• Meta-Analysis •

# Vasculature alteration of foveal zone in systemic lupus erythematosus: a Meta-analysis

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## Abstract

● **AIM:** To summarize and quantitatively evaluate vasculature alteration of foveal zone in systemic lupus erythematosus (SLE) patients by secondary literature analysis.

● **METHODS:** A systematic search of PubMed, Embase, Web of Science, Cochrane Library, CBM, CNKI WanFang Data and VIP was conducted. Studies were about retinal vessel density in SLE patients from January 2000 to April 2023 and valid data were extracted. The Joanna Briggs Institute (JBI) critical appraisal checklist was used to evaluate the cross-sectional studies and prospective studies. The measurement data for combined effect size were weighted mean difference (WMD) and 95% confidence interval (CI). The heterogeneity was evaluated by $I^2$ test. The fixed-effect model was adopted when $P$>0.1 or $I^2$<50%, and random-effect model was adopted in the contrary. Subgroup and sensitivity analysis were utilized to analyze the sources of heterogeneity. The publication bias was evaluated by Egger tests and funnel plots.

● **RESULTS:** A total of 14 studies with 445 subjects and 441 healthy controls from 9 countries were enrolled and 11 studies were included in Meta-analysis. The JBI scores of studies were no less than 14 points. The Meta-analysis results indicated that mean parafoveal superficial vessel density (SVD; WMD=-1.22, 95%CI: -1.67, -0.76), mean perifoveal SVD (WMD=-1.42, 95%CI: -1.95, -0.89), mean whole SVD (WMD=-1.66, 95%CI: -2.53, -0.79), mean parafoveal deep vessel density (WMD=-1.67, 95%CI: -2.75, -0.59) and mean whole deep vessel density (WMD= -4.09, 95%CI: -7.67, -0.52) was significantly lower than the control, while mean foveal SVD (WMD=-1.71, 95%CI: -4.65, 1.24), mean foveal avascular zone (FAZ) area (WMD=0.04, 95%CI: -0.01, 0.09) and mean acircularity index (AI; WMD=0.00, 95%CI: -0.02, 0.02) were not different between SLE patients and controls. Subgroup analysis indicated that the heterogeneity in SVD was partially due to the scanning area. Ocellus or binoculus data contributed partially to the heterogeneity in parafoveal deep vessel density and FAZ area. Sensitivity analysis indicated that the results were robust after changing the analysis model except for foveal SVD and FAZ area. There was no bias in included studies except whole SVD.

● **CONCLUSION:** Parafoveal superficial and deep vessel density are significantly lower in SLE patients while FAZ area and AI are not different between SLE patients and the control.

● **KEYWORDS:** systemic lupus erythematosus; retinal vessel density; optical coherence tomography; Meta-analysis
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## INTRODUCTION

Systemic lupus erythematosus (SLE) is a connective tissue disease with systemic inflammation, characterized by autoantibodies and immune complex deposition. It involves many systems and tissue including kidney, nervous system, blood vessels and eye[1]. Dry eye disease (DED) and lupus retinopathy are the common ocular complications of SLE, and the latter is recognized as the signal of systemic disease activity[2]. Optical coherence tomography angiography (OCTA) can produce images of blood flow that have unprecedented resolution of all the vascular layers of the retina in a new

non-invasive fashion[3], and is widely applied in the common ophthalmic diseases such as retinal vein occlusion, age-related macular degeneration and diabetic retinopathy. Cogniliro *et al*[4] investigated the retinal vessel densities in SLE patients by OCTA in 2019. He revealed that the superficial and deep retinal vessel densities in SLE patients were lower than healthy people and the decrease of vessel densities in patients with lupus nephritis was more significant. Similar studies follows but contrary conclusions exist partly due to the sample size and different image processing. Therefore, this Meta-analysis aims to quantify foveal vasculature alteration of SLE patients compared to controls, providing new insight for other studies.

## MATERIALS AND METHODS

**Search Strategy** We performed a systematic literature search in PubMed, Embase, Web of Science, Cochrane Library, CBM, CNKI, WangFang Data and VIP from January 2000 to April 2023, utilizing database-specific subject headings and keywords for "systemic lupus erythematosus" and "optical coherence tomography angiography" and "retinal vessel density". The searches were modified to accommodate the unique terminology and syntax of each database. We conducted backward and forward citation tracking of the eligible full text articles to identify additional studies. PRISMA guidelines was followed in this study. The protocol for this Meta-analysis is registered in International Prospective Register of Systematic Reviews (PROSPERO) and obtained a registration number CRD42023414572.

