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The correlation between nailfold capillaroscopic findings and adaptive optics imaging of retinal microvasculature in patients with systemic sclerosis

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Abstract

Background. Vascular injury is a central and early feature of systemic sclerosis (SSc) pathogenesis. Although nailfold capillaroscopy (NC) effectively visualizes characteristic peripheral arteriolar and capillary changes, the retinal microcirculation provides a noninvasive, high-resolution view into subtler vascular dysfunction. Consequently, retinal vascular imaging may offer an ideal modality for monitoring microvascular injury and detecting early manifestations of SSc.

Objectives. To compare retinal microvascular parameters between SSc patients and healthy controls using adaptive optics (AO) imaging, and to evaluate the correlation between adaptive optics-derived retinal measurements and NC findings in SSc.

Materials and methods. The study included 31 patients with SSc and 41 healthy controls. The AO images of the retinal arteries were obtained in both groups and the measurements were compared. Nailfold capillaroscopy was also performed in the SSc cohort, and its findings were directly compared with the AO imaging results.

Results. Retinal arterial wall thickness was significantly lower in SSc patients than in healthy controls ($p = 0.016$), and the wall-to-lumen ratio was similarly reduced in the SSc group ($p = 0.048$). Within the SSc cohort, hypertensive patients exhibited a significantly greater wall cross-sectional area compared to those without hypertension ($p = 0.026$).

Conclusions. Adaptive optics retinal imaging demonstrated a significant reduction in mean arterial wall thickness in SSc patients compared with healthy controls. However, no correlation was identified between the AO findings and the NC parameters or the disease stage. Our analysis revealed that alterations in retinal vascular parameters were confined to SSc patients with comorbid hypertension or those receiving sildenafil therapy. To fully establish the clinical utility of adaptive optics imaging in SSc, and to elucidate its relationship with NC findings, larger, multicenter studies with more diverse patient cohorts are warranted.

Key words: systemic sclerosis, scleroderma, adaptive optics, nailfold capillaroscopy, retinal microvasculature

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Highlights

- Adaptive optics unveils retinal microvascular changes in systemic sclerosis (SSc): First study to apply high-resolution AO imaging in scleroderma patients.
- Concordance between nailfold capillaroscopy and adaptive optics metrics: Combined modalities enhance accuracy in detecting SSc microangiopathy.
- Thinner retinal vessel walls in SSc vs controls: Quantitative AO analysis shows significant retinal wall thinning.
- Adaptive optics as a novel diagnostic tool for SSc microvascular injury: Promises noninvasive, early detection and monitoring of microvascular changes in scleroderma.

Background

Systemic sclerosis (SSc) is a connective tissue disorder caused by autoimmunity. It is characterized by obliterative vasculopathy, widespread fibrosis and a dysregulated immune response.[1,2] Vascular involvement represents an initial and pivotal factor in the pathogenesis of the disease, as well as in the development of multiple organ dysfunction. The vasculopathy in SSc includes thrombosis, vasospasm and vessel lumen obliteration leading to microangiopathy.[2] Microcirculatory changes observed in the capillaries are the hallmark of the disease.

Nailfold capillaroscopy (NC), as a noninvasive imaging technique, is routinely used to assess peripheral capillary abnormalities in scleroderma patients and is included in the diagnostic criteria for SSc.[3,4] Therefore, this tool plays a pivotal role in both diagnosing and monitoring the progression of the disease.

A range of ocular manifestations have been observed in patients with scleroderma, including those affecting the posterior segment of the eye.[5–10] Recent research has concentrated on retinal and choroidal alterations observed in these individuals. Advanced imaging methods, such as optical coherence tomography angiography (OCTA), have facilitated the detection of structural changes in the retinal microvasculature linked to systemic diseases.

Adaptive optics (AO) imaging represents a noninvasive tool for the visualization of retinal structures, including photoreceptors, blood vessels and nerve fibers, in vivo at the microscopic level. The camera employs infrared illumination with a wavelength of 850 nm.[11] The AO technology is employed for the evaluation of retinal vessels in healthy eyes and arterial hypertension, as well as in ocular pathologies such as diabetic retinopathy, glaucoma, retinal vessel occlusion and retinal vasculitis.[12–22]

Objectives

The study aimed to assess and compare the retinal microvasculature parameters in scleroderma patients and healthy controls using AO imaging. Furthermore, we aimed to evaluate the relationship between NC findings, disease characteristics and AO results within the SSc group.

Materials and methods

The study was conducted at the Military Institute of Aviation Medicine (Warsaw, Poland) between March 2022 and May 2023. The study received approval from the Ethics Committee Reviewing Biometric Research at the Military Institute of Aviation Medicine (approval No. 1/2022) and followed the tenets of the Declaration of Helsinki.

The purpose and procedures of the study were thoroughly explained to the participants, and written consent was subsequently obtained from individuals. The study sample comprised patients with SSc from the Department and Polyclinic of Systemic Connective Tissue Diseases at the National Institute of Geriatrics, Rheumatology and Rehabilitation in Warsaw. Healthy participants were enrolled during routine appointments at the Department of Ophthalmology in the Military Institute of Aviation Medicine.

