Journal of Translational Autoimmunity 13 (2026) 100381

Contents lists available at ScienceDirect

Journal of Translational Autoimmunity

journal homepage: www.sciencedirect.com/journal/journal-of-translational-autoimmunity

The clinical profile of systemic sclerosis without a 'scleroderma pattern' at nailfold capillaroscopy: results from the multicenter SPRING registry of the Italian Society of Rheumatology

Antonio Tonutti [a,b], Maria De Santis [a,b], Francesca Motta [a,b], Gianluigi Bajocchi [c], Dilia Giuggioli [d], Silvia Bellando-Randone [e], Cosimo Bruni [e], Giovanni Zanframundo [f], Roberta Foti [g], Giovanna Cuomo [h], Alarico Ariani [i], Edoardo Rosato [j], Gemma Lepri [e], Francesco Girelli [k], Elisabetta Zanatta [l], Silvia Laura Bosello [m], Ilaria Cavazzana [n], Francesca Ingegnoli [o], Fabio Cacciapaglia [p], Giuseppe Murdaca [q], Giuseppina Abignano [r], Giorgio Pettiti [s], Alessandra Della Rossa [t], Maurizio Caminiti [u], Anna Maria Iuliano [v], Giovanni Ciano [w], Lorenzo Beretta [x], Gianluca Bagnato [y], Ennio Lubrano [z], Ilenia De Andres [aa], Luca Idolazzi [ab], Marta Saracco [ac], Cecilia Agnes [ad], Corrado Campochiaro [ae,af], Giacomo De Luca [ae,af], Martina Orlandi [d], Marco Di Battista [t], Mariangela Nivuori [ag], Livio Milazzo [ah], Edoardo Cipolletta [ai], Federica Lumetti [d], Amelia Spinella [d], Emanuele Cocchiara [c], Veronica Codullo [f], Beatrice Moccaldi [l], Elisa Visalli [g], Carlo Iandoli [h], Antonietta Gigante [j], Greta Pellegrino [aj,ak], Erika Pigatto [al], Maria Grazia Lazzaroni [n], Enrico De Lorenzis [m], Gianna Mennillo [r], Giuseppa Pagano-Mariano [u], Federica Furini [am], Licia Vultaggio [am], Simone Parisi [an], Clara Lisa Peroni [an], Enrico Fusaro [an], Gerolamo Bianchi [ao], Gian Domenico Sebastiani [v], Marcello Govoni [am], Salvatore D'Angelo [r], Franco Cozzi [ap], Franco Franceschini [n], Serena Guiducci [e], Valeria Riccieri [aq], Lorenzo Dagna [ae,af], Carlo Salvarani [c], Florenzo Iannone [ag], Marco Matucci-Cerinic [ae,af,ar], Clodoveo Ferri [d], Rossella De Angelis [ah,*]

[a] *Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, 20072, Italy*
[b] *Rheumatology and Clinical Immunology, IRCCS Humanitas Research Hospital, Rozzano, Milan, 20089, Italy*
[c] *Rheumatology Unit, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy*
[d] *Rheumatology Unit, School of Medicine, Department of Medical and Surgical Sciences for Children and Adults, University of Modena and Reggio Emilia, Modena, Italy*
[e] *Division of Rheumatology, Department of Experimental and Clinical Medicine, University of Florence, Careggi Hospital, Florence, Italy*
[f] *Department of Rheumatology, Policlinico San Matteo, Pavia, Italy*
[g] *Rheumatology Unit, A.O.U Policlinico S. Marco, Catania, Italy*
[h] *Department of Precision Medicine – University of Campania "Luigi Vanvitelli", Naples, Caserta, Italy*
[i] *Department of Medicine, Internal Medicine and Rheumatology, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy*
[j] *Department of Translational and Precision Medicine, Sapienza University of Rome, Italy, Roma, Italy*
[k] *Department of Medicine, Rheumatology Unit, Ospedale Morgagni – Pierantoni, Forlì, Italy*
[l] *Department of Rheumatology, University of Padua, Padua, Italy*
[m] *Division of Rheumatology and Clinical Immunology, Fondazione Policlinico Universitario A. Gemelli-IRCCS and Catholic University of the Sacred Heart, Rome, Italy*
[n] *Rheumatology and Clinical Immunology, ASST Spedali Civili of Brescia, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy*
[o] *Rheumatology Clinic, Department of Rheumatology and Medical Sciences, ASST Gaetano Pini-CTO, Department of Clinical Sciences and Community Health, Dipartimento di Eccellenza 2023-2027, Università degli Studi di Milano, Milan, Italy*
[p] *Department of Medicine and Surgery, LUM University "Giuseppe Degennaro" Casamassima - Rheumatology Unit "F. Miulli" General Hospital Acquaviva delle Fonti, Bari, Italy*
[q] *Research Hospital San Martino, University of Genoa, Genoa, Italy*
[r] *Rheumatology Institute of Lucania (IReL), San Carlo Hospital, Potenza and University of Basilicata, Department of Health of Science, Potenza, Italy*

* Corresponding author.
E-mail address: r.deangelis@staff.univpm.it (R. De Angelis).

https://doi.org/10.1016/j.jtauto.2026.100381
Received 8 April 2026; Received in revised form 24 May 2026; Accepted 8 June 2026
Available online 13 June 2026

[s] Azienda Ospedaliera S. Croce e Carle, Cuneo, Italy
[t] Department of Rheumatology, University of Pisa, Pisa, Italy
[u] Departmental Rheumatology Unit, Grande Ospedale Metropolitano, Reggio Calabria, Italy
[v] Rheumatology Unit, San Camillo - Forlanini Hospital, Rome, Italy
[w] Hospital of Ariano Irpino, Local Health Department, Ariano Irpino, Avellino, Italy
[x] Referral Center for Systemic Autoimmune Diseases, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico di Milano, Milan, Italy
[y] Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy
[z] Department of Rheumatology, University of Molise, Campobasso, Italy
[aa] Rheumatology Unit, Azienda Ospedaliera di Rilievo Nazionale ed Alta Specializzazione "Garibaldi", Catania, Italy
[ab] Rheumatology Section, Department of Medicine, University of Verona, Verona, Italy
[ac] Rheumatology Unit, Mauriziano-Umberto I Hospital, Turin, Italy
[ad] Department of Medicine, San Lorenzo Hospital, Carmagnola, Turin, Italy
[ae] Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR), IRCCS Ospedale San Raffaele, Milan, Italy
[af] Vita-Salute San Raffaele University, Milan, Italy
[ag] Unit of Rheumatology, Department of Precision and Regenerative Medicine, Area Jonica (DiMePRe-J) University of Bari, Italy
[ah] Rheumatology Unit, Department of Clinical and Molecular Sciences, Polytechnic University of Marche, Ancona, Italy
[ai] Department of Internal Medicine, Marche University Hospital, Ancona, Italy
[aj] IRCCS Ospedale Galeazzi Sant'Ambrogio, Milan, Italy
[ak] Dipartimento di Scienze Biomediche e Cliniche, Università degli Studi di Milano, Milan, Italy
[al] UOC Medicina Generale, Azienda Pedemontana 7, San Bassiano Hospital, Bassano del Grappa, Italy
[am] Rheumatology Unit, Department of Medical Sciences, University of Ferrara and Azienda Ospedaliera-Universitaria S. Anna, Ferrara, Italy
[an] Rheumatology Unit, Città della Salute e della Scienza, Turin, Italy
[ao] Rheumatology Unit, Department of Musculoskeletal Sciences, Local Health Trust La Colletta Hospital, Genoa, Italy
[ap] Department of Medicine, Villa Salus Hospital, Venice, Italy
[aq] Department of Medical and Cardiovascular Sciences, Sapienza University of Rome, Rome, Italy
[ar] Inflammation Fibrosis and Ageing Initiative (INFLAGE), Division of Genetics and Cell Biology, IRCCS San Raffaele Scientific Institute, Milan, Italy

ARTICLE INFO

Keywords:
Nailfold capillaroscopy
Phenotype
Scleroderma pattern
Systemic sclerosis

ABSTRACT

Background: Microvascular alterations can be detected with nailfold videocapillaroscopy, useful for systemic sclerosis (SSc) diagnosis upon identification of the “scleroderma pattern” (NVC-SP). However, this pattern is missing in a subset of SSc patients.
Methods: This retrospective analysis on the multicenter Italian SPRING cohort of SSc patients assessed the prevalence and characteristics of patients without NVC-SP. Associations with demographic and clinical features were evaluated using logistic regression (cross-sectional) and mixed-effects models (longitudinal).
Results: Out of 1689 SSc patients with available NVC information, 90 (5.3%) did not have the NVC-SP. These patients were older at SSc onset (53 vs. 49 years) and more frequently sine scleroderma (31% vs 12%, $p < 0.001$). The overall burden of vascular complications was milder in this subset, with a lower prevalence of pitting scars (33% vs 48%), telangiectasias (52% vs 74%), and calcinosis (3.4% vs 12%). During the follow-up, mRSS remained lower (60-month mean 4 vs 7, $p = 0.002$), as well as the estimated probability of vascular complications. Moreover, despite comparable values at baseline, DLCO remained significantly higher in patients without NVC-SP at the following time points (12, 24, and 60 months, $p < 0.05$). The presence of “late” NVC-SP was independently associated with ILD (OR 1.83, 95% CI 1.05-3.18).
Conclusions: The absence of NVC-SP in 5.3% of SPRING SSc patients may identify a subset characterized by milder disease, with a lower burden of vascular and organ complications. Conversely, lung involvement was more frequently observed in patients with more severe NVC microangiopathy.

1. Introduction

In systemic sclerosis (SSc), the microvascular alterations are a hallmark of the vascular involvement [1], which includes skin telangiectasias, pitting scars, digital ulcers, pulmonary arterial hypertension (PAH), and renal crisis [2]. Modifications of the microcirculation can be observed on nailfold videocapillaroscopy (NVC), for which a qualitative classification of the ‘scleroderma pattern’ (SP) has been provided [3,4] and is part of the 2013 SSc classification criteria [5]. Remarkably, the presence of a NVC-SP is also a criterion for the very early diagnosis of SSc (i.e., VEDOSS) [6].