**Inclusion and Exclusion Criteria** Publications were eligible for inclusion if they reported retinal vessel densities between SLE patients and healthy controls. Included studies had to detail the diagnostic criteria for SLE or how SLE patients were ascertained. Patients in the included studies must had no lupus retinopathy or hydroxychloroquine (HCQ) toxicity maculopathy in slit lamp, visual field examination or optical coherence tomography by ophthalmologist. Full-text articles and conference abstracts with sufficient data of cross-sectional, retrospective or prospective studies were included. Studies had to report on at least one of the following retinal vessel densities: foveal superficial vessel density (SVD), parafoveal SVD, perifoveal SVD, whole SVD, parafoveal deep vessel density (DVD), perifoveal DVD, whole DVD, foveal avascular zone (FAZ) area and FAZ acircularity index (AI). Studies published in English or Chinese language were included. Articles were excluded if they were editorials, opinion pieces, case reports, systematic reviews, or conference abstracts with insufficient data on retinal vessel densities or to determine eligibility of SLE and control groups.

**Quality Assessment and Data Extraction** After duplicates were removed, all records were imported into Endnote software. Two reviewers independently reviewed titles and abstracts and then full-text articles. Study data were extracted and recorded on a standardized form by two reviewers. The following data were extracted from each study: name of author(s), year of publication, country where the study was conducted, study design, patient characteristics, diagnostic criteria, duration of disease, treatment, OCTA facilities, scan area, retinal vessel densities, FAZ area and AI. In studies with multiple study groups, data were extracted for those study groups that met the inclusion criteria. As all included articles were observational studies, the Joanna Briggs Institute (JBI) critical appraisal checklist was used to assess study quality. Those studies with scores five or more in JBI criteria will be considered to have a good quality[5]. Abstracts included in this review were not evaluated using this checklist and were of low quality. If there is a disagreement between the two reviewers, a third reviewer was joined and the result was discussed.

**Statistical Analysis** We used Revman 5.4 software and STATA 16.0 software to conduct our Meta-analysis. Mean and standard deviation (SD) were used to calculate a mean difference in SLE patients compared to controls. Standard errors were converted into SDs using the sample size provided. These outcomes were summarized as weighted mean differences (WMD) in SLE patients compared to controls. The study data in Işık *et al*[6] were reported by median and quartiles so we used the approach by Luo *et al*[7] and Wan *et al*[8] to convert into mean and SD. The confidence interval (CI) was set at 95%, and $P<0.05$ was considered statistically significant. Perifoveal DVD were not Meta-analyzed because only 2 studies were included. We tested for heterogeneity using the $I^2$ statistics. If the heterogeneity was obvious, subgroup analysis and sensitivity analysis were used. Sensitivity analysis was performed by changing analysis model or stepwise removal of each study. If not changed, it indicated the merged results was robust. Funnel plots and Egger's teat were generated to assess publication bias.

## RESULTS

**Search Results** The search strategy identified 721 records. Totally 479 articles remained after removal of duplicates. After screening titles and abstracts, a total of 64 records remained. In total, 14 studies from 9 countries (445 subjects and 441 healthy controls) met our inclusion criteria in this review and 11 were included in Meta-analysis. The study inclusion process is detailed in Figure 1.

**Study Characteristics** All included articles were observational studies including design from cross-sectional[6,9-16], retrospective case-control study[17] and prospective study[18]. Studies were conducted in China[9,13], Egypt[10], USA[17], Turkey[6,14,18], Germany[11], Abu Dhabi[12], Poland[15], and Spain[16]. Study characteristics are listed in Table 1. The quality of studies was medium to high except for the study of Shah *et al*[17]. Results

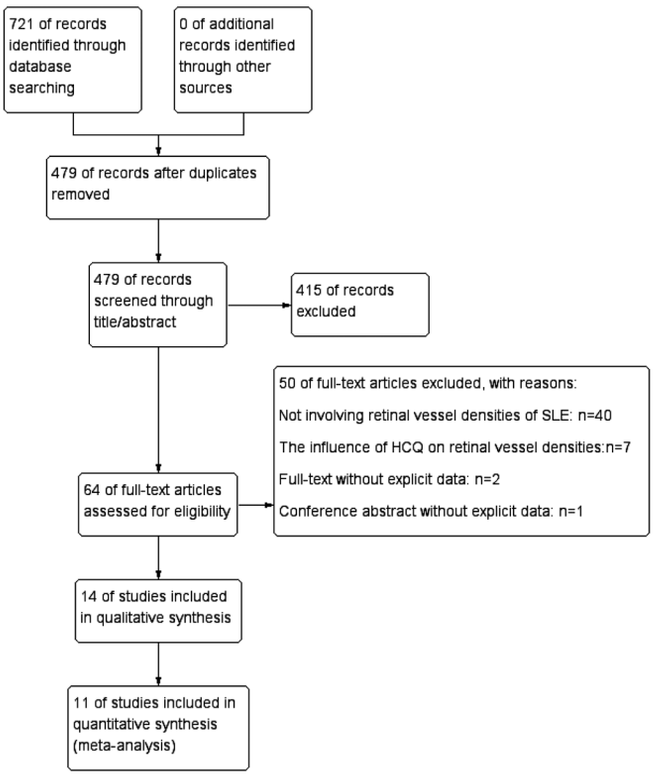


**Figure 1 PRISMA flow diagram detailing selection of the studies included in this review** HCQ: Hydroxychloroquine; SLE: Systemic lupus erythematosus.

were extracted from the studies included. The studies involving foveal SVD, parafoveal SVD, perifoveal SVD, whole SVD, parafoveal DVD, whole DVD, FAZ area and AI were more than 3 and further analyzed, while the studies involving perifoveal DVD were excluded to avoid bias in the results.