Participants

A total of 31 patients (61 eyes) diagnosed with SSc and 41 healthy controls (81 eyes) were included in this and our previous study.[23] No significant differences were observed between the scleroderma patients and the control group regarding age, gender distribution or axial length (Table 1,2). Within the study cohort, 71.4% of patients were diagnosed with diffuse cutaneous SSc, while 28.6% were diagnosed with limited cutaneous SSc. Nailfold capillaroscopy revealed an early scleroderma pattern in 5 patients, an active pattern in 12 and a late pattern in 9. Within the SSc cohort, 2 patients had pulmonary arterial hypertension (PAH), 8 developed digital ulcers and 8 were hypertensive. A total of 13 participants were treated with sildenafil, while 12 were treated with amlodipine. Interstitial lung disease was identified in 11 patients, of whom 64% were classified as having nonspecific interstitial pneumonia (NSIP) and 36% as having usual interstitial pneumonia (UIP). Elevated pro-B-type natriuretic peptide (proBNP) levels were observed in 16.1% of the studied cases (Table 3).

Table 1. Baseline characteristics of the study cohort

Analyzed trait*		Statistic
Number of participants, n (%)		72 (100.00)
Number of eyes, n (%)		142 (100.00)
Gender	female	49 (60.06)
	male	23 (31.94)
Age [years], Me (Q_1–Q_3)		46 (36–55)
Shapiro–Wilk W test for normality		W = 0.933 p < 0.001

*Statistic parameters used: n – absolute number; % – percentage; Me – median; Q – quartiles.

Table 2. Baseline characteristics of the study cohort by occurrence of scleroderma

Analyzed trait		Scleroderma		p-value
		present	absent	
Number of participants, n (%)		31 (43.06)	41 (56.94)	–
Number of eyes, n (%)		61 (42.96)	81 (57.04)	–
Gender, n (%)	female	22 (70.97)	27 (65.85)	χ^2 = 0.209 df = 1 p = 0.647
	male	9 (29.03)	14 (34.15)	
Age [years], Me (Q_1–Q_3) Shapiro–Wilk test		48 (40–54) W = 0.935 p = 0.003	41 (35–55) W = 0.0867 p < 0.001	Levene's test F (1, 140) = 1.137 p = 0.288 Mann–Whitney test U = 2070.000 $Z_{corr.}$ = 1.651 p = 0.099
AL [mm], Me (Q_1–Q_3) Shapiro–Wilk test		23.53 (22.88–24.20) W = 0.968 p = 0.114	23.78 (23.13–24.35) W = 0.970 p = 0.129	Levene's test F (1, 121) = 0.475 p = 0.492 ANOVA F (1, 121) = 0.138 p = 0.711

*Statistic parameters used: n – absolute number; % – percentage; Me – median; Q – quartiles; ANOVA – analysis of variance; df – degrees of freedom; AL – axial length.

Table 3. Baseline characteristics of the scleroderma group (n = 31)

Trait		n M (SD)	% Me (Q_1–Q_3)
Gender	female	22	71.0
	male	9	29.0
Scleroderma	localized	8	28.6
	systemic	20	71.4
	capillaroscopy	27	96.4
Scleroderma pattern	none	2	7.1
	early	5	17.9
	active	12	42.9
	late	9	32.1
anti-PM/SCL		1	3.6
PC TH fibrillarin		3	10.7
anti-Scl-70-antibodies		17	54.8
Centromere		8	25.8
Number of vessels	normal	2	7.1
	reduced	20	71.5
	very reduced	6	21.4
Avascular are		16	57.1
Giant capillaries		14	50.0
Hemorrhages		11	39.3
Branched vessels		10	35.7
MES Shapiro–Wilk test		2.2 (1.1) W = 0.848	2.5 (1.1–3.1) p < 0.001
Interstitial lung disease		12	42.9
PAH		2	7.1
NSIP		7	22.6
UIP		4	14.3
MMF		13	41.9
MTX		7	25.0
mRSS Shapiro–Wilk test		8.1 (7.9) W = 0.771	2.0 (2.0–12.0) p < 0.001
Finger ulcers		8	28.6
RVSP > 35 mm Hg		3	1.1
Elevated proBNP		5	18.5
Arterial hypertension		8	25.8
Administration of sildenafil		13	41.9
Administration of amlodipine		12	38.7

Missing data were pair-wise deleted. For discrete variables: n – number; % – percentage. For numerical traits: M – mean; SD – standard deviation; Me – median; Q – quartiles; anti-PM/SCL – anti-polymyositis/scleroderma antibodies; PAH – pulmonary arterial hypertension; NSIP – non-specific interstitial pneumonia; UIP – usual interstitial pneumonia, MMF – mycophenolat mofetil; MTX – methotrexate, mRSS – modified Rodnan Skin Score; RVSP – right ventricle systolic pressure; MES – the microangiopathy evolution score.

Methods

A comprehensive ophthalmic examination was performed on all participants. This included assessments of best-corrected visual acuity (BCVA), intraocular pressure, refraction, anterior segment examination, fundoscopy with pupillary dilatation, and axial length (AL) measurement. Exclusion criteria were refractive errors beyond –3.0 or +3.0 diopters and any pathological ocular condition, including glaucoma or retinal and choroidal diseases. Moreover, eyes with low-quality AO images were also excluded. The BCVA was measured monocularly using LogMAR charts (Lighthouse International, New York, USA) at 5 m, while AL was assessed using the IOL Master 500 (Carl Zeiss Meditec AG, Jena, Germany).

