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ORIGINAL PAPER

Capillaroscopic Characteristics in Patients with Primary Sjögren's Syndrome: Insights from a Pilot Study / A Retrospective Observational Cross-Sectional Study

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Abstract

Objective. The principal aim of this study was to evaluate nailfold videocapillaroscopic (NVC) findings in patients with primary and secondary Sjögren's syndrome (pSS and sSS), with a particular focus on their association with Raynaud's phenomenon (RP), serological markers, as well as extraglandular involvement.

Methods. A retrospective cross-sectional study was conducted on a cohort of 22 patients diagnosed with Sjögren's syndrome (SS), 18 with pSS and 4 with sSS. Demographic, clinical, serological, and capillaroscopic data were collected and analyzed. NVC images (magnification 250x) were acquired using a high-resolution device (Smart G-Scope) to evaluate both normal and pathological patterns. The statistical analysis was performed using IBM SPSS software, version 20 for Windows.

Results. A non-specific capillary pattern was predominant in 88.89 of pSS patients, with tortuous (94%), crossing (78%), and dilated capillaries (67%) being the most frequently observed findings. Pathological capillaries including megacapillaries, branching capillaries, and microhemorrhages were mutually exclusive with normal patterns (p=0.01, p=0.03). RP was present in 18.18% of patients (16.67% in pSS and 25% in sSS). Both tortuous and crossing capillaries were negatively associated with the presence of RP (p=0.02, p=0.04). Low complement C3 levels were correlated with dilated capillaries (p=0.02), and microhemorrhages were significantly associated with hematologic involvement (p=0.03).

Conclusions. According to our findings, NVC could serve as a valuable tool in identifying patients at greater risk of systemic complications in SS, offering critical insights into disease progression, and further research is warranted to explore these associations in larger cohorts.

Keywords: Sjögren's syndrome, nailfold capillaroscopy, Raynaud's phenomenon, capillary abnormalities, primary Sjögren's syndrome, secondary Sjögren's syndrome, microvascular involvement, complement C3, extraglandular manifestations, autoimmune disease.

Introduction

Primary Sjögren's syndrome (pSS) is a complex systemic autoimmune disorder. This enigmatic condition continues to pose significant challenges to the global medical community due to its profound impact on patients' quality of life and its intricate clinical presentation.

Although traditionally associated with the destruction of exocrine glands, resulting in hallmark symptoms such as xerophthalmia and xerostomia, pSS often manifests with a broader spectrum of systemic complications, including hematologic, pulmonary, neurological, and articular involvement, which further complicates diagnosis and management [1,2,3].

The diagnostic criteria for pSS have evolved considerably since their initial proposal in 1965, with successive revisions reflecting the increasing complexity of the disease [4]. Despite these advances, early diagnosis remains challenging, highlighting the necessity of incorporating reliable diagnostic tools capable of identifying systemic involvement before irreversible damage occurs.

Capillaroscopy, a non-invasive method for assessing microcirculation, has emerged as an invaluable tool in the rheumatologist's diagnostic arsenal. This technique is particularly renowned for its ability to distinguish primary from secondary Raynaud's phenomenon and for its utility in the early detection of vascular abnormalities associated with autoimmune diseases such as dermatomyositis, mixed connective tissue disease, and systemic sclerosis. Its integration into the classification criteria of the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) for systemic sclerosis underscores its significant clinical value [5,6,7].

In pSS, Raynaud's phenomenon, with an estimated prevalence ranging from 10% to 35%, represents the

most commonly observed cutaneous vascular manifestation. Of particular interest, RP often precedes other clinical manifestations and systemic complications by several years, which elevates the importance of capillaroscopy as a crucial diagnostic tool for early detection [2,8,9,10]. Nevertheless, the current body of evidence regarding capillaroscopic findings in pSS is limited, with few studies investigating microvascular differences between pSS patients and control groups.

This study aims to deepen the understanding of capillaroscopy's role in the early diagnosis of extraglandular involvement and in the ongoing monitoring of primary Sjögren's syndrome.

Materials and Methods

Study Design

This retrospective, observational cross-sectional study was conducted on a cohort of 22 patients diagnosed with Sjögren's syndrome, who were hospitalized in the Internal Medicine Departments II and III of Colentina Clinical Hospital in Bucharest, between October 2023 and June 2024.

Study Population

This study initially comprised 18 patients, all over 18 years of age, diagnosed exclusively with pSS based on the 2016 classification criteria. To enhance the statistical significance of the analysis, 4 additional patients with sSS, associated with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), were subsequently included, bringing the total cohort to 22 patients.

The comparative assessment of clinical, serological, and capillaroscopic data between the pSS and sSS groups revealed no significant differences (as indicated in Table 1), confirming that the inclusion of sSS patients did not alter the results or distort the capillaroscopic findings. Therefore, further statistical correlations and capillaroscopic evaluations were performed on the complete cohort without impacting the original objective of examining capillaroscopic features in pSS patients. Patients with secondary Sjögren's syndrome related to other autoimmune conditions, such as scleroderma, mixed connective tissue disease (MCTD), or dermatomyositis (DM), were excluded, to avoid potential confounding effects due to distinct capillaroscopic patterns characteristic of these diseases [11].

Data Collection

The necessary data for constructing the study database were extracted from the patients' medical records. Table 1 provides a detailed presentation of the variables incorporated into the study.

Capillaroscopic Technique

Nailfold videocapillaroscopy (NVC) was performed under controlled environmental conditions to minimize physiological capillary constriction. The procedure was applied to all fingers, except the thumbs of both hands, following the application of a drop of immersion oil to the nailfold to improve visualization, and the fourth and fifth fingers of the non-dominant hand were selected for standardized evaluation. The examination was conducted using a high-resolution Smart G-Scope videocapillaroscope with 250x magnification, equipped with automatic focusing and HD imaging capabilities, ensuring precision in capturing detailed images of the distal capillary row. Each session lasted approximately 15 minutes per patient, with the images subsequently analyzed using proprietary microscope software compatible with both Windows and Android platforms. Comprehensive measurements of capillary structure and microarchitecture were performed, adhering to the guidelines established by the European League Against Rheumatism (EULAR) and the Scleroderma Clinical Trials Consortium (SCTC).

The capillaroscopic parameters evaluated encompassed capillary architecture, density, and diameters (dilated and megacapillaries), as well as the presence of tortuous, crossing, and branching capillaries, and microhemorrages.

Statistical Analysis

Data were initially collected and structured in a database developed using Microsoft Excel. The statistical analysis was performed using IBM SPSS Statistics (version 20 for Windows). Numerical variables were expressed as mean ± standard deviation (SD) for normally distributed data or as median (min, max) for data that did not follow a normal distribution. The Student t-test was used for parametric variables, while the Mann-Whitney U test was applied for non-parametric variables. Categorical data were examined with the Chi-square test. To assess the strength of associations, odds ratios (OR) with corresponding 95% confidence intervals (CI) were calculated. Statistical significance was determined using a p-value <0.05, provided the 95% CI did not include 1. All reported p-values were two-tailed.

Results

There were no statistically significant differences between the two groups (pSS and sSS) across the evaluated demographic, clinical, serological, and capillaroscopic parameters (Table1.).

Demographic Profile

The mean age at inclusion was 52 years for patients with pSS and 54 years for the overall cohort. The mean age at diagnosis was approximately 48 years. Disease duration varied considerably, with a median duration of 2 years, ranging from a few months to several decades, reflecting heterogeneity in disease progression. There was a clear predominance of female patients, with women representing 90.91% of the cohort (Table1).

Systemic Involvement

Extraglandular manifestations were present in 68% of the patients, with hematologic and pulmonary involvement being the most frequent, occurring in 50% and 45% of cases, respectively. Lymphadenopathy (exclusively observed in female patients) and neurological involvement were identified solely in the pSS group, with prevalences of 36% and 23%, respectively.

RP was diagnosed in 18.18% of patients, with no significant difference between the pSS group and the sSS group (Table 1). Notably, the presence of RP was associated with a reduced probability of developing tortuous and crossing capillaries, suggesting a potential protective effect against these capillaroscopic abnormalities (Table 2). Hypergammaglobulinemia was more prevalent in RP-positive patients compared to those without RP; however, this difference did not reach statistical significance (Table 2, Table 3).

Table 1. *Demographic, serological, extraglandular, and capillaroscopic features of Sjögren's syndrome patients.*

Variable	pSS (N=18) 82%	sSS (N=4) 18%	Total (N=22) 100%	OR (CI 95%)	*p* value
Demographic variables					
Sex F/M (F%)	16/2 (88.88%)	4/0 (100%)	20/2 (90.91%)	1.13 (0.09-13.14)	0.92
Age at inclusion (years)	52.44±12.22	63.75±13.45	54.50±12.91	-	0.19
Age at disease onset (years) *[Mean ± SD]*	48.06±12.89	51.25±16.93	48.64±13.31	-	0.74
Duration of disease (years) *[Median (min, max)]*	2 (0, 14)	11 (0, 37)	2 (0, 37)	-	0.41
Autoantibodies/ serological analysis					
ANA (Y/N)	16/2 (89%)	3/1 (75%)	19/3 (86%)	2.66 (0.17-39.62)	0.46
Anti-Ro (SSA) (Y/N)	15/3 (83%)	2/2 (50%)	17/5 (77%)	3.5 (0.36-33.30)	0.25
Anti-La (SSB) (Y/N)	10/8 (56%)	0/4	10/12 (45%)	6.11 (0.60-62.23)	0.12
RF (Y/N)	12/6 (67%)	3/1 (75%)	15/7 (68%)	0.66 (0.05-7.85)	0.74
HPC (C3/C4) (Y/N)	1/17 (5.5%)	1/3 (25%)	2/20 (9%)	0.17 (0.00-3.65)	0.22
Hypergammaglobulinemia(Y/N)	11/7 (61%)	2/2 (50%)	13/9 (59%)	1.57 (1.17-13.86)	0.68
Extraglandular involvement(Y/N)	12/6 (67%)	3/1 (75%)	15 (68%)	0.66 (0.05-7.85)	0.74
RP (Y/N) (%)	3/15 (16.67%)	1/3 (25%)	4/18 (18.18%)	0.60 (0.04-7.92)	0.69
Hematologic (Y/N)	9/9 (50%)	2/2 (50%)	11 (50%)	1.00 (0.11-8.73)	1.00
Pulmonary (Y/N)	7/11 (38.8%)	2/2 (50%)	9/13 (40.9%)	0.63 (0.07-5.61)	0.68
Neurological (Y/N)	5/13 (28%)	0/4	5/17 (23%)	2.14 (0.20-22.47)	0.52
Lymphadenopathy (Y/N)	8/10 (44%)	0/4	8/14 (36%)	4.09 (0.40-41.66)	0.23
Capillaroscopic findings					
ACA (Y/N)	0/18	0/4	0/22	-	-
RCD (Y/N)	0/18	1/3 (25%)	1/21 (5%)	-	-
Tortuous capillaries (Y/N)	17/1 (94%)	3/1 (75%)	20/2 (91%)	5.66 (0.27-117.44)	0.22
Branching capillaries (Y/N)	7/11 (39%)	0/4	7/15 (32%)	3.33 (0.32-34.12)	0.31
Crossing capillaries (Y/N)	14/4 (78%)	2/2 (50%)	16/6 (73%)	3.50 (0.36-33.30)	0.25
Megacapillaries (Y/N)	2/16 (11%)	2/2 (50%)	4/18 (18%)	0.12 (0.01-1.44)	0.06
Microhemorrhages (Y/N)	7/11 (39%)	2/2 (50%)	9/13 (41%)	0.63 (0.07-5.61)	0.68
Dilated capillaries (Y/N)	12/6 (67%)	4/0 (100%)	16/6 (73%)	0.37 (0.03-3.83)	0.40

Abbreviations: pSS – primary Sjögren's syndrome; sSS – secondary Sjögren's syndrome; ANA – antinuclear antibodies; RF – rheumatoid factor; HPC – Hypocomplementemia; RP – Raynaud's phenomenon; F/M – Female/Male; ACA – Abnormal Capillary Architecture; RCD – Reduced Capillary Density; Y=yes(present), N=no(absent).

Table 2. *Comparative evaluation of SS patients with and without RP.*

Variable	RP (+) (N=4) 18.18%	RP (-) (N=18) 81.81%	OR (CI 95%)	P value
Demographic variables				
Sex F/M (%)	3/1 (75%)	17/1 (94.44)	0.17 (0.00-3.65)	0.22
Age at inclusion (years) *[Mean ± SD]*	57.00±15.97	53.94±12.61	-	0.73
Age at disease onset (years) *[Mean ± SD]*	53.00±16.57	47.67±12.84	-	0.53
Duration of disease (years) *[Median (min, max)]*	3.5 (0, 9)	2 (0, 37)	-	0.90
Autoantibodies/ serological analysis				
ANA (Y/N)	4/0 (100%)	15/3 (83.3%)	1.25 (0.11-13.92)	0.85
Anti-Ro (SSA) (Y/N)	3/1 (75%)	13/5 (72.2%)	1.15 (0.09-13.87)	0.91
Anti-La (SSB (Y/N)	1/3 (25%)	9/9 (50%)	0.88 (0.06-12.88)	0.93
RF (Y/N)	4/0 (100%)	11/7 (61.1%)	3.33 (0.32-34.12)	0.31

Variable	RP (+) (N=4) 18.18%	RP (-) (N=18) 81.81%	OR (CI 95%)	P value
HPC (C3/C4) (Y/N)	1/3 (25%)	1/17 (5.5%)	5.66 (0.27-117.44)	0.22
Hypergammaglobulinemia(Y/N)	4/0 (100%)	9/9 (50%)	5.00 (0.49-50.83)	0.17
Extraglandular involvement(Y/N)	4/0 (100%)	11/7 (61.1%)	3.33 (0.32-34.12)	0.31
Hematologic (Y/N)	3/1 (75%)	8/10 (44.4%)	3.75 (0.32-43.31)	0.26
Pulmonary (Y/N)	3/1 (75%)	6/12 (33.3%)	6.00 (0.50-70.66)	0.12
Neurological (Y/N)	1/3 (25%)	4/14 (22.2%)	1.16 (0.09-14.51)	0.90
Lymphadenopathy (Y/N)	1/3 (25%)	7/11 (38.8%)	0.52 (0.04-6.09)	0.60
Capillaroscopic findings				
ACA (Y/N)	0/4 (0%)	0/18 (0%)	-	-
RCD (Y/N)	1/3 (25%)	0/18 (0%)	-	-
Tortuous capillaries (Y/N)	2/2 (50%)	18/0 (100%)	0.05 (0.00-0.68)	0.02
Crossing capillaries (Y/N)	1/3 (25%)	15/3 (83.3%)	0.06 (0.00-0.88)	0.01
Branching capillaries (Y/N)	2/2 (50%)	5/13 (27.7%)	2.60 (0.28-28.81)	0.38
Dilated capillaries (Y/N)	3/1 (75%)	13/5 (72.2%)	1.15 (0.09-13.87)	0.91
Megacapillaries (Y/N)	2/2 (50%)	2/16 (11.1%)	0.12 (0.01-1.44)	0.06
Microhemorrhages (Y/N)	3/1 (75%)	6/12 (33.3%)	6.0 (0.50-70.66)	0.12

Abbreviations: ANA – antinuclear antibodies; RF – rheumatoid factor; HPC – Hypocomplementemia; RP – Raynaud's phenomenon; F/M – Female/Male; ACA – Abnormal Capillary Architecture; RCD – Reduced Capillary Density; Y=yes(present), N=no(absent).

Table 3. *Capillaroscopic features: TC-Tortuous capillaries; CC-Crossing capillaries; BC- Branching capillaries; DC-Dilated capillaries; MC-Megacapillaries; MH-Microhemorrhages.*

Variable	TC		OR (CI 95 %)	P	CC		OR (CI 95%)	P	BC		OR (CI 95 %)	P	DC		OR (CI 95 %)	P	MC		OR (CI 95%)	P	MH		OR (CI 95%)	P
	Y	N			Y	N			Y	N			Y	N			Y	N			Y	N		
Demographic variables																								
Sex F/M (F%)	18/2	2/0	2.11 (0.16-27.58)	0.56	15/1	5/1	3.00 (0.15-57.36)	0.44	6/1	14/1	0.42 (0.02-8.04)	0.56	14/2	6/0	0.71 (0.06-8.15)	0.78	4/0	16//2	0.58 (0.04-7.91)	0.68	7/2	13/0	0.19 (0.01-2.15)	0.18
Age at inclusion (years) *[Mean ± SD]*	55.30±13 .27	46.50±3 .53	-	0.07	52.13±11 .30	60.83±15 .84	-	0.25	55.87±11 .72	53.87±13 .77	-	0.73	56.31±12 .27	49.67±14 .47	-	0.34	55.25±17 .29	54.33±12 .37	-	0.92	54.67±12 .72	54.38±13 .55	-	0.96
Age at disease onset (years) *[Mean ± SD]*	49.30±13 .62	42.00±9 .89	-	0.47	46.56±12 .30	54.17±15 .47	-	0.31	49.14±13 .18	48.40±13 .82	-	0.90	49.13±13 .34	47.33±14 .40	-	0.79	49.50±14 .27	48.44±13 .51	-	0.88	45.89±14 .22	50.54±13 .55	-	0.44
Duration of disease (years) *[Median (min, max)]*	2 (0, 37)	4.5 (0, 9)	-	0.70	2 (0, 37)	6 (0, 13)	-	0.49	8 (1, 13)	2 (0, 37)	-	0.23	5 (0, 37)	2 (1, 5)	-	0.54	5.5 (0, 12)	2 (0, 37)	-	0.83	5 (0, 37)	2 (0, 14)	-	0.26
Serological analysis																								
ANA (Y/N)	17/3	2/0	1.50 (0.12-18.44)	0.75	14/2	5/1	1.4 (0.10-19.01)	0.8	6/1	13/2	0.92 (0.06-12.28)	0.95	13/3	6/0	0.50 (0.04-5.35)	0.56	4/0	15/3	0.93 (0.07-11.05)	0.95	9/0	10/3	3.63 (0.34-38.23)	0.28
Anti-Ro (SSA) (Y/N)	15/5	1/1	3.0 (0.15-57.36)	0.44	12/4	4/2	1.5 (0.19-11.53)	0.69	6/1	10/5	3.00 (0.27-32.20)	0.35	12/4	4/2	1.50 (0.19-11.53)	0.69	3/1	13/5	1.15 (0.09-13.87)	0.91	7/2	9/4	1.55 (0.21-11.08)	0.65
Anti-La (SSB) (Y/N)	10/9	0/2	3.30 (0.29-37.10)	0.33	8/7	2/4	2.28 (0.31-16.51)	0.41	3/4	7/7	0.75 (0.12-4.66)	0.75	6/9	4/2		0.55	1/3	9/8	0.29(0.02-3.45)	0.33	4/4	6/7	1.16 (0.20-6.80)	0.86
RF (Y/N)	13/7	2/0	0.58 (0.05-6.58)	0.43	11/5	4/2	1.10 (0.14-8.12)	0.92	4/3	11/4	0.48 (0.07-3.19)	0.44	10/6	5/1	0.33 (0.03-3.57)	0.35	4/0	11/7	3.33 (0.32-37.2)	0.31	6/3	9/4	0.88 (0.14-5.47)	0.89
HPC (C3/C4) (Y/N)	1/19	1/1	0.05 (0.00-1.61)	0.03	0/16	2/4	0.09 (0.00-1.16)	0.06	1/6	1/14	2.33 (0.12-43.79)	0.56	2/14	0/6	1.40 (0.12-15.97)	0.78	1/3	1/17	5.66 (0.27-117.44)	0.22	2/7	0/13	5.25 (0.46-59.28)	0.18
Hypergammaglobulinemia (Y/N)	11/9	2/0	0.23 (0.01-5.53)	0.37	10/6	3/3	1.66 (0.25-11.07)	0.59	4/3	9/6	0.88 (0.14-5.47)	0.89	9/7	4/2	0.64 (0.09-4.58)	0.65	3/1	10/7	2.40 (0.20-27.72)	0.47	6/3	7/6	1.71(0.29-9.99)	0.54
Extraglandular involvement	13/7	2/0	0.87 (0.06-11.23)	0.91	10/6	5/1	0.33 (0.03-3.57)	0.35	6/1	9//6	4.00 (0.37-42.17)	0.22	12/4	3/3	3.00 (0.42-21.29)	0.26	3/1	12/6	1.5 (0.12-17.66)	0.74	7/2	8/5	2.18 (0.31-15.04)	0.42
RP (Y/N) (%)	2/18	2/0	0.05 (0.00-0.68)	0.02	1/15	3/3	0.06 (0.00-0.88)	0.01	2/5	2/13	2.60 (0.28-28.81)	0.38	3/13	1/15	1.15 (0.09-13.87)	0.91	2/2	2/16	0.12 (0.01-1.44)	0.06	3/6	1/12	6.0 (0.50-70.66)	0.12
Hematologic (Y/N)	9/11	2/0	0.27 (0.02-3.10)	0.29	7/9	4/2	0.38(0.05-2.77)	0.33	4/3	7/8	1.52 (0.25-9.29)	0.64	9/7	2/4	2.57 (0.36-18.32)	0.33	3/1	8/10	3.75(0.32-43.31)	0.26	7/2	4/9	7.87 (1.10-56.12)	0.03
Pulmonary (Y/N)	8/12	1/1	0.66 (0.03-12.27)	0.78	5/11	4/2	0.22 (0.03-1.67)	0.13	4/3	5/10	2.66 (0.42-16.82)	0.29	7/9	2/4	1.55 (0.21-11.08)	0.65	2/2	7/11	1.57 (0.17-13.86)	0.68	4/5	5/8	1.28 (0.22-7.18)	0.77
Neurological (Y/N)	5/15	0/2	1.2 (0.09-13.03)	0.92	3/13	2/4	0.46 (0.05-3.81)	0.46	3/4	2/13	4.87 (0.59-40.25)	0.12	4/12	1/5	1.66 (0.14-18.87)	0.67	0/4	5/13	0.46 (0.04-4.89)	0.52	3/6	2/11	2.75 (0.35-21.30)	0.32
Lymphadenopathy	7/13	1/1	0.53	0.6	6/10	2/4	1.20	0.8	3/4	5/10	1.50	0.6	5/11	3/3	0.45	0.4	1/3	7/11	0.52	0.6	1/8	7/6	0.10	0.0

Variable	TC		OR (CI 95 %)	P	CC		OR (CI 95%)	P	BC		OR (CI 95 %)	P	DC		OR (CI 95 %)	P	MC		OR (CI 95%)	P	MH		OR (CI 95%)	P
(Y/N)			(0.02-9.98)	7			(0.16-8.65)	5			(0.23-9.46)	6			(0.06-3.09)	1			(0.04-6.09)	8			(0.01-1.12)	4
Capillaroscopic findings																								
TC (Y/N)	-	-	-	-	16/0	4/2	5.00 (2.08-12.01)	0.01	6/1	14/1	0,42 (0.02-8.04)	0.56	14/2	6/0	0.17 (0.06-8.15)	0.78	2/2	18/0	0.05 (0.00-0.68)	0.02	7/2	13/0	0.19 (0.01-2.15)	0.18
CC (Y/N)	16/4	0/2	10.20 (0.86-120.96)	0.06	-	-	-	-	3/4	13/2	0.11 (0.01-0.95)	0.03	10/6	6/0	0.22 (0.02-2.23)	0.20	1/3	15/3	0.06 (0.00-0.88)	0.01	5/4	11/2	0.22 (0.03-1.67)	0.13
BC (Y/N)	6/14	1/1	0.42 (0.23-8.04)	0.56	3/13	4/2	0.11 (0.01-0.95)	0.03	-	-	-	-	7/9	0/6	5.6 (0.39-0.90)	0.05	1/3	6/12	0.66 (0.05-5.85)	0.74	4/5	3/10	2.66 (0.42-16.82)	0.29
DC (Y/N)	14/6	2/0	0.71 (0.06-8.15)	0.78	10/6	6/0	0.22 (0.02-2.23)	0.20	7/0	9/6	5.60 (0.56-55.42)	0.14	-	-	-	-	4/0	12/6	2.69(0.26-27.82)	0.40	8/1	8/5	5.00 (0.47-52.96)	0.15
MC (Y/N)	2/18	2/0	0.05 (0.00-0.68)	0.02	1/15	3/3	0.06 (0.00-0.88)	0.01	1/6	3/12	0.66 (0.05-7.85)	0.74	4/12	0/6	2.69 (0.26-27.82)	0.40	-	-	-	-	3/6	1/12	6.00 (0.50-70.66)	0.12
MH (Y/N)	7/13	2/0	0.19 (0.01-2.15)	0.18	5/11	4/2	0.22 (0.03-1.67)	0.13	4/3	5/10	2.66 (0.42-16.82)	0.29	8/8	1/5	5.00 (0.47-52.96)	0.15	3/1	6/12	6.00(0.50-70.66)	0.12	-	-	-	-

Abbreviations: ANA – antinuclear antibodies; RF – rheumatoid factor; HPC – Hypocomplementemia; RP – Raynaud's phenomenon; F/M – Female/Male; ACA – Abnormal Capillary Architecture; RCD – Reduced Capillary Density; Y=yes(present), N=no(absent).

Serological Analysis

Anti-SSA/Ro antibody titers were markedly elevated, with a median value of 125.57 IU/mL and a maximum recorded value of 867 IU/mL (normal reference range: <20 IU/mL).

Antinuclear antibodies (ANA) were positive in 19 patients (86%), of whom 16 had pSS and 3 had sSS. Furthermore, 17 patients (77%) tested positive for anti-Ro antibodies, with 15 from the pSS group and 2 from the sSS group. Anti-La antibodies were detected solely in the pSS cohort, being present in 10 patients (45%), all of whom also tested positive for anti-Ro. Rheumatoid factor (RF) was found in 15 patients (68%), with 12 from the pSS group and 3 from the sSS group. Hypergammaglobulinemia was observed in 13 patients (59%), with 11 from the pSS group and 2 from the sSS group. Hypocomplementemia was present in 2 patients (9%), one from each diagnostic category (Table1).

Capillaroscopic Findings

Capillaroscopic analysis demonstrated a high prevalence of abnormalities in patients with pSS. Tortuous capillaries were the most frequently observed, present in 94% of cases, followed by crossing capillaries (78%) and dilated capillaries (67%). Additional findings included branching capillaries and microhemorrhages in 39% of cases, while megacapillaries were identified in 11% of patients.

All patients, regardless of whether they had pSS or sSS, exhibited at least one capillaroscopic abnormality, with the majority of findings being non-specific (88.89% in the pSS group and 81.82% in the overall cohort).

Opposite relationships were observed between the presence of megacapillaries and both tortuous and crossing capillaries. Branching capillaries were significantly negatively correlated with crossing capillaries. Conversely, tortuous capillaries emerged as a risk factor for the development of crossing capillaries. At the threshold of statistical significance, dilated capillaries and megacapillaries were positive predictors for microhemorrhages.

Significant statistical associations were observed between the presence of dilated capillaries and low complement C3 levels, suggesting that reduced C3 titers may be a risk factor for the development of these capillaroscopic abnormalities. Similarly, microhemorrhages were significantly associated with hematologic involvement, with patients displaying hematologic abnormalities having a heightened risk of developing microhemorrhages. Paradoxically, lymphadenopathy appeared to have a protective effect against the development of microhemorrhages, although this was at the borderline of statistical significance.

An important observation of the study was that hypocomplementemia may act as a protective factor against the development of tortuous capillaries. Low complement levels were also borderline significant as a negative predictor for crossing capillaries (Table3.). These results suggest that hypocomplementemia is positively correlated with abnormal capillaroscopic patterns and negatively associated with more physiological structures, highlighting the need for further research into the pathogenic relationships between serological abnormalities and various capillaroscopic patterns.

Discussions

Although 4 patients with sSS—2 with SLE, 2 with AR—were included, their capillaroscopic patterns of these sSS cases aligned with those seen in patients with pSS, suggesting that their inclusion did not impact the study's findings, which support the hypothesis that microvascular involvement, as identified through nailfold capillaroscopy, is a characteristic feature of SS, regardless of whether it is classified as primary or secondary classification.

The age distribution and gender ratio in our cohort align closely with existing literature on SS, reinforcing the well-established predominance of the disease in middle-aged women. Notably, our findings corroborate those of Ohtsuka and other researchers, which suggest a similar age of onset for pSS (52.1 years) and a comparable female-to-male ratio[12,13,14,15].

RP was present in a modest proportion of our cohort (18.18% overall; 16.67% in pSS and 25% in sSS). While our results are somewhat lower than the 32% prevalence reported by Corominas et al., this discrepancy likely reflects differences in sample size and recruitment methods [16]. In our cohort, the presence of tortuous or crossing capillaries emerged as a protective factor against the development of RP (P=0.02, P=0.04). This finding contrasts with previous reports, such as those by Tektonidou *et al*., who, despite the absence of statistical significance (P = 0.26), noted a higher frequency of crossing capillaries in patients with SS and RP [17].

The systemic involvement observed in our study, particularly the high prevalence of hematologic and pulmonary manifestations, underscores the complex, multisystem nature of SS. Capobianco et al. reported a systemic involvement rate of 57%, including lower rates of hematologic (16.3%) and pulmonary (6.55%) manifestations [18]. The pattern of extraglandular involvement we documented, especially the absence of lymphadenopathy in male patients and the higher rates of pulmonary disease in those with pSS, provides important clinical insights.