**Vessel Densities in Region of Interests and Foveal Avascular Zone** Heterogeneity was significant between studies that investigated foveal SVD ($I^2$=84%, $P$<0.0001), whole SVD ($I^2$=79%, $P$=0.0003), parafoveal DVD ($I^2$=58%, $P$=0.07), whole DVD ($I^2$=92%, $P$<0.00001), FAZ area ($I^2$=94%, $P$<0.00001) and AI ($I^2$=66%, $P$=0.01) and random model were applied. Five studies (387 subjects) reported on foveal SVD[6,13-15,18], 6 studies (379 subjects) on whole SVD[6,10-11,14-15,18], 4 studies (350 subjects) on parafoveal DVD[9,14-15,18], 4 studies (309 subjects) on whole DVD[10,14-15,18], 10 studies (720 subjects) on FAZ area[6,9-12,14-18] and 6 studies (498 subjects) reported on AI[6,9-10,14-16]. Mean whole SVD (WMD=-1.66, 95%CI: -2.53, -0.79), mean parafoveal DVD (WMD=-1.67, 95%CI: -2.75, -0.59), mean whole DVD (WMD=-4.09, 95%CI: -7.67, -0.52) were significantly lower, indicating poor whole SVD, parafoveal DVD and whole DVD in SLE patients compared to controls. Mean foveal SVD (WMD=-1.71, 95%CI: -4.65, 1.24), mean FAZ area (WMD=0.04, 95%CI: -0.01, 0.09) and AI (WMD=0.00, 95%CI: -0.02, 0.02) were not different between SLE patients and controls (Figures 2-7).

**Table 1 Characteristics of included studies**

mean±SD or medium, range

| Study | Study location | Study design | Mono- or binocular | Sample (SLE/control) | Age (y) | | Duration of disease (y) | HCQ (y) | Scan area |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | SLE | Control | | | |
| Isik 2021[6] | Turkey | CS | OD | 35/35 | 42.6±9.2 | 42.5±7.9 | 10.6±4.4 | NA | 6 mm×6 mm |
| An 2021[9] | China | CS | Monocular | 41/40 | 37.61±12.73 | 35.53±10.17 | NA | No | 6 mm×6 mm |
| Arfeen 2020[10] | Egypt | CS | Binocular | 20/20 | 29.20±7.90 | 27.60±4.43 | NA | NA | 6 mm×6 mm |
| Mihailovic 2020[11] | Germany | CS | OD | 19/19 | 40.1±11.5 | 38.2±12.6 | NA | 5.76±5.18 | 3 mm×3 mm |
| Pichi 2020[12],a | Abu Dhabi | CS | Binocular | 15/15 | 42.3±13.4 | Age-matched | 11.3±6.8 | No current treatment | 3 mm×3 mm |
| Liu 2022[13] | China | CS | Average of binocular | 12/12 | 33.80±9.49 | 33.20±9.41 | 4.33±2.67 | NA | 3 mm×3 mm |
| Ermurat 2022[14] | Turkey | CS | Monocular | 47/41 | 39, 21-55 | 36, 18-55 | NA | NA | 6 mm×6 mm |
| Mimier-Janczak 2022[15],b | Poland | CS | Average of binocular | 30/31 | 46.07±14.09 | 44.55±14.11 | 101.8±89.98 (mo) | 391.23±425.52 (mo) | 6 mm×6 mm |
| Pelegrin 2023[16],c | Spain | CS | Lower one of two eyes | 78/80 | 45, 43-50 | 47, 40.9-50.4 | 8.6, 7.3-12.4 | 6, 5-8 | 3 mm×3 mm |
| Shah 2019[17],a | USA | Retrospective | Binocular | 5/5 | NA | NA | NA | NA | 3 mm×3 mm |
| Subasi 2022[18] | Turkey | Prospective | Monocular | 60/60 | 43.36±12.05 | 39.73±7.74 | 11.63±6.94 | >5y, 44 subjects; <5y, 16 subjects | 6 mm×6 mm |

CS: Cross-sectional; HCQ: Hydroxychloroquine; NA: Not available; OD: *Oculus dexter;* SLE: Systemic lupus erythematosus; FAZ: Foveal avascular zone. [a]The data in the study was evaluated from the skeletonized figure of OCTA; [b]The border line of FAZ area was manually drawn; [c]The data was recorded as median and 95% confidence interval.