All participants with scleroderma underwent a clinical evaluation and NC. The clinical data collected from each SSc patient comprised the following: The type of SSc (either limited or diffuse cutaneous scleroderma), the presence of interstitial lung disease (classified as either NSIP or UIP), hypertension, elevated proBNP, and the treatment method (administrations of sildenafil or amlodipine). The NC was conducted using the CapillaryScope 200 Pro (Dino-Lite, Taipei, Taiwan),

following the manufacturer's guidelines. To ensure consistency, all images were captured by the same expert, maintaining uniformity in lighting, focus and positioning.

The study aimed to categorize scleroderma microangiopathy using the Cutolo classification and to assess multiple capillaroscopic parameters – vessel density, hemorrhages, capillary morphology, giant capillaries, and avascular areas. The classification was based on identifying specific capillary abnormalities linked to different disease stages. In each NC image, vessel density was classified as normal (≥7 capillaries), reduced (4–6 capillaries) or severely reduced (≤3 capillaries). This classification offered valuable insights into the microvascular changes linked to the progression of scleroderma. For each participant, we recorded capillaroscopic features – including hemorrhages, tortuous (branched) vessels, giant capillaries, and avascular zones – offering crucial insight into the microvascular abnormalities characteristic of SSc.[24] The Dino-Lite capillaroscope underwent routine quality control checks, during which calibration images were acquired to confirm accurate color reproduction and resolution.

Images of retinal arterioles using an AO retinal camera (rtx1™; Imagine Eyes, Orsay, France) were captured in both patient groups. Before imaging, participants received 1 drop of 1% tropicamide for pupil dilation. Retinal artery images were analyzed with AOdetectArtery software (rtx1™; Imagine Eyes), focusing on the superior quadrant arterioles with a lumen diameter of at least 40 µm and no bifurcations. Two measurements were taken, and the highest-quality scan was selected for analysis.

The main vascular parameters obtained with AO were total vessel diameter (TD), lumen diameter (LD) and wall thickness (WT). The software also calculates 2 additional vascular metrics: The wall-to-lumen ratio (WLR), defined as wall thickness (WT) divided by lumen diameter (LD), and the wall cross-sectional area (WCSA), computed as $\pi \times [(TD/2)^2 - (LD/2)^2]$, which represents the area occupied by the vessel wall (Fig. 1,2).

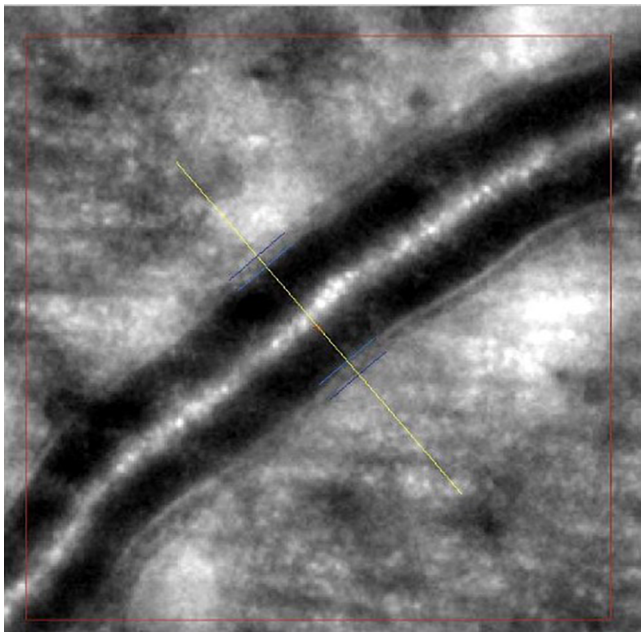

Fig. 1. Adaptive optics (AO) image of the retinal artery in a patient with scleroderma

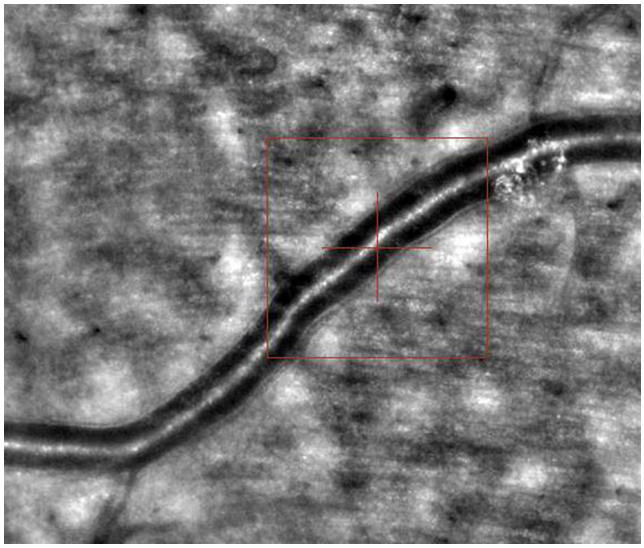

Fig. 2. Adaptive optics (AO) image of the retinal artery in a patient with scleroderma

Statistical analyses

Qualitative variables were shown as integers with percentages. Quantitative parameters were presented according to their weighted arithmetic mean, median, standard deviation (SD), and min–max values. Relationships among the examined qualitative variables were illustrated using contingency tables. Relationships among categorical variables were assessed using Pearson's χ^2 test when all expected cell counts were ≥5, and Fisher's two-tailed exact test when any expected count fell below 5. The Shapiro–Wilk W test was used to assess the normality of distribution and Levene's test was fitted to check the homogeneity of variances. Differences between independent groups for normally distributed numerical variables with homogeneous variances were assessed by one-way analysis of variance (ANOVA) without replication. Variables failing to meet normality or homogeneity of variance assumptions were analyzed with nonparametric tests – namely, the Mann–Whitney U test for dichotomous independent variables and the Kruskal–Wallis H test for variables with more than 2 categories. A level of $p < 0.050$ was deemed statistically significant. All the statistical procedures were performed using STATISTICA v. 13.3 (TIBCO Software Inc., Palo Alto, USA).

