Emerging Role of Nailfold Capillaroscopy in Assessment of Microvascular Affection in Patients with Systemic lupus erythematosus

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Abstract:

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disorder characterized by immune dysregulation, persistent inflammation, and a broad spectrum of clinical manifestations affecting several organs, including the skin, joints, kidneys, lungs, nervous system, and vascular system. Although immune-mediated tissue injury represents the hallmark of the disease, increasing evidence indicates that vascular dysfunction, particularly at the microvascular level, plays a pivotal role in disease progression, organ involvement, and irreversible damage. Both macrovascular complications, mainly related to accelerated atherosclerosis, and microvascular abnormalities contribute substantially to the increased morbidity and mortality observed in patients with SLE.

Nailfold capillaroscopy (NFC) is a simple, non-invasive imaging technique that permits direct visualization of the peripheral microcirculation and has become an established method for evaluating structural microvascular abnormalities in rheumatic diseases. Besides its well-recognized role in the assessment of patients with Raynaud's phenomenon and the identification of characteristic capillaroscopic patterns such as the scleroderma pattern, NFC has gained increasing attention as a potential tool for investigating microvascular involvement in SLE. Accumulating evidence suggests that capillaroscopic abnormalities may parallel disease activity, reflect internal organ involvement, and provide valuable information regarding the extent of vascular damage. Therefore, NFC has emerged as a promising adjunctive modality for the assessment of microvascular dysfunction in SLE. This review summarizes the current evidence regarding the role of nailfold capillaroscopy in evaluating microvascular involvement in systemic lupus erythematosus and discusses its potential clinical applications.

Keywords: Systemic lupus erythematosus; Microvascular Affection; Nailfold Capillaroscopy

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Introduction

Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disorder characterized by involvement of several organ systems, including the skin, musculoskeletal system, kidneys, respiratory system, nervous system, and vascular structures. It affects approximately 3.4 million individuals globally, with nearly 400,000 newly diagnosed cases reported annually. The disease predominantly affects females during their reproductive years and shows a greater prevalence and severity among individuals of African ancestry. Geographical variations in SLE incidence have been observed, with increased rates documented in countries such as Poland, the United States, Barbados, and China. Although the precise etiology of SLE remains incompletely defined, its development is believed to involve a complex interaction between genetic susceptibility, environmental exposures, and hormonal influences. (1)

The diagnosis and clinical assessment of SLE rely on recognized classification and evaluation tools, including the criteria established by the American College of Rheumatology (ACR) and the SLE Disease Activity Index (SLEDAI). Due to its multisystem nature and association with several comorbidities, SLE requires continuous follow-up involving strategies such as malignancy surveillance and cardiovascular risk evaluation. The underlying pathogenesis involves immune system dysregulation, leading to the generation of pathogenic autoantibodies, particularly anti-Smith antibodies. These antibodies are considered highly specific for SLE and have been associated with disease activity and distinct clinical manifestations. (2)

Vascular involvement represents a major component of SLE and contributes substantially to disease-related morbidity and mortality. Vascular abnormalities may occur in the form of vasculopathy, which is characterized by non-inflammatory structural vascular changes, or vasculitis, where inflammatory processes result in vascular injury and infiltration by inflammatory cells. Such vascular manifestations may develop as

a consequence of active disease or may coexist as associated comorbid conditions. (3)

Microvascular abnormalities have increasingly been recognized as an important contributor to SLE pathogenesis. Nailfold capillaroscopy (NFC) has emerged as a valuable, non-invasive method for evaluating microvascular alterations. Current evidence supports the utility of NFC in identifying and describing microcirculatory abnormalities among patients with SLE. (4)

This review aims to explore the challenges associated with microvascular impairment in SLE, provide an overview of the major capillaroscopic abnormalities linked to disease-related microangiopathy, and highlight the evolving role of nailfold capillaroscopy in evaluating microvascular involvement in systemic lupus erythematosus.

Epidemiology of SLE

SLE demonstrates a marked female predominance, with an estimated female-to-male ratio of nearly 9:1 among adults. The disease is associated with an increased risk of early mortality, with this risk being particularly pronounced in individuals of African, Chinese, and Hispanic ancestry. Lupus nephritis (LN) represents one of the most significant complications of SLE and is associated with increased mortality. The distribution of SLE varies considerably across different geographical regions. In the United States, reported incidence rates range between 2 and 7.6 cases per 100,000 population, whereas prevalence estimates range from 19 to 159 cases per 100,000 population. Individuals of African ancestry, particularly those residing in America or Europe, have been reported to develop SLE more frequently and at a younger age compared with individuals of Northern European ancestry. (5)

Pathogenesis

SLE develops through a complex interaction of immunological, hormonal, environmental, and genetic factors that impair immune tolerance toward self-antigens. This loss of tolerance, together with pro-inflammatory mediators including type 1 interferons and cytokines, promotes extensive immune dysregulation involving multiple immune pathways and eventually contributes to the development of autoimmunity. In lupus, abnormalities involve both innate and adaptive immune responses, leading to impaired T-cell function with a shift toward Th17 cell differentiation rather than regulatory T (Treg) cell activity, accompanied by reduced IL-2 production. Despite an overall decrease in circulating B-cell numbers, autoreactive B cells persist and contribute to disease pathogenesis. This concept has supported the development of biologic treatments targeting the overactive BLyS pathway, which plays a central role in B-cell survival. (6)

The identification of a strong type 1 interferon signature in lupus highlights the significant contribution of innate immunity to disease mechanisms. Dendritic cells contribute to this process by producing type 1 interferon and participating in the recognition and clearance of immune complexes and nucleic acids that act as autoantigens in lupus. Important antigenic stimuli include endogenous and exogenous nucleic acids, which promote the generation of autoantibodies directed against nucleic acid-associated antigens, mainly originating from NETs and apoptotic cells. Increased NET degradation has been linked to greater disease severity, lupus nephritis, anti-dsDNA antibody positivity, and complement consumption**. (Figure 1)** (7)