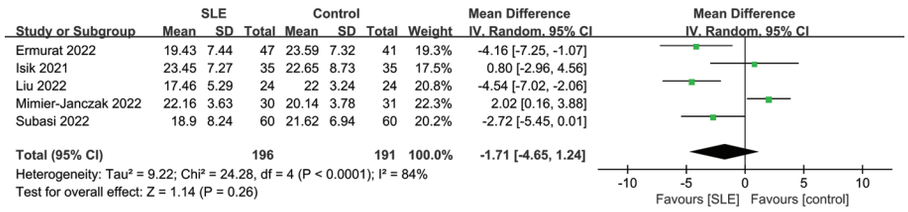


**Figure 2 Forest plot of WMD of foveal SVD in SLE patients compared to control** WMD: Weighted mean differences; SVD: Superficial vessel density; SLE: Systemic lupus erythematosus; IV: Inverse variance; SD: Standard deviation; CI: Confidence internal.

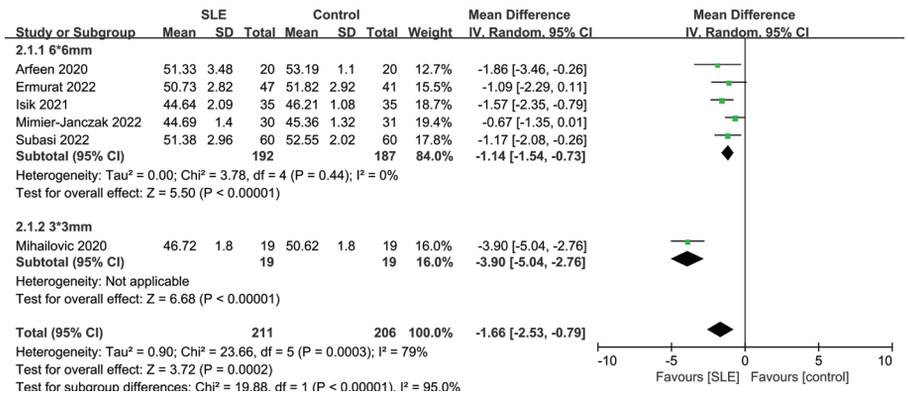


**Figure 3 Forest plot of WMD of whole SVD in SLE patients compared to control** WMD: Weighted mean differences; SVD: Superficial vessel density; SLE: Systemic lupus erythematosus; IV: Inverse variance; SD: Standard deviation; CI: Confidence internal.

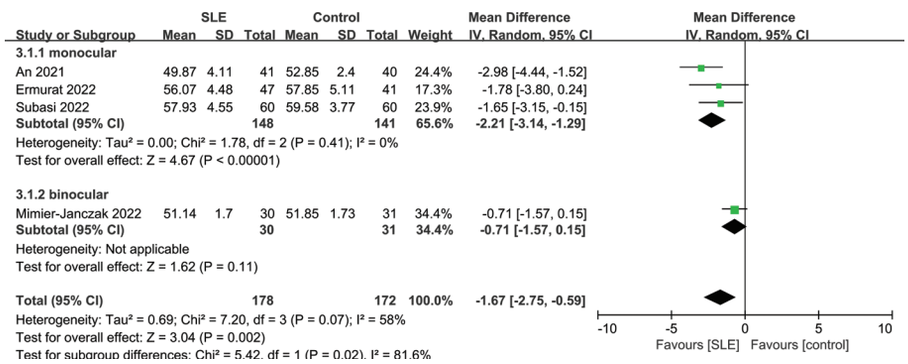


**Figure 4 Forest plot of WMD of parafoveal DVD in SLE patients compared to control** WMD: Weighted mean differences; DVD: Deep vessel density; SLE: Systemic lupus erythematosus; IV: Inverse variance; SD: Standard deviation; CI: Confidence internal.

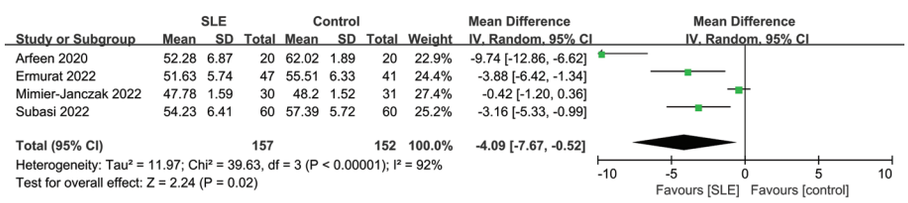


**Figure 5 Forest plot of WMD of whole DVD in SLE patients compared to control** WMD: Weighted mean differences; DVD: Deep vessel density; SLE: Systemic lupus erythematosus; IV: Inverse variance; SD: Standard deviation; CI: Confidence internal.

Heterogeneity was not significant between studies that investigated parafoveal SVD ($I^2$=0, $P$=0.97) and perifoveal SVD ($I^2$=0, $P$=0.68) and fixed model was applied. Six studies (468 subjects) reported on parafoveal SVD[6,9,13-15,18] and 3 studies on perifoveal SVD (278 subjects)[6,14,18]. Mean parafoveal SVD (WMD=-1.22, 95%CI: -1.67, -0.76) and mean perifoveal SVD (WMD=-1.42, 95%CI: -1.95, -0.89) were significantly lower, indicating poor parafoveal SVD and perifoveal SVD in SLE patients compared to controls (Figures 8-9).

