SUPPLEMENTARY FILE

Nailfold Videocapillaroscopic and Other Clinical Risk Factors for Digital Ulcers in Systemic Sclerosis: A Multicenter, Prospective Cohort Study

Maurizio Cutolo MD, Ariane L. Herrick MD, Oliver Distler MD, Mike Becker MD, Emma Beltran PhD, Patrick Carpentier MD, Clodoveo Ferri MD, Murat Inanç MD, Panayiotis Vlachoyiannopoulos MD, Harbajan Chadha-Boreham PhD, Emmanuelle Cottreel MSc, Thomas Pfister PhD, Daniel Rosenberg PhD, Juan V. Torres MSc, Vanessa Smith MD PhD, on behalf of the videoCAPillaroscopy (CAP) study investigators.

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1. CAP study Steering Committee members

Maurizio Cutolo, *Research Laboratory and Academic Division of Clinical Rheumatology, University of Genova, IRCCS AOU S. Martino, Genova, Italy;* **Ariane L. Herrick**, *Centre for Musculoskeletal Research, The University of Manchester, Salford Royal NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester and NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK;* **Oliver Distler,** *Rheumatology, University Hospital, Zürich, Switzerland;* **Mike Becker**, *Rheumatology, University Hospital, Zürich, Switzerland, Rheumatology and Clinical Immunology, Charité University Hospital, Berlin, Germany;* **Emma Beltran**, *Hospital Universitario y Politécnico La Fe, Valencia, Spain;* **Patrick Carpentier**, *Vascular Medicine, La Tronche Hospital, Grenoble, France;* **Clodoveo Ferri,** *Chair & Rheumatology Unit, University of Modena & Reggio Emilia, Modena, Italy;* **Murat Inanç**, *Division of Rheumatology, Department of Internal Medicine, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkey;* **Panayiotis Vlachoyiannopoulos,** *Department of Pathophysiology, Medical School, National and Kapodistrian University of Athens, Athens, Greece;* **Vanessa Smith,** *Department of Rheumatology, Ghent University Hospital; Ghent University, Ghent, Belgium.*

2. CAP study Principal Investigators

The CAP study Investigators are as follows:

Austria – *Sozialmedizinisches Zentrum Süd-Kaiser-Franz-Josef-Spital, Vienna*: **L Erlacher;** *Hanusch Krankenhaus der Gebietskrankenkasse, Vienna*: **M Hirschl;** *Medizinische Universität Wien, Vienna*: **HP Kiener;** *Medizinische Universität Graz, Graz*: **E Pilger**.

Belgium – *Universitair Ziekenhuis Gent, Ghent:* **V Smith**; *Universitair Ziekenhuis Gasthuisberg, Leuven:* **D Blockmans;** *Université Libre de Bruxelles Hôpital Erasme, Brussels:* **J-C Wautrecht.**

Czech Republic – *Revmatologický ústav, Prague:* **R Becvár.**

France – *Centre Hospitalier Universitaire de Grenoble, La Tronche:* **P Carpentier;** *Hôpital Tenon, Paris:* **C Frances;** *Centre Hospitalier Universitaire Amiens, Amiens:* **C Lok;** *CHU Dupuytren, Limoges:* **A Sparsa;** *CHRU de Lille, Hôpital Claude Huriez, Lille:* **E Hachulla;** *CHU de Montpellier, Montpellier:* **I Quere;** *Groupe Hospitalier Cochin Saint Vincent de Paul, Paris:* **Y Allanore;** *Centre Hospitalier Universitaire de Nantes, Nantes:* **C Agard.**

Germany – *Charité Universitätsmedizin Berlin, Berlin:* **G Riemekasten;** *Universitätsklinik Köln, Cologne:* **N Hunzelmann;** *Sankt Josef-Hospital, Klinikum der Ruhr-Universität Bochum, Bochum-Gerthe:* **M Stücker;** *Asklepios Klinik Altona, Hamburg:* **K Ahmadi-Simab;** *Universitätsklinikum Münster, Münster:* **C Sunderkötter;** *Universitätsklinikum Halle (Saale), Halle:* **J Wohlrab;** *Kerckhoff-Klinik GmbH, Bad Nauheim*: **U Müller-Ladner**; *Universitätsklinikum Düsseldorf, Düsseldorf:* **M Schneider.**

Greece – *Laiko General Hospital, Athens:* **P Vlachoyianopoulos;** *General Hospital of Athens, Hippokration, Athens:* **D Vassilopoulos;** *University General Hospital of Ioannina, Ioannina:* **A Drosos;** *Hospital Board of General University Hospital of Patras, Patra:* **A Antonopoulos.**

Israel – *Rambam Medical Center, Haifa:* **A Balbir-Gurman;** *Sheba Medical Center, Tel-Hashomer:* **P Langevitz;** *Bnai Zion Medical Center, Haifa:* **I Rosner;** *Meir Medical Center, Kfar Saba:* **Y Levy.**

Italy – *Azienda Ospedale San Martino, Genova:* **M Cutolo;** *Azienda Ospedaliera Pisana Ospedale Santa Chiara, Pisa:* **S Bombardieri;** *Università Cattolica Sacro Curoe, Complesso Integrato Columbus, Rome:* **G Ferraccioli;** *Azienda Ospedaliera 'Pugliese Ciaccio' di Catanzaro, Catanzaro:* **S Mazzuca;** *Ospedale Murri-Università Politecnica delle Marche, Jesi:* **W Grassi;** *Azienda Ospedaliera Universitaria Integrata di Verona, Verona:* **C Lunardi;** *Azienda Ospedaliera Spedali Civili di Brescia, Brescia:* **P Airó;** *Policlinico Umberto I, Rome:* **V Riccieri.**

The Netherlands – *Vrije Universiteit Medisch Centrum, Amsterdam:* **AE Voskuyl;** *Leiden University Medical Center, Leiden:* **A Schuerwegh.**

Portugal – *Hospitais da Universidade de Coimbra, Coimbra:* **L Santos;** *Hospital Curry Cabral, Lisbon:* **AC Rodrigues, A Grilo;** *Hospital Fernando Fonseca, Lisbon:* **MC Amaral.**

Spain – *Hospital Universitario La Fe, Valencia:* **JA Román Ivorra;** *Hospital de la Santa Creu i Sant Pau, Barcelona:* **I Castellvi.**

Switzerland – *Universitäts-Spital Zürich, Zürich:* **O Distler;** *Centre Hospitalier Universitaire Vaudoise, Lausanne:* **F Spertini;** *Kantonspital Sankt Gallen, St Gallen:* **R Müller.**

Turkey – *Istanbul Üniversitesi Istanbul Tip Fakültesi, Istanbul:* **M Inanç;** *Ege Üniversitesi Tip Fakültesi, Izmir:* **F Oksel;** *Ankara Üniversitesi Tip Fakültesi Ibni Sina Hastanesi, Ankara:* **N Turkcapar.**

United Kingdom – *Hope Hospital, Salford:* **A Herrick;** *Royal Free Hospital, London:* **C Denton;** *Bath Institute for Rheumatic Diseases, Bath:* **N McHugh;** *Wrightington Hospital, Wigan:* **C Chattopadhyay;** *Addenbrookes Hospital Cambridge, Cambridge:* **F Hall;** *Leeds Teaching Hospitals NHS Trust, Leeds:* **M Buch.**

3. Selection of covariables potentially associated with future development of new digital ulcers through ULR to MLR

Supplementary Table S1. Bundle 1: Demographics

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
Number of variables (V = 14)						**3**	**1**
1. Sex							
Female, n (%)	79 (76.7)	293 (80.3)	1.236* (0.732–2.089)	0.428*	0.518 (0.472–0.564)		
Male, n (%)	24 (23.3)	72 (19.7)					
2. Age at enrollment (years): mean (SD); n	51.5 (13.9); 103	54.8 (13.6); 365	0.983 (0.967–0.999)	0.033	0.573 (0.509–0.636)	X	X
3. Race							
White/Caucasian, n (%)	98 (95.1)	346 (94.8)	0.929 (0.338–2.552)	0.887	0.502 (0.478–0.526)		
Other, n (%)	5 (4.9)	19 (5.2)					
4. Height† (cm): mean (SD), n	166.4 (10.2); 102	164.3 (8.5); 363	1.026 (1.002–1.052)	0.035	0.559 (0.493–0.625)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
5. Weight (kg), mean (SD); n	65.9 (13.2); 102	65.5 (14.2); 364	1.002 (0.987–1.018)	0.790	0.516 (0.452–0.579)		
6. Body surface area (m^2), mean (SD); n	1.7 (0.2); 102	1.7 (0.2); 363	1.552 (0.553–4.357)	0.404	0.529 (0.465–0.594)		
7. Manual labor†, yes, n/N (%)	13/103 (12.6)	71/365 (19.5)	0.598 (0.316–1.131)	0.114	0.534 (0.496–0.572)		
8. Smoking behavior,							
Never, n/N (%)	63/103 (61.2)	234/365 (64.1)					
Past, not current, n/N (%)	19/103 (18.4)	82/365 (22.5)	0.861‡ (0.486–1.524)	0.607‡	0.544 (0.489–0.600)		
Current, n/N (%)	21/103 (20.4)	49/365 (13.4)	1.592§ (0.889–2.849)	0.117§			
9. Currently smoking, n/N (%)	21/103 (20.4)	49/365 (13.4)	1.652 (0.938–2.909)	0.082	0.535 (0.492–0.578)	X	

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
10. Cigarette packs per day, mean (SD); n	0.24 (0.41); 100	0.28 (0.48); 356	0.804 (0.490–1.322)	0.390	0.509 (0.457–0.561)		
11. Years smoking, mean (SD); n	7.8 (12.7); 99	7.3 (13.4); 353	1.003 (0.986–1.020)	0.755	0.512 (0.457–0.567)		
12. Smoking Index Duration, mean (SD); n	5.4 (9.6); 99	5.7 (10.5); 353	0.997 (0.975–1.019)	0.783	0.490 (0.437–0.543)		
13. Comprehensive Smoking Index: mean (SD); n	0.1 (0.2); 99	0.1 (0.3); 351	–[¶]	0.032	0.535 (0.480–0.590)	X	
14. Hand dominancy							
Right, n/N (%)	100/103 (97.1)	348/365 (95.3)	0.614[‖] (0.176–2.138)	0.444[‖]	0.509 (0.489–0.528)		
Left or ambidextrous, n/N (%)	3/103 (2.9)	17/365 (4.7)					

Reduction of covariables through Step 1: ULR (Retention criterion: $p < 0.15$ for linear term or $p < 0.05$ for quadratic term), Step 2: MLR within-bundle (Entry criterion: $p < 0.15$; Retention criterion: $p < 0.10$), and Step 3: MLR across-bundles (Entry criterion: $p < 0.15$; Retention criterion: $p < 0.05$).