Nonetheless, patients may be diagnosed with—and fulfil the classification criteria for—SSc even in the absence of NVC-SP in approximately 10% cases [7], yet it remains poorly defined whether these subjects harbor a distinct clinical profile. Preliminary evidence suggests a correlation between the presence of ‘active’ or ‘late’ NVC-SP and the likelihood of onset and progression of visceral manifestations in SSc [8]. However, it is less clear whether the risk of developing distinct complications differs when comparing patients with or without NVC-SP [8]. The SSc Progression Investigation (SPRING) project, started in 2015 under the endorsement of the Italian Society of Rheumatology (SIR), includes more than 1900 classified SSc patients, along with more than 250 VEDOSS cases. Within the SPRING cohort, our study aimed to: [1] determine the prevalence of SSc without NVC-SP; [2] characterize the cross-sectional clinical, serological, and therapeutic profile of these patients compared to those with NVC-SP, including comparisons with 'early', 'active', and 'late' NVC-SP subgroups; [3] assess longitudinal disease trajectories over a five-year follow-up; and [4] perform an exploratory comparison of VEDOSS patients with and without NVC-SP. Notably, while patients without NVC-SP were included in a previous SPRING-SIR publication as a comparator group [9], no dedicated analysis of this subset has been performed to date.

2. Methods

2.1. Study design, data source, and setting

SPRING is a retrospective, multicenter, nationwide cohort involving 38 tertiary referral centers for SSc. Data were collected using the REDCap (Research Electronic Data Capture) platform. Clear definitions for all variables were established and shared “a priori” to minimize heterogeneity across participating centers, and periodic quality checks were performed by the coordinating team [9]. The study was approved by the Ethics Committee of the Azienda Ospedaliera Universitaria

Careggi (Florence), reference number OSS 15.010. All participants provided informed consent prior to enrollment. The extracted data includes information entered up to July 15, 2022. For each patient, follow-up visits were scheduled annually (±2 months) after enrolment (hereafter referred to as 'baseline' visit), with a maximum follow-up duration of five years.

2.2. Study population and recorded variables

Patients from the SPRING registry were eligible for inclusion in this study if they were aged ≥18 years at enrollment, met the 2013 SSc classification criteria [5] or the VEDOSS criteria [6,10]. These patients underwent NVC, and were classified as: 'without NVC-SP' vs. 'with NVC-SP,' which was further categorized as 'early', 'active', or 'late' [3,4]. The NVC data were recorded at baseline, and NVC patterns were classified by trained rheumatologists at each center according to the standardized criteria published [3,4]. Patients lacking NVC information at enrolmentwere excluded from the analysis. SSc onset was defined as the time of appraisal of the first non-Raynaud's phenomenon manifestation [11].

Collected data included demographic [12] and clinical characteristics at baseline and at yearly intervals thereafter. These included: skin subsets (diffuse cutaneous—dcSSc, limited cutaneous—lcSSc, and sine scleroderma—ssSSc) [13]; oesophageal (dysphagia, reflux) and intestinal symptoms (diarrhoea, abdominal bloating, constipation, malabsorption); sicca syndrome (dry eyes and/or mouth); scleroderma renal crisis (sudden onset of severe arterial hypertension with acute renal failure); skin and peripheral vascular signs (puffy fingers, calcinosis, telangiectasia, pitting scars, digital ulcers); and musculoskeletal involvement (tenosynovitis and/or arthritis, defined as inflammatory changes observed in more than two joints; joint contractures; tendon friction rubs—TFR; clinically defined muscle weakness and atrophy). The Unified Vascular Phenotype (UVP) score was calculated by assigning one point each for the presence of puffy hands, skin telangiectasias, pitting scars, and digital ulcers (range 0-4), as described elsewhere [14,15].

Further variables included: the modified Rodnan skin score (mRSS); predicted forced vital capacity (FVC%) and diffusion capacity for carbon monoxide (DLCO%); presence of interstitial lung disease (ILD) on high-resolution computed tomography (HRCT); systolic pulmonary artery pressure (sPAP, mmHg), left ventricular ejection fraction (LVEF%) and diastolic dysfunction on echocardiography [9,13,16]; antinuclear (ANA) and SSc-related antibodies (anticentromere—ACA, anti-topoisomerase I—TOPO1, and anti-RNA polymerase III—POLR3). Pulmonary arterial hypertension (PAH) was confirmed by right heart catheterization and classified as WHO group 1, in accordance with the diagnostic criteria in use at the time of data collection [17]: PAH was absent when there was no suspicion according to the low probability of pulmonary hypertension on the DETECT algorithm [18], or when right heart catheterization excluded PAH.

Comorbidities included ischemic heart disease, stroke, arterial hypertension, dyslipidaemia, and diabetes mellitus [19,20]. Treatment data included use of immunosuppressive agents (cyclophosphamide, methotrexate, azathioprine, mycophenolate mofetil, rituximab, tocilizumab)and vasoactive/vasodilating therapies (endothelin receptor antagonists—bosentan, macitentan; phosphodiesterase-5 inhibitors—sildenafil, tadalafil; intravenous iloprost; calcium channel blockers). No patient in the study group was on prednisone or its equivalent at doses of 10 mg/day or more.

The VEDOSS case report form was shared with the one adopted for patients with established SSc, provided that no patient presented with skin sclerosis or sclerodactyly, nor fulfilled the 2013 SSc classification criteria.

2.3. Exposure and outcomes

The main exposure was the absence of NVC-SP [3,4] in patients classified as SSc [5].

In the cross-sectional analysis, the outcomes of interests were baseline characteristics of patients with SSc, including demographic, clinical and therapeutic features. A sensitivity analysis was performed to compare the characteristics of patients with SSc without NVC-SP vs. those of patients with 'early', active', or 'late' NVC-SP.

In the longitudinal analysis, the outcomes of interest were changes in disease manifestations (expressed as expected prevalence for categorical variables and expected means for continuous variables, as detailed in the statistical methods), evaluated at 12, 24, and 60 months of follow-up from the baseline visit.

A cross-sectional comparison between VEDOSS patients with and without the NVC-SP was performed as a complementary analysis.

2.4. Statistical analysis

Given the retrospective registry-based design, no formal a priori sample size calculation was performed. The study included all eligible patients with available baseline NVC and the effective sample size was determined by existing data.

After assessing for normality using the Shapiro-Wilk test, continuous variables were summarized as means (± standard deviation−SD) or medians (interquartile range—IQR), as appropriate. Categorical variables were expressed as numbers and counts and percentages (n/N, %).

Group comparisons were performed using appropriate statistical tests: Pearson's chi-square or Fisher's exact test for categorical variables, and Student's t-test or Mann-Whitney *U* test for continuous variables. To account for multiple comparisons, p-values were adjusted using the Benjamini-Hochberg procedure.

Multivariable logistic regression was used to explore associations of SSc without NVC-SP with the outcomes of interest. For binary logistic regression, results were reported as odds ratios (OR) with 95% confidence intervals (CI); for multinomial logistic regression, results were reported as relative risk ratios (RRR) with 95% CIs for each outcome category relative to the reference category (base outcome). In multivariable models, the UVP score was considered as an ordinal variable (0-4). Individual components of the UVP score were also evaluated separately to reduce reliance on the composite vascular index. Vasoactive treatment was considered a descriptive variable reflecting clinical management and vascular disease burden, rather than a core confounder in the primary adjusted models, because its prescription may occur downstream of peripheral vascular manifestations and NVC.

Multivariable models were fitted using clinically informed adjustment sets defined a priori, based on prior literature and expert opinion. Core covariates included age at SSc onset, sex, disease duration, cutaneous subset, and SSc-related autoantibodies, where appropriate according to the outcome under investigation. The specific adjustment set was adapted to each outcome to avoid overadjustment or adjustment for variables lying on the causal pathway. Exploratory univariable analyses were used to characterize the cohort and contextualize the clinical relevance of observed associations but were not used as an automated variable-selection procedure.

To evaluate the impact of SSc without NVC-SP on repeated measurements over time, longitudinal analyses were performed.

For binary outcomes (arthritis, calcinosis, digital ulcers, pitting scars, ILD, evidence of sPAP >40 mmHg on echocardiography), generalized estimating equations (GEE) were used to account for within-subject correlations. For continuous outcomes (predicted FVC% and DLCO%, mRSS, UVP score), mixed-effects models with random intercepts for participants were adopted. Although the UVP score is an ordinal variable (range 0–4), it was included in mixed-effects models as an approximately continuous measure for exploratory purposes, consistent with published applications of this score. Predicted marginal means and differences between groups were estimated, and contrasts were used to derive ORs (for binary outcomes) or mean differences (for continuous outcomes) with corresponding 95% CIs. For longitudinal analyses, the number of available observations was reported by NVC-SP group and

Table 1
Cross-sectional comparison of demographic, clinical, serological, and therapeutic features between SSc patients with and without the NVC scleroderma pattern (NVC-SP) at enrollment in the SPRING-SIR registry. Categorical variables are reported as counts (percentages); continuous variables as medians (IQR) [number of patients with available data].

