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The relationship of nailfold capillaroscopy patterns with clinical features, functional status, pain and fatigue in patients with systemic sclerosis

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ABSTRACT

Aim: To identify the frequency of scleroderma-type capillaroscopic patterns and evaluate the association of capillaroscopic patterns with clinical parameters, functional status, fatigue, and pain in systemic sclerosis (SSc).

Material and Method: This cross-sectional study included SSc patients consecutively between January 2017 and January 2019. Cutaneous involvement was evaluated with the modified Rodnan skin score (mRSS). The presence of digital ulcers, Raynaud phenomenon, interstitial lung disease, pulmonary hypertension, cardiac, gastrointestinal system (GIS), renal, joint and muscle involvement were recorded. The severity of the Raynaud phenomenon, fatigue, pain, and patient global assessment (PGA) was assessed on the Visual Analogue Scale (VAS). The Health Assessment Questionnaire (HAQ) and the Duruoz Hand Index (DHI) were used to assess physical disability and hand function, respectively. Nailfold videocapillaroscopic examinations of the patients were performed, and they were classified into four groups, including normal/non-specific, early, active, and late scleroderma patterns.

Results: The mean age of 32 patients with SSc (31 female, one male) was 48.93±12.77. Anormal capillaroscopic examination findings were detected in 93.7% of the patients, and the most common capillaroscopic pattern was the active pattern. The comparison of scleroderma pattern groups revealed no difference in age (p=0.224), but disease duration was shorter in the early pattern group (p=0.005). The duration and severity of the Raynaud phenomenon, and mean mRSS were lower in the early pattern group (p=0.004, p=0.009, and p=0.001, respectively). The digital ulcer (p=0.011) and diffuse cutaneous SSc (p=0.016) were more common in the late pattern group. The percentage of pulmonary hypertension (p=0.011), GIS involvement (p<0.001), and arthralgia (p=0.027) were higher in the late pattern group. Fatigue (p=0.575), pain (p=0.536), PGA (p=0.861), HAQ (p=0.164) and DHI (p=0.064) scores were not different between the capillaroscopy pattern groups.

Conclusion: Digital ulcer, pulmonary hypertension, and GIS involvement were more common in SSc patients with the late pattern. The fatigue, pain, physical disability, and hand function were similar between capillaroscopy pattern groups.

Keywords: Scleroderma, nailfold capillaroscopy, functional status

INTRODUCTION

Systemic sclerosis (SSc) is an autoimmune disease with microvascular changes followed by progressive tissue fibrosis. Characteristic microvascular changes in the nailfold area occur early and can be assessed with simple, non-invasive methods that allow early diagnosis of SSc (1-4).

The gold standard method for the evaluation of nailfold capillaries is videocapillaroscopy (2,4). It enables to differentiate primary Raynaud phenomenon and SSc. Capillaroscopy findings that occur in the majority of patients are specific for SSc (4). These capillaroscopy findings were described by Maricq et al. (5-7) as "scleroderma patterns". Cutolo et al. (8) classified the "scleroderma" type capillaroscopic patterns into three phases including "early" phase (few enlarged or giant

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capillaries, few capillary haemorrhages, no capillary loss), "active" phase (frequent giant capillaries and capillary haemorrhages, mild disorganization, moderate capillary loss) and "late" phase (few or no giant capillaries and haemorrhages, extensive avascular areas, disorganization, ramified/bushy capillaries). Findings of "scleroderma pattern" on capillaroscopy were included in the criteria for (very) early diagnosis of SSc and 2013 American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) classification criteria (9,10).

Nail fold videocapillaroscopic (NVC) examinations provide information for early diagnosis, prognosis and treatment efficacy in SSc (11), but its effects on functional status, hand function, fatigue, and pain are currently not known. This study aimed to 1) determine the frequency of scleroderma-type capillaroscopic patterns and 2) identify the associations of capillaroscopic scleroderma patterns with clinical parameters, functional status, fatigue, and pain in SSc.

MATERIAL AND METHOD

The study was carried out with the permission of Marmara University Faculty of Medicine Clinical Researches Ethics Committee (Date: 06.01.2017, Decision No: 09.2017.095). All procedures were performed in accordance with the 1964 Helsinki declaration. Informed consent was obtained from all participants.