*Male vs female

[†]Exclusion criterion: Not retained following Step 1 (ULR) based on Steering Committee Decision

[‡]Past, not current vs never smoker

[§]Current vs never smoker

[¶]OR is not given since the functional relationship is quadratic. Associated *p* value and ROC-AUC are of quadratic term

[‖]Left/ambidextrous vs right handed

Abbreviations: AUC, area under the curve; CI, confidence interval; MLR, multivariable logistic regression; OR, odds ratio; ROC, receiver operating characteristic; SD, standard deviation; ULR, univariable logistic regression

Supplementary Table S2. Bundle 2: Systemic sclerosis clinical characteristics

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
Number of variables (V = 30)						**6**	**3**
1. Age at first Raynaud's phenomenon (years): mean (SD); n	39.2 (16.0); 103	40.9 (14.2); 361	0.992 (0.977–1.007)	0.299	0.542 (0.476–0.609)		
2. Years since first Raynaud's phenomenon: mean (SD); n	12.4 (12.0); 103	13.9 (11.7); 361	0.988 (0.969–1.008)	0.241	0.557 (0.494–0.619)		
3. Age at first physician-documented non-Raynaud's clinical feature* (years): mean (SD); n	43.1 (14.8); 103	45.6 (13.6); 363	0.987 (0.971–1.003)	0.106	0.561 (0.496–0.626)	X	X
4. Years since first physician-documented non-Raynaud's clinical feature*: mean (SD); n	8.5 (7.0); 103	9.4 (8.4); 363	0.987 (0.959–1.015)	0.362	0.514 (0.452–0.575)		
5. Years between first Raynaud's and first physician-documented non-Raynaud's clinical feature*: mean (SD); n	4.3 (9.5); 103	4.9 (8.8); 359	0.991 (0.966–1.018)	0.523	0.564 (0.501–0.626)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
6. SSc subtype							
Diffuse cutaneous SSc, n/N (%)	48/103 (46.6)	140/365 (38.4)	0.713† (0.459–1.108)	0.133†	0.541 (0.487–0.596)	X	
Limited cutaneous SSc, n/N (%)	55/103 (53.4)	225/365 (61.6)					
7. Extent of skin involvement (modified mRSS), mean (SD); n	13.0 (9.0); 100	11.3 (8.4); 354	1.023 (0.998–1.048)	0.076	0.562 (0.496–0.627)	X	
8. Sclerodactyly, yes, n/N (%)	94/103 (91.3)	319/365 (87.4)	1.505 (0.711–3.188)	0.285	0.519 (0.487–0.552)		
Organ involvement (of the below mentioned variables)							
9. Any organ involvement							
10. Kidney involvement: proteinuria, n/N (%)	7/103 (6.8)	31/365 (8.5)	0.786 (0.335–1.840)	0.579	0.509 (0.480–0.537)		
11. Kidney involvement: SSc renal crisis, kidney failure, n/N (%)	2/103 (1.9)	22/365 (6.0)	0.309 (0.071–1.336)	0.116	0.520 (0.502–0.539)	X	X
12. Heart involvement, n/N (%)	22/103 (21.4)	55/365 (15.1)	1.531 (0.882–2.658)	0.130	0.532 (0.488–0.575)	X	X

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
13. Lung involvement – pulmonary arterial hypertension, n/N (%)	19/103 (18.4)	63/365 (17.3)	1.084 (0.615–1.912)	0.780	0.506 (0.464–0.548)		
14. Lung interstitial disease or respiratory failure, n/N (%)	46/103 (44.7)	157/365 (43.0)	1.069 (0.688–1.661)	0.766	0.508 (0.454–0.563)		
15. Gastrointestinal tract, n/N (%)	71/103 (68.9)	241/365 (66.0)	1.142 (0.713–1.827)	0.581	0.515 (0.464–0.566)		
16. Muscles, n/N (%)	13/103 (12.6)	45/365 (12.3)	1.027 (0.531–1.988)	0.936	0.502 (0.465–0.538)		
17. Joint involvement, n/N (%)	45/103 (43.7)	127/365 (34.8)	1.454 (0.932–2.269)	0.099	0.545 (0.491–0.599)	X	
18. Pleural effusion, n/N (%)	8/103 (7.8)	19/365 (5.2)	1.534 (0.651–3.613)	0.328	0.513 (0.484–0.541)		
19. Nervous system‡, n/N (%)	4/103 (3.9)	7/365 (1.9)	2.066 (0.593–7.202)	0.255	0.510 (0.490–0.530)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
20. Any other organ system involvement other than the above, n/N (%)	3/103 (2.9)	21/365 (5.8)	0.491 (0.144–1.681)	0.258	0.514 (0.494–0.534)		
(Connective) tissue disease							
21. Systemic lupus erythematosus‡, n/N (%)	3/103 (2.9)	13/365 (3.6)	0.812 (0.227–2.907)	0.749	0.503 (0.484–0.522)		
22. Sjogren's syndrome, n/N (%)	7/103 (6.8)	42/365 (11.5)	0.561 (0.244–1.289)	0.173	0.524 (0.494–0.553)		
23. Dermatomyositis‡, n/N (%)	2/103 (1.9)	1/365 (0.3)	7.208 (0.647–80.301)	0.108	0.508 (0.495–0.522)		
24. Polymyositis‡, n/N (%)	3/103 (2.9)	6/365 (1.6)	1.795 (0.441–7.305)	0.414	0.506 (0.489–0.524)		
25. Rheumatoid arthritis, n/N (%)	6/103 (5.8)	16/365 (4.4)	1.349 (0.514–3.541)	0.543	0.507 (0.482–0.532)		
26. Marfan syndrome‡, n/N (%)	0/103 (0.0)	0/365 (0.0)	–	–	–		
27. Ehlers-Danlos syndrome‡, n/N (%)	0/103 (0.0)	1/365 (0.3)	0.000 (0.000–+Inf)	0.989	0.501 (0.499–0.504)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
28. Osteogenesis imperfecta‡, n/N (%)	1/103 (1.0)	1/365 (0.3)	3.569 (0.221–57.554)	0.370	0.504 (0.494–0.513)		
29. Stickler syndrome‡, n/N (%)	0/103 (0.0)	0/365 (0.0)	–	–	–		
30. Any other (connective) tissue disease than the above mentioned‡, n/N (%)	2/103 (1.9)	6/365 (1.6)	1.185 (0.236–5.960)	0.837	0.502 (0.487–0.516)		

Reduction of covariables through Step 1: ULR (Retention criterion: p < 0.15 for linear term or p < 0.05 for quadratic term), Step 2: MLR within-bundle (Entry criterion: p < 0.15; Retention criterion: *p* < 0.10), and Step 3: MLR across-bundles (Entry criterion: p < 0.15; Retention criterion: *p* < 0.05).

*Potential non-Raynaud's clinical features: swollen hands, face or feet, skin thickening, multiple digital and facial telangiectasia, digital ulcers, arthritis, calcinosis, flexion contractures, myositis, sicca syndrome, kidney involvement, heart involvement, lung involvement, gut involvement, esophagus involvement, pleura involvement, pericardium involvement, pleura involvement, CNS involvement, and other

†Limited vs diffuse SSc

‡Exclusion Criterion: Not retained following Step 1(ULR) due to a frequency of fewer than 20 patients

Abbreviations: AUC, area under the curve; CI, confidence interval; CNS, central nervous system; mRSS, Modified Rodnan Skin Score; MLR, multivariable logistic regression; OR, odds ratio; ROC, receiver operating characteristic; SD, standard deviation; SSc, systemic sclerosis; ULR, univariable logistic regression

Supplementary Table S3. Bundle 3: Digital ulcer characteristics

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
Number of variables (V = 24)						**8**	**3**
1. Number of DUs, n/N (%)							
0	41 /103 (39.8)	262/365 (71.8)					
1	24/103 (23.3)	57/365 (15.6)	2.691* (1.507–4.803)	0.001*	0.678 (0.622–0.734)	X	X
2	16/103 (15.5)	27/365 (7.4)	3.787† (1.879–7.630)	<0.001†			
≥3	22/103 (21.4)	19/365 (5.2)	7.399‡ (3.687–14.848)	<0.001‡			
2. Presence of DUs§, n/N (%)	62/103 (60.2)	103/365 (28.2)	3.847 (2.439–6.067)	<0.001	0.660 (0.607–0.713)		
3. At least one DU in fingertips§, n/N (%)	33/103 (32.0)	54/365 (14.8)	2.715 (1.639–4.498)	<0.001	0.586 (0.537–0.635)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
4. At least one DU in finger joints[§], n/N (%)	17/103 (16.5)	12/365 (3.3)	5.814 (2.677–12.628)	<0.001	0.566 (0.529–0.603)		
Previous complications							
5. Soft tissue infection requiring antibiotics	52/103 (50.5)	142/361 (39.3)	1.594 (1.027–2.475)	0.038	0.557 (0.503–0.612)	X	
6. Auto-amputation, n/N (%)	13/103 (12.6)	14/365 (3.8)	3.621 (1.644–7.977)	0.001	0.544 (0.510–0.578)	X	X
7. Critical digital ischemia, n/N (%)	35/103 (34.0)	94/362 (26.0)	1.473 (0.920–2.358)	0.107	0.540 (0.489–0.592)	X	
8. Gangrene, n/N (%)	16/103 (15.5)	37/365 (10.1)	1.630 (0.866–3.068)	0.130	0.527 (0.489–0.565)	X	
9. Osteomyelitis, n/N (%)	7/102 (6.9)	16/364 (4.4)	1.591 (0.636–3.979)	0.320	0.512 (0.486–0.539)		
Current (at enrollment) complications							
10. Soft tissue infection requiring antibiotics, n/N (%)	23/103 (22.3)	24/365 (6.6)	4.085 (2.194–7.606)	<0.001	0.579 (0.536–0.621)	X	

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
11. Critical digital ischemia	15/103 (14.6)	12/365 (3.3)	5.014 (2.266–11.094)	<0.0001	0.556 (0.521–0.592)	X	X
Previous or current complications							
12. Soft tissue infection requiring antibiotics[§], n/N (%)	57/103 (55.3)	143/365 (39.2)	1.924 (1.237–2.992)	0.004	0.581 (0.526–0.635)		
13. Auto-amputation[§], n/N (%)	13/103 (12.6)	15/365 (4.1)	3.370 (1.548–7.338)	0.002	0.543 (0.509–0.576)		
14. Critical digital ischemia[§], n/N (%)	39/103 (37.9)	98/365 (26.8)	1.661 (1.048–2.632)	0.031	0.555 (0.503–0.607)		
15. Gangrene[§], n/N (%)	17/103 (16.5)	38/365 (10.4)	1.701 (0.916–3.160)	0.093	0.531 (0.491–0.570)		
16. Osteomyelitis, n/N (%)	7/103 (6.8)	16/365 (4.4)	1.591 (0.636–3.979)	0.320	0.512 (0.486–0.539)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
17. Any current or previous complication[§], n/N (%)	71/103 (68.9)	194/365 (53.2)	1.956 (1.228–3.114)	0.005	0.579 (0.527–0.631)		
Previous DU-associated interventions							
18. Hospitalization for DUs, n/N (%)	55/103 (53.4)	144/365 (39.5)	1.759 (1.132–2.732)	0.012	0.570 (0.515–0.624)	X	
19. Surgical amputation, n/N (%)	6/103 (5.8)	20/364 (5.5)	1.064 (0.416–2.723)	0.897	0.502 (0.476–0.527)		
20. Other intervention, n/N (%)	7/103 (6.8)	23/362 (6.4)	1.075 (0.448–2.580)	0.872	0.502 (0.475–0.530)		
Current DU-associated interventions							
21. Wound debridement[§], n/N (%)	14/99 (14.1)	11/311 (3.5)	4.492 (1.967–10.256)	<0.001	0.553 (0.517–0.589)		
22. Antiseptics[§], n/N (%)	21/99 (21.2)	32/311 (10.3)	2.347 (1.282–4.299)	0.006	0.555 (0.511–0.599)		
23. Supportive gels/creams[§], n/N (%)	24/99 (24.2)	35/311 (11.3)	2.523 (1.415–4.501)	0.002	0.565 (0.519–0.611)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
24. Any current or previous intervention[§], n/N (%)	68/103 (66.0)	178/365 (48.8)	2.041 (1.293–3.222)	0.002	0.586 (0.534–0.639)		

Reduction of covariables through Step 1: ULR (Retention criterion: p < 0.15 for linear term or p < 0.05 for quadratic term), Step 2: MLR within-bundle (Entry criterion: p < 0.15; Retention criterion: p < 0.10), and Step 3: MLR across-bundles (Entry criterion: p < 0.15; Retention criterion: *p* < 0.05).