	SSc SPRING cohort (N = 1903)	NVC-SP present (N = 1599)	NVC-SP absent (N = 90)	p	Adj.p
Demographic features					
Sex, n/N (%)	1681/1893 (88.8)	1409/1595 (88.3)	83/90 (92.2)	0.339	0.694
Age at entry, median (IQR)	60 (50-70) [1895]	60 (49-69) [1597]	63 (52-72) [90]	0.067	0.328
Age at RP onset, median (IQR)	45 (34-56) [1879]	45 (34-56) [1586]	48 (35-60) [89]	0.323	0.694
Age at SSc onset, median (IQR)	50 (39-60) [1745]	49 (39-59) [1488]	53 (45-63) [81]	**0.008**	0.087
Disease duration, median (IQR)	8 (4-15) [1744]	8 (4-14) [1487]	9 (4-14) [81]	0.969	>0.99
RP to SSc onset, median (IQR)	1 (0-4) [1741]	1 (0-4) [1485]	1 (0-5) [80]	0.088	0.388
Smoke, n/N (%)	559/1693 (33)	477/1451 (32.9)	29/77 (37.7)	0.456	0.746
Comorbidities					
Coronary artery disease, n/N (%)	55/1903 (2.9)	44/1599 (2.8)	5/90 (5.6)	0.181	0.556
Stroke, n/N (%)	17/1903 (0.9)	15/1599 (0.9)	2/90 (2.2)	0.228	0.560
Arterial hypertension, n/N (%)	450/1903 (23.6)	390/1599 (24.4)	20/90 (22.2)	0.734	0.915
Peripheral artery disease, n/N (%)	103/1903 (5.4)	81/1599 (5.1)	4/90 (4.4)	>0.99	>0.99
Dyslipidemia, n/N (%)	209/1903 (11)	184/1599 (11.5)	6/90 (6.7)	0.214	0.560
Diabetes mellitus, n/N (%)	56/1903 (2.9)	45/1599 (2.8)	6/90 (6.7)	**0.050**	0.302
Overlap AT disease, n/N (%)	204/1889 (10.8)	166/1593 (10.4)	11/90 (12.2)	0.715	0.915
Clinical features					
LeRoy subset, n/N (%)				**<0.001**	**<0.001**
ssSSc	229/1849 (12.4)	190/1582 (12)	27/88 (30.7)		**<0.001**
lcSSc	1255/1849 (67.9)	1063/1582 (67.2)	56/88 (63.6)		0.487
dcSSc	365/1849 (19.7)	329/1582 (20.8)	5/88 (5.7)		**<0.001**
mRSS, median (IQR)	4 (2-9) [1736]	4 (2-9) [1469]	3 (0-6) [85]	**0.001**	**0.013**
Pitting scars, n/N (%)	880/1867 (47.1)	760/1591 (47.8)	30/90 (33.3)	**0.010**	0.094
Digital ulcers, n/N (%)	407/1873 (21.7)	344/1596 (21.6)	14/90 (15.6)	0.222	0.560
Telangiectasias, n/N (%)	1135/1872 (60.6)	983/1595 (61.6)	47/90 (52.2)	0.095	0.388
UVP score, median (IQR)	2 (1-3) [1875]	2 (1-3) [1597]	1 (1-2) [90]	**0.001**	**0.013**
Calcinosis, n/N (%)	219/1866 (11.7)	193/1591 (12.1)	3/89 (3.4)	**0.020**	0.137
Arthritis, n/N (%)	209/1858 (11.2)	181/1583 (11.4)	9/88 (10.2)	0.861	>0.99
Tendon friction rubs, n/N (%)	156/1868 (8.4)	145/1592 (9.1)	4/90 (4.4)	0.185	0.556
Muscle weakness, n/N (%)	267/1867 (14.3)	228/1591 (14.3)	10/90 (11.1)	0.486	0.750
Muscle atrophy, n/N (%)	96/1866 (5.1)	83/1590 (5.2)	0/90 (0)	**0.020**	0.137
Oesophageal symptoms, n/N (%)	937/1872 (50.1)	801/1595 (50.2)	39/90 (43.3)	0.245	0.575
Intestinal symptoms, n/N (%)	366/1868 (19.6)	325/1592 (20.4)	13/90 (14.4)	0.215	0.560
Sicca syndrome, n/N (%)	542/1869 (29)	467/1594 (29.3)	27/90 (30)	0.981	>0.99
Scleroderma renal crisis, n/N (%)	22/1868 (1.2)	16/1592 (1)	1/90 (1.1)	0.609	0.885
LVEF <50%, n/N (%)	23/1489 (1.5)	22/1288 (1.7)	1/77 (1.3)	>0.99	>0.99
Diastolic dysfunction, n/N (%)	343/1514 (22.7)	308/1318 (23.4)	13/74 (17.6)	0.312	0.694
sPAP >40 mmHg, n/N (%)	168/1553 (10.8)	138/1345 (10.3)	9/79 (11.4)	0.896	>0.99
PAH on RHC, n/N (%)	31/1421 (2.2)	27/1240 (2.2)	1/71 (1.4)	>0.99	>0.99
ILD, n/N (%)	660/1903 (34.7)	562/1599 (35.1)	24/90 (26.7)	0.126	0.425
FVC%, median (IQR)	102 (87-116) [1411]	102 (87-116) [1214]	107 (89-123) [74]	0.064	0.328
DLCO%, median (IQR)	69 (55-82) [1342]	69 (55-82) [1158]	72 (59-85) [68]	0.115	0.414
Autoantibodies					
ACA, n/N (%)	771/1903 (40.5)	669/1599 (41.8)	37/90 (41.1)	0.979	>0.99
anti-TOPO1, n/N (%)	666/1858 (35.8)	552/1592 (34.7)	26/89 (29.2)	0.347	0.694
anti-POLR3, n/N (%)	40/1569 (2.5)	34/1348 (2.5)	3/77 (3.9)	0.448	0.746
Therapy					
Immunosuppressants, n/N (%)	712/1633 (43.6)	599/1378 (43.5)	26/78 (33.3)	0.101	0.388
Vasoactive treatments, n/N (%)	1621/1858 (87.2)	1395/1565 (89.1)	67/89 (75.3)	**<0.001**	**0.004**

AT: autoimmune; ACA: anticentromere antibodies; dcSSc: diffuse cutaneous systemic sclerosis; lcSSc: limited cutaneous systemic sclerosis; ssSSc: systemic sclerosis sine scleroderma; DLCO%: predicted diffusing capacity of the lungs for carbon monoxide; FVC%: predicted forced vital capacity; ILD: interstitial lung disease; LVEF: left ventricle ejection fraction; mRSS: modified Rodnan's skin score; NVC-SP: nailfold videocapillaroscopy scleroderma pattern; PAH: pulmonary arterial hypertension; POLR3: anti-RNA polymerase III; RHC: right heart catheterization; RP: Raynaud's phenomenon; sPAP: systolic pulmonary artery pressure; TOPO1: topoisomerase 1; UVP: unified vascular phenotype score.

follow-up timepoint. Given the retrospective registry-based design, missing follow-up data reflected real-world data availability across visits and outcomes. To assess the potential impact of missing follow-up data, a complete-case/available-case sensitivity analysis was performed using observations available at each follow-up timepoint. Because of the limited number of patients without NVC-SP at later visits, this analysis was considered exploratory.

A two-sided p-value <0.05 was considered statistically significant. All statistical analyses were conducted using RStudio (version 2024.12.0 + 467; R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Characteristics of SSc patients without NVC-SP at baseline

The SPRING registry enrolled 1903 SSc patients: 88.8% female (1681/1893), median age at disease onset 50 years-IQR 39-60, median disease duration at entry 8 years, IQR 4-15. Cutaneous subsets were dcSSc in 19.7% (365/1849) of patients, lcSSc in 67.9% (1255/1849), and ssSSc in 12.4% (229/1849). Disease manifestations included digital ulcers in 21.7% (407/1873) of patients, telangiectasias in 60.6% (1135/1872), calcinosis in 11.7% (219/1866), arthritis in 11.2% (209/1858),

ILD in 34.7% (660/1903), PAH on right heart catheterization in 2.2% (31/1421), and oesophageal involvement in 50.1% (937/1872). SSc-specific autoantibodies included ACA in 40.5% (771/1903), anti-TOPO1 in 35.8% (666/1858), and anti-POLR3 in 2.5% (40/1569). Immunosuppressive treatments were administered to 43.6% (712/1633) of patients, and vasoactive/vasodilating therapies to 87.2% (1621/1858) (Table 1).

In 1689 patients, NVC data were available and 90 had SSc without NVC-SP (5.3%). Compared to those with NVC-SP, these patients had a higher median age at SSc onset (53 years, IQR 45-63 vs. 49 years, IQR 39-59; $p = 0.008$), while the disease duration at entry, sex, and comorbidities distribution were similar.

Notably, SSc patients without NVC-SP were more frequently ssSSc (30.7%, 27/88 vs 12%, 190/1582; $p < 0.001$) and less frequently dcSSc (5.7%,5/88 vs 20.8%, 329/1582; $p < 0.001$), while the prevalence of lcSSc was similar in the two groups (63.6%, 56/88 vs 67.2%. 1063/1582; $p = 0.487$). Pitting scars (33.3%, 30/90 vs 47.8%, 760/1591; $p = 0.010$) and calcinosis cutis (3.4%, 3/89 vs 12.1%, 193/1591; $p = 0.020$) were significantly less frequent in this group, and the UVP score was lower (1, IQR 1-2 vs 2, IQR 1-3; $p = 0.001$), reflecting a lower overall burden of vascular complications. Accordingly, vasoactive treatments were less frequently prescribed in this disease subset (75.3%, 67/89 vs 89.1%, 1395/1565; $p < 0.001$).

After adjustment for confounders (Table 2), SSc without NVC-SP remained positively associated with the ssSSc phenotype (multinomial RRR 2.97, 95% CI 1.74-5.06; $p < 0.001$) and negatively with dcSSc (RRR 0.36, 95% CI 0.14-0.94; $p = 0.036$), compared to lcSSc as the reference category.

On binary logistic models, no association was observed for pitting scars and calcinosis, while telangiectasias were less common in patients without NVC-SP (OR 0.62, 95% CI 0.39-1.00; $p = 0.047$). Most importantly, we observed a negative association between the UVP score and the lack of NVC-SP (OR 0.57, 95% CI 0.38-0.86; $p = 0.007$). In adjusted models, absent NVC-SP was associated with lower odds of puffy hands (OR 0.62, 95% CI 0.39–0.98; p=0.040), whereas no significant association was observed with digital ulcers (OR 0.71, 95% CI 0.34–1.36; p=0.333).

Table 2
Multivariable logistic regression models evaluating the association of absent NVC-SP with clinical outcomes showing $p < 0.10$ on univariable analysis. For cutaneous subsets, multinomial logistic regression was fit, lcSSc represented the reference category.