Results

The study included 31 SSc patients (61 eyes) and 41 healthy controls (81 eyes). No significant differences between the 2 groups regarding retinal arteries TD, LD, second wall thickness, and WCSA were found (Table 4).

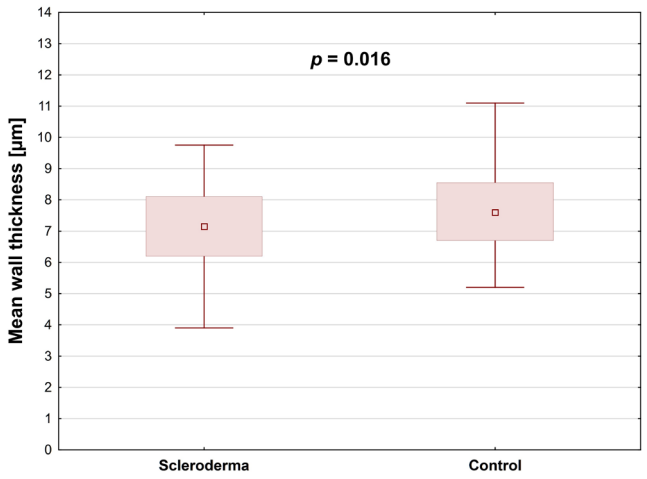

Fig. 3. Graphical presentation of the measures of location (median, quartiles) and dispersion (min–max values) of the mean wall thickness [µm] in the study participants' eyes by occurrence of scleroderma

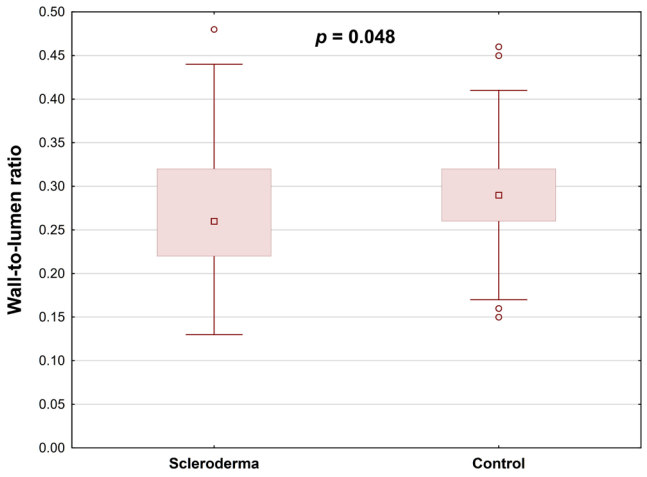

Fig. 4. Graphical presentation of the measures of location (median, quartiles) and dispersion (min–max values) of the wall-to-lumen ratio in the study participants' eyes by occurrence of scleroderma

Mean retinal arterial wall thickness was significantly lower in SSc patients than in healthy controls (p = 0.016), and the wall-to-lumen ratio was also notably decreased in the SSc group (p = 0.048) (Table 4; Fig. 3,4).

Retinal vessel parameters obtained through AO, including TD, LD, wall thicknesses, WLR, and WCSA, were analyzed in relation to NC findings and clinical features of SSc. No statistically significant correlation was observed between retinal vessel parameters and capillaroscopic patterns, nor between these parameters and the type of SSc (Table 5–7). The WCSA was significantly higher in hypertensive SSc patients compared to those without hypertension (p = 0.026; Table 7).

Discussion

Vascular damage is a hallmark of SSc and plays a pivotal role in its pathogenesis. It has been established that microvascular changes primarily affect peripheral arterioles and capillaries. Generalized vasculopathy has been demonstrated to contribute significantly to perfusion disorders in both the retina and the choroid. Therefore, the retinal microvasculature offers an ideal window for monitoring disease progression and detecting early pathological changes. Previous studies have shown that retinal findings, such as hard exudates, vascular tortuosity and arterial narrowing, as well as microhemorrhages, have been discovered in patients with SSc during fundus examination.[25–27] The presence of small retinal capillary abnormalities can be detected through a range of diagnostic techniques, including OCTA and fluorescein angiography (FA). The morphological changes in the retinal caliber, shape, or lumen diameter are valuable for assessing the state of microcirculatory perfusion. Therefore, we hypothesized that adaptive optics retinal imaging, as a novel noninvasive method, could aid in the detection of abnormalities in the structure of retinal vessels.

In this study, AO was used for retinal artery assessment in both groups. To the best of our knowledge, our study is the first to use AO imaging in SSc. A comparison of the 2 groups revealed no statistically significant differences in terms of LD, TD and WLR. According to previous studies, WLR and WCSA are optimal parameters for evaluating vascular remodeling in cases of diabetic retinopathy and arterial hypertension.[11,28–32] Żmijewska et al. analyzed arterial measurements using AO in 36 patients with nonproliferative diabetic retinopathy (DR). Their results demonstrated thicker arterial walls, increased WLR and WCSA in DR group than in controls.[29] Matuszewski et al.[33] and Cristescu et al.[34] also demonstrated comparable outcomes. However, our results showed that the WLR was significantly decreased among SSc patients compared to the healthy group (p = 0.048).

Lombardo et al.[35] reported that, in eyes with nonproliferative DR, the parafoveal capillary lumen diameter was significantly reduced compared to healthy controls. Similarly, Zaleska-Żmijewska et al.[18] demonstrated that prediabetic patients exhibit distinct alterations in both capillary lumen diameter and wall-to-lumen ratio relative to control subjects.

An elevated WLR reflects both thickening of the vessel wall and concomitant narrowing of the lumen. Piantoni et al.[36] used AO in patients with active rheumatoid arthritis treated with abatacept to evaluate cardiovascular risk factors. Their results indicated a significant reduction in the WLR of the arterioles after abatacept treatment. However, our results showed that the mean arterial wall was thinner in the scleroderma group than in the controls (p = 0.016). It is possible that the observed results may be attributed to the vasodilator treatment employed in the management of SSc.[37]

Pache et al.[37] demonstrated that in 10 healthy volunteers, a single dose of sildenafil induced significant dilation of both retinal arterioles and venules 30 minutes

Table 4. Descriptive statistics for the adaptive optics by occurrence of scleroderma (n = 142 eyes)

Adaptive optics	Study group	Statistical parameter				Statistical tests
		M	SD	Me	Q_1–Q_3	
Total diameter [µm]	scleroderma	67.25	11.37	67.15	58.00–75.50	normality test W = 0.979, p = 0.411 W = 0.966, p = 0.033 Levene's test F (1, 135) = 1.083 p = 0.300 Mann–Whitney test U = 2130.000 $Z_{corr.}$ = –0.699 p = 0.484
	control	69.03	12.88	69.30	58.00–78.40	
Wall 1 thickness [µm]	scleroderma	6.53	1.44	6.60	5.60–7.40	normality test W = 0.985, p = 0.677 W = 0.325, p < 0.001 Levene's test F (1, 135) = 1.337 p = 0.250 Mann–Whitney test U = 1323.000 $Z_{corr.}$ = –4.216 **p < 0.001**
	control	8.20	4.78	7.50	6.60–8.90	
Wall 2 thickness [µm]	scleroderma	7.46	1.72	7.45	6.10–8.50	normality test W = 0.976, p = 0.317 W = 0.950, p = 0.004 Levene's test F (1, 135) = 0.686 p = 0.409 Mann–Whitney test U = 2284.500 $Z_{corr.}$ = –0.026 p = 0.979
	control	7.52	1.61	7.20	6.40–8.10	
Mean wall thickness [µm]	scleroderma	6.99	1.34	7.15	6.20–8.10	normality test W = 0.983, p = 0.589 W = 0.512, p < 0.001 Levene's test F (1, 135) = 0.285 p = 0.594 Mann–Whitney test U = 1740.000 $Z_{corr.}$ = –2.398 **p = 0.016**
	control	7.86	2.52	7.60	6.70–8.55	
Lumen diameter [µm]	scleroderma	53.25	10.49	52.65	44.80–61.10	normality test W = 0.983, p = 0.585 W = 0.962, p = 0.018 Levene's test F (1, 135) = 2.123 p = 0.147 Mann–Whitney test U = 2279.000 $Z_{corr.}$ = 0.050 p = 0.960
	control	53.64	14.03	53.30	44.20–62.40	
Wall-to-lumen ratio	scleroderma	0.2710	0.0681	0.2600	0.2200–0.3200	normality test W = 0.970, p = 0.159 W = 0.946, p = 0.002 Levene's test F (1, 135) = 0.024 p = 0.878 Mann–Whitney test U = 1837.000 $Z_{corr.}$ = –1.976 **p = 0.048**
	control	0.2940	0.0724	0.2600	0.2200–0.3300	
Wall cross-sectional area [µm^2]	scleroderma	1338.3	410.0	1386	983–1594	normality test W = 0.952, p = 0.024 W = 0.960, p = 0.015 Levene's test F (1, 135) = 0.006 p = 0.941 Mann–Whitney test U = 1843.000 $Z_{corr.}$ = 0.051 p = 0.051
	control	1479.3	431.3	1498	1129–1724	

M – mean; SD – standard deviation; Me – median; Q – quartiles. Values in bold are statistically significant.

Table 5. Descriptive statistics for the lumen diameter [µm] in the study participants with scleroderma by selected capillaroscopic assessments (n = 61 eyes)