*1 vs 0 DUs

[†]2 vs 0 DUs

[‡]≥3 vs 0 DUs

[§]Exclusion criterion: Not retained following Step 1 (ULR) based on Steering Committee Decision

Abbreviations: AUC, area under the curve; CI, confidence interval; DU, digital ulcer; MLR, multivariable logistic regression; OR, odds ratio; ROC, receiver operating characteristic; SD, standard deviation; ULR, univariable logistic regression

Supplementary Table S4. Bundle 4: Other clinical characteristics

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
Number of variables (V = 16)						**3**	**1**
1. Known peripheral arterial disease, n/N (%)	3/103 (2.9)	23/365 (6.3)	0.446 (0.131–1.516)	0.196	0.517 (0.496–0.538)		
2. Diabetes, n/N (%)	2/103 (1.9)	19/365 (5.2)	0.361 (0.083–1.575)	0.175	0.516 (0.499–0.534)		
3. Other relevant concomitant disease, n/N (%)	38/103 (36.9)	145/365 (39.7)	0.887 (0.565–1.394)	0.603	0.514 (0.461–0.567)		
Allen test							
4. Number of abnormal hands*, n/N (%)							
0	61/95 (64.2)	226/338 (66.9)					
1	2/95 (2.1)	27/338 (8.0)	0.274† (0.063–1.186)	0.083†	0.561 (0.508–0.615)		
2	32/95 (33.7)	85/338 (25.1)	1.395‡ (0.850–2.289)	0.188‡			

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
5. Both hands abnormal, n/N (%)	32/95 (33.7)	85/338 (25.1)	0.661 (0.405–1.081)	0.099	0.543 (0.490–0.596)	X	
6. Either hand abnormal, n/N (%)	34/95 (35.8)	112/338 (33.1)	0.889 (0.552–1.432)	0.629	0.513 (0.459–0.568)		
7. Left hand abnormal, n/N (%)	33/96 (34.4)	96/338 (28.4)	1.320 (0.815–2.140)	0.259	0.530 (0.476–0.583)		
8. Right hand abnormal, n/N (%)	33/95 (34.7)	101/338 (29.9)	1.249 (0.771–2.023)	0.366	0.524 (0.470–0.578)		
Digital lesions other than DUs							
Fissure							
9. Presence, n/N (%)	17/103 (16.5)	54/365 (14.8)	1.258 (0.708–2.236)	0.433	0.516 (0.474–0.558)		
10. Number, mean (SD); n	3.1 (2.9); 17	3.1 (2.5); 54	1.022 (0.887–1.177)	0.764	0.508 (0.467–0.549)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103)	Non-cases (N=365)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
Paronychia							
11. Presence, n/N (%)	20/103 (19.4)	38/365 (10.4)	2.048 (1.132–3.705)	0.018	0.545 (0.503–0.586)	X	X
12. Number, mean (SD); n	2.5 (2.9); 20	2.9 (1.9); 38	1.112 (0.948–1.304)	0.192	0.541 (0.500–0.582)		
Pitting scars							
13. Presence, n/N (%)	60/103 (58.3)	182/365 (49.9)	1.498 (0.958–2.342)	0.076	0.550 (0.496–0.604)	X	
14. Number*, mean (SD); n	4.2 (3.0); 60	3.9 (3.6); 182	1.049 (0.985–1.118)	0.133	0.564 (0.502–0.626)		
Calcinosis							
15. Presence, n/N (%)	21/103 (20.4)	67/365 (18.4)	1.090 (0.637–1.866)	0.753	0.507 (0.462–0.552)		
16. Number, mean (SD); n	2.9 (2.5); 21	3.2 (3.3); 67	0.995 (0.882–1.122)	0.930	0.491 (0.447–0.536)		

Reduction of covariables through Step 1: ULR (Retention criterion: $p < 0.15$ for linear term or $p < 0.05$ for quadratic term), Step 2: MLR within-bundle (Entry criterion: $p < 0.15$; Retention criterion: $p < 0.10$), and Step 3: MLR across-bundles (Entry criterion: $p < 0.15$; Retention criterion: $p < 0.05$)

*Exclusion criterion: Not retained following Step 1 (ULR) based on Steering Committee Decision

†1 vs 0 abnormal hands (Allen test)

‡2 vs 0 abnormal hands (Allen test)

Abbreviations: AUC, area under the curve; CI, confidence interval; DU, digital ulcer; MLR, multivariable logistic regression; OR, odds ratio; ROC, receiver operating characteristic; SD, standard deviation; ULR, univariable logistic regression

Supplementary Table S5. Bundle 5: Nailfold videocapillaroscopic characteristics: quantitative assessment (6 sub-bundles)

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103) mean (SD); n	Non-cases (N=365) mean (SD); n	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
						31	**3**
Patient level (V = 6): both hands, 8 fingers (Sub-bundle 5.1)							
1. Number of capillaries/mm*	4.2 (1.6); 103	4.8 (1.8); 362	0.800 (0.696–0.920)	0.002	0.605 (0.546–0.665)	X	
2. Number of giants/mm	0.6 (0.7); 103	0.5 (0.6); 362	1.055 (0.755–1.474)	0.753	0.506 (0.445–0.568)		
3. Number of irregularly enlarged capillaries/mm	1.3 (1.0); 103	1.3 (1.1); 362	0.975 (0.795–1.196)	0.810	0.502 (0.437–0.566)		
4. Number of microhemorrhages/mm	0.2 (0.3); 103	0.2 (0.3); 362	0.543 (0.249–1.183)	0.124	0.565 (0.506–0.625)	X	
5. Number of neoangiogeneses/mm*	0.7 (0.7); 103	0.5 (0.6); 362	1.529 (1.093–2.140)	0.013	0.572 (0.507–0.636)	X	

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103) mean (SD); n	Non-cases (N=365) mean (SD); n	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
6. Maximum capillary diameter	88.5 (29.6); 85	86.2 (27.6); 284	0.998 (0.991–1.006)	0.670	0.501 (0.440–0.562)		
Hand level (V = 6): dominant hand, 4 fingers (Sub-bundle 5.2)							
1. Number of capillaries/mm*	4.0 (1.7); 101	4.7 (1.8); 359	0.803 (0.701–0.921)	0.002	0.606 (0.547–0.665)	X	
2. Number of giants/mm	0.5 (0.7); 101	0.5 (0.7); 359	0.991 (0.715–1.375)	0.958	0.518 (0.455–0.581)		
3. Number of irregularly enlarged capillaries/mm	1.3 (1.1); 101	1.4 (1.2); 359	0.955 (0.787–1.157)	0.637	0.508 (0.443–0.573)		
4. Number of microhemorrhages/mm	0.2 (0.4); 101	0.2 (0.4); 359	0.662 (0.348–1.258)	0.208	0.552 (0.495–0.609)		
5. Number of neoangiogeneses/mm	0.6 (0.7); 101	0.5 (0.6); 359	1.303 (0.946–1.795)	0.105	0.549 (0.484–0.613)	X	
6. Maximum capillary diameter	89.0 (26.7); 67	87.1 (29.5); 242	0.998 (0.992–1.005)	0.655	0.514 (0.452–0.577)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103) mean (SD); n	Non-cases (N=365) mean (SD); n	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
Hand level (V = 6): non-dominant hand, 4 fingers (Sub-bundle 5.3)							
1. Number of capillaries/mm*	4.2 (1.7); 101	4.9 (1.9); 359	0.819 (0.719–0.933)	0.003	0.599 (0.538–0.659)	X	
2. Number of giants/mm	0.6 (0.8); 101	0.5 (0.7); 359	1.063 (0.779–1.450)	0.699	0.524 (0.464–0.585)		
3. Number of irregularly enlarged capillaries/mm	1.3 (1.1); 101	1.3 (1.1); 359	0.995 (0.816–1.214)	0.963	0.501 (0.436–0.566)		
4. Number of microhemorrhages/mm	0.2 (0.3); 101	0.2 (0.4); 359	0.612 (0.300–1.247)	0.176	0.543 (0.485–0.600)		
5. Number of neoangiogeneses/mm*	0.7 (0.7); 101	0.5 (0.6); 359	1.501 (1.089–2.069)	0.013	0.577 (0.513–0.640)	X	
6. Maximum capillary diameter	88.6 (35.0); 75	87.3 (31.1); 244	0.998 (0.991–1.005)	0.593	0.497 (0.437–0.557)		
Finger level (V = 24): both hands, 4 pairs of fingers (Sub-bundle 5.4)							
Index fingers							
1. Number of capillaries/mm	4.2 (1.9); 100	4.7 (2.1); 353	0.879 (0.784–0.985)	0.026	0.577 (0.516–0.638)	X	

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103) mean (SD); n	Non-cases (N=365) mean (SD); n	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
2. Number of giants/mm	0.4 (0.7); 100	0.5 (0.7); 353	0.936 (0.671–1.304)	0.694	0.518 (0.459–0.578)		
3. Number of irregularly enlarged capillaries/mm	1.3 (1.3); 100	1.3 (1.3); 353	1.018 (0.858–1.207)	0.837	0.511 (0.447–0.574)		
4. Number of microhemorrhages/mm*	0.1 (0.3); 100	0.2 (0.4); 353	0.418 (0.190–0.917)	0.030	0.575 (0.528–0.623)	X	
5. Number of neoangiogeneses/mm*	0.7 (0.8); 100	0.4 (0.6); 353	1.616 (1.195–2.185)	0.002	0.587 (0.523–0.650)	X	
6. Maximum capillary diameter	87.2 (33.9); 47	85.7 (31.2); 176	0.997 (0.990–1.004)	0.382	0.520 (0.460–0.579)		
Middle fingers							
7. Number of capillaries/mm*	4.0 (1.7); 103	4.7 (2.0); 358	0.816 (0.719–0.926)	0.002	0.600 (0.541–0.659)	X	
8. Number of giants/mm	0.6 (0.9); 103	0.5 (0.7); 358	1.198 (0.919–1.563)	0.182	0.532 (0.471–0.592)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103) mean (SD); n	Non-cases (N=365) mean (SD); n	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
9. Number of irregularly enlarged capillaries/mm	1.3 (1.2); 103	1.4 (1.2); 358	0.971 (0.811–1.161)	0.744	0.510 (0.447–0.573)		
10. Number of microhemorrhages/mm	0.2 (0.5); 103	0.3 (0.5); 358	0.810 (0.493–1.333)	0.408	0.529 (0.477–0.581)		
11. Number of neoangiogeneses/mm	0.6 (0.8); 103	0.5 (0.7); 358	1.316 (0.978–1.769)	0.070	0.546 (0.484–0.607)	X	
12. Maximum capillary diameter	87.9 (36.1); 63	86.5 (29.4); 198	1.002 (0.997-1.008)	0.472	0.521 (0.461–0.581)		
Ring fingers							
13. Number of capillaries/mm	4.2 (1.8); 102	4.8 (1.9); 360	0.846 (0.746–0.959)	0.009	0.591 (0.529–0.652)	X	
14. Number of giants/mm	0.6 (0.9); 102	0.7 (0.9); 360	0.923 (0.710–1.198)	0.546	0.524 (0.463–0.584)		
15. Number of irregularly enlarged capillaries/mm	1.3 (1.2); 102	1.4 (1.3); 360	0.953 (0.797–1.139)	0.594	0.509 (0.445–0.574)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103) mean (SD); n	Non-cases (N=365) mean (SD); n	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
16. Number of microhemorrhages/mm	0.2 (0.4); 102	0.3 (0.5); 360	0.689 (0.397–1.195)	0.185	0.539 (0.485–0.593)		
17. Number of neoangiogeneses/mm	0.7 (0.9); 102	0.6 (0.7); 360	1.309 (1.001–1.710)	0.049	0.537 (0.473–0.600)	X	
18. Maximum capillary diameter	92.0 (31.9); 63	92.4 (35.7); 220	0.996 (0.991–1.002)	0.196	0.526 (0.467–0.586)		
Little fingers							
19. Number of capillaries/mm	4.3 (1.8); 102	5.0 (1.9); 358	0.811 (0.714–0.921)	0.001	0.614 (0.551–0.677)	X	
20. Number of giants/mm	0.5 (0.8); 102	0.5 (0.7); 358	1.077 (0.795–1.459)	0.630	0.511 (0.452–0.571)		
21. Number of irregularly enlarged capillaries/mm	1.3 (1.2); 102	1.2 (1.2); 358	1.042 (0.865–1.256)	0.662	0.508 (0.442–0.574)		
22. Number of microhemorrhages/mm	0.2 (0.4); 102	0.2 (0.4); 358	0.773 (0.441–1.353)	0.367	0.527 (0.475–0.580)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103) mean (SD); n	Non-cases (N=365) mean (SD); n	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
23. Number of neoangiogeneses/mm	0.7 (0.8); 102	0.6 (0.8); 358	1.226 (0.935–1.607)	0.140	0.549 (0.487–0.612)	X	
24. Maximum capillary diameter	87.8 (26.4); 50	85.0 (30.2); 179	1.000 (0.993–1.006)	0.880	0.503 (0.443–0.563)		
Finger-level (V = 24): dominant hand, 4 individual fingers (Sub-bundle 5.5)							
Index fingers							
1. Number of capillaries/mm	3.9 (2.2); 89	4.5 (2.3); 325	0.879 (0.787–0.981)	0.022	0.603 (0.538–0.668)	X	
2. Number of giants/mm	0.3 (0.7); 89	0.5 (0.8); 325	0.785 (0.556–1.109)	0.170	0.547 (0.492–0.601)		
3. Number of irregularly enlarged capillaries/mm	1.4 (1.5); 89	1.4 (1.4); 325	1.038 (0.881–1.224)	0.656	0.508 (0.441–0.575)		
4. Number of microhemorrhages/mm	0.1 (0.4); 89	0.2 (0.5); 325	0.592 (0.305–1.150)	0.122	0.552 (0.512–0.593)	X	X
5. Number of neoangiogeneses/mm	0.6 (0.8); 89	0.4 (0.8); 325	1.212 (0.911–1.614)	0.187	0.547 (0.486–0.608)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103) mean (SD); n	Non-cases (N=365) mean (SD); n	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
6. Maximum capillary diameter	93.1 (37.3); 26	85.9 (32.0); 119	0.998 (0.992–1.005)	0.568	0.529 (0.470–0.587)		
Middle fingers							
7. Number of capillaries/mm	3.8 (1.9); 97	4.7 (2.2); 339	0.801 (0.707–0.907)	0.001	0.614 (0.553–0.674)	X	X
8. Number of giants/mm	0.5 (0.8); 97	0.5 (0.8); 339	1.018 (0.764–1.356)	0.902	0.491 (0.432–0.550)		
9. Number of irregularly enlarged capillaries/mm	1.4 (1.4); 97	1.3 (1.4); 339	1.015 (0.868–1.188)	0.849	0.510 (0.446–0.575)		
10. Number of microhemorrhages/mm	0.2 (0.8); 97	0.3 (0.6); 339	–[†]	0.007	0.565 (0.524–0.605)	X	
11. Number of neoangiogeneses/mm	0.6 (0.9); 97	0.4 (0.8); 339	1.326 (1.024–1.718)	0.032	0.558 (0.498–0.617)	X	X
12. Maximum capillary diameter	92.3 (40.3); 36	87.1 (30.6); 143	0.999 (0.994–1.005)	0.807	0.513 (0.454–0.571)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103) mean (SD); n	Non-cases (N=365) mean (SD); n	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
Ring fingers							
13. Number of capillaries/mm	4.2 (2.1); 99	4.6 (2.1); 343	0.902 (0.807–1.009)	0.070	0.564 (0.500–0.629)	X	
14. Number of giants/mm	0.6 (0.9); 99	0.7 (1.0); 343	0.895 (0.701–1.142)	0.372	0.532 (0.473–0.590)		
15. Number of irregularly enlarged capillaries/mm	1.2 (1.4); 99	1.4 (1.5); 343	0.890 (0.754–1.050)	0.166	0.555 (0.491–0.619)		
16. Number of microhemorrhages/mm	0.2 (0.4); 99	0.3 (0.6); 343	0.734 (0.451–1.195)	0.214	0.510 (0.462–0.557)		
17. Number of neoangiogeneses/mm	0.6 (0.9); 99	0.5 (0.8); 343	1.118 (0.869–1.439)	0.385	0.524 (0.465–0.582)		
18. Maximum capillary diameter	93.4 (29.4); 42	92.9 (38.8); 167	0.997 (0.991–1.002)	0.186	0.532 (0.474–0.591)		
Little fingers							
19. Number of capillaries/mm	4.1 (1.8); 97	5.0 (2.1); 347	0.808 (0.715–0.913)	0.001	0.620 (0.558–0.681)	X	