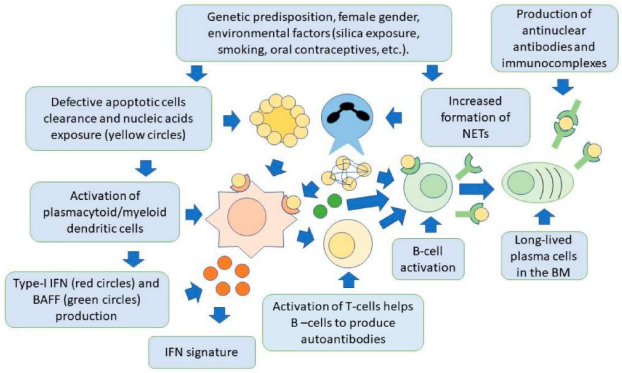

Figure 1: Innate and adaptive immunity are both involved in the pathophysiology of SLE [8]

Microvascular affection in SLE

Vascular involvement, whether representing a direct manifestation of SLE or occurring as an associated comorbidity, has a considerable impact on patients' quality of life and represents a major contributor to mortality in advanced disease. Vascular abnormalities in SLE can involve vessels of different sizes throughout the body. Diseases affecting medium and large vessels may include accelerated atherosclerosis, thrombosis related to antiphospholipid syndrome, and vasculitis involving visceral, coronary, and cerebral arteries. In addition, microvascular manifestations may appear as livedo reticularis, cutaneous vasculitis, lupus nephritis, pulmonary arterial hypertension (PAH), and intestinal vasculitis. (9)

- **Pathogenesis**

Although the precise mechanisms responsible for vascular involvement in lupus

remain incompletely defined, they are believed to result from complex interactions between vascular endothelial cells, inflammatory cells, cytokines, autoantibodies, and immune complexes. LV is considered a secondary form of vasculitis that may present with acute or subacute manifestations resulting from immune complex deposition within vessel walls. Furthermore, vascular abnormalities may develop as associated conditions, such as steroid-induced atherosclerosis, or may occur due to enhanced atherosclerotic processes within a persistent pro-inflammatory environment. (10)

Autoantibody binding to specific antigens leads to the formation of circulating immune complexes, which subsequently accumulate within vascular walls. This process is facilitated by defective clearance through the reticuloendothelial system and increased vascular permeability induced by platelet-derived amines and IgE-mediated reactions. The deposition of immune complexes activates the complement cascade, resulting in inflammatory responses and depletion of complement components. Certain complement factors promote recruitment of polymorphonuclear leukocytes, which infiltrate the vessel wall and release tissue-damaging enzymes. Consequently, vascular injury may progress to thrombosis, occlusion, hemorrhage, and ischemic alterations in surrounding tissues. Moreover, factors including hydrostatic pressure and disturbed blood flow may contribute to the preferential localization of immune complexes in specific vascular regions, thereby affecting the distribution of vascular lesions. (9)

Among the autoantibodies implicated in vascular injury, anti-endothelial cell antibodies (AECA) are considered major mediators of endothelial damage. Binding of AECA to endothelial cells induces cellular activation, resulting in increased expression of adhesion molecules, including E-selectin, intercellular adhesion molecule 1 (ICAM-1), and vascular cell adhesion molecule 1 (VCAM-1). This activation also stimulates the release of cytokines and chemokines, promoting an inflammatory response characterized by interleukin-1 (IL-1), IL-6, and IL-8. Furthermore, it enhances tissue factor production, thereby promoting coagulation and endothelial cell cytotoxicity. More than 80% of patients with SLE have detectable AECA. Additional autoantibodies implicated in the pathogenesis of lupus vasculitis (LV) include antineutrophil cytoplasmic antibodies (ANCA), antiphospholipid antibodies (aPL), and anti-double-stranded DNA antibodies (anti-dsDNA). Although ANCA are predominantly associated with primary systemic vasculitis, they may also be detected in secondary vasculitides associated with systemic connective tissue diseases, including SLE, with reported positivity in 15–20% of patients. ANCA interact with proteinase 3 (PR3) or myeloperoxidase (MPO) antigens to form immune complexes, promoting neutrophil adhesion to endothelial cells. This process facilitates extravascular migration of neutrophils, vascular injury, and endothelial cell apoptosis. (11)

Activated neutrophils and monocytes trapped within the microcirculation may induce focal necrosis involving capillaries, venules, and, less frequently, arterioles. Antiphospholipid (aPL) antibodies bind to phospholipids exposed on damaged endothelial cells, resulting in further endothelial activation and injury. They also activate the complement cascade, producing pro-adhesive, pro-inflammatory, and pro-thrombotic effects. In addition, anti-dsDNA antibodies enhance endothelial activation by stimulating the release of interleukin-6 (IL-6) and interleukin-8 (IL-8). Although these antibodies exhibit anti-endothelial activity, direct cytotoxic effects have not yet been demonstrated. (12)

Alterations in programmed cell death pathways, particularly apoptosis and NETosis, play a key role in the pathogenesis of SLE and LV. Impaired balance between the generation and clearance of apoptotic cells and DNA-containing neutrophil extracellular traps (NETs) promotes the formation of autoantigens, which subsequently contribute to immune complex formation. These immune complexes are removed by macrophages and dendritic cells, leading to the secretion of pro-inflammatory cytokines that sustain inflammation and tissue injury in patients with SLE. NETs are extracellular DNA networks enriched with a variety of proteins and can promote thromboinflammation in disorders such as sepsis, SLE, