Evaluation of retinal microvascular density in patients affected by systemic lupus erythematosus: an optical coherence tomography angiography study

Retinopathy in systemic lupus erythematosus (SLE) has an incidence of 7%–29% and is suggestive of high disease activity being a marker of poor visual outcome and prognosis for survival.[1] Recently, we demonstrated a subclinical retinal involvement in patients with SLE that seems to be related to kidney involvement where hydroxychloroquine had a protective role.[2] The pathogenesis of lupus retinopathy is attributed to a vasculopathy most commonly immune complex-mediated microangiopathy.[1] Optical coherence tomography angiography (OCTA) is a non-invasive technique for imaging the microvasculature of the retina and choroid that may quantify foveal avascular zone, non-perfused or low-perfused areas. Quantitative measurements based on OCTA may have value in managing retinopathy but also correlate with visual outcome and mirror vascular involvement in systemic diseases.[3] The aim of this study was to evaluate retinal microvasculature using OCTA in patients with SLE without signs of retinopathy according to standard lupus retinopathy

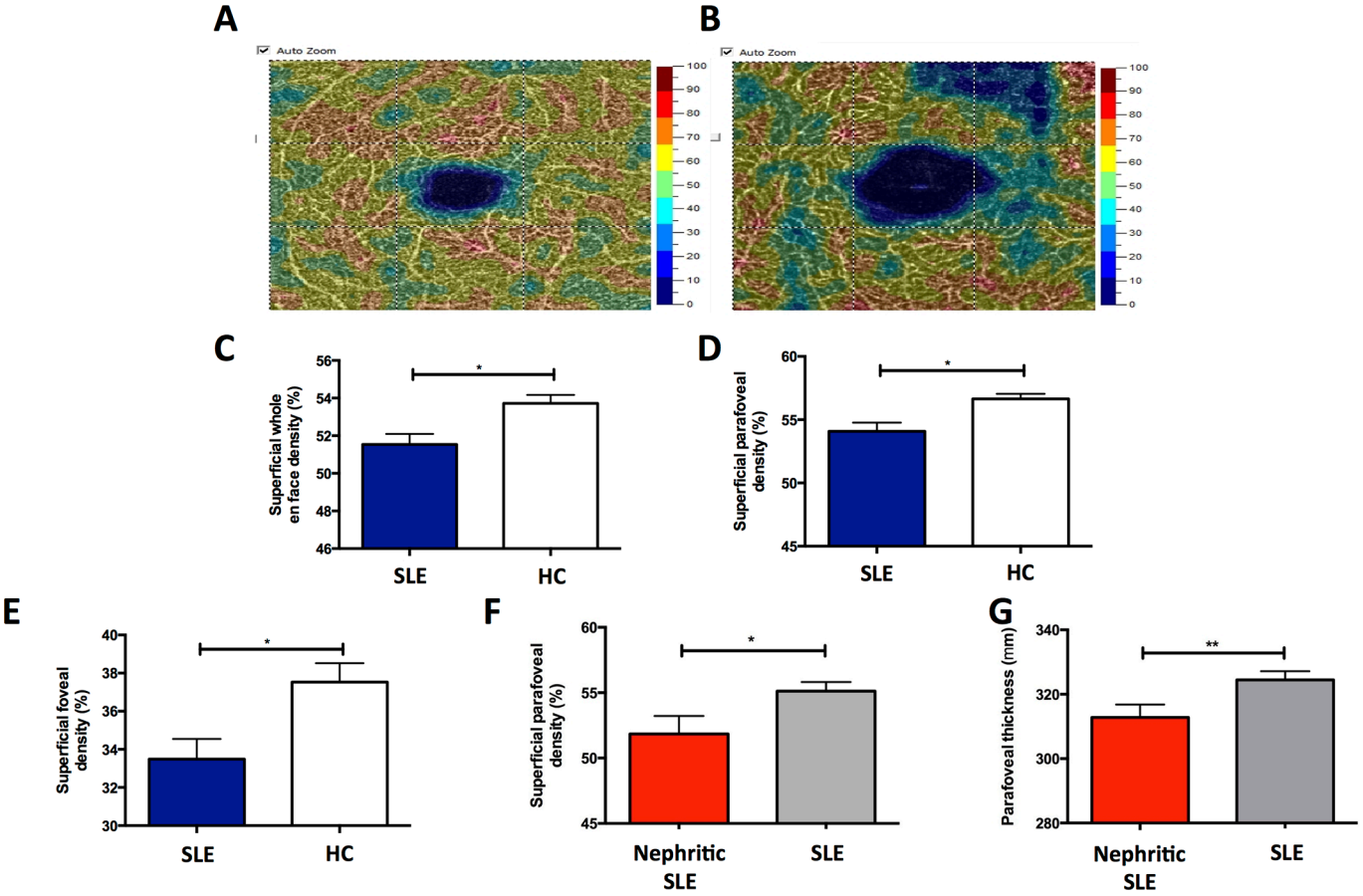

Figure 1 Superficial whole en face vessel density (%, colour-coded) maps in a (A) healthy control (HC) and a (B) patient with systemic lupus erythematosus (SLE). (B) Enlargement of the foveal avascular zone (central dark blue area) and parafoveal areas of reduced perfusion (light and dark blue areas). Patients with SLE displayed reduced superficial whole en face (C), parafoveal (D) and foveal (E) vessel density (%) compared with those in healthy eyes. Patients with SLE with lupus nephritis showed superficial parafoveal vessel density (%) compared with those in patients without nephritis (F). Parafoveal thickness in patients with SLE with nephritis was reduced than that in patients without kidney involvement (G). *P<0.05; **P<0.01.