Study Design and Cohort

This cross-sectional study included 32 patients diagnosed as SSc, according to the ACR/EULAR criteria for SSc (10). The SSc patients aged ≥18 years who presented to the outpatient clinic of Rheumatology were consecutively included in the study between January 2017 and January 2019. The exclusion criteria for the study were being younger than 18 years of age, having hand disorders related to Diabetes mellitus, neurological disorders, erosive osteoarthritis, and hand surgery or trauma.

Demographic and Clinical Variables

Data on age, sex, disease duration, age at diagnosis, smoking status, and body mass index (BMI) were recorded, and physical examinations were performed. Skin involvement was assessed using the modified Rodnan skin score (mRSS), and patients were grouped into diffuse cutaneous SSc (dcSSc) or limited cutaneous SSc (lcSSc) according to the extent of skin involvement (12,13). The presence of the Raynaud phenomenon and digital ulcer were evaluated separately, and the severity of these parameters was assessed on Visual Analogue Scales (VAS). Interstitial lung disease, pulmonary hypertension, cardiac, gastrointestinal system (GIS), renal, joint and muscle involvement were recorded in each patient. Pain, fatigue, and patient global assessment (PGA) were evaluated on VAS. The Health Assessment Questionnaire (HAQ) was used to evaluate physical disability (14). Hand function was assessed with Duruoz Hand Index (DHI), which is a valid scale for SSc (15,16).

NVC examinations of the patients were performed, and they were classified into four groups according to the findings of capillaroscopy: normal/non-specific, early, active, and late scleroderma patterns (8). The second-fifth fingernails were examined bilaterally in each patient. Before the examination, the patients rested for at least 15 minutes at room temperature (22–25 °C). Fingers affected by recent local trauma were excluded from analysis (17).

Statistical analysis

The statistical analysis was done using SPSS Statistics (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). A two-tailed P-value of <0.05 was considered significant. Categorical variables were summarized as frequency and percentages, and continuous variables were summarized as mean, standard deviation, median, minimum, maximum, 25th and 75th percentiles. Continuous variables were compared using the Mann-Whitney U and Kruskal-Wallis tests (with a post hoc test) because the variables had a non-normal distribution, according to the normality tests. Chi-square and Fisher's exact tests were used to assess the differences between categorical variables.

RESULTS

The mean age of 32 patients with SSc (31 female, one male) was 48.93±12.77. The median disease duration was 24 months (min-max: 3-216), and the mean age at diagnosis was 45.21±12.84 (**Table 1**).

Normal capillaroscopy findings were found in 6.3% of the patients. Capillaroscopic examination findings of the patients are given in **Table 2**. Capillary loss was detected in 53% of the patients, and digital ulcer (p=0.006), dcSSc (p=0.003), telangiectasia (p=0.031), pulmonary hypertension (p=0.006), and GIS involvement (p<0.001) were more common in those with capillary loss.

The comparison of scleroderma pattern groups revealed no difference in age (p=0.224) and age at diagnosis (p=0.677), but disease duration was shorter in the early pattern group (p=0.005). Although groups were not different regarding the presence of the Raynaud phenomenon (p=0.819), the duration and severity of the Raynaud phenomenon were lower in the early pattern group (p=0.004, and p=0.009, respectively). The digital ulcer was more common in the late pattern group (p=0.011). Mean mRSS was lower in the early pattern group (p=0.001). The dcSSc (p=0.016) was more common in the late pattern. The percentage of interstitial lung disease (p=0.274), renal

disease (p=0.470), and six-minute walking test (p=0.335) were similar between the capillaroscopy patterns. The percentage of pulmonary hypertension (p=0.011) and GIS involvement (p<0.001) were higher in the late pattern group. The percentage of arthralgia was higher in the late pattern group (p=0.027), but arthritis was not (p=0.254). Fatigue (p=0.575), pain (p=0.536), PGA (p=0.861), HAQ (p=0.164) and DHI (p=0.064) scores were not different between the capillaroscopy pattern groups (**Table 3**).