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103) mean (SD); n	Non-cases (N=365) mean (SD); n	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
20. Number of giants/mm	0.6 (1.0); 97	0.5 (0.8); 347	1.155 (0.907–1.469)	0.242	0.513 (0.453–0.573)		
21. Number of irregularly enlarged capillaries/mm	1.2 (1.3); 97	1.3 (1.4); 347	0.974 (0.822–1.153)	0.756	0.502 (0.439–0.565)		
22. Number of microhemorrhages/mm	0.2 (0.5); 97	0.3 (0.6); 347	0.791 (0.504–1.242)	0.308	0.525 (0.476–0.574)		
23. Number of neoangiogeneses/mm	0.6 (0.8); 97	0.6 (0.9); 347	1.034 (0.807–1.326)	0.790	0.519 (0.460–0.578)		
24. Maximum capillary diameter	89.1 (28.7); 37	86.1 (33.5); 147	1.001 (0.996–1.007)	0.692	0.497 (0.436–0.558)		
Finger level (V = 24): non-dominant hand, 4 individual fingers (Sub-bundle 5.6)							
Index fingers							
1. Number of capillaries/mm	4.4 (2.0); 92	4.9 (2.4); 343	0.902 (0.811–1.003)	0.056	0.562 (0.499–0.624)	X	
2. Number of giants/mm	0.5 (0.9); 92	0.4 (0.8); 343	1.103 (0.839–1.449)	0.484	0.497 (0.439–0.555)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103) mean (SD); n	Non-cases (N=365) mean (SD); n	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
3. Number of irregularly enlarged capillaries/mm	1.2 (1.3); 92	1.3 (1.5); 343	0.959 (0.815–1.129)	0.619	0.503 (0.440–0.567)		
4. Number of microhemorrhages/mm*	0.1 (0.3); 92	0.2 (0.5); 343	0.460 (0.225–0.941)	0.033	0.550 (0.507–0.593)	X	
5. Number of neoangiogeneses/mm*	0.7 0.9); 92	0.5 (0.8); 343	1.472 (1.137–1.904)	0.003	0.579 (0.516–0.643)	X	
6. Maximum capillary diameter	86.2 (35.8); 30	88.6 (34.9); 128	0.997 (0.991–1.003)	0.341	0.526 (0.470–0.523)		
Middle fingers							
7. Number of capillaries/mm	4.1 (2.0); 97	4.8 (2.3); 341	0.864 (0.773–0.965)	0.010	0.582 (0.518–0.646)	X	
8. Number of giants/mm	0.7 (1.0); 97	0.6 (0.9); 341	1.129 (0.892–1.428)	0.312	0.537 (0.478–0.597)		
9. Number of irregularly enlarged capillaries/mm	1.2 (1.4); 97	1.4 (1.4); 341	0.942 (0.798–1.112)	0.480	0.528 (0.464–0.592)		

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103) mean (SD); n	Non-cases (N=365) mean (SD); n	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
10. Number of microhemorrhages/mm	0.2 (0.4); 97	0.2 (0.5); 341	0.829 (0.517–1.328)	0.435	0.509 (0.461–0.557)		
11. Number of neoangiogeneses/mm	0.5 (0.8); 97	0.5 (0.8); 341	1.088 (0.820–1.443)	0.558	0.523 (0.464–0.581)		
12. Maximum capillary diameter	88.3 (39.9); 49	89.3 (34.6); 152	1.002 (0.997–1.007)	0.532	0.524 (0.464–0.584)		
Ring fingers							
13. Number of capillaries/mm*	4.2 (2.0); 94	4.9 (2.2); 352	0.831 (0.739–0.934)	0.002	0.607 (0.545–0.670)	X	
14. Number of giants/mm	0.6 (1.0); 94	0.7 (1.0); 352	0.951 (0.747–1.212)	0.687	0.526 (0.466–0.587)		
15. Number of irregularly enlarged capillaries/mm	1.4 (1.5); 94	1.3 (1.4); 352	1.049 (0.899–1.223)	0.545	0.517 (0.450–0.584)		
16. Number of microhemorrhages/mm	0.2 (0.5); 94	0.3 (0.6); 352	0.816 (0.524–1.270)	0.368	0.533 (0.484–0.581)		
17. Number of neoangiogeneses/mm	0.8 (1.1); 94	0.6 (0.9); 352	1.276 (1.017–1.601)	0.035	0.548 (0.484–0.612)	X	

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103) mean (SD); n	Non-cases (N=365) mean (SD); n	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
18. Maximum capillary diameter	93.0 (38.3); 42	96.3 (41.6); 172	0.998 (0.993–1.003)	0.354	0.529 (0.469–0.590)		
Little fingers							
19. Number of capillaries/mm	4.3 (2.1); 100	4.9 (2.2); 348	0.871 (0.783–0.971)	0.012	0.592 (0.528–0.656)	X	
20. Number of giants/mm	0.4 (0.7); 100	0.4 (0.8); 348	0.954 (0.710–1.282)	0.755	0.497 (0.444–0.550)		
21. Number of irregularly enlarged capillaries/mm	1.3 (1.5); 100	1.2 (1.3) 348	1.074 (0.913–1.263)	0.386	0.506 (0.440–0.571)		
22. Number of microhemorrhages/mm	0.2 (0.5); 100	0.2 (0.5); 348	0.928 (0.596–1.443)	0.739	0.505 (0.459–0.551)		
23. Number of neoangiogeneses/mm	0.8 (0.9); 100	0.6 (0.9); 348	1.216 (0.969–1.525)	0.091	0.560 (0.499–0.621)	X	
24. Maximum capillary diameter	88.0 (37.6); 35	88.1 (39.1) 119	0.999 (0.993–1.004)	0.631	0.504 (0.449–0.558)		

Reduction of covariables through Step 1: ULR (Retention criterion: $p < 0.15$ for linear term or $p < 0.05$ for quadratic term), Step 2: MLR within-bundle (Entry criterion: $p < 0.15$; Retention criterion: $p < 0.10$), and Step 3: MLR across-bundles (Entry criterion: $p < 0.15$; Retention criterion: $p < 0.05$).

*For the NVC bundle, several types of assessments, sub-bundles met the statistical criteria mentioned above to be retained after Step 2. However, in order to retain only one type of NVC assessment in the final model (for practicability), the Steering Committee decided on only retaining the sub-bundle with the highest AUC (i.e. sub-bundle 5.5). The other NVC covariables were subsequently not retained (*)

†OR is not given since the functional relationship is quadratic. Associated *p* value and ROC-AUC are of quadratic term

Abbreviations: AUC, area under the curve; CI, confidence interval; MLR, multivariable logistic regression; NVC, nailfold videocapillaroscopy; OR, odds ratio; ROC, receiver operating characteristic; SD, standard deviation; ULR, univariable logistic regression

Supplementary Table S6. Nailfold videocapillaroscopic characteristics: qualitative assessment (1 covariable)

Variable	Summary statistics		ULR			Variables selected	
	Cases (N=103) n/N (%)	Non-cases (N=365) n/N (%)	OR (95% CI)	Wald Chi-square *p* value	ROC-AUC (95% CI)	MLR within-bundle	MLR across-bundles
Number of variables (V = 1)						**1**	**0**
NVC qualitative assessment							
1. NVC pattern*							
Normal/early	4/103 (3.9)	44/363 (12.1)					
Active	25/103 (24.3)	123/363 (33.9)	2.234† (0.736–6.779)	0.156†	0.597 (0.548–0.647)	X	
Late	74/103 (71.8)	196/363 (54.0)	4.150‡ (1.441–11.950)	0.008‡			

Reduction of covariables through Step 1: ULR (Retention criterion: p < 0.15 for linear term or *p* < 0.05 for quadratic term), Step 2: MLR within-bundle (Entry criterion: *p* < 0.15; Retention criterion: *p* < 0.10), and Step 3: MLR across-bundles (Entry criterion: *p* < 0.15; Retention criterion: p < 0.05).

*For the NVC bundle, several types of assessments, sub-bundles met the statistical criteria mentioned above to be retained after Step 2. However, in order to retain only one type of NVC assessment in the final model (for practicability), the Steering Committee decided on only retaining the sub-bundle with the highest AUC (i.e., sub-bundle 5.5). The other NVC covariables were subsequently not retained (*).

†Active vs Normal/early

‡Late vs Normal/early

Abbreviations: AUC, area under the curve; CI, confidence interval; MLR, multivariable logistic regression; NVC, nailfold videocapillaroscopy; OR, odds ratio; ROC, receiver operating characteristic; SD, standard deviation; ULR, univariable logistic regression

4. Definitions of DUs, critical digital ischemia, and other digital lesions

Supplementary Table S7. Definitions of digital ulcer (DU), critical digital ischemia, and other (than DU) digital lesions

Digital lesion	Definition used
Digital ulcer	A DU was defined as a denuded area located on the fingers of the hands and with defined border and loss of epithelization, loss of epidermis and dermis. It did not include fissures, paronychia, pitting scars, or ulcers located over the metacarpo-phalangeal joints or elbows.
Digital critical ischemia	This is not Raynaud's phenomenon. It is a prolonged, severe, persistent reduction in digital tissue perfusion without re-warming.
Fissures	Linear cleavage of skin that extends into the dermis.
Paronychia	Skin infection that occurs around the nails.
Pitting scars	Small-sized hyperkeratosis.
Calcinosis	Deposits of calcium-containing salts in soft tissues, visible to the naked eye and/or confirmed by X-ray.