**Subgroup Analysis** Subgroups of whole SVD were divided according to scanning area. In 6 mm×6 mm subgroup consisting 5 studies[6,10,14-15,18], mean whole SVD was significantly lower in SLE patients than controls (WMD=-1.44, 95%CI: -1.54, -0.73) with $I^2$ decreasing to 0. Only one study was included in 3 mm×3 mm subgroup with whole SVD still significantly lower in SLE[11]. The result revealed that the scanning area contributed parts of heterogeneity.

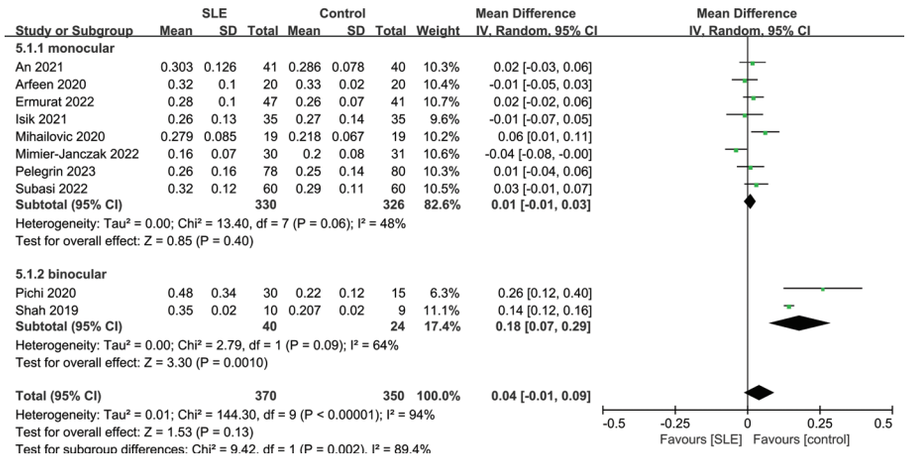


**Figure 6 Forest plot of WMD of FAZ area in SLE patients compared to control** WMD: Weighted mean differences; FAZ: Foveal avascular zone; SLE: Systemic lupus erythematosus; IV: Inverse variance; SD: Standard deviation; CI: Confidence internal.

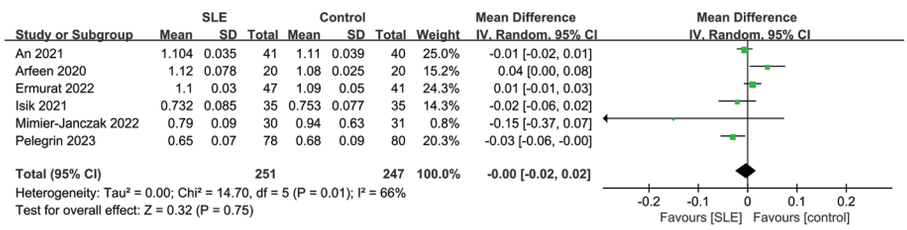


**Figure 7 Forest plot of WMD of AI in SLE patients compared to control** WMD: Weighted mean differences; AI: Acircularity index; SLE: Systemic lupus erythematosus; IV: Inverse variance; SD: Standard deviation; CI: Confidence internal.

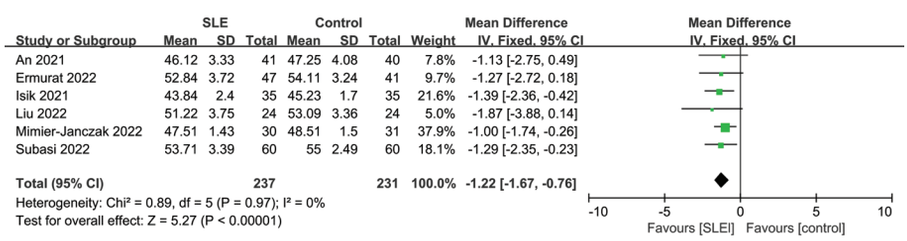


**Figure 8 Forest plot of WMD of parafoveal SVD in SLE patients compared to control** WMD: Weighted mean differences; SVD: Superficial vessel density; SLE: Systemic lupus erythematosus; IV: Inverse variance; SD: Standard deviation; CI: Confidence internal.

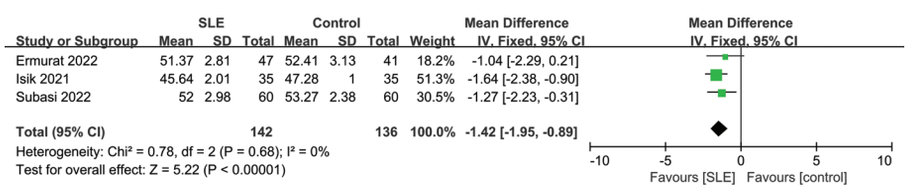


**Figure 9 Forest plot of WMD of perifoveal SVD in SLE patients compared to control** WMD: Weighted mean differences; SVD: Superficial vessel density; SLE: Systemic lupus erythematosus; IV: Inverse variance; SD: Standard deviation; CI: Confidence internal.