Table 1. Demographic and clinical characteristics of the patients

Variable	
Female (n, %)	31 (96.9)
Age (mean±SD)	48.93±12.77
Body Mass Index, kg/m2, (mean±SD)	29.40±5.79
Smoker (n, %)	7 (21.9)
Duration of disease, months, (median, min-max)	24 (3-216)
Age at diagnosis, year, (mean±SD)	45.21±12.84
Raynaud phenomenon (n, %)	30 (93.8)
Duration, months, (median, min-max)	24 (3-192)
Severity, VAS, (mean±SD)	6±2.21
Digital ulcers (n, %)	6 (18.8)
Severity, VAS, (mean±SD)	4.3±2.16
History of digital ulcers (n, %)	11 (34.4)
mRSS (median, min-max)	6.5 (0-29)
Diffuse cutaneous SSc (n, %)	8 (25.0)
Limited cutaneous SSc (n, %)	17 (53.1)
Telangiectasia (n, %)	5 (15.6)
Calcinosis (n, %)	3 (9.4)
Interstitial lung disease (n, %)	11 (34.4)
Pulmonary hypertension (n, %)	6 (18.8)
Cardiac disease (n, %)	0
Renal disease (n, %)	1 (3.1)
Gastrointestinal involvement (n, %)	8 (25.0)
Arthralgia (n, %)	21 (65.6)
Arthritis (n, %)	2 (6.3)
Myositis (n, %)	0
Tendon friction rub (n, %)	0
Fatigue, VAS, (mean±SD)	4.29±3.37
Pain, VAS, (median, min-max)	2 (0-9)
PGA, VAS, (mean±SD)	5.09±1.93
HAQ (median, min-max)	0.42 (0-1.35)
DHI (median, min-max)	3 (0-66)

SSc: Systemic Sclerosis, VAS: Visual Analogue Scale, mRSS: modified Rodnan skin scores, PGA: Patient global assessment, HAQ: Health Assessment Questionnaire, DHI: Duruoz Hand Index.

Table 2. Capillaroscopic examination findings of the patients

Variable	
Hemorrhages (n, %)	22 (68.8)
Enlarged/dilated capillaries (n, %)	19 (59.4)
Giant capillary (n, %)	24 (75.0)
Avascular area (n, %)	17 (53.1)
Disorganization of capillary architecture (n, %)	17 (53.1)
Neoangiogenesis (n, %)	3 (9.4)
Patterns	
Normal/non-specific pattern (n, %)	2 (6.3)
Early scleroderma pattern (n, %)	12 (37.5)
Active scleroderma pattern (n, %)	13 (40.6)
Late scleroderma pattern (n, %)	5 (15.6)

Table 3. Comparisons of patients between capillaroscopic pattern groups

	Normal/ Early Pattern N=14	Active Pattern N=13	Late Pattern N=5	P value
Age	45 (30.5-58)	52 (45.5-60.5)	54 (48.5-60)	0.224
Female	13 (92.9)	13 (100)	5 (100)	0.515
Body Mass Index	27.5 (20.7-32.5)	31.2 (26.6-34.5)	32.4 (23.9-35.4)	0.385
Smoking	3 (23.1)	4 (30.8)	0 (0)	0.458
Disease duration	12 (7-19.5)	48 (24-72)	60 (30-174)	0.005
Age at diagnosis	44 (27.7-56.5)	47 (37-57)	46 (43-50)	0.677
Raynaud phenomenon	13 (92.9)	12 (92.3)	5 (100)	0.819
Duration	12 (5-24)	48 (24-99)	132 (36-186)	0.004
Severity, VAS	4 (4-5.5)	7 (3.5-8)	8 (7.5-8.5)	0.009
Digital ulcers	0	3 (23.1)	3 (60)	0.011
Severity, VAS	0	4 (3-7)	3 (2-7)	0.500
History of digital ulcers	0	6 (46.2)	5 (100)	<0.001
mRSS	2 (0-5.5)	7 (4-11)	17 (9.5-26.5)	0.001
Diffuse cutaneous SSc	0	5 (38.5)	3 (60)	0.016
Limited cutaneous SSc	8 (57.1)	7 (53.8)	2 (40)	
Telangiectasia	0	3 (23.1)	2 (40)	0.067
Calcinosis	0	2 (15.4)	1 (20)	0.264
Interstitial lung disease	3 (21.4)	5 (38.5)	3 (60)	0.274
Pulmonary hypertension	0	3 (23.1)	3 (60)	0.011
Cardiac disease	0	0	0	
Renal disease	0	1	0	0.470
Gastrointestinal involvement	0	3 (23.1)	5 (100)	<0.001
Arthralgia	12 (85.7)	5 (38.5)	4 (80)	0.027
Arthritis	2 (14.3)	0	0	0.254
Myositis	0	0	0	
Fatigue, VAS	3.5 (0-7.5)	5 (1.2-7.7)	4 (3-7)	0.575
Pain, VAS	3.5 (0-7.5)	0.5 (0-6.5)	1 (0-5)	0.536
PGA, VAS	5 (3.7-6.2)	5.5 (4.2-6)	5 (3.5-7)	0.861
HAQ	0.25 (0-0.5)	0.5 (0.2-0.7)	0.55 (0.2-0.8)	0.164
DHI	1.5 (0-6)	4 (1-16.5)	6 (4-12.5)	0.064