classification[4] and correlate abnormal vascular density with disease activity, damage accrual, treatment and visual outcome. From 20 November 2015 to 31 December 2017, a total of 52 eyes of patients with SLE, diagnosed according to the American College of Rheumatology classification criteria,[5] and 40 eyes of healthy controls (HC) were examined by means of a 6 mm OCTA scan (Optovue XR Avanti, Fremont, CA). Split-spectrum amplitude-decorrelation angiography generated optical coherence tomography angiograms of both superficial and deep retinal capillaries referred to the whole en face, foveal and parafoveal zone from patients with SLE and HC (figure 1A,B). Capillary density values were compared with clinical data by Spearman's rank correlation coefficient, and groups were compared using analysis of variance and Kruskal-Wallis analyses. Values of $p<0.05$ were considered statistically significant. Demographic and clinical features of enrolled subjects are summarised in table 1. The eyes from patients with SLE had a lower mean superficial whole en face density, superficial parafoveal density and superficial foveal density ($p=0.02$ for all comparisons) compared with healthy eyes (figure 1C–E). Patients with SLE with nephritis displayed reduced parafoveal vessel density and parafoveal thickness compared with those of patients without nephritis ($p=0.02$ and $p=0.008$, figure 1F,G). A negative correlation was demonstrated in patients with SLE between age and superficial whole en face density ($p=0.0005$, $r=-0.5$), superficial foveal density ($p=0.006$, $r=-0.4$), superficial parafoveal density ($p=0.004$, $r=-0.4$), deep whole en face density ($p=0.003$, $r=-0.4$) and deep parafoveal density ($p=0.001$, $r=-0.4$). Systemic Lupus Erythematosus Disease Activity Index correlated inversely with superficial en face density ($p=0.002$, $r=-0.4$), superficial parafoveal density ($p=0.0003$, $r=-0.5$ and $p=0.002$), deep whole en face density ($p=0.01$, $r=-0.4$) and deep parafoveal density ($p=0.002$, $r=-0.4$). A negative correlation was also found between Systemic Lupus International Collaborating Clinics (SLICC) and superficial whole en face density ($p=0.0001$, $r=-0.5$), superficial parafoveal density ($p<0.0001$, $r=-0.6$), deep whole en face density ($p<0.0001$, $r=-0.6$) and deep parafoveal density ($p<0.0001$, $r=-0.7$). A positive correlation was found between hydroxychloroquine cumulative dose and both superficial and deep parafoveal density ($p=0.009$, $r=0.4$ and $p=0.04$, $r=0.3$). Best corrected visual acuity in SLE positively correlated with superficial whole en face density, superficial parafoveal density, deep whole en face density and deep parafoveal density ($p<0.0001$, $r=0.7$ for all correlations).

Patients with SLE displayed a reduced retinal microvascular density compared with normal subjects, in particular those with kidney involvement. Vessel density provides a quantitative metric of capillary network that correlated with age, best corrected visual acuity and clinical features as SLE disease activity and damage accrual. Hydroxychloroquine might have a protective role preserving the microvascular structures.

Table 1 Demographic and clinical characteristics of enrolled subjects

	HC (n=20)	SLE (n=26)
Age (years)	46±8.9	49.6±13.6
Female, n (%)	16 (80)	23 (88.5)
Disease duration (years)	NA	15.1±7.7
Anti-dsDNA positive Abs, n (%)	NA	13 (50)
aPL positive Abs, n (%)	NA	10 (40)
C3 (mg/L)	NA	98.9±21.7
C4 (mg/L)	NA	19.6±5.8
SLEDAI-2K	NA	4.3±4.4
SLICC	NA	1.9±1.5
HCQ, n (%) HCQ cumulative dose (g)	NA	16 (61.5) 738.8±486.8
BCVA (logMAR)	0.0±0.1	0.0±0.1
Kidney involvement*, n (%)	NA	10 (40)

*Kidney involvement was defined as the presence of biopsy-proven glomerulonephritis class III, IV or V according to the International Society of Nephrology/Renal Pathology Society glomerulonephritis classification criteria.[6]
Continuous variables were shown using mean and SD.
aPL, antiphospholipid; BCVA, best corrected visual acuity; HC, healthy controls; HCQ, hydroxychloroquine; NA, not applicable; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SLICC, SLICC/ACR damage index score.

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