Subgroups of parafoveal DVD were divided by mono- or binocular OCTA. In monocular subgroup consisting 3 studies[9,14,18], mean parafoveal DVD was lower in SLE patients (WMD=-2.21, 95%CI: -3.14, -1.29) with $I^2$ decreasing to 0. The data of the resting one study was originated from the average OCTA of two eyes[15]. The origin of ocular OCTA data contributed parts of heterogeneity.

Subgroups of FAZ area were divided by monocular or binocular OCTA. In monocular subgroup consisting 8 studies[6,9-11,14-16,18], mean FAZ area was not different between SLE patients and controls (WMD=0.01, 95%CI: -0.01, 0.03) with $I^2$ decreasing to 48%. In binocular subgroup, mean FAZ area was significant larger in SLE patients compared to controls (WMD=0.18, 95%CI: 0.07, 0.29) but heterogeneity was still significant ($I^2$=64%). The result revealed that the origin of ocular OCTA data contributed parts of heterogeneity. Although subgroups were divided in whole DVD by country and the heterogeneity decreased to 0, the studies in each subgroup were less than 3 and the merged result was interpreted. Foveal SVD was divided into subgroups according to the origin of

ocular OCTA and country and no origin of heterogeneity was found. AI was divided into subgroups according to the design, country, male-to-female ratio and scanning area and no origin of heterogeneity was found.

**Sensitivity Analysis and Publication Bias** The sensitivity analysis was achieved by changing the analysis model and the results were robust for parafoveal SVD, perifoveal SVD, whole SVD, parafoveal DVD, whole DVD and AI. The result of foveal SVD was changed by changing analysis model ($P$=0.04) or exclude the study of Mimier-Janczak *et al*[15] ($P$=0.006). The result of FAZ area was also changed after changing the analysis model. It indicated the analysis model for foveal SVD and FAZ area weren't robust. Since the studies were less than 10, Egger's test was applied and indicated there wasn't publication bias for foveal SVD ($P$=0.997), parafoveal SVD ($P$=0.25), perifoveal SVD ($P$=0.443), parafoveal DVD ($P$=0.648), whole DVD ($P$=0.244) and AI ($P$=0.175). There are more than 10 studies involving FAZ area, and funnel plot and Egger's test were applied. Visual inspection of funnel plots was basically symmetry (Figure 10). Although Egger's test indicated $P$ value was 0.03, small-sample-size studies may increase heterogeneity of random-effect model, so there was no publication bias for FAZ area according to funnel plot. Studies of small sample size like Shah *et al*[17] contributed to the different results after changing analysis model and there was no obvious change in merged results if excluded these studies.

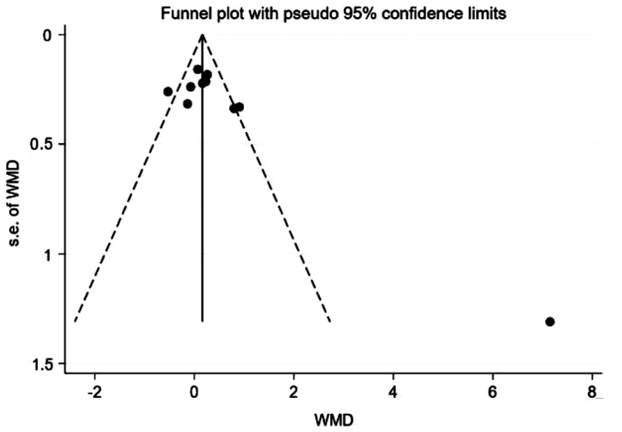


**Figure 10 Funnel plot for studies reporting FAZ area in SLE patients compared to control** WMD: Weighted mean differences; FAZ: Foveal avascular zone; SLE: Systemic lupus erythematosus.

## DISCUSSION

This Meta-analysis included 445 subjects and 441 healthy controls from January 2000 to April 2023. To our knowledge, this review is the first of its kind to summarize and quantify retinal microcirculation differences in SLE and healthy people. Compared to previous observational studies, this Meta-analysis included more subjects to provide overall and robust results and increased the statistical power of each individual study. Our Meta-analysis found that SLE patients have decreased retinal microcirculation in superficial parafoveal, superficial perifoveal, whole superficial, deep parafoveal and whole deep zone compared with healthy control while foveal SVD, FAZ area and AI were not significantly different.

Our Meta-analysis suggests that SLE patients have lower retinal vessel densities in superficial parafoveal zone, superficial perifoveal zone and whole superficial zone with a reduction of 1.22%, 1.42% and 1.66% respectively. Vessel densities in deep parafoveal zone and whole deep zone were also impaired with a reduction of 1.67% and 4.09%. Although vessel density in deep perifoveal zone couldn't be merged due to limited number of studies, there was a significant difference in SLE and control with a reduction of 4.29% and 3.26% in each study. It's recognized that in SLE patients, autoantibodies and immune complex are deposited in the wall of blood vessels with inflammation triggered by complements and thus retinal microcirculation could be impaired. This finding is reinforced by immunofluorescence studies that autoantibodies and immune complex depositing in the walls of retinal and choroidal vessels and the basement membrane of choroidal epithelium[19].