Outcomes	Covariates	OR/RRR	95% CI	p
ssSSc vs. lcSSc	Age at SSc onset	0.98	0.97-0.99	<0.001
	Disease duration	0.92	0.90-0.94	<0.001
	Sex	1.95	1.07-3.57	0.030
	Anti-TOPO1	0.56	0.38-0.82	0.003
	Absent NVC-SP	2.97	1.74-5.06	**<0.001**
dcSSc vs. lcSSc	Age at SSc onset	0.98	0.97-0.99	<0.001
	Disease duration	0.98	0.96-1.00	0.021
	Sex	0.65	0.44-0.95	0.027
	Anti-TOPO1	4.64	3.51-6.14	**<0.001**
	Absent NVC-SP	0.36	0.14-0.94	0.036
Pitting scars	Age at SSc onset	0.98	0.98-0.99	<0.001
	Disease duration	1.06	1.04-1.07	<0.001
	Sex	0.53	0.38-0.75	<0.001
	Anti-TOPO1	1.81	1.42-2.31	<0.001
	dcSSc	3.04	2.26-4.11	<0.001
	Absent NVC-SP	0.73	0.43-1.19	0.208
Telangiectasias	Age at SSc onset	1.01	1.00-1.02	0.002
	Disease duration	1.08	1.06-1.10	<0.001
	Sex	1.19	0.86-1.65	0.296
	Anti-TOPO1	0.88	0.69-1.12	0.297
	dcSSc	1.56	1.17-2.09	0.003
	Absent NVC-SP	0.62	0.39-1.00	**0.047**
Calcinosis	Age at SSc onset	0.99	0.98-1.00	0.185
	Disease duration	1.07	1.05-1.09	<0.001
	Sex	1.39	0.81-2.56	0.262
	Anti-TOPO1	0.51	0.33-0.75	0.001
	dcSSc	2.46	1.63-3.68	<0.001
	Absent NVC-SP	0.37	0.09-1.02	0.096
UVP score	Age at SSc onset	1.00	0.99-1.00	0.143
	Disease duration	1.05	1.03-1.06	<0.001
	Sex	0.72	0.54-0.95	0.021
	Anti-TOPO1	1.20	0.97-1.48	0.089
	dcSSc	1.94	1.52-2.49	<0.001
	Absent NVC-SP	0.57	0.38-0.86	**0.007**
Puffy fingers	Age at SSc onset	1.00	0.99-1.01	0.533
	Disease duration	0.97	0.95-0.98	<0.001
	Sex	0.95	0.69-1.3	0.734
	Anti-TOPO1	0.65	0.52-0.81	<0.001
	Absent NVC-SP	0.62	0.39-0.98	0.041
Digital ulcers	Age at SSc onset	0.99	0.98-1.00	0.005
	Disease duration	1.04	1.03-1.06	<0.001
	Sex	0.65	0.45-0.95	0.023
	Anti-TOPO1	1.68	1.27-2.23	<0.001
	dcSSc	1.91	1.41-2.59	<0.001
	Absent NVC-SP	0.71	0.34-1.36	0.333

dcSSc: diffuse cutaneous SSc; NVC-SP: nailfold videocapillaroscopy scleroderma pattern; OR: odds ratio of the binomial logistic regression; RRR: relative risk ratio of the multinomial logistic regression; ssSSc: SSc sine scleroderma; TOPO1: topoisomerase 1; UVP: unified vascular phenotype score.

3.2. Characteristics of SSc without NVC-SP versus 'early', 'active', and 'late' NVC-SP

Supplementary Table 1 shows the comparison of baseline demographic and clinical features of SSc without NVC-SP versus patients showing 'early', 'active', or 'late' NVC-SP. Patients without a NVC-SP had a lower burden of cutaneous and visceral manifestations when compared to those with a 'late' and 'active' NVC-SP, while no major differences were observed with those showing a 'early' NVC-SP.

On multivariable logistic regression (Supplementary Table 2), patients with 'early' (OR 0.55, 95% CI 0.31-0.97; $p = 0.038$), 'active' (OR 0.29, 95% CI 0.17-0.51; $p < 0.001$), and 'late' (OR 0.11, 95% CI 0.06-0.23; $p < 0.001$) NVC-SP were less likely to be ssSSc compared to those without NVC-SP. The UVP score was significantly higher with 'active' (OR 2.35, 95% CI 1.26-4.39; $p = 0.007$) and 'late' (OR 2.40, 95% CI 1.19-4.85; $p = 0.015$) NVC-SP, while ILD remained associated with the 'late' NVC-SP (OR 1.83, 95% CI 1.05-3.18; $p = 0.033$).

3.3. Longitudinal phenotype of patients with SSc without NVC-SP

According to generalized effects models, the estimated probability of experiencing vascular outcomes (new evidence of calcinosis, pitting scars, digital ulcers, or sPAP >40 mmHg on echocardiography) during follow-up was numerically lower in patients with SSc without NVC-SP than in those with NVC-SP. In particular, at the 12-month follow-up, patients without NVC-SP showed a significantly lower probability of having pitting scars (32%, 95% CI 22-43 vs 47%, 95% CI 45-50), corresponding to an absolute risk reduction of 15% (OR 0.52, 95% CI 0.32-0.87; $p = 0.012$). Likewise, their probability of having calcinosis was significantly lower at both 24 months (2.7%, 95% CI 0.7-10 vs 14%, 95% CI 11-16; absolute risk reduction 11%; OR 0.18, 95% CI 0.04-0.76; $p = 0.020$) and 60 months (3.1%, 95% CI 0.7-13 vs 15%, 95% CI 11-19; absolute risk reduction 12%; OR 0.18, 95% CI 0.04-0.86; $p = 0.031$). Notably, no association was found between SSc without NVC-SP and ILD or arthritis over time (Fig. 1).

Compared to patients with the NVC-SP, those without NVC-SP exhibited a significantly lower burden of skin and vascular involvement throughout the follow-up. Mean mRSS values were consistently lower at 12 months (4, 95% CI 2-6 vs 7, 95% CI 6.5-7; mean difference −3, $p = 0.001$), 24 months (4, 95% CI 2-6 vs 7, 95% CI 7-8; mean difference −3, $p = 0.001$), and 60 months (4, 95% CI 1-6 vs 7, 95% CI 7-8; mean difference −4, $p = 0.002$). UVP scores also remained significantly lower at 12 months (mean UVP 1.4, 95% CI 1.1-1.6, vs 1.8, 95% CI 1.7-1.9; mean difference −0.4, 95% CI −0.7 to −0.2; $p = 0.001$), at 24 months

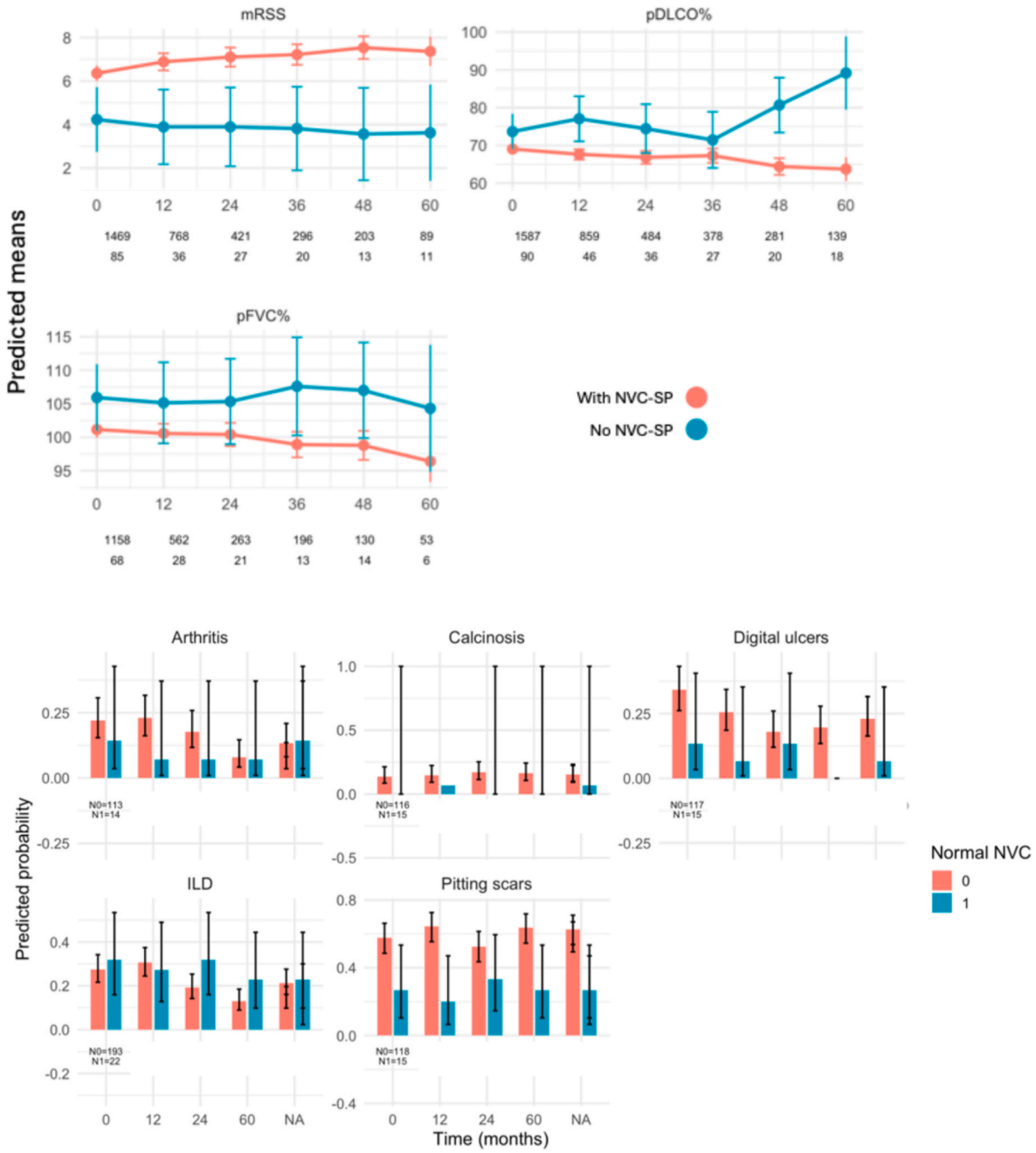

Fig. 1. Predicted mean values of continuous variables at 12, 24, and 60 months in SSc without NVC-SP (green) or with the NVC-SP (coral). Patient numbers at each timepoint are reported below each panel and correspond to the number of available observations contributing to the outcome-specific model at that visit. The upper row refers to patients with NVC-SP, whereas the lower row refers to patients without NVC-SP. Estimated probability (from GEE models) of having selected disease manifestations at 12, 24, and 60 months of follow up in patients with SSc without NVC-SP (green) or with the NVC-SP (coral).