5. Chart for DU location

Supplementary Figure S1. Coding of the location of digital ulcers

R or L	1, 2, 3, 4 or 5	1, 2, 3, a or b	D, P or L
Hand: R = right L = left	Digit number: 1 = thumb 2 = index finger 3 = middle finger 4 = ring finger 5 = little finger	Phalange: 1 = proximal phalange 2 = intermediate phalange 3 = distal phalange a = proximal interphalangeal joint b = distal interphalangeal joint	Side: D = dorsal P = palmar L = lateral

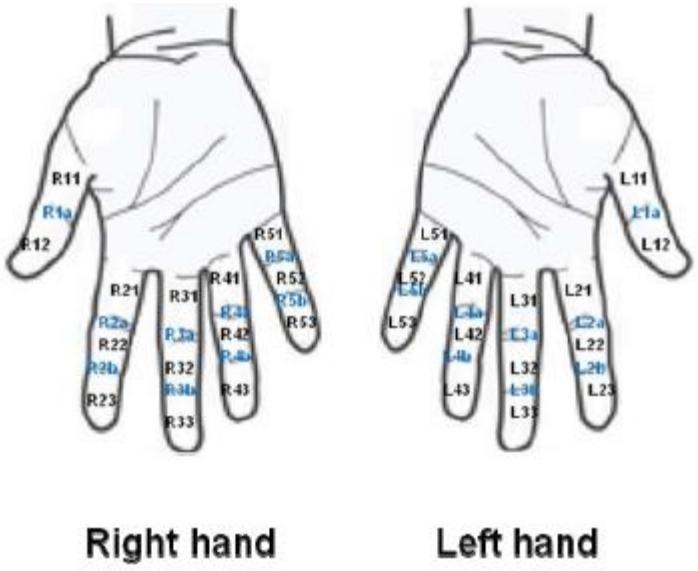
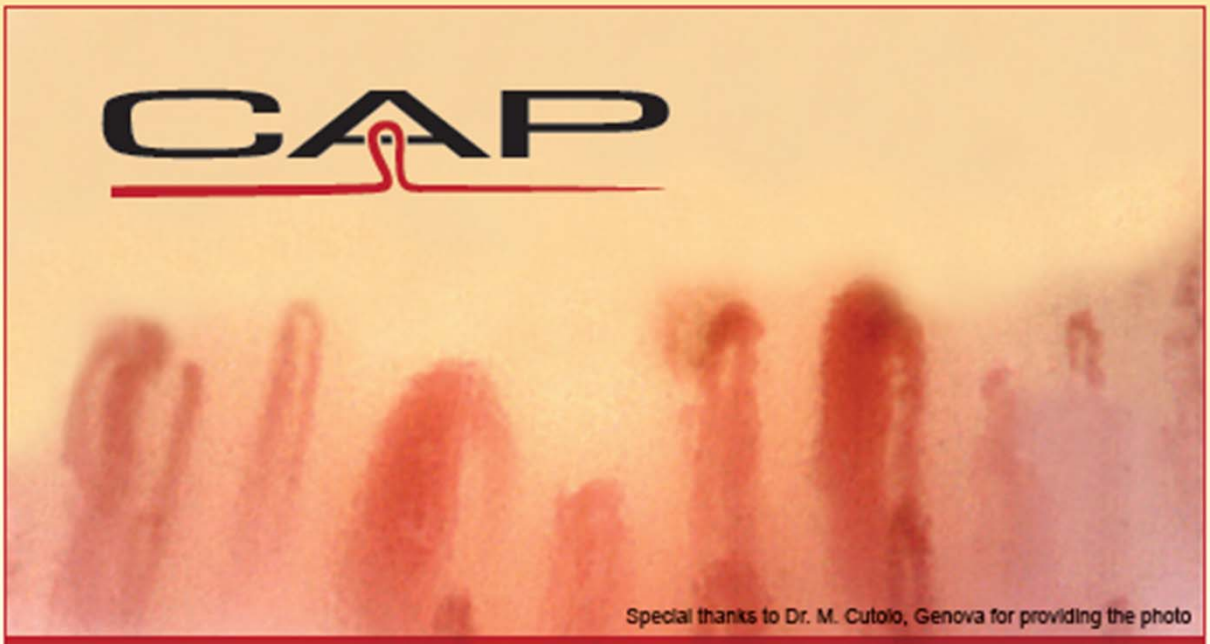


Table and sketch illustrating how the location of DU is coded.

6. Investigator booklet

Images on page 1, 4–7 and 9–13 by Dr R. De Angelis, Dr Del Medico, Dr Riccieri and Dr Sulli from M. Cutolo “Atlas of capillaroscopy in rheumatic diseases” Elsevier Srl Milano 2010

CAP



Special thanks to Dr. M. Cutolo, Genova for providing the photo

Investigator booklet

ACTELION

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General guidelines

Prior to examination the patient must have been for 15 minutes in a room at 22-23°C prior to NVC assessment. He/she must refrain from smoking and drinking caffeinated drinks for 4 hours prior to NVC assessment.

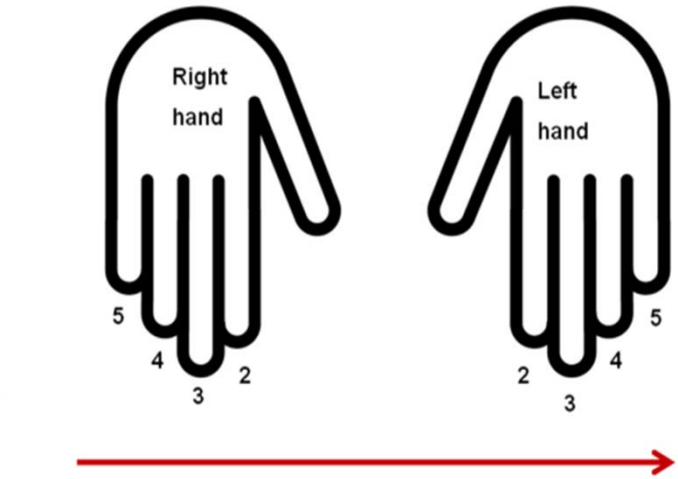
Do not analyze fingers which underwent recent trauma since this could entail microvascular abnormalities.

NVC assessment can be hampered by recent manicure, chemical substances, radiations, vibrating tools, gardening, and intensive guitar playing. In such cases, the NVC assessment must be rescheduled.

For the evaluation of the NVC parameters, a 200x lens is used.

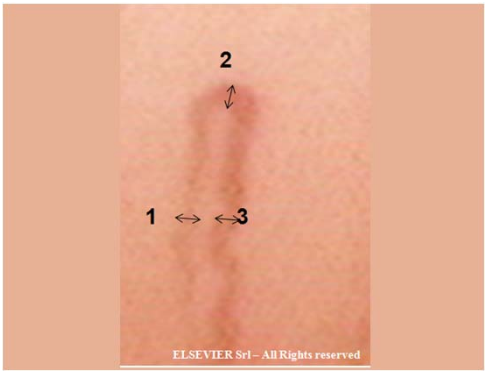
Two adjacent non overlapping fields located in the center of the nailbed for each of fingers 2 to 5 of each hand are evaluated (16 fields in total). Working on adjacent fields is essential to avoid bias in the image selection.

We recommend that you always take capillaroscopic images from left to right (like when you read): starting with the patient's right hand, 5th (little) finger, moving on to the right hand, 4th (ring) finger, ending with the left hand, 5th (little) finger as shown below.



Normal (healthy) morphology

In a healthy person, hairpin-shaped capillaries can be observed. The average density is 9-12 capillaries per mm.
Normal capillaries can also have tortuosities and crossings.

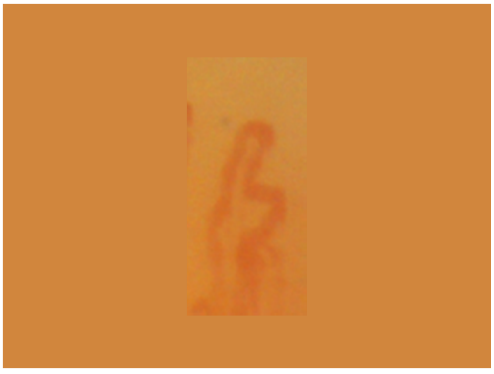


Normal hairpin-shaped capillary

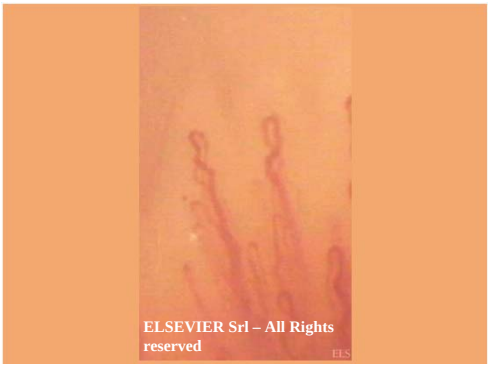
1 – afferent (arterial) limb

2 – apical (transitional) limb

3 – efferent (venous) limb (diameter <20μm)



Tortuosity: Bending of afferent and efferent limb but not apical limb.

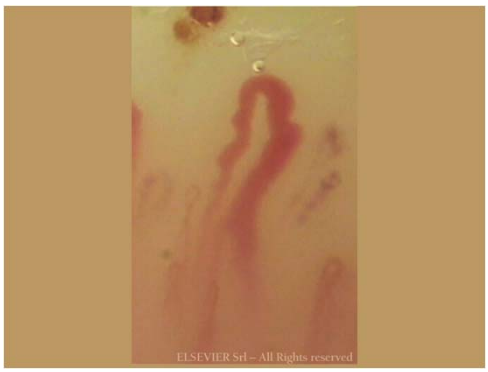


Crossing capillary: Capillary whose limbs cross once or twice.

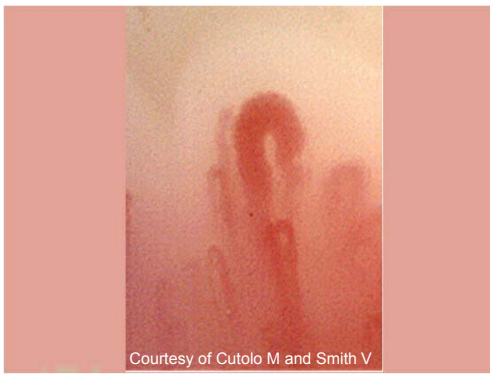
Abnormal morphology

Abnormal capillaries are not pathologic if they occur isolated.

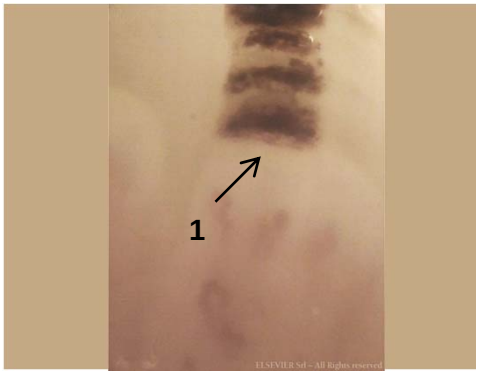
In SSc patients, irregularly enlarged capillaries, giant capillaries, microhemorrhages and neoangiogeneses (meandering, ramified, branching, bushy and bizarre capillaries) may be observed.



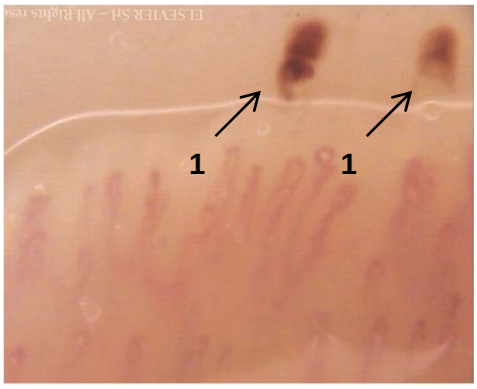
Irregularly enlarged capillary: Capillary with a diameter >20μm. Morphology can be hairpin-shaped, tortuous or crossing once.

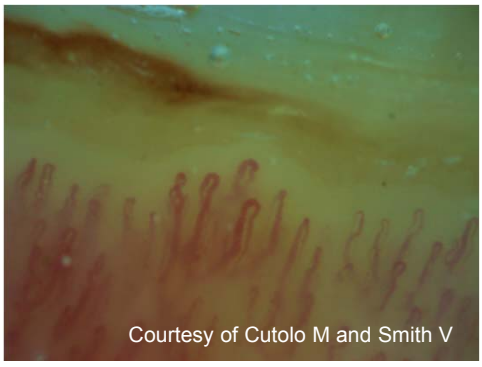


Giant capillary: Hairpin-shaped or horseshoe-shaped homogeneously large capillary with diameter >50μm. (Horseshoe shape: diameter of apical limb is larger than that of afferent and efferent limb.)