But scholars hold different opinions about the order of impairment in superficial and deep capillary plexus (DCP). Most believe that DCP was vulnerable than superficial capillary plexus (SCP). An *et al*[9] found that parafoveal vessel density in the DCP layer of SLE group was significantly lower than that in the control group while no significant difference was found in the parafoveal vessel density in SCP and FD-300. Shi *et al*[20] observed that deeper total microvascular (DTMI) density was significantly lower in SLE patients while no significant changes in superficial microvascular (SMIR), superficial total microvascular (STMI) and superficial macrovascular (SMAR) densities of SLE patients compared to the normal group. Arfeen *et al*[10] and Ermurat and Koyuncu[14] found that SLE patients have more sectors of decreased vessel densities in DCP than SCP. Subasi *et al*[18] found that superficial and DCP were all decreased in SLE patients with the decrease in DCP more significant. Other scholars believed the SCP was more sensitive to the impairment of inflammation. The so-called severe vaso-occlusive retinopathy is characterized by small arterial occlusions and diffuse capillary non-perfusion. It was reported that the characteristics of the superficial retinal capillary plexuses (SRCP) tends to be arterial, but on the contrary, the deep retinal capillary plexuses (DRCP) consists of veins[21]. Therefore, SCP is more vulnerable. Our Meta-analysis suggests that DCP shows a more significant reduction in vessel densities than SCP. We believe the reasons may as follows. First, DCP derives from the vertical branches of SCP[22] and have slow blood flow, resulting in the deposition

of autoantibodies and immune complex easier. Second, the DCP supplies the outer retina and requires more oxygen, which makes it more sensitive to ischemia. Finally, the SLE patients in the included studies were all inspected with fundus scope ensuring no lupus retinopathies and the retina should be the kind of micro vasculopathy. In this case, alteration of microcirculation in DCP may be more obvious.

Although some scholars found FAZ area in SLE patients was significantly larger owing to inperfusion and ischemia of retina[11-12,23], our Meta-analysis suggests that no change in FAZ area between SLE patients and healthy control in merge group or in monocular group. In binocular group which including only two studies, the conclusion of larger FAZ area in SLE isn't steady due to the high heterogeneity. Some studies suggests that FAZ area is influenced by various factors such as age, axial length, vascular layer segmentation and the method of calculating FAZ parameters and AI is more sensitive for evaluating the morphological irregularity of FAZ. It also fingers out that mechanical stretch and damage to capillaries due to macular edema are important reason for FAZ irregularity[24]. Our Meta-analysis suggests that AI between SLE and control group were not different although the high heterogeneity. In the included studies, lupus retinopathy or hydroxychloroquine toxicity associated retinopathy was excluded under fundus scope and vessel density in foveal zone is less affected, therefore the structure of FAZ may not be damaged and that's the reason for indifference of FAZ area and AI between SLE patients and control group.

This Meta-analysis has limitations. First, only studies written in Chinese or English were included. Second, random-effect model was chosen for deep vessel densities due to the high heterogeneity since country, male-to female ratio and the treatment scheme including hydroxychloroquine or not may increase the heterogeneity. Publication bias appeared to influence the Meta-analysis of SVD and more studies should be included in the future. Lastly, some subjects took hydroxychloroquine in the treatment scheme even though toxicity associated maculopathy were excluded, but it was hard to eliminate the influence of hydroxychloroquine in retinal microcirculation and structure. Future studies may include patients with other kinds of autoimmune disease who taking hydroxychloroquine as positive control.

Our Meta-analysis investigated the quantitative alternation of retinal microcirculation in SLE. The superficial and deep vessel densities in perifoveal zone were decreased significantly in SLE while FAZ area and AI were not significantly different from healthy control. We wish to raise the awareness of ophthalmologists and rheumatologists about the ocular complications of SLE especially in retina and we believe it's a promising way to evaluate the disease activity of SLE by quantifying retinal vessel densities. Given the heterogeneity and paucity of studies in SLE retinopathy, future researches including more subjects and positive control are needed.

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**Authors' Contributions:** He XY: conceptualization, methodology, formal analysis, investigation, data curation and writing-original draft. Chen WW: data curation. Wang Q: conceptualization, validation, writing-review & editing and supervision.

**Information on author access to data:** Xing-Yu He, email-address: 493952089@qq.com.

**Conflicts of Interest: He XY,** None; **Chen WW,** None; **Wang Q,** None.

## REFERENCES

1 Conigliaro P, Cesareo M, Chimenti MS, *et al*. Take a look at the eyes in systemic lupus erythematosus: a novel point of view. *Autoimmun Rev* 2019;18(3):247-254.

2 Kharel Sitaula R, Shah DN, Singh D. Role of lupus retinopathy in systemic lupus erythematosus. *J Ophthalmic Inflamm Infect* 2016;6(1):15.

3 Spaide RF, Fujimoto JG, Waheed NK, *et al*. Optical coherence tomography angiography. *Prog Retin Eye Res* 2018;64:1-55.