(mean UVP 1.4, 95% CI 1.1-1.7, vs 1.7, 95% CI 1.6-1.8; mean difference −0.3, 95% CI −0.6 to 0.0; p = 0.047), and at 60 months (mean UVP 1.4, 95% CI 1.0-1.7, vs 1.8, 95% CI 1.7-1.9; mean difference −0.4, 95% CI −0.8 to −0.1; p = 0.024).

Predicted DLCO% was significantly higher in SSc without NVC-SP at all time points: 12 months (77%, 95% CI 71-83, vs 68%, 95% CI 66-69; mean difference 9.4%, 95% CI 3.3-16; p = 0.003), 24 months (74%, 95% CI 68-81, vs 67%, 95% CI 65-69; mean difference 7.6%, 95% CI 0.9-14; p = 0.026), and 60 months (89%, 95% CI 79-99, vs 64%, 95% CI 61-67; mean difference 25%, 95% CI 15-36; p < 0.001). By contrast, no significant differences in predicted FVC% were observed between the two groups at any time point (Fig. 1).

Since the number of available observations decreased over time in both groups, a complete-case/available-case sensitivity analysis was performed and reported in Supplementary Fig. 1. Although the small number of patients without NVC-SP at later timepoints prevents robust statistical inference, the observed trajectories were qualitatively similar to those obtained in the primary longitudinal models.

3.4. Clinical relevance of absent NVC-SP in VEDOSS patients

SPRING included 268 patients with VEDOSS (Table 3): 92% were females, and the median age at RP onset was 44 years (IQR 32-56); ANA were detected in 97.7% (255/261) patients, with ACA in 45.1% (121/

Table 3
Comparison of baseline characteristics of VEDOSS patients with and without the NVC scleroderma pattern.

	SPRING-VEDOSS cohort (N = 268)	NVC-SP present (N = 162)	NVC-SP absent (N = 85)	p	adj.p
Demographic features					
Age at entry, median (IQR)	54 (43-66) [267]	52 (41-64) [162]	54 (44-65) [85]	0.474	>0.99
Age at RP onset, median (IQR)	44 (32-56) [265]	43 (30-54) [162]	46 (33-56) [84]	0.352	>0.99
Sex, n/N (%)	245/266 (92.1)	146/160 (91.2)	80/85 (94.1)	0.584	>0.99
Smoke, n/N (%)	84/239 (35.1)	49/148 (33.1)	30/75 (40)	0.385	>0.99
Menopause, n/N (%)	131/222 (59)	75/133 (56.4)	46/75 (61.3)	0.584	>0.99
Comorbidities					
Arterial hypertension, n/N (%)	37/268 (13.8)	21/162 (13)	13/85 (15.3)	0.760	>0.99
Dyslipidaemia, n/N (%)	27/268 (10.1)	12/162 (7.4)	13/85 (15.3)	0.084	0.745
Diabetes mellitus, n/N (%)	6/268 (2.2)	4/162 (2.5)	1/85 (1.2)	0.662	>0.99
COPD, n/N (%)	2/268 (0.7)	1/162 (0.6)	0/85 (0)	>0.99	>0.99
Cancer, n/N (%)	17/268 (6.3)	9/162 (5.6)	6/85 (7.1)	0.850	>0.99
Clinical features					
Oesophageal symptoms, n/N (%)	89/257 (34.6)	51/158 (32.3)	33/83 (39.8)	0.310	>0.99
Intestinal symptoms, n/N (%)	31/257 (12.1)	19/159 (11.9)	10/83 (12)	>0.99	>0.99
Sicca syndrome, n/N (%)	75/257 (29.2)	44/158 (27.8)	24/83 (28.9)	0.981	>0.99
Pitting scars, n/N (%)	6/257 (2.3)	4/159 (2.5)	1/83 (1.2)	0.663	>0.99
Digital ulcers, n/N (%)	4/257 (1.6)	2/159 (1.3)	1/83 (1.2)	>0.99	>0.99
Telangiectasias, n/N (%)	29/256 (11.3)	14/158 (8.9)	13/83 (15.7)	0.169	0.865
UVP score, n/N (%)	0 (0-1) [256]	0 (0-1) [158]	1 (0-1) [83]	**0.002**	**0.060**
Calcinosis, n/N (%)	5/256 (2)	2/158 (1.3)	1/83 (1.2)	>0.99	>0.99
Arthritis, n/N (%)	19/256 (7.4)	11/157 (7)	6/83 (7.2)	>0.99	>0.99
ILD, n/N (%)	26/268 (9.7)	16/162 (9.9)	7/85 (8.2)	0.848	>0.99
FVC%, median (IQR)	107 (93-120) [187]	111 (92-122) [116]	107 (98-118) [62]	0.839	>0.99
DLCO%, median (IQR)	78 (68.75-88.25) [192]	78 (68-89) [121]	80 (70-87) [62]	0.938	>0.99
Conduction block, n/N (%)	2/130 (1.5)	2/85 (2.4)	0/39 (0)	>0.99	>0.99
Arrhythmia, n/N (%)	6/130 (4.6)	4/85 (4.7)	0/39 (0)	0.307	>0.99
PASP >40 mmHg, n/N (%)	6/185 (3.2)	2/116 (1.7)	2/62 (3.2)	0.611	>0.99
LVEF <50%, n/N (%)	4/177 (2.3)	2/112 (1.8)	2/59 (3.4)	0.609	>0.99
Diastolic dysfunction, n/N (%)	24/171 (14)	10/105 (9.5)	13/62 (21)	0.066	0.745
Autoantibodies					
ANA, n/N (%)	255/261 (97.7)	155/161 (96.3)	84/84 (100)	0.097	0.745
ACA, n/N (%)	121/268 (45.1)	67/162 (41.4)	45/85 (52.9)	0.109	0.745
anti-TOPO1, n/N (%)	36/261 (13.8)	21/161 (13)	12/84 (14.3)	0.942	>0.99
anti-POLR3, n/N (%)	6/234 (2.6)	4/142 (2.8)	1/79 (1.3)	0.657	>0.99
Treatments					
Immunosuppressants, n/N (%)	30/231 (13)	21/146 (14.4)	5/68 (7.4)	0.215	0.978
Vasoactive treatments, n/N (%)	154/253 (60.9)	102/158 (64.6)	44/77 (57.1)	0.339	>0.99

ACA: anticentromere antibodies; ANA: antinuclear antibodies; COPD: chronic obstructive pulmonary disease; DLCO%: predicted diffusing capacity of the lungs for carbon monoxide; FVC%: predicted forced vital capacity; ILD: interstitial lung disease; POLR3: RNA polymerase III; RP: Raynaud's phenomenon; sPAP: systolic pulmonary artery pressure; TOPO1: topoisomerase 1; UVP: unified vascular phenotype score.

268), anti-TOPO1 in 13.8% (36/261), and anti-POLR3 in 2.6%. Gastrointestinal manifestations included oesophageal and intestinal symptoms in 34.6% (89/257) and 12.1% (31/257), respectively;29.2% (75/257) patients complained of sicca syndrome and 7.4% (19/256) of arthritis. ILD was recorded in 9.7% (26/268) patients, the median FVC% predicted values being 107% (IQR 93-120) and DLCO% predicted 78 (IQR 69-88). Pitting scars were reported in 2.3% (6/234) of subjects, telangiectasias in 11.3% (29/256), calcinosis in 2% (5/256), and digital ulcers in 1.6% (4/257); the median UVP score was 0 (IQR 0-1).

Among VEDOSS patients, 32% had no detectable NVC-SP. Overall, the characteristics of VEDOSS patients with and without NVC-SP were similar, despite the latter group showing a lower burden of vascular manifestations, represented by the UVP score (Table 3). After adjusting for age at RP onset, sex, and anti-TOPO1 positivity, multivariable logistic regression confirmed that the absence of NVC-SP was associated with decreasing UVP score in VEDOSS (OR 2.44, 95% CI 1.41-4.22; $p = 0.001$).

4. Discussion

Our data show that in some SSc patients NVC capillary modifications may be not yet detectable, suggesting a very slow progression of the microvascular disease [1,9,21]. The prevalence and clinical relevance of absent NVC-SP among patients fulfilling the 2013 SSc classification criteria has been poorly described. In a previous EUSTAR study, 13.7% of patients did not have a NVC-SP [7], and similar results were reported in another well-characterized monocentric cohort [22]. Herein, we report a prevalence of SSc without NVC-SP as high as 5.3% in the Italian SPRING registry, relatively lower but still representing a relevant proportion of SSc patients. The cross-sectional baseline data were partially and preliminarly presented [9]; however, that study did not include longitudinal analyses, UVP score assessments, or VEDOSS comparisons for this subgroup. [12].

In our study, aligning with smaller cohorts [8,22], SSc without NVC-SP was associated with a lower prevalence of peripheral vascular manifestations (telangiectasias, pitting scars, and calcinosis). However, we could not detect significant associations between NVC findings and digital ulcers [7,23], possibly due to class imbalance and the relatively small size of the group without NVC-SP. Nevertheless, the use of vasoactive medications and the overall vascular burden—reflected by the proposed UVP score—were significantly lower in patients without NVC-SP compared to those with NVC-SP. Overall, such vascular findings could be due to differences observed between patients without NVC-SP compared to those with ‘active’ and ‘late’—but not ‘early’— NVC-SP [22].