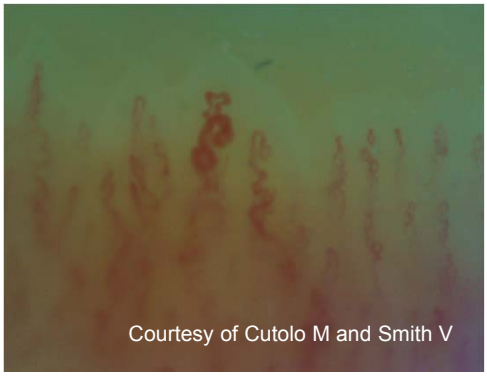
Microhemorrhage (1): Dark mass due to hemosiderin deposit which can be linked to a disappearing capillary. One microhemorrhage refers to one capillary that bled. Large confluent bleedings that cannot be linked to a disappearing capillary are not counted.





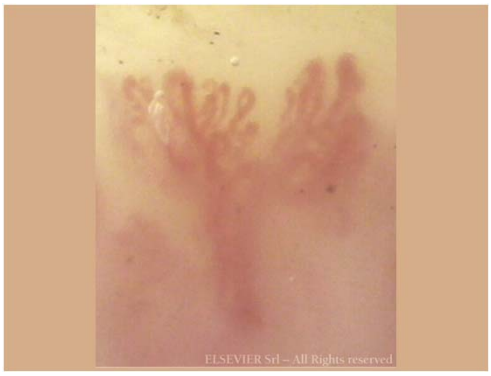
Large, confluent bleeding (not counted in CAP)

Meandering, ramified, branching, bushy, and bizarre capillaries are the result of neoangiogenesis.



Meandering: Capillary in which all three limbs (afferent, apical and efferent) cross upon themselves or with each other several times.

Meandering should not be confused with tortuosities, in which only afferent and efferent limbs are bended.



Ramified, branching, bushy capillary

Bizarre capillary (no picture): Abnormal capillary not matching any of the definitions provided above.

NVC variables assessed in CAP

This guide explains how to fill in the section “Nailfold Videocapillaroscopy“ of the eCRF.

" " indicates an assessment as listed in the eCRF.

SSc pattern according to NVC (if several patterns coexist, please select most severe manifestation pattern.

SSc pattern

Among the 16 fields (8 fingers, 2 fields per finger), please choose the most severe manifestation pattern: early, active, or late. For example, if a patient has some fields with an active pattern and others with a late pattern, please select the late pattern.

In case of doubt and in borderline cases, the following rules may be applied:

Early SSc pattern: Presence of giant capillaries and microhemorrhages. The worst field has at least 6 capillaries.

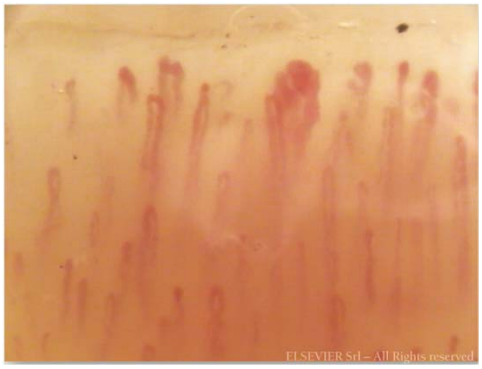
Active SSc pattern: There are always giant capillaries and sometimes ramifications. The worst field has 4-6 capillaries.

Late SSc pattern: The worst field has 3 capillaries or less, or more than two-thirds neoangiogeneses.

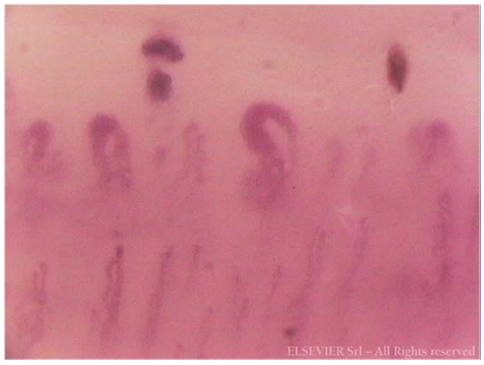
Normal may be selected if no abnormal morphology is observed.

Illustrations on next page

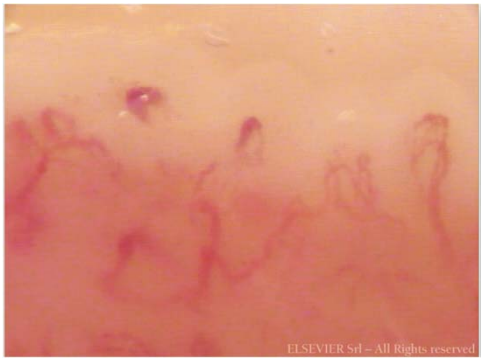
SSc pattern according to NVC (if several patterns coexist, please select most severe manifestation pattern.



Early SSc pattern: Few giant capillaries, few capillary microhemorrhages, relatively well-preserved capillary distribution, no evident loss of capillaries.



Active SSc pattern: Frequent giant capillaries, frequent capillary microhemorrhages, moderate loss of capillaries, mild disorganization of the capillary architecture, absent or mild ramified capillaries. Usually this pattern is associated with 4-6 capillaries / mm.



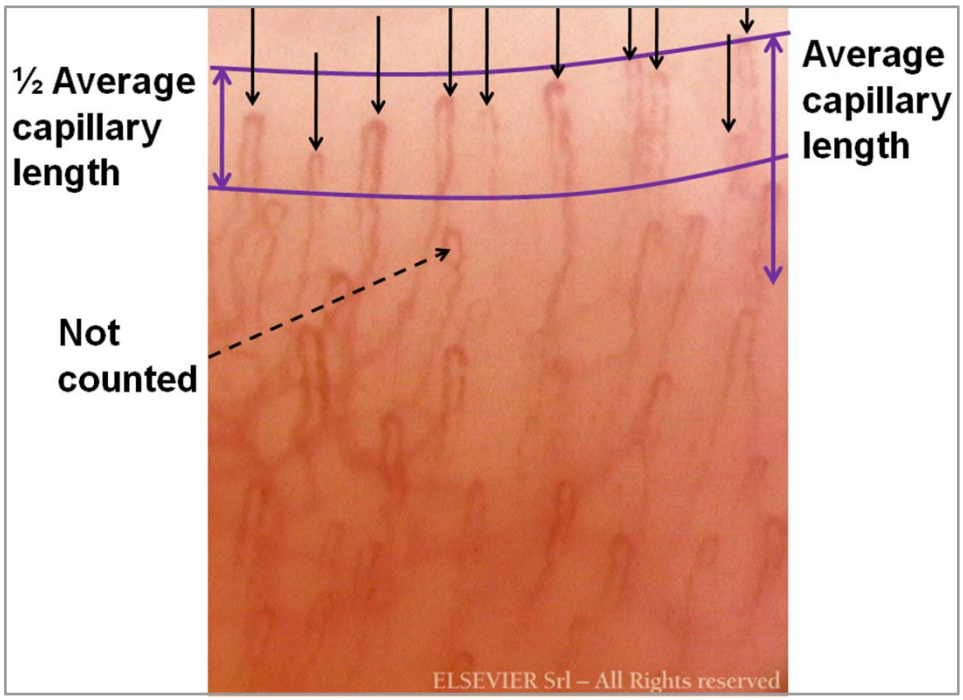
Late SSc pattern: Irregular enlargement of the capillaries, few or absent giant capillaries and microhemorrhages, severe loss of capillaries with avascular areas, disorganization of the normal capillary array, and ramified/bushy capillaries. Usually this pattern is associated with < 4 capillaries / mm.

Capillaries | # Irregularly enlarged capillaries | # Giant capillaries | # Microhemorrhages | # neoangiogeneses | Max capillary diameter (µm)

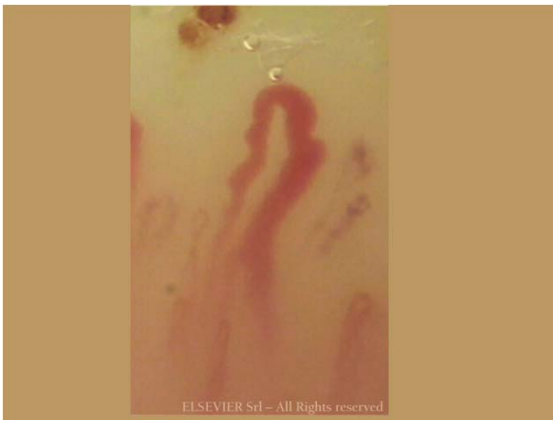
Number of capillaries

Please count the number of normal and abnormal capillaries which refers to the number of capillaries counted along one linear millimeter within the distal row of the nailfold.

Distal row: The distal row is the row of capillaries closest to the nail side corresponding to the entire front line. All capillaries which are longer than half of the average capillary length are counted.



Capillaries | # Irregularly enlarged capillaries | # Giant capillaries | # Microhemorrhages | # Neoangiogeneses | Max capillary diameter (μm)



Number of irregularly enlarged capillaries

Please count all capillaries within the distal row and with a diameter >20 μm in a linear millimeter. Morphology can be normal, tortuous or crossing once.

Capillaries | # Irregularly enlarged capillaries | # Giant capillaries | # Microhemorrhages | # neoangiogeneses | Max capillary diameter (μm)

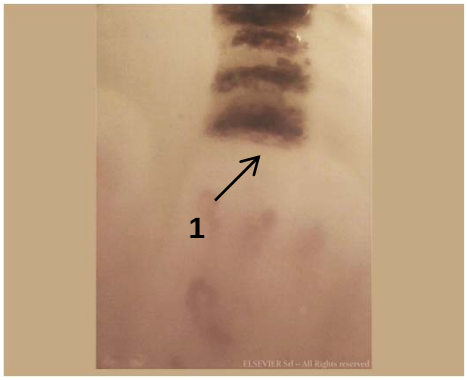
Number of giant capillaries

Please count all hairpin-shaped or horseshoe-shaped homogeneously large capillaries within the distal row and with a diameter >50μm in a linear millimeter. (Horseshoe shape: diameter of apical limb is larger than that of afferent and efferent limb.)

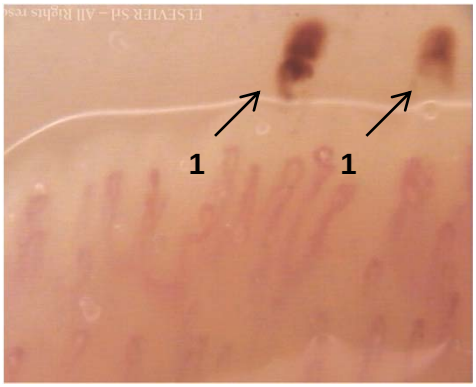
Capillaries | # Irregularly enlarged capillaries | # Giant capillaries | # Microhemorrhages | # neoangiogeneses | Max capillary diameter (µm)

Number of microhemorrhages

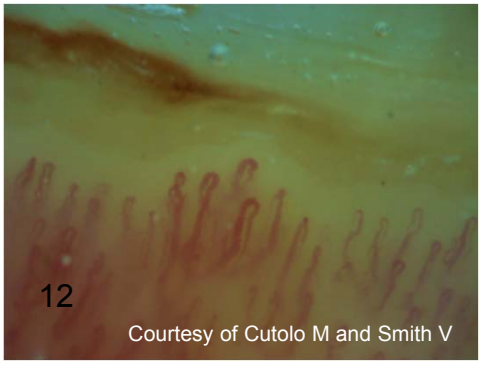
Please count all dark masses due to hemosiderin deposit and which can be linked to a disappearing capillary in a linear millimeter. One microhemorrhage refers to one capillary that bled. Large confluent bleedings that cannot be linked to a disappearing capillary are not counted.



One microhemorrhage.



Two microhemorrhages.