Investigated trait		Statistical parameter		Statistics
		M (SD)	Me (Q_1–Q_3)	
Scleroderma	localized	55.81 (13.23)	58.20 (41.83–61.18)	normality test W = 0.980, p = 0.721 W = 0.929, p = 0.261 Levene's test F (1, 50) = 4.027, p = 0.051 ANOVA F (1, 50) = 2.244 p = 0.140
	systemic	51.15 (8.65)	50.00 (44.73–57.20)	
Scleroderma pattern	early	48.80 (9.92)	52.40 (41.33–55.83)	normality test W = 0.964, p = 0.841 W = 0.970, p = 0.692 W = 0.959, p = 0.612 Levene's test. F (3, 48) = 1.884, p = 0.145 ANOVA F (3, 48) = 1.718 p = 0.176
	active	55.94 (11.75)	57.20 (45.85–64.53)	
	late	49.78 (7.85)	49.00 (43.63–55.97)	
Number of vessels	normal	52.23 (11.12)	58.20 (42.53–58.95)	normality test W = 0.784, p = 0.077 W = 0.982, p = 0.811 W = 0.932, p = 0.403 Levene's test F (2, 49) = 0.365, p = 0.696 ANOVA F (2, 49) = 1.718 p = 0.498
	reduced	51.51 (9.43)	50.00 (44.57–59.77)	
	very reduced	55.59 (12.71)	54.50 (44.07–62.04)	
Avascular areas	yes	52.83 (11.23)	51.35 (44.52–61.70)	normality test W = 0.968, p = 0.667 W = 0.980, p = 0.820 Levene's test F (1, 50) = 0.797, p = 0.376 ANOVA F (1, 50) = 0.072 p = 0.789
	no	52.04 (9.03)	52.50 (43.95–58.83)	
Giant capillaries	yes	52.66 (12.52)	49.95 (42.23–61.24)	normality test W = 0.970, p = 0.613 W = 0.968, p = 0.576 Levene's test F (1, 50) = 6.718, p = 0.012 ANOVA F (3, 48) = 0.014 p = 0.907
	no	52.33 (7.64)	52.90 (44.78–58.28)	
Hemorrhages	yes	49.38 (12.18)	46.65 (40.92–55.28)	normality test W = 0.978, p = 0.726 W = 0.906, p = 0.054 Levene's test F (1, 50) = 1.244, p = 0.270 ANOVA F (1, 50) = 3.127 p = 0.083
	no	54.45 (8.51)	54.55 (48.30–61.49)	
Branched vessels	yes	50.38 (9.78)	49.10 (44.56–57.58)	normality test W = 0.959, p = 0.232 W = 0.975, p = 0.878 Levene's test F (1, 50) = 0.116, p = 0.735 ANOVA F (1, 50) = 1.175 p = 0.283
	no	53.62 (10.49)	53.35 (43.68–59.27)	

Table 5. Descriptive statistics for the lumen diameter [μm] in the study participants with scleroderma by selected capillaroscopic assessments (n = 61 eyes) – cont.

Investigated trait		Statistical parameter		Statistics
		M (SD)	Me (Q_1–Q_3)	
Finger ulcers	yes	54.05 (12.26)	52.70 (46.08–60.95)	normality test W = 0.951, p = 0.114 W = 0.954, p = 0.586 Levene's test F (1, 49) = 0.168, p = 0.683 ANOVA F (1, 50) = 0.399 p = 0.530
	no	52.04 (9.54)	52.50 (43.21–59.10)	
Arterial hypertension	yes	56.30 (13.02)	55.15 (49.00–65.50)	normality test W = 0.975, p = 0.566 W = 0.961, p = 0.731 Levene's test F (1, 49) = 1.248, p = 0.269 ANOVA F (1, 49) = 2.871 p = 0.097
	no	52.29 (9.52)	52.50 (44.70–59.10)	
Sildenafil	yes	48.92 (8.21)	49.00 (44.10–53.60)	normality test W = 0.972, p = 0.676 W = 0.985, p = 0.957 Levene's test F (1, 49) = 2.625, p = 0.112 ANOVA F (1, 49) = 6.062 **p = 0.017**
	no	56.54 (10.94)	58.20 (48.50–64.20)	
Amlodipine	yes	54.44 (10.87)	54.80 (47.80–59.10)	normality test W = 0.967, p = 0.491 W = 0.955, p = 0.392 Levene's test F (1, 49) = 0.024, p = 0.877 ANOVA F (1, 49) = 1.554 p = 0.218
	no	52.53 (10.34)	49.95 (44.70–61.45)	

M – mean; SD – standard deviation; Me – median; Q – quartiles; ANOVA – analysis of variance. Values in bold are statistically significant.

Table 6. Descriptive statistics for the wall-to-lumen ration in the study participants with scleroderma by selected capillaroscopic assessments (n = 61 eyes)

Investigated trait		Statistical parameter		Statistics
		M (SD)	Me (Q_1–Q_3)	
Scleroderma	localized	0.2593 (0.0794)	0.2500 (0.2300–0.2850)	normality test W = 0.983, p = 0.835 W = 0.876, p = 0.041 Levene's test F (1, 50) = 0.009, p = 0.925 Mann–Whitney test U = 212.000 $Z_{corr.}$ = 1.315 p = 0.188
	systemic	0.2816 (0.0641)	0.2800 (0.2267–0.3233)	
Scleroderma pattern	early	0.2989 (0.0924)	0.3000 (0.2500–0.3500)	normality test W = 0.964, p = 0.837 W = 0.917, p = 0.057 W = 0.886, p = 0.040 Levene's test F (3, 48) = 0.574, p = 0.635 Kruskal–Wallis test H (3, n = 52) = 3.453 p = 0.327
	active	0.2626 (0.0726)	0.2500 (0.2117–0.2900)	
	late	0.2753 (0.0516)	0.2700 (0.2267–0.3300)	
Number of vessels	normal	0.2367 (0.0971)	0.2600 (0.1517–0.3100)	normality test W = 0.957, p = 0.600 W = 0.968, p = 0.368 W = 0.963, p = 0.820 Levene's test F (2, 49) = 1.151, p = 0.229 ANOVA F (2, 49) = 2.972 p = 0.061
	reduced	0.2895 (0.0696)	0.2800 (0.2500–0.3300)	
	very reduced	0.2408 (0.0448)	0.2350 (0.2142–0.2658)	

Table 6. Descriptive statistics for the wall-to-lumen ration in the study participants with scleroderma by selected capillaroscopic assessments (n = 61 eyes) – cont.