NVC-SP is a VEDOSS criterion and might represent a potential hallmark of progression to established SSc, particularly in cases that were negative at disease onset. Our explorative analysis identified that the NVC-SP was absent in 32% SPRING-VEDOSS cases, in agreement with the EUSTAR-VEDOSS data [6]. Remarkably, the association between the presence of NVC-SP and the increased overall vascular burden was confirmed in VEDOSS cases. Therefore, despite the sample size prevents

any sound conclusion, these results may first suggest that the correlation between capillary alterations and vascular burden—observed in established SSc—may be already present in the very early disease phases. Further evidence is required to assess whether NVC-SP could help stratify VEDOSS patients at higher risk of long-term vascular complications, since these subjects might represent a target population more likely to benefit from preventive pharmacological and non-pharmacological measures.

Previous works have postulated that SSc patients without a NVC-SP have a lower chance of developing vascular complications during follow-up, compared to those with pathologic NVC changes [8]. In our study, peripheral vascular manifestations were consistently more prevalent among patients with a NVC-SP at 12, 24, and 60 months after baseline, despite a statistical significance being reached only in selected comparisons. Nonetheless, the trend of the UVP score throughout the follow-up remained lower in SSc patients without NVC-SP compared to those showing the NVC-SP.

We observed that SSc patients without NVC-SP had a milder cutaneous phenotype. Indeed, the absence of NVC-SP was positively associated with the ssSSc phenotype and negatively with dcSSc, aligning with previous evidence from EUSTAR [7]. Interestingly, a higher prevalence of skin sclerosis was also reported among patients with mixed connective tissue disease and NVC-SP, compared to patients without specific NVC alterations [24]. Thus, an association between microvascular alterations and the severity of skin involvement across scleroderma spectrum disorders may be postulated[25]. Remarkably, in our analysis, SSc patients without NVC-SP retained lower mRSS values across follow-up visits compared to their counterpart.

The recent, single-center study on a mixed connective tissue disease, ILD was associated with reduced NVC capillary density but not with the presence of the NVC-SP [24]. In SPRING-SIR, we could not describe any difference comparing the prevalence of ILD in patients with or without NVC-SP. Nevertheless, ILD was associated with the 'late' NVC-SP after adjusting for notable risk factors like dcSSc and anti-TOPO1. Aligning with previous reports [21,22], we observed significantly decreased values of predicted DLCO% but not FVC% over time in patients with the NVC-SP compared to those without. Despite this finding might suggest a sufferance of the pulmonary microvasculature, we were not able to demonstrate that patients with and without NVC-SP differed in terms of right-heart catheterization-diagnosed PAH or increased echocardiographic sPAP [26].

Several limitations should be discussed. First, referral bias should be considered, since all SPRING centers were tertiary care units, likely selecting patients with a more severe SSc phenotype, generally linked with more severe NVC findings as confirmed in this analysis [11,12,14,23]. Second, while information on NVC was available for most patients, class imbalance could have affected the statistical power of our analysis, despite the genuine prevalence of microvascular alterations in SSc patients. This also applies to selected outcomes, such as PAH and SRC, which are underrepresented in the SPRING registry [9,12,13,16].Third, the UVP score includes vascular manifestations that conceptually overlap with NVC-captured microangiopathy, raising the risk of circular interpretation. To partially address this, associations between absent NVC-SP and individual vascular components were tested, yielding inconsistent results. Additionally, vasoactive therapy may act as a confounder, mediator, or effect modifier in this context, and this distinction could not be formally tested. Fourth, the small size of the SSc without NVC-SP group — particularly at later follow-up visits, where the number of available observations decreased substantially — prevented confounder-adjusted longitudinal analyses and introduced sensitivity to attrition bias. A complete-case/available-case sensitivity analysis showed qualitatively similar trajectories, but without robust statistical confirmation; accordingly, all longitudinal estimates should be considered exploratory. In particular, apparent fluctuations in the model-predicted probability of ILD and calcinosis likely reflect selective loss to follow-up of patients with more severe disease, rather than genuine disease remission. Additionally, the follow-up duration was limited to five years, which may be insufficient to capture long-term complications. Fifth, we could not evaluate the longitudinal trend of NVC alterations in patients without a baseline NVC-SP, since these were not recorded in the CRF of the registry. Sixth, due to the sample size and the cross-sectional design, our findings on VEDOSS patients must be interpreted cautiously and as purely speculative to inform further research.

In conclusion, the present analysis from the SPRING-SIR registry demonstrates that approximately 5% of classified SSc patients lack the NVC-SP, and that this subset is characterized by a milder overall phenotype, with lower vascular burden, lower mRSS, and better-preserved DLCO over time. The relationship with pulmonary vascular disease and fibrosing manifestations remains less clear, since a more severe skin involvement is observed in patients with the NVC-SP, while ILD shows only signals restricted to the 'late' NVC-SP. Notably, the absence of NVC-SP might have a prognostic implication, as these patients have a lower probability of developing new vascular complications, calcinosis, and worsening mRSS. Further multicenter studies with repeated assessment [25–27] should assess the longitudinal trend of NVC alterations and their correlation with the incidence and progression of SSc-related complications. Continued research is needed to elucidate the mechanistic interplay between vasculopathy and fibrosing manifestations of the SSc disease.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or non-profit sectors.

CRediT authorship contribution statement

Antonio Tonutti: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Writing – original draft, Writing – review & editing. **Maria De Santis:** Data curation, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Francesca Motta:** Data curation, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Gianluigi Bajocchi:** Data curation, Investigation, Visualization, Writing – review & editing. **Dilia Giuggioli:** Data curation, Investigation, Visualization, Writing – review & editing. **Silvia Bellando-Randone:** Data curation, Investigation, Visualization, Writing – review & editing. **Cosimo Bruni:** Data curation, Investigation, Visualization, Writing – review & editing. **Giovanni Zanframundo:** Data curation, Investigation, Visualization, Writing – review & editing. **Roberta Foti:** Data curation, Investigation, Visualization, Writing – review & editing. **Giovanna Cuomo:** Data curation, Investigation, Visualization, Writing – review & editing. **Alarico Ariani:** Data curation, Investigation, Visualization, Writing – review & editing. **Edoardo Rosato:** Data curation, Investigation, Visualization, Writing – review & editing. **Gemma Lepri:** Data curation, Investigation, Visualization, Writing – review & editing. **Francesco Girelli:** Data curation, Investigation, Visualization, Writing – review & editing. **Elisabetta Zanatta:** Data curation, Investigation, Visualization, Writing – review & editing. **Silvia Laura Bosello:** Data curation, Investigation, Visualization, Writing – review & editing. **Ilaria Cavazzana:** Data curation, Investigation, Visualization, Writing – review & editing. **Francesca Ingegnoli:** Data curation, Investigation, Visualization, Writing – review & editing. **Fabio Cacciapaglia:** Data curation, Investigation, Visualization, Writing – review & editing. **Giuseppe Murdaca:** Data curation, Investigation, Visualization, Writing – review & editing. **Giuseppina Abignano:** Data curation, Investigation, Visualization, Writing – review & editing. **Giorgio Pettiti:** Data curation, Investigation, Visualization, Writing – review & editing. **Alessandra Della Rossa:** Data curation, Investigation, Visualization, Writing – review & editing. **Maurizio Caminiti:** Data curation, Investigation, Visualization, Writing – review & editing. **Anna Maria Iuliano:** Data

curation, Investigation, Visualization, Writing – review & editing. **Giovanni Ciano:** Data curation, Investigation, Visualization, Writing – review & editing. **Lorenzo Beretta:** Data curation, Investigation, Visualization, Writing – review & editing. **Gianluca Bagnato:** Data curation, Investigation, Visualization, Writing – review & editing. **Ennio Lubrano:** Data curation, Investigation, Visualization, Writing – review & editing. **Ilenia De Andres:** Data curation, Investigation, Visualization, Writing – review & editing. **Luca Idolazzi:** Data curation, Investigation, Visualization, Writing – review & editing. **Marta Saracco:** Data curation, Investigation, Visualization, Writing – review & editing. **Cecilia Agnes:** Data curation, Investigation, Visualization, Writing – review & editing. **Corrado Campochiaro:** Data curation, Investigation, Visualization, Writing – review & editing. **Giacomo De Luca:** Data curation, Investigation, Visualization, Writing – review & editing. **Martina Orlandi:** Data curation, Investigation, Visualization, Writing – review & editing. **Marco Di Battista:** Data curation, Investigation, Visualization, Writing – review & editing. **Mariangela Nivuori:** Data curation, Investigation, Visualization, Writing – review & editing. **Livio Milazzo:** Data curation, Investigation, Visualization, Writing – review & editing. **Edoardo Cipolletta:** Data curation, Investigation, Visualization, Writing – review & editing. **Federica Lumetti:** Data curation, Investigation, Visualization, Writing – review & editing. **Amelia Spinella:** Data curation, Investigation, Validation, Writing – review & editing. **Emanuele Cocchiara:** Data curation, Investigation, Visualization, Writing – review & editing. **Veronica Codullo:** Data curation, Investigation, Visualization, Writing – review & editing. **Beatrice Moccaldi:** Data curation, Investigation, Visualization, Writing – review & editing. **Elisa Visalli:** Data curation, Investigation, Visualization, Writing – review & editing. **Carlo Iandoli:** Data curation, Investigation, Visualization, Writing – review & editing. **Antonietta Gigante:** Data curation, Investigation, Visualization, Writing – review & editing. **Greta Pellegrino:** Data curation, Investigation, Visualization, Writing – review & editing. **Erika Pigatto:** Data curation, Investigation, Visualization, Writing – review & editing. **Maria Grazia Lazzaroni:** Data curation, Investigation, Visualization, Writing – review & editing. **Enrico De Lorenzis:** Data curation, Investigation, Visualization, Writing – review & editing. **Gianna Mennillo:** Data curation, Investigation, Visualization, Writing – review & editing. **Giuseppa Pagano-Mariano:** Data curation, Investigation, Visualization, Writing – review & editing. **Federica Furini:** Data curation, Investigation, Visualization, Writing – review & editing. **Licia Vultaggio:** Data curation, Investigation, Validation, Writing – review & editing. **Simone Parisi:** Data curation, Investigation, Visualization, Writing – review & editing. **Clara Lisa Peroni:** Data curation, Investigation, Visualization, Writing – review & editing. **Enrico Fusaro:** Data curation, Investigation, Visualization, Writing – review & editing. **Gerolamo Bianchi:** Data curation, Investigation, Visualization, Writing – review & editing. **Gian Domenico Sebastiani:** Data curation, Investigation, Visualization, Writing – review & editing. **Marcello Govoni:** Data curation, Investigation, Visualization, Writing – review & editing. **Salvatore D'Angelo:** Data curation, Investigation, Visualization, Writing – review & editing. **Franco Cozzi:** Data curation, Investigation, Visualization, Writing – review & editing. **Franco Franceschini:** Data curation, Investigation, Visualization, Writing – review & editing. **Serena Guiducci:** Data curation, Investigation, Visualization, Writing – review & editing. **Valeria Riccieri:** Data curation, Investigation, Visualization, Writing – review & editing. **Lorenzo Dagna:** Data curation, Investigation, Visualization, Writing – review & editing. **Carlo Salvarani:** Visualization, Writing – review & editing. **Florenzo Iannone:** Data curation, Investigation, Visualization, Writing – review & editing. **Marco Matucci-Cerinic:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Clodoveo Ferri:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Rossella De Angelis:** Conceptualization, Data curation, Formal analysis, Investigation, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The Authors acknowledge the Italian Society for Rheumatology (SIR) for supporting the development of the SPRING research.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jtauto.2026.100381.