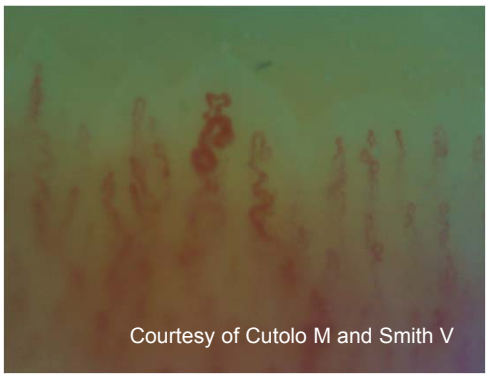
Large, confluent bleeding (not counted in CAP)

CAP

Capillaries | # Irregularly enlarged capillaries | # Giant capillaries | # Microhemorrhages | # neoangiogeneses | Max capillary diameter (µm)

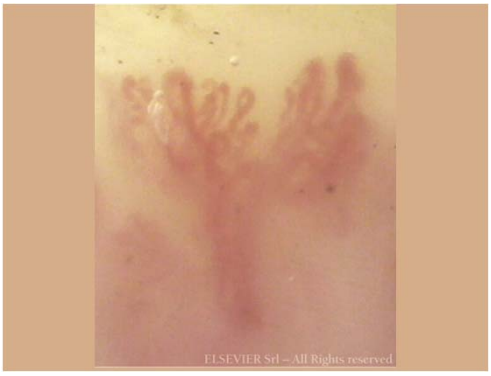
Number of neoangiogeneses

Please count all meandering, ramified, branching, bushy, bizarre capillaries, and capillaries with more than two crossings. Count within the distal row in one linear millimeter.



=

Meandering: Capillary in which all three limbs (afferent, apical and efferent) cross upon themselves or with each other several times.



+

Ramified, branching, bushy capillary

+

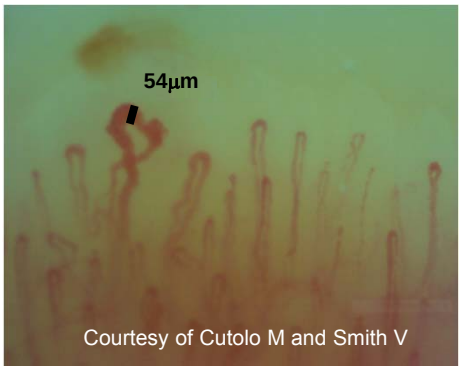
Capillaries with more than two crossings (no picture).

+

Bizarre capillary (no picture): Abnormal capillary not matching any of the definitions provided above.

Maximum capillary diameter

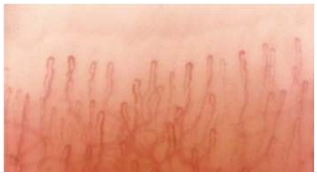
Please choose among all homogeneously large (diameter ≥50μm) capillaries in the 1-mm field, (if any) maximum diameter, irrespective of morphology.



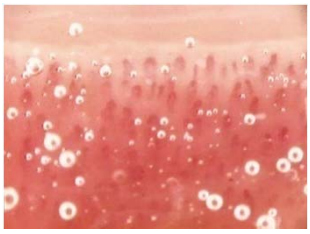
Frequently asked questions

What does a normal NVC pattern look like?

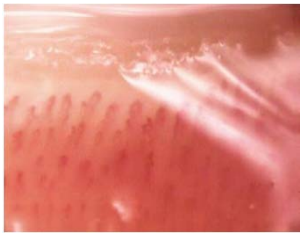
It has thin, parallel capillaries. 9-12 capillaries / mm in the distal row.



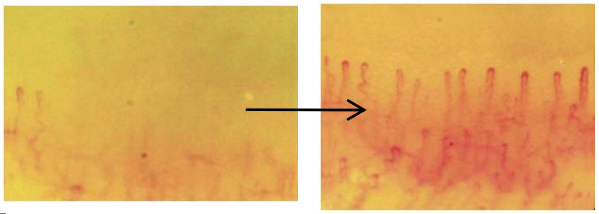
Why do I see bubbles on the image?
It is probable that the operator used too much immersion oil. Reducing the amount of oil could improve the image quality.




Why are there reflections on the image?
It is probable that the operator used too little immersion oil. Increasing the amount of oil could improve the image quality



Why can't I clearly see capillaries?
It is probable that the operator pressed too hard on the nailfold, therefore preventing blood cells from flowing in the capillaries. Releasing the pressure could improve the image visibility.



7. Interactions – bundle 6

Supplementary Table S8. Interactions investigated and grouped into a separate bundle on Steering Committee advice

Interactions grouped into a separate bundle on Steering Committee advice
Sex and age at enrollment
Sex and age at first physician-documented non-Raynaud's clinical feature
Age at enrollment and years since first physician-documented non-Raynaud's clinical feature
Age at enrollment and years since first Raynaud's phenomenon
Age at enrollment and age at first physician-documented non-Raynaud's clinical feature
Age at enrollment and age at first Raynaud's clinical phenomenon
SSc subtype and age at first physician-documented non-Raynaud's clinical feature
SSc subtype and mRSS

Following the advice from the Steering Committee, pre-specified interactions were investigated in Step 2, within a separate bundle, using a stepwise forward selection procedure with specific selection criteria (Entry criterion: $p < 0.15$; Retention criterion: $p < 0.10$). For all pairs of covariables the *p* value was > 0.10, so none of them were retained.
Abbreviations: mRSS, Modified Rodnan Skin Score; SSc, systemic sclerosis

8. Excluded variables

Supplementary Table S9. Overview of variables excluded because they consisted of fewer than 20 patients

Binary variables with a frequency of fewer than 20 patients	
Bundle 1: Demographics	None
Bundle 2: SSc clinical characteristics	Organ involvement: - Nervous system (Connective) Tissue disease: - Systemic Lupus Erythematosus - Dermatomyositis - Polymyositis - Marfan syndrome - Ehlers-Danlos syndrome - Osteogenesis imperfecta - Stickler syndrome - Any other (connective) tissue disease
Bundle 3: Digital ulcer characteristics	None
Bundle 4: Other clinical characteristics	None
Bundle 5: Nailfold videocapillaroscopic characteristics	None

Abbreviations: SSc, systemic sclerosis

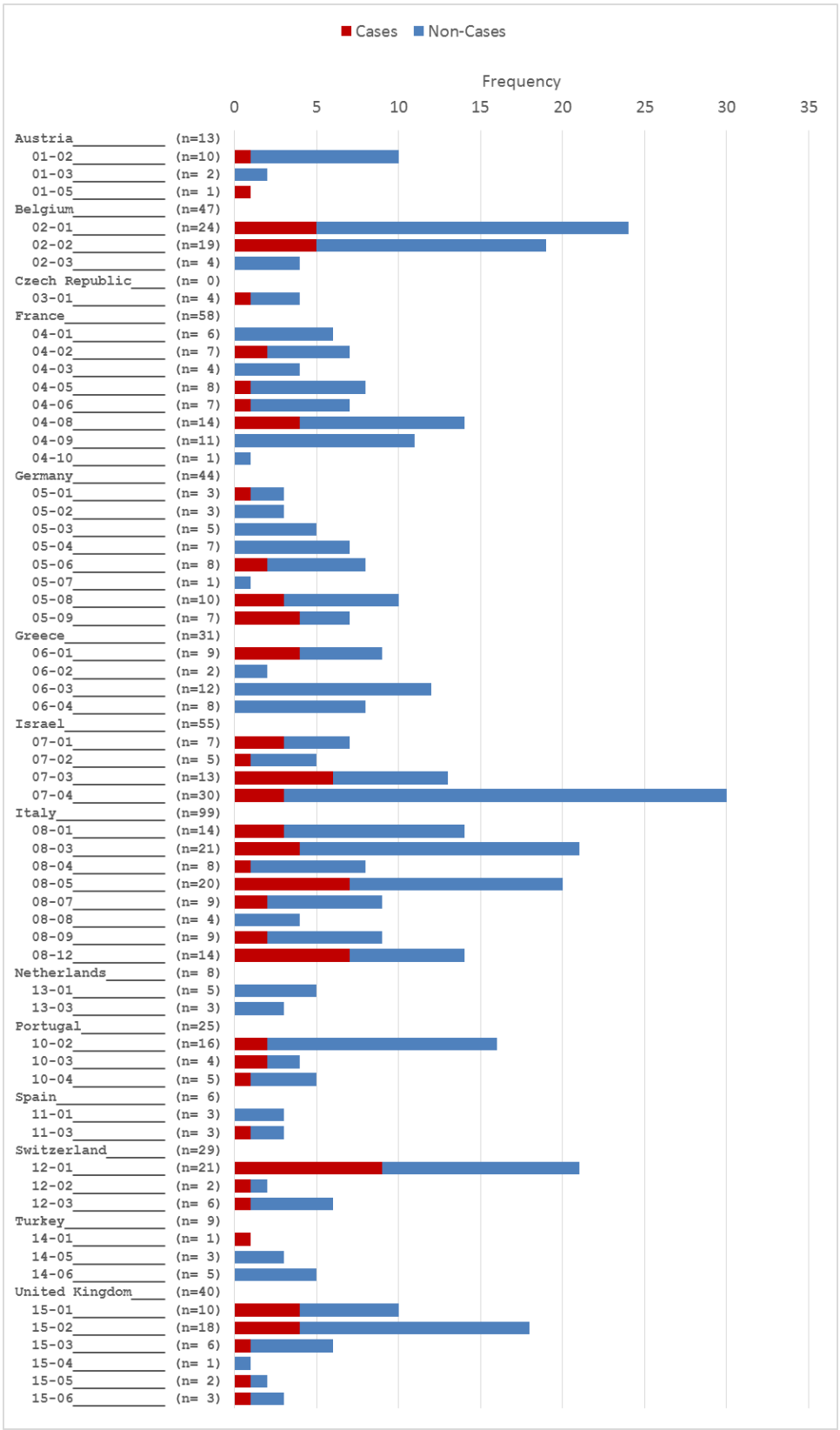
Supplementary Table S10. Overview of variables excluded on clinical advice from the Steering Committee

Variables excluded on clinical advice from the Steering Committee	
Bundle 1: Demographics	- Height (cm) - Conduct manual labor
Bundle 2: SSc clinical characteristics	None
Bundle 3: DU characteristics	- Presence of DU - At least one DU in fingertips - At least one DU in finger joints - Previous or current (= at enrollment) complications: • Soft tissue infection requiring antibiotics • Auto-amputation • Critical digital ischemia • Gangrene • Any previous or current complication - Current DU-associated interventions: • Current wound debridement • Current antiseptics • Current wound supportive gels/creams - Any previous or current intervention
Bundle 4: Other clinical characteristics	- Allen test: number of abnormal hands - Number of pitting scars
Bundle 5: Nailfold videocapillaroscopic characteristics	• None

Abbreviations: DU, digital ulcer; SSc, systemic sclerosis

9. New digital ulcer occurrence by Center

Figure S2. Frequency of Patients, Cases, and Non-Cases per Center



The median (minimum, maximum) number of patients/center was 1 (0, 31) and Cases/center was 1 (0,9).