The high frequency of ANA positivity (86%) in our cohort is consistent with prior research, which has reported similar findings (87%) by Corominas et al. [16]. Additionally, anti-Ro antibodies were positive in 77% of patients (83% in pSS and 50% in sSS), aligning with the 75% frequency reported by Corominas et al. [16]. The exclusive presence of anti-La antibodies in pSS patients (45%) in our cohort further strengthens the association between this autoantibody and the primary form of the disease,

compared to the 39.7% reported by Capobianco[18].

Capillaroscopic analysis revealed a variety of microvascular abnormalities in nearly all patients, with the majority exhibiting non-specific patterns. Tortuous capillaries were the most frequently observed abnormalities. Bernardino et al. similarly reported tortuous capillaries in 100% of their cohort [19]. Dilated capillaries were present in 73% of patients, which mirrors Bernardino's findings of 73.33% [19].

In terms of capillary density, our findings are consistent with the research by Bernardino (2020) and Cakmakci (2015), which reported a normal capillary density in patients with SS [15,19]. However, earlier studies by Capobianco (2005) and Tektonidou (1999) observed lower capillary density in SS patients compared to healthy controls [17,18]. These discrepancies emphasize the need for additional research to clarify the clinical significance of capillary density variations in SS.

The presence of megacapillaries, though observed in a minority of our cohort (18%), echoes findings from prior studies such as Bernardino et al. (33.3%), highlighting the heterogeneity of capillaroscopic patterns in SS [19]. Furthermore, the significant association between megacapillaries and microhemorrhages in our study highlights the potential link between structural capillary alterations and endothelial damage. This hypothesis is supported by our observation of a higher prevalence of microhemorrhages in patients with concurrent systemic involvement, particularly hematologic manifestations.

Additionally, our findings suggest a positive association between hypocomplementemia and pathological capillaroscopic patterns, alongside a negative association with normal capillary morphology. To our knowledge, existing literature has not yet explored correlations between hypocomplementemia, and capillaroscopic manifestations in patients with pSS, emphasizing the relevance of our observations.

One of the more intriguing findings from our study was the inverse relationship between tortuous capillaries and megacapillaries, suggesting distinct pathophysiological mechanisms underlying these capillary abnormalities. This warrants further investigation, as understanding the different capillary morphologies could offer new insights into the progression and systemic implications of Sjögren's syndrome. Moreover, the strong association between capillary tortuosity and cross-capillaries, both of which are considered variants of normal morphology, contrasts sharply with the pathological nature of megacapillaries. This dichotomy emphasizes the importance of detailed capillaroscopic analysis in clinical assessments.

Despite the relatively small sample size and cross-sectional nature of the study, our findings contribute to the growing body of evidence regarding the capillaroscopic features and systemic associations in Sjögren's syndrome. The significant associations observed between capillary abnormalities and systemic involvement, particularly hematologic and pulmonary manifestations, highlight the clinical utility of capillaroscopy in identifying patients at higher risk for severe extraglandular disease.

Limitations and Future Directions

The limited sample size curtails the broader applicability of the results and weakens the statistical power of the analysis. Moreover, the retrospective design and absence of longitudinal follow-up hinder the ability to establish causality or monitor capillaroscopic evolution over time. Future research should seek to overcome these limitations by incorporating larger, prospective cohorts with standardized capillaroscopic and serological assessments.

Conclusions

The predominant finding in this study was the presence of a non-specific capillaroscopic pattern, observed in 88.89% of patients with pSS. Importantly, our results reveal a mutual exclusivity between minor capillary anomalies, such as tortuous and crossed capillaries, which are often considered non-pathological or non-specific, and major pathological abnormalities, including dilated capillaries, megacapillaries, branched capillaries, and microhemorrhages. Within each category, a strong tendency to co-occur was identified, suggesting that the presence of one abnormality increases the probability of others, reinforcing their interrelationship as risk factors for more severe disease progression.

A particularly notable observation was the apparent protective role of tortuous and crossed capillaries against the development of RP. This finding indicates that routine capillaroscopic evaluation may offer critical predictive value in assessing disease progression and the risk of developing RP. Such insights emphasize the potential of capillaroscopy to serve as a non-invasive tool for early detection of vascular involvement in SS, facilitating timely clinical interventions.

Conflicts of Interest: The authors declare no conflicts of interest.

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