Data availability

Data will be made available on request.

References

[1] M. Matucci-Cerinic, B. Kahaleh, F.M. Wigley, Evidence that systemic sclerosis is a vascular disease, Arthritis Rheum. 65 (2013) 1953–1962, https://doi.org/10.1002/art.37988.

[2] C.P. Denton, D. Khanna, Systemic sclerosis, Lancet 390 (2017) 1685–1699, https://doi.org/10.1016/S0140-6736(17)30933-9.

[3] V. Smith, A. Vanhaecke, A.L. Herrick, O. Distler, M.G. Guerra, C.P. Denton, E. Deschepper, I. Foeldvari, M. Gutierrez, E. Hachulla, F. Ingegnoli, S. Kubo, U. Müller-Ladner, V. Riccieri, A. Sulli, J.M. van Laar, M.C. Vonk, U.A. Walker, M. Cutolo, EULAR Study Group on Microcirculation in Rheumatic Diseases, Fast track algorithm: how to differentiate a "scleroderma pattern" from a "non-scleroderma pattern", Autoimmun. Rev. (2019) 102394 https://doi.org/10.1016/j.autrev.2019.102394.

[4] V. Smith, A.L. Herrick, F. Ingegnoli, N. Damjanov, R. De Angelis, C.P. Denton, O. Distler, K. Espejo, I. Foeldvari, T. Frech, B. Garro, M. Gutierrez, G. Gyger, E. Hachulla, R. Hesselstrand, A. Iagnocco, C. Kayser, K. Melsens, U. Müller-Ladner, S. Paolino, C. Pizzorni, M. Radic, V. Riccieri, M. Snow, W. Stevens, A. Sulli, J. M. van Laar, M.C. Vonk, A. Vanhaecke, M. Cutolo, EULAR study group on microcirculation in rheumatic diseases and the scleroderma clinical trials consortium group on capillaroscopy, standardisation of nailfold capillaroscopy for the assessment of patients with Raynaud's phenomenon and systemic sclerosis, autoimmun, Rev (2020) 102458, https://doi.org/10.1016/j.autrev.2020.102458.

[5] F. van den Hoogen, D. Khanna, J. Fransen, S.R. Johnson, M. Baron, A. Tyndall, M. Matucci-Cerinic, R.P. Naden, T.A. Jr Medsger, P.E. Carreira, G. Riemekasten, P. J. Clements, C.P. Denton, O. Distler, Y. Allanore, D.E. Furst, A. Gabrielli, M. D. Mayes, J.M. van Laar, J.R. Seibold, L. Czirjak, V.D. Steen, M. Inanc, O. Kowal-Bielecka, U. Müller-Ladner, G. Valentini, D.J. Veale, M.C. Vonk, U.A. Walker, L. Chung, D.H. Collier, M. Ellen Csuka, B.J. Fessler, S. Guiducci, A. Herrick, V. M. Hsu, S. Jimenez, B. Kahaleh, P.A. Merkel, S. Sierakowski, R.M. Silver, R. W. Simms, J. Varga, J.E. Pope, Classification criteria for systemic sclerosis: an American college of rheumatology/European league against rheumatism collaborative initiative, Ann. Rheum. Dis. 72 (2013) 1747–1755, https://doi.org/10.1136/annrheumdis-2013-204424, 2013.

[6] S. Bellando-Randone, F. Del Galdo, G. Lepri, T. Minier, D. Huscher, D.E. Furst, Y. Allanore, O. Distler, L. Czirják, C. Bruni, S. Guiducci, J. Avouac, M. Cutolo, V. Smith, M. Matucci-Cerinic M, Very early diagnosis of systemic sclerosis collaborators, progression of patients with Raynaud's phenomenon to systemic sclerosis: a five-year analysis of the European scleroderma trial and research group multicentre, longitudinal registry study for very early diagnosis of systemic sclerosis (VEDOSS), Lancet Rheumatol. 3 (2021) e834–e843, https://doi.org/10.1016/S2665-9913(21)00244-7.

[7] F. Ingegnoli, I. Ardoino, P. Boracchi, M. Cutolo, EUSTAR co-authors, nailfold capillaroscopy in systemic sclerosis: data from the EULAR scleroderma trials and research (EUSTAR) database, Microvasc. Res. 89 (2013) 122–128, https://doi.org/10.1016/j.mvr.2013.06.003.

[8] A. Vanhaecke, M. Cutolo, O. Distler, V. Riccieri, Y. Allanore, C.P. Denton, E. Hachulla, F. Ingegnoli, E. Deschepper, J. Avouac, S. Jordan, D. Launay, K. Melsens, C. Pizzorni, A. Sulli, M. Vasile, A.L. Herrick, V. Smith, Nailfold capillaroscopy in SSc: innocent bystander or promising biomarker for novel severe organ involvement/progression? Rheumatology 61 (2022) 4384–4396, https://doi.org/10.1093/rheumatology/keac079.

[9] R. De Angelis, C. Ferri, E. Cipolletta, V. Riccieri, M. Di Battista, G. Bajocchi, S. Bellando-Randone, C. Bruni, M. Orlandi, G. Zanframundo, R. Foti, G. Cuomo,

A. Ariani, E. Rosato, G. Lepri, F. Girelli, E. Zanatta, S.L. Bosello, I. Cavazzana, F. Ingegnoli, M. De Santis, F. Cacciapaglia, G. Murdaca, G. Abignano, G. Pettiti, A. Della Rossa, M. Caminiti, A.M. Iuliano Am, et al., SPRING-SIR (systemic sclerosis progression investigation group of the Italian society for rheumatology), prevalence, distribution and associations of the scleroderma capillaroscopic patterns: new insights from the Italian SPRING-SIR registry, Rheumatology 65 (2025), https://doi.org/10.1093/rheumatology/keaf672 keaf672.

[10] J. Avouac, J. Fransen, U.A. Walker, V. Riccieri, V. Smith, C. Muller, I. Miniati, I. H. Tarner, S. Bellando-Randone, M. Cutolo, Y. Allanore, O. Distler, G. Valentini, L. Czirjack, U. Muller-Ladner, D.E. Furst, A. Tyndall, M. Matucci-Cerinic, EUSTAR Group, Preliminary criteria for the very early diagnosis of systemic sclerosis: results of a Delphi consensus study from EULAR scleroderma trials and research group, Ann. Rheum. Dis. 70 (2011) 476–481, https://doi.org/10.1136/ard.2010.136929.

[11] A. Tonutti, F. Motta, G. Bajocchi, S. Bellando-Randone, C. Bruni, M. Orlandi, et al., Elderly-onset systemic sclerosis defines a distinct clinical subset: analysis from the SPRING registry of the Italian society for rheumatology, J. Autoimmun. 157 (2025) 103501, https://doi.org/10.1016/j.jaut.2025.103501.

[12] C. Ferri, R. De Angelis, D. Giuggioli, G. Bajocchi, L. Dagna, G. Zanframundo, R. Foti, F. Cacciapaglia, G. Cuomo, A. Ariani, E. Rosato, S. Guiducci, F. Girelli, V. Riccieri, E. Zanatta, S. Bosello, I. Cavazzana, F. Ingegnoli, M. De Santis, G. Murdaca, G. Abignano, N. Romeo, A. Della Rossa, M. Caminiti, A. Iuliano, G. Ciano, L. Beretta, G. Bagnato, E. Lubrano, I. De Andres, A. Giollo, M. Saracco, C. Agnes, F. Lumetti, A. Spinella, L. Magnani, C. Campochiaro, G. De Luca, V. Codullo, E. Visalli, F. Masini, A. Gigante, S. Bellando-Randone, G. Pellegrino, E. Pigatto, M.G. Lazzaroni, F. Franceschini, E. Generali, G. Mennillo, S. Barsotti, G. P. Mariano, F. Calabrese, F. Furini, L. Vultaggio, S. Parisi, C.L. Peroni, D. Rozza, A. Zanetti, G. Carrara, G. Landolfi, C.A. Scirè, G. Bianchi, E. Fusaro, G. D. Sebastiani, M. Govoni, S. D'Angelo, F. Cozzi, A. Doria, F. Iannone, C. Salvarani, M. Matucci-Cerinic, SPRING-SIR (systemic sclerosis PRogression INvestiGation group of the Italian society of rheumatology), geographical heterogeneity of clinical and serological phenotypes of systemic sclerosis observed at tertiary referral centres. The experience of the Italian SIR-SPRING registry and review of the world literature, Autoimmun. Rev. 21 (2022) 103159, https://doi.org/10.1016/j.autrev.2022.103159.