10. Within-bundle MLR models

Table S11. Bundle 1: Demographics within-bundle MLR model

Variable	Category	Coefficient estimate	Standard error	MLR (within-bundle) OR (95% CI)	Wald Chi-square	*P* value
Intercept		-0.3249	0.4515	0.723 (0.298–1.751)	0.5178	0.4718
Age at enrollment		-0.0177	0.0084	0.982 (0.966–0.999)	4.4803	0.0343

ROC-AUC (95% CI): 0.574 (0.508–0.639)

Multivariable logistic regression equation

Probability (new DU within 6 months) = exp (linear predictor)/(1 + exp (linear predictor)), where

linear predictor = -0.325

-0.018*age at enrollment

Hosmer-Lemeshow goodness-of-fit test: Chi-Square = 4.3621, df = 8, p value = 0.823

Abbreviations: AUC, area under the curve; CI, confidence interval; DU, digital ulcer; MLR, multivariable logistic regression; OR, odds ratio; ROC, receiver operating characteristic

Table S12.Bundle 2: Systemic sclerosis clinical characteristics within-bundle MLR model

Variable	Category	Coefficient estimate	Standard error	MLR (within-bundle) OR (95% CI)	Wald Chi-square	*P* value
Intercept		-0.5921	0.3824	0.553 (0.261–1.170)	2.3975	0.1215
Age at first physician-documented non-Raynaud clinical feature		-0.0163	0.0084	0.984 (0.968–1.000)	3.7777	0.0519
Kidney involvement: SSc renal crisis, kidney failure	Yes	-1.3314	0.7540	0.264 (0.060–1.158)	3.1180	0.0774
Heart involvement	Yes	0.5874	0.2904	1.799 (1.018–3.179)	4.0908	0.0431

ROC-AUC (95% CI): 0.601 (0.537–0.664)

Multivariable logistic regression equation

Probability (new DU within 6 months) = exp (linear predictor)/(1 + exp (linear predictor)), where

linear predictor = –0.592

– 0.016*age at first physician-documented non-Raynaud clinical feature

+ (-1.331 if Kidney involvement = YES)

+ (0.587 if Heart involvement = YES)

Hosmer-Lemeshow goodness-of-fit test: Chi-Square = 20.0667, df = 8, *p* value = 0.010

Abbreviations: AUC, area under the curve; CI, confidence interval; df, degrees of freedom; DU, digital ulcer; MLR, multivariable logistic regression; OR, odds ratio; ROC, receiver operating characteristic; SSc, systemic sclerosis

Table S13. Bundle 3: Digital ulcer characteristics within-bundle MLR model

Variable	Category	Coefficient estimate	Standard error	OR (95% CI)	MLR (within-bundle) Wald Chi-square	*P* value
Intercept		-1.8948	0.1705	0.150 (0.108–0.210)	123.5659	<0.0001
Number of DUs at enrollment categorized	1	0.8362	0.3169	2.308 (1.240–4.295)	6.9624	0.0083
	2	1.0603	0.3808	2.887 (1.369–6.090)	7.7538	0.0054
	≥3	1.9168	0.3659	6.799 (3.319–13.930)	27.4362	<0.0001
Previous complication: auto-amputation	Yes	0.8375	0.4470	2.310 (0.962–5.549)	3.5095	0.0610
Presence of CDI at enrollment	Yes	0.8440	0.4510	2.326 (0.961–5.629)	3.5026	0.0613

ROC-AUC (95% CI): 0.694 (0.637, 0.751)

Multivariable logistic regression equation

Probability (new DU within 6 months) = exp (linear predictor)/(1 + exp (linear predictor)), where

linear predictor = -1.895

+ (0.836 if 1 DU or 1.060 in 2 DU or 1.917 if ≥3 DU)

+ (0.838 if previous auto-amputation = YES)

+ (0.844 if CDI = YES)

Hosmer-Lemeshow goodness-of-fit test: Chi-Square = 0.7316, df = 2, *p* value = 0.694

Abbreviations: AUC, area under the curve; CDI, critical digital ischemia; CI, confidence interval; df, degrees of freedom; DU, digital ulcer; MLR, multivariable logistic regression; OR, odds ratio; ROC, receiver operating characteristic; SSc, systemic sclerosis

Table S14. Bundle 4: Other clinical characteristics within-bundle MLR model

Variable	Category	Coefficient estimate	Standard error	MLR (within-bundle) OR (95% CI)	Wald Chi-square	*P* value
Intercept		-1.3730	0.1284	0.253 (0.197–0.326)	114.3192	<0.0001
Presence of paronychia	Yes	0.7066	0.3101	2.027 (1.104–3.722)	5.1923	0.0227

ROC-AUC (95% CI): 0.545 (0.501, 0.589)

Multivariable logistic regression equation

Probability (new DU within 6 months) = exp (linear predictor)/(1 + exp (linear predictor)), where

linear predictor = -1.373

+ (0.707 if presence of paronychia = YES)

Hosmer-Lemeshow goodness-of-fit test: Chi-Square = 0.000, df = 0

Abbreviations: AUC, area under the curve; CI, confidence interval; df, degrees of freedom; DU, digital ulcer; MLR, multivariable logistic regression; OR, odds ratio; ROC, receiver operating characteristic

Table S15. Bundle 5: Quantitative NVC characteristics* within-bundle MLR model

				MLR (within-bundle)		
Variable	**Category**	**Coefficient estimate**	**Standard error**	**OR (95% CI)**	**Wald Chi-square**	***P* value**
Intercept		-0.3538	0.3108	0.702 (0.382–1.291)	1.2961	0.2549
Finger level: dominant hand, 4 individual fingers (Sub-bundle 5.5)	IF: Number of microhemorrhages	-1.0510	0.4956	0.350 (0.132–0.923)	4.4974	0.0339
	MF: Number of capillaries	-0.2384	0.0700	0.788 (0.687–0.904)	11.5852	0.0007
	MF: Number of neoangiogeneses	0.2993	0.1441	1.349 (1.017–1.789)	4.3126	0.0378
ROC-AUC (95% CI): 0.677 (0.614–0.740)						
Multivariable logistic regression equation						
Probability (new DUs within 6 months) = exp (linear predictor)/(1 + exp (linear predictor)), where linear predictor = –0.354 –1.051*nb IF microhemorrhages –0.238 *nb MF capillaries +0.299 *nb MF neoangiogeneses						

Hosmer-Lemeshow goodness-of-fit test: Chi-Square = 7.9131, df = 8, *p* value = 0.442

Abbreviations: AUC, area under the curve; CI, confidence interval; df, degrees of freedom; DU, digital ulcer; IF, index finger; MF, middle finger; MLR, multivariable logistic regression; NVC, nailfold videocapillaroscopy; OR, odds ratio; ROC, receiver operating characteristic

Table S16. Comparison of the within-bundle MLR models of NVC sub-bundles

Sub-bundle	5.1 Both hands	5.2 Dominant hand	5.3 Non-dominant hand	5.4 Finger pairs	5.5 Individual fingers dominant hand	5.6 Individual fingers non-dominant hand
N* (of 468)	465	460	460	447	382	399
ROC-AUC	0.617	0.606	0.613	0.655	0.677	0.638
ROC-AUC 95% CI	0.555–0.678	0.547–0.665	0.551–0.676	0.593–0.716	0.614–0.740	0.570–0.705
Selected variables						
# Capillaries	X	X	X	X	X	X
# Neoangiogeneses	X		X	X	X	X
# Microhemorrhages				X	X	X

*Number of patients for whom data on all variables used in MLR are available

Abbreviations: AUC, area under the curve; CI, confidence interval; MLR, multivariable logistic regression; NVC, nailfold videocapillaroscopy; ROC, receiver operating characteristic

11. NVC characteristics carried forward during multivariable analyses

Supplementary Table S17. Complete list of NVC variables carried forward from MLR within-bundle to MLR across-bundles analysis

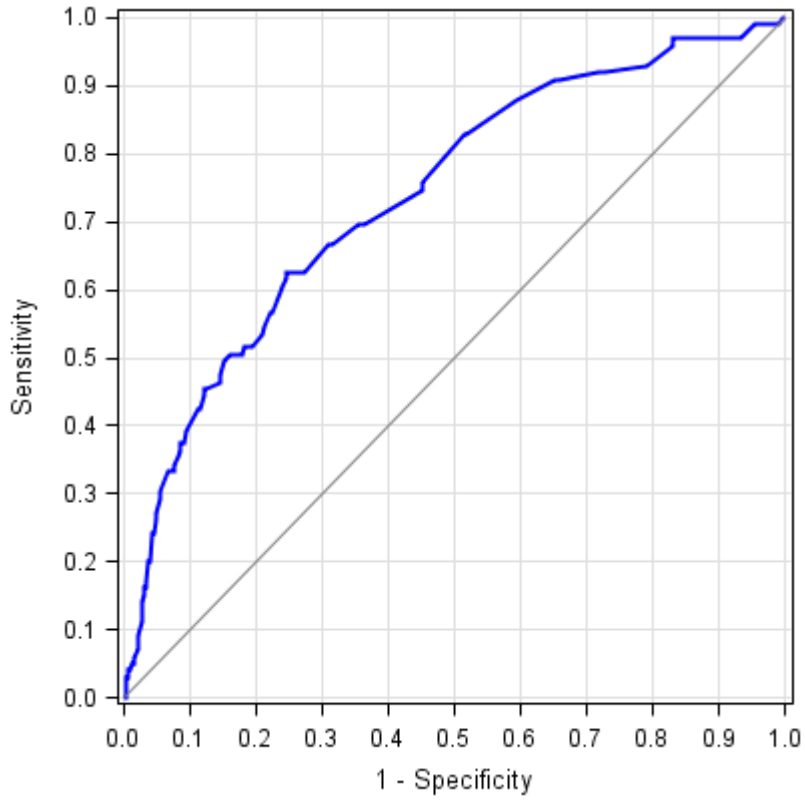
NVC Sub-bundle	Variables retained to enter MLR across-bundles	ROC-AUC (95% CI)
Qualitative NVC characteristics		
NVC pattern	NVC pattern	0.597 (0.548–0.647)
Quantitative NVC characteristics		
Patient level: both hands, 8 fingers (=sub-bundle 5.1)	Number of capillaries Number of neoangiogeneses	0.617 (0.555–0.678)
Hand level: dominant hand, 4 fingers (=sub-bundle 5.2)	Number of capillaries	0.606 (0.547–0.665)
Hand level: non-dominant hand, 4 fingers (=sub-bundle 5.3)	Number of capillaries Number of neoangiogeneses	0.613 (0.551–0.676)
Finger level: both hands, 4 pairs of fingers (=sub-bundle 5.4)	IF: Number of microhemorrhages IF: Number of neoangiogeneses MF: Number of capillaries	0.655 (0.593–0.716)
Finger level: dominant hand, 4 individual fingers (=sub-bundle 5.5)	IF: Number of microhemorrhages MF: Number of capillaries MF: Number of neoangiogeneses	0.677 (0.614–0.740)
Finger level: non-dominant hand, 4 individual fingers (=sub-bundle 5.6)	IF: Number of microhemorrhages IF: Number of neoangiogeneses RF: Number of capillaries	0.638 (0.570–0.705)

Abbreviations: AUC, area under the curve; CI, confidence interval; IF, index finger; MF, middle finger; MLR, multivariable logistic regression; NVC, nailfold videocapillaroscopy; RF, ring finger; ROC, receiver operating characteristic

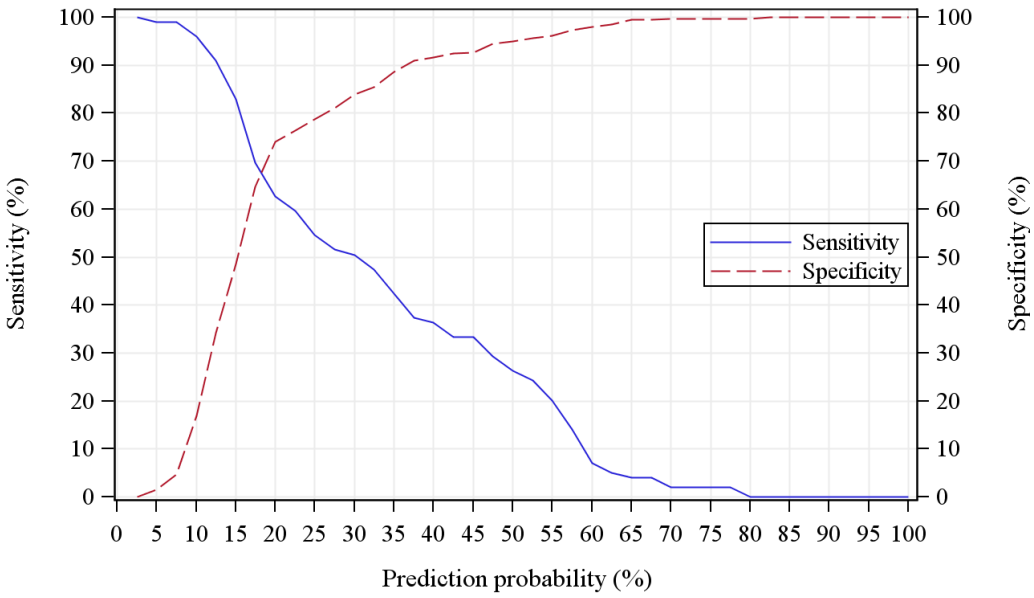
12. Operating characteristics of the final MLR model

Supplementary Figure S3. Receiver operating characteristic curve (A) and sensitivity/specificity* curves (B) of the final MLR model

A



B



*vs 2.5% cut-offs

13. CAP study Statisticians

In addition to the acknowledged and author statisticians, the following statisticians were involved in the statistical analysis plan and/or performing analyses:

Sophie Collingborn, *PRA International GmbH, Mannheim, Germany;* **Hans-Peter Duerr** & **Martin Scott,** *Numerus Ltd, Tübingen, Germany.*