Investigated trait		Statistical parameter		Statistics
		M (SD)	Me (Q_1–Q_3)	
Avascular areas	yes	0.2753 (0.0707)	0.2700 (0.2292–0.3300)	normality test W = 0.911, p = 0.049 W = 0.975, p = 0.678 Levene's test F (1, 50) = 0.445, p = 0.508 ANOVA F (1, 50) = 0.0003 p = 0.986
	no	0.2750 (0.0678)	0.2600 (0.2475–0.3200)	
Giant capillaries	yes	0.2838 (0.0784)	0.2600 (0.2292–0.3208)	normality test W = 0.953, p = 0.269 W = 0.933, p = 0.090 Levene's test F (1, 50) = 0.447, p = 0.235 ANOVA F (1, 50) = 0.819 p = 0.370
	no	0.2665 (0.0580)	0.2750 (0.2292–0.3200)	
Hemorrhages	yes	0.2945 (0.0833)	0.2750 (0.2383–0.3300)	normality test W = 0.966, p = 0.393 W = 0.943, p = 0.271 Levene's test F (1, 50) = 3.232, p = 0.078 ANOVA F (1, 50) = 2.639 p = 0.111
	no	0.2631 (0.0561)	0.2650 (0.2242–0.3158)	
Branched vessels	yes	0.2861 (0.0750)	0.2750 (0.2200–0.3317)	normality test W = 0.944, p = 0.080 W = 0.939, p = 0.277 Levene's test F (1, 50) = 0.818, p = 0.370 ANOVA F (1, 50) = 0.688 p = 0.411
	no	0.2694 (0.0658)	0.2600 (0.2300–0.3200)	
Finger ulcers	yes	0.2728 (0.0684)	0.2600 (0.2242–0.3200)	normality test W = 0.968, p = 0.373 W = 0.939, p = 0.374 Levene's test F (1, 49) = 0.279, p = 0.599 ANOVA F (1, 49) = 0.001 p = 0.914
	no	0.2720 (0.0652)	0.2700 (0.2300–0.3067)	
Arterial hypertension	yes	0.2760 (0.0626)	0.2600 (0.2300–0.3300)	normality test W = 0.960, p = 0.200 W = 0.978, p = 0.958 Levene's test F (1, 49) = 0.081, p = 0.777 ANOVA F (1, 49) = 0.0002 p = 0.989
	no	0.2700 (0.0704)	0.2650 (0.2200–0.3150)	
Sildenafil	yes	0.2910 (0.0648)	0.2800 (0.2400–0.3300)	normality test W = 0.944, p = 0.162 W = 0.949, p = 0.239 Levene's test F (1, 49) = 0.011, p = 0.918 ANOVA F (1, 49) = 2.449 p = 0.124
	no	0.2560 (0.0677)	0.2600 (0.2200–0.2900)	
Amlodipine	yes	0.2560 (0.0643)	0.2550 (0.2200–0.3000)	normality test W = 0.938, p = 0.089 W = 0.980, p = 0.914 Levene's test F (1, 49) = 0.143, p = 0.707 ANOVA F (1, 49) = 3.051 p = 0.087
	no	0.2800 (0.0697)	0.2700 (0.2250–0.3200)	

M – mean; SD – standard deviation; Me – median; Q – quartiles; ANOVA – analysis of variance.

Table 7. Descriptive statistics for the wall cross-sectional area [μm²] in the study participants with scleroderma by selected capillaroscopic assessments (n = 61 eyes)

Investigated trait		Statistical parameter		Statistics
		M (SD)	Me (Q_1–Q_3)	
Scleroderma	localized	1399.9 (540.5)	1438 (874–1619)	normality test W = 0.907, p = 0.122 W = 0.959, p = 0.187 Levene's test F (1, 50) = 3.233, p = 0.078 ANOVA F (1, 50) = 0.802 p = 0.375
	systemic	1291.3 (323.1)	1379 (1032–1534)	
Scleroderma pattern	early	1235.8 (382.5)	1389 (840–1601)	normality test W = 0.787, p = 0.015 W = 0.951, p = 0.315 W = 0.946, p = 0.391 Levene's test F (3, 48) = 1.493, p = 0.228 Kruskal–Wallis test H (3, n = 52) = 3.104 p = 0.376
	active	1420.4 (458.6)	1428 (1079–1703)	
	late	1210.5 (314.5)	1244 (897–1434)	
Number of vessels	normal	1078.3 (413.4)	912 (796–1444)	normality test W = 0.879, p = 0.322 W = 0.964, p = 0.265 W = 0.828, p = 0.020 Levene's test. F (2, 49) = 0.124, p = 0.883 Kruskal–Wallis test H (2, n = 52) = 1.857 p = 0.395
	reduced	1350.1 (362.8)	1389 (1067–1608)	
	very reduced	1298.8 (493.5)	1325 (922–1446)	
Avascular areas	yes	1322.3 (392.2)	1381 (1048–1496)	normality test W = 0.919, p = 0.025 W = 0.915, p = 0.060 Levene's test F (1, 50) = 0.535, p = 0.468 Mann–Whitney test U = 310.000 $Z_{corr.}$ = –0.361 p = 0.718
	no	1323.0 (409.1)	1433 (866–1605)	
Giant capillaries	yes	1278.2 (461.3)	1405 (892–1620)	normality test W = 0.931, p = 0.083 W = 0.952, p = 0.262 Levene's test F (1, 50) = 1.790, p = 0.187 ANOVA F (1, 50) = 0.657 p = 0.421
	no	1323.0 (319.5)	1356 (981–1532)	
Hemorrhages	yes	1249.4 (440.7)	1195 (864–1467)	normality test W = 0.857, p = 0.007 W = 0.968, p = 0.437 Levene's test F (1, 50) = 0.443, p = 0.509 Mann–Whitney test U = 248.000 $Z_{corr.}$ = 1.345 p = 0.179
	no	1358.3 (364.1)	1397 (1059–1600)	
Branched vessels	yes	1260.5 (324.7)	1353 (899–1530)	normality test W = 0.945, p = 0.353 W = 0.935, p = 0.045 Levene's test. F (1, 50) = 0.925, p = 0.341 Mann–Whitney test U = 267.000 $Z_{corr.}$ = –0.741 p = 0.459
	no	1355.5 (429.1)	1397 (981–1605)	