4 Conigliaro P, Cesareo M, Chimenti MS, *et al*. Evaluation of retinal microvascular density in patients affected by systemic lupus erythematosus: an optical coherence tomography angiography study. *Ann Rheum Dis* 2019;78(2):287-289.

5 Masresha SA, Alen GD, Kidie AA, *et al*. First line antiretroviral treatment failure and its association with drug substitution and sex among children in Ethiopia: systematic review and meta-analysis. *Sci Rep* 2022;12(1):18294.

6 Işık MU, Akmaz B, Akay F, *et al*. Evaluation of subclinical retinopathy and angiopathy with OCT and OCTA in patients with systemic lupus erythematosus. *Int Ophthalmol* 2021;41(1):143-150.

7 Luo DH, Wan X, Liu JM, *et al*. Optimally estimating the sample mean from the sample size, Median, mid-range, and/or mid-quartile range. *Stat Methods Med Res* 2018;27(6):1785-1805.

8 Wan X, Wang WQ, Liu JM, *et al*. Estimating the sample mean and standard deviation from the sample size, Median, range and/or interquartile range. *BMC Med Res Methodol* 2014;14:135.

9 An Q, Gao J, Liu L, *et al*. Analysis of foveal microvascular abnormalities in patients with systemic lupus erythematosus using optical coherence tomography angiography. *Ocul Immunol Inflamm* 2021;29(7-8):1392-1397.

10 Arfeen SA, Bahgat N, Adel N, *et al*. Assessment of superficial and deep retinal vessel density in systemic lupus erythematosus patients using optical coherence tomography angiography. *Graefes Arch Clin Exp Ophthalmol* 2020;258(6):1261-1268.

11 Mihailovic N, Leclaire MD, Eter N, *et al*. Altered microvascular density in patients with systemic lupus erythematosus treated with hydroxychloroquine-an optical coherence tomography angiography study. *Graefes Arch Clin Exp Ophthalmol* 2020;258(10):2263-2269.

12 Pichi F, Woodstock E, Hay S, *et al*. Optical coherence tomography angiography findings in systemic lupus erythematosus patients with no ocular disease. *Int Ophthalmol* 2020;40(8):2111-2118.

13 Liu R, Wang Y, Xia Q, *et al*. Retinal thickness and microvascular alterations in the diagnosis of systemic lupus erythematosus: a new approach. *Quant Imaging Med Surg* 2022;12(1):823-837.

14 Ermurat S, Koyuncu K. Evaluation of subclinical retinal microvascular changes in systemic lupus erythematosus patients using optical coherence tomography angiography and its relationship with disease activity. *Lupus* 2022;31(5):541-554.

15 Mimier-Janczak M, Kaczmarek D, Proc K, *et al*. Evaluation of subclinical retinal disease in patients affected by systemic lupus erythematosus with No evidence of ocular involvement-an optical coherence tomography angiography original study. *J Clin Med* 2022;11(24):7417.

16 Pelegrín L, Morató M, Araújo O, *et al*. Preclinical ocular changes in systemic lupus erythematosus patients by optical coherence tomography. *Rheumatology* (*Oxford*) 2023;62(7):2475-2482.

17 Shah C, Gabriel R, Kedhar S, *et al*. Subclinical foveal vasculopathy in patients with systemic lupus erythematosus using optical coherence tomography angiography. *J VitreoRetinal Dis* 2019;3(5):283-288.

18 Subasi S, Kucuk KD, San S, *et al*. Macular and peripapillary vessel density alterations in a large series of patients with systemic lupus erythematosus without ocular involvement. *Graefes Arch Clin Exp Ophthalmol* 2022;260(11):3543-3552.

19 Nguyen QD, Uy HS, Akpek EK, *et al*. Choroidopathy of systemic lupus erythematosus. *Lupus* 2000;9(4):288-298.

20 Shi WQ, Han T, Liu R, *et al*. Retinal microvasculature and conjunctival vessel alterations in patients with systemic lupus erythematosus-an optical coherence tomography angiography study. *Front Med* (*Lausanne*) 2021;8:724283.

21 Bao LL, Zhou R, Wu YF, *et al*. Unique changes in the retinal microvasculature reveal subclinical retinal impairment in patients with systemic lupus erythematosus. *Microvasc Res* 2020;129:103957.

22 Campbell JP, Zhang M, Hwang TS, *et al*. Detailed vascular anatomy of the human retina by projection-resolved optical coherence tomography angiography. *Sci Rep* 2017;7:42201.

23 Pelegrin L, Figueras-Roca M, Olate-Perez A, *et al*. Changes in macular capillary network measured with optical coherence tomography-angiography in patients with systemic lupus erythematosus. *Arthritis and Rheumatology* 2020,72(SUPPL 10):3654-3655.

24 Han RY, Gong RW, Liu W, *et al*. Optical coherence tomography angiography metrics in different stages of diabetic macular edema. *Eye Vis* (*Lond*) 2022;9(1):14.