 (100)	0 (0)	0.013
	Normal	10 (66.7)	5 (33.3)	
Microhemorrhage	Abnormal	27 (84.4)	5 (15.6)	0.999
	Normal	1 (100)	0 (0)	
Dimension ab ^a	Abnormal	23 (85.2)	4 (14.8)	0.999
	Normal	5 (83.3)	1 (16.7)	
Capillary density changes	Abnormal	26 (83.9)	5 (16.1)	0.999
	Normal	2 (100)	0 (0)	

BMD, bone mineral density; NSP: non-scleroderma pattern.

^a Enlarged loops and mega capillary.

^b Angiogenesis and architectural derangement.

Table 4. Assessing hip BMD level according to capillaroscopy pathologic results

Capillaroscopy pathology results		Hip BMD		P value
		Normal	Osteopenia	
Morphological ab ^b	Abnormal	15 (83.3)	3 (16.7)	0.013
	Normal	103 (66.7)	5 (33.3)	
Microhemorrhage	Abnormal	25 (78.1)	7 (21.9)	0.999
	Normal	1 (100)	0 (0)	
Dimension ab ^a	Abnormal	20 (74.1)	7 (25.9)	0.999
	Normal	5 (83.3)	1 (16.7)	
Capillary density changes	Abnormal	24 (77.4)	7 (22.6)	0.999
	Normal	1 (50)	1 (50)	

BMD, bone mineral density; NSP: non-scleroderma pattern.

^a Enlarged loops and mega capillary.

^b Angiogenesis and architectural derangement.

SLE, however the rate of normal NFC was different in these two studies. This difference may be due to the different races in these two studies. The participants of these two studies were approximately similar in terms of age. In the current study, the mean age was 43 years, and in the study by Lambova et al, it was 49 years. The presence of elongated capillaries in 43% of SLE patients, increased tortuosity in 70%, and a sizeable sub-papillary plexus in 60% of cases were the most common capillaroscopic abnormalities. Dilated capillaries were observed in 80% of the patients, large capillary loops in 6.6%, and bleeding in 16.6%. Our study showed abnormal morphology in 45.5%, abnormal bleeding in 3%, dimension abnormality in 18.2%, capillary density changes, and 6.1% of patients with the SLE. The results obtained for different types of abnormalities were inconsistent with the study by Lambova et al (23).

In the study by Xia et al, osteopenia was observed in 13% of SLE patients. The frequency of osteoporosis was found to be more prevalent in the lumbar spine in patients. In our study, osteopenia was 24.2% in the hip BMD and 15.2% spine BMD. These results show a lower BMD value in the hip area than in the spine area in the patients with SLE. Accordingly, our study findings were inconsistent with the findings of Xia et al in this issue. In the report by Xia et al, BMD of the spine was assessed in patients with lupus, and its results were approximately similar to our study (24).

The study by Ruaro et al was conducted on patients with rheumatoid arthritis, systemic sclerosis, and normal participants. They showed that bone quality is lower in rheumatic disorders. Besides, in systemic sclerosis patients with changed microvasculature, bone quality appeared to be worse. In the present study, we found morphological change in the NFC in patients with SLE correlated with osteopenia in the spine. In addition, the morphology of nail capillaries has a significant relationship with lower BMD in the spine area. These findings were similar to the findings of the study by Ruaro et al, since spine BMD was evaluated in their study; however there is a difference in the study population. In this study, patients with SLE were evaluated, however in the report by Ruaro et al, patients with systemic sclerosis and rheumatoid arthritis were

evaluated. Nevertheless, there were similar findings of correlation of NFC abnormality with BMD in these two studies. In the future, more studies should be conducted to evaluate this correlation in different types of rheumatic disorders (25). Lower BMD in the spine area in patients with SLE has been seen in the study of Mendoza-Pinto et al, which is consistent with the results of above mentioned studies (26).

Likewise, the study by Atlan et al showed a relationship between low BMD and abnormal changes in NFC findings, including micro-architectural indices in patients with systemic sclerosis. In line with the study by Atlan et al, the current study scrutinized similar findings of the BMD of the spine (27).

Conclusion

There is a relationship between nail scleroderma-pattern of SLE with spinal BMD. In SLE patients with non-scleroderma-pattern and normal NFC, normal BMD is more prevalent but in patients with scleroderma-pattern, osteopenia should be considered. However, no relationship between scleroderma-pattern and hip BMD was detected. Nailfold scleroderma pattern has no relationship with age and gender in patients with SLE. There is a relationship between scleroderma-pattern with dimension abnormality and morphology in capillaroscopy results. The prevalence of scleroderma pattern is significantly higher in SLE patients with abnormally dimension results than other abnormalities. Besides, in patients with normal morphology results, the scleroderma pattern does not exist. According to capillaroscopy findings and BMD of the spine or hip, a correlation between the morphological abnormality of nail capillaries and spinal BMD and in patients who have spinal osteopenia should be considered. Accordingly, no significant relationship between BMD of the hip and capillaroscopy findings was seen.

Limitations of the study

This study was conducted on a relatively small size population. We suggest further investigation of our findings on larger samples.

Authors' contribution

AR and HS were the principal investigators of the study. AR, HS, PD, ME, AA, FF, ZA participated in preparing the concept and design. AR, MM and FF revisited the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Shahid Beheshti University of Medical Sciences approved this study (Ethical code #IR.SBMU.MSP.REC.1398.881). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from M.D thesis of Haleh Sadraee at this university (Thesis #193434). Additionally, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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