Table 7. Descriptive statistics for the wall cross-sectional area [μm²] in the study participants with scleroderma by selected capillaroscopic assessments (n = 61 eyes) – cont.

Investigated trait		Statistical parameter		Statistics
		M (SD)	Me (Q_1–Q_3)	
Finger ulcers	yes	1291.3 (376.8)	1353 (896–1576)	normality test W = 0.884, p = 0.054 W = 0.934, p = 0.033 Levene's test. F (1, 49) = 0.154, p = 0.696 Mann–Whitney test U = 263.000 $Z_{corr.}$ = –0.134 p = 0.893
	no	1377.9 (450.1)	1389 (1079–1489)	
Arterial hypertension	yes	1517.5 (476.9)	1466 (1259–1717)	normality test W = 0.929, p = 0.295 W = 0.940, p = 0.047 Levene's test F (1, 49) = 0.296, p = 0.589 ANOVA F (1, 49) = 5.252 **p = 0.026**
	no	1281.2 (374.6)	1324 (905–1547)	
Sildenafil	yes	1224.4 (300.2)	1244 (987–1428)	normality test W = 0.963, p = 0.478 W = 0.931, p = 0.080 Levene's test F (1, 49) = 2.494, p = 0.121 ANOVA F (1, 49) = 2.821 p = 0.099
	no	1424.6 (462.6)	1466 (983–1717)	
Amlodipine	yes	1316.4 (422.9)	1356 (912–1541)	normality test W = 0.895, p = 0.023 W = 0.958, p = 0.291 Levene's test F (1, 49) = 0.015, p = 0.903 Mann–Whitney test U = 308.000 $Z_{corr.}$ = –0.200 p = 0.842
	no	1351.6 (407.4)	1392 (985–1612)	

M – mean; SD – standard deviation; Me – median; Q – quartiles; ANOVA – analysis of variance. Values in bold are statistically significant.

after administration (p < 0.001). Moreover, Polak at al.[38] reported increased retinal blood flow in healthy controls after sildenafil administration. Sildenafil can enhance the vasodilatory effect of nitric oxide (NO), the primary regulator of vascular smooth muscle tone. In addition, we compared the measurements of the retinal arteries obtained in AO with the results of the NC. However, we did not find a statistically significant correlation with the type of scleroderma, finger ulcers and scleroderma patterns, number of vessels, avascular areas, hemorrhages, or branched vessels visualized in NC. In our previous study, we found that scleroderma microangiopathy patterns correlated significantly with both superficial and deep foveal avascular zone (FAZ) areas, as well as with deep retinal vessel density measured by OCTA.[23] Several studies have explored the relationship between peripheral capillary density measured with nailfold capillaroscopy and both choriocapillaris vessel density[39] and overall retinal perfusion.[40] However, these findings have been inconsistent. It is therefore possible that high-resolution imaging of the retinal microvasculature may yield stronger correlations with NC abnormalities.

These findings corroborate earlier reports that hypertension is associated with increased wall cross-sectional area, reflecting arteriolar remodeling.[11] Furthermore, in our study, we evaluated the impact of vasodilator medications employed for the management of complications associated with scleroderma vasculopathy. Contrary to expectations, the findings of this study indicated a decreased LD in patients treated with sildenafil (p = 0.017). It is worth noting that most patients in our NC cohort exhibited a late scleroderma pattern – reflecting severe vasculopathy and advanced disease – so the observed arterial lumen narrowing likely reflects the chronicity and severity of SSc.

Limitations

It is important to acknowledge the limitations of the research, including the relatively small number of participants and the cross-sectional nature of the study.

Conclusions

Our study analysis of the AO retinal imaging data set revealed a reduced mean arterial wall thickness in patients with SSc compared to healthy controls. However, no correlation was identified between the AO findings and the NC parameters or the disease stage. The retinal vessel parameters revealed significant differences only in hypertensive or sildenafil-treated patients. Further studies on a larger cohort of patients are necessary to draw reliable conclusions about the usefulness of AO in the diagnosis of SSc and its possible correlation with capillaroscopic findings.

Data Availability Statement

All data generated or analyzed during this study are included in this article.

Consent for publication

Not applicable.

Use of AI and AI-assisted technologies

Not applicable.

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