[13] R. De Angelis, C. Ferri, D. Giuggioli, G. Bajocchi, L. Dagna, S. Bellando-Randone, G. Zanframundo, R. Foti, F. Cacciapaglia, G. Cuomo, A. Ariani, E. Rosato, G. Lepri, F. Girelli, V. Riccieri, E. Zanatta, S.L. Bosello, I. Cavazzana, F. Ingegnoli, M. De Santis, G. Murdaca, G. Abignano, N. Romeo, A. Della Rossa, M. Caminiti, A. M. Iuliano, G. Ciano, L. Beretta, G. Bagnato, E. Lubrano, I. De Andres, A. Giollo, M. Saracco, C. Agnes, E. Cipolletta, F. Lumetti, A. Spinella, L. Magnani, C. Campochiaro, G. De Luca, V. Codullo, E. Visalli, C. Di Vico, A. Gigante, G. Pellagrino, E. Pigatto, M.G. Lazzaroni, F. Franceschini, E. Generali, G. Mennillo, S. Barsotti, G.P. Mariano, F. Furini, L. Vultaggio, S. Parisi, C.L. Peroni, D. Rozza, A. Zanetti, G. Carrara, G. Landolfi, C.A. Scirè, G. Bianchi, E. Fusaro, G. D. Sebastiani, M. Govoni, S. D'Angelo, F. Cozzi, S. Guiducci, A. Doria, C. Salvarani, F. Iannone, M. Matucci-Cerinic, SPRING-SIR (systemic sclerosis PRogression INvestiGation group of the Italian society of rheumatology), systemic sclerosis sine scleroderma: clinical and serological features and relationship with other cutaneous subsets in a large series of patients from the national registry “SPRING” of the Italian society for rheumatology, RMD Open 9 (2023) e002890, https://doi.org/10.1136/rmdopen-2022-002890.

[14] S. Di Donato, M. Hughes, M. Matucci-Cerinic, C.P. Denton, E. Jude, J. Pauling, S. Ramjug, L.A. Bissell, Y. Allanore, M.E. Truchetet, F. Del Galdo, Op0093 towards a unified vascular endotype in systemic sclerosis. Prognostic value of vascular disease in the eustar database, Ann. Rheum. Dis. 83 (Suppl 1) (2024) 71–72.

[15] J.D. Pauling, Y. Allanore, M.H. Buch, M. Cutolo, F. Del Galdo, C.P. Denton, S. Di Donato, R.T. Domsic, T. Frech, A.L. Herrick, M. Matucci-Cerinic, V. Smith, M. E. Truchetet, M. Hughes, Exploiting a unified vascular framework to predict organ-specific complications and accomplish disease modification in systemic sclerosis, Lancet Rheumatol. 7 (2025) e895–e906, https://doi.org/10.1016/S2665-9913(25)00251-6.

[16] R. De Angelis, D. Giuggioli, G. Bajocchi, L. Dagna, G. Zanframundo, R. Foti, F. Cacciapaglia, G. Cuomo, A. Ariani, E. Rosato, S. Guiducci, F. Girelli, V. Riccieri, E. Zanatta, S. Bosello, I. Cavazzana, F. Ingegnoli, M. De Santis, G. Murdaca, G. Abignano, N. Romeo, A. Della Rossa, M. Caminiti M, A.M. Iuliano, et al., Sex-related differences in systemic sclerosis: a multicenter cross-sectional study from the national registry of the Italian society for rheumatology, J. Rheumatol. 49 (2022) 176–185, https://doi.org/10.3899/jrheum.210794.

[17] M. Humbert, G. Kovacs, M.M. Hoeper, R. Badagliacca, R.M.F. Berger, M. Brida, J. Carlsen, A.J.S. Coats, P. Escribano-Subias, P. Ferrari, D.S. Ferreira, H. A. Ghofrani, G. Giannakoulas, D.G. Kiely, E. Mayer, G. Meszaros, B. Nagavci, K. M. Olsson, J. Pepke-Zaba, J.K. Quint, G. Rådegran, G. Simonneau, O. Sitbon, T. Tonia, M. Toshner, J.L. Vachiery, A. Vonk Noordegraaf, M. Delcroix, S. Rosenkranz, ESC/ERS Scientific Document Group, 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension, Eur. Respir. J. 6 (2023) 2200879, https://doi.org/10.1183/13993003.00879-2022.

[18] J.G. Coghlan, C.P. Denton, E. Grünig, D. Bonderman, O. Distler, D. Khanna, U. Müller-Ladner, J.E. Pope, M.C. Vonk, M. Doelberg, H. Chadha-Boreham, H. Heinzl, D.M. Rosenberg, V.V. McLaughlin, J.R. Seibold, DETECT study group, evidence-based detection of pulmonary arterial hypertension in systemic sclerosis: the DETECT study, Ann. Rheum. Dis. 73 (2014) 1340–1349, https://doi.org/10.1136/annrheumdis-2013-203301.

[19] M. Orlandi, S. Bellando-Randone, R. De Angelis, C. Ferri, D. Giuggioli, F. Cacciapaglia, et al., Towards a comprehensive approach to the management and prognosis of systemic sclerosis's patients: the role of comorbidities in the SPRING-SIR registry, Eur. J. Intern. Med. 130 (2024) 130–136, https://doi.org/10.1016/j.ejim.2024.07.040.

[20] C. Ferri, D. Giuggioli, S. Guiducci, F. Lumetti, G. Bajocchi, L. Magnani, V. Codullo, A. Ariani, F. Girelli, V. Riccieri, G. Pellegrino, S. Bosello, R. Foti, E. Visalli, G. Amato, A. Benenati, G. Cuomo, F. Iannone, F. Cacciapaglia, R. De Angelis, F. Ingegnoli, R. Talotta, C. Campochiaro, L. Dagna, G. De Luca, S. Bellando-Randone, A. Spinella, G. Murdaca, N. Romeo, M. De Santis, E. Generali, S. Barsotti, A. Della Rossa, I. Cavazzana, F. Dall'Ara, M.G. Lazzaroni, F. Cozzi, A. Doria, E. Pigatto, E. Zanatta, G. Ciano, L. Beretta, G. Abignano, S. D'Angelo, G. Mennillo, G. Bagnato, F. Calabrese, M. Caminiti, G. Pagano Mariano, E. Battaglia, E. Lubrano, G. Zanframundo, A. Iuliano, F. Furini, A. Zanetti, G. Carrara, F. Rumi, C.A. Scirè, M. Matucci-Cerinic, Italian society for rheumatology (SIR). Systemic sclerosis progression INvestiGation (SPRING) Italian registry: demographic and clinico-serological features of the scleroderma spectrum, Clin. Exp. Rheumatol. 38 (Suppl 125) (2020) 40–47.

[21] M. Yang, V. Goh, J. Lee, M. Espinoza, Y. Yuan, M. Carns, K. Aren, L. Chung, D. Khanna, Z.H. McMahan, R. Agrawal, L. Beussink Nelson, S.J. Shah, M. L. Whitfield, M. Hinchcliff, Clinical phenotypes of patients with systemic sclerosis with distinct molecular signatures in skin, Arthritis Care Res. 75 (2023) 1469–1480, https://doi.org/10.1002/acr.24998.

[22] V. Smith, V. Riccieri, C. Pizzorni, S. Decuman, E. Deschepper, C. Bonroy, A. Sulli, Y. Piette, F. De Keyser, M. Cutolo, Nailfold capillaroscopy for prediction of novel future severe organ involvement in systemic sclerosis, J. Rheumatol. 40 (2013) 2023–2028, https://doi.org/10.3899/jrheum.130528.

[23] C. Ghizzoni, M. Sebastiani, A. Manfredi, F. Campomori, M. Colaci, D. Giuggioli, C. Ferri, Prevalence and evolution of scleroderma pattern at nailfold videocapillaroscopy in systemic sclerosis patients: clinical and prognostic implications, Microvasc. Res. 99 (2015) 92–95, https://doi.org/10.1016/j.mvr.2015.03.005.

[24] C. Kasser, G. Boleto, Y. Allanore, J. Avouac, Nailfold videocapillaroscopy findings and associations with organ involvement in mixed connective tissue disease, Clin. Exp. Rheumatol. 43 (2025) 418–424, https://doi.org/10.55563/clinexprheumatol/xshsd7.

[25] C. Boulon, S. Aiouaz, S. Blaise, M. Mangin, J. Decamps-Le Chevoir, P. Senet, I. Lazareth, N. Baudot, L. Tribout, B. Imbert, F.X. Lapebie, P. Lacroix, M. E. Truchetet, J. Seneschal, A. Solanilla, S. Skopinski, E. Lazaro, I. Quéré, M. A. Pistorius, C. Le Hello, P. Perez, P. Carpentier, J. Constans, Correlation between capillaroscopic classifications and severity in systemic sclerosis: results from SCLEROCAP study at inclusion. Correlation between capillaroscopic classifications and severity in systemic sclerosis: results from SCLEROCAP study at inclusion, Clin. Exp. Rheumatol. 37 (Suppl 119) (2019) 63–68.

[26] R. De Angelis, V. Riccieri, E. Cipolletta, N. Del Papa, F. Ingegnoli, S. Bosello, A. Spinella, G. Pellegrino, M. de Pinto, S. Papa, G. Armentaro, D. Giuggioli, Significant nailfold capillary loss and late capillaroscopic pattern are associated with pulmonary arterial hypertension in systemic sclerosis, Rheumatology 63 (2024) 1616–1623, https://doi.org/10.1093/rheumatology/kead445.

[27] H.A. Dundar, A. Adrovic, S. Demir, F. Demir, F. Cakmak, N.A. Ayaz, B. Sözeri, Y. Bilginer, O. Kasapçopur, E. Unsal, Description of the characteristics of the nailfold capillary structure in healthy children: a multi-centric study, Rheumatology 63 (2024) SI152–SI159, https://doi.org/10.1093/rheumatology/keae296.