SSc: Systemic Sclerosis, VAS: Visual Analogue Scale, mRSS: modified Rodnan skin scores, PGA: Patient global assessment, HAQ: Health Assessment Questionnaire, DHI: Duruoz Hand Index.

DISCUSSION

The present study identified the frequency of scleroderma-type capillaroscopic patterns and the associations of capillaroscopic patterns with clinical features and functional status in SSc patients.

Anormal capillaroscopic examination findings were detected in 93.7% of the patients, and the most common capillaroscopic pattern was the active pattern in our study. Similarly, scleroderma-type patterns have been reported to be present in more than 90% of SSc patients with clinically significant disease (2).

In the present study, disease duration, duration and severity of Raynaud phenomenon, and mRSS were lower in the early pattern group. However, digital ulcers, dcSSc, and arthralgia were more common in the late pattern group. Although there were no differences in interstitial lung disease and the six-minute walking test between the groups, pulmonary hypertension and GIS involvement were more common in patients with late capillaroscopy pattern. Our study results are in line with data on the associations of NVC patterns with organ involvement in SSc. Previous reports have found capillaroscopy to be useful in detecting patients with more severe disease who will have new involvement in the future, and there is an increased risk for moderate to severe organ involvement in SSc patients with late pattern (3,11,18-20).

In our study, the capillary loss was detected in 53% of the patients, and digital ulcer, pulmonary hypertension, and GIS involvement were more common in those with capillary loss. Similarly, a previous study found capillary loss as a risk factor for new digital ulcers (21). Nailfold capillary density was also associated with pulmonary arterial hypertension in another study (22).

Additionally, we found no significant differences in fatigue, pain, PGA, HAQ and DHI scores between the SSc patients regarding NVC patterns. Impaired hand function was identified as the major contributor to overall disability in SSc patients (23,24). A previous study found that patients with early dcSSc had a high burden of disability, fatigue, and pain (23). Other studies reported that patients with dcSSc had poorer hand functions (25), and in early dcSSc, the degree of hand impairment correlated with skin thickening (23). Digital ulcers have been identified as one of the disease manifestations affecting hand function (26).

On the other hand, to the best of our knowledge, there is no data revealing the relationship between NVC patterns and function, pain, and fatigue in SSc patients. The fact that there was no difference between the scleroderma type capillaroscopic patterns in terms of function, fatigue, and pain in our study may be due to the small sample size and needs to be confirmed in larger epidemiologic studies.

CONCLUSION

NVC provides valuable data on the diagnosis, activity, and prognosis of SSc. Digital ulcers, pulmonary hypertension, and GIS involvement are more common in SSc patients with late scleroderma-type capillaroscopic pattern and capillary loss. Since hand function is an important determinant of physical function in patients with SSc, it should be determined by further studies whether this can be predicted with capillaroscopy findings.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Marmara University Faculty of Medicine Clinical Researches Ethics Committee (Date: 06.01.2017, Decision No: 09.2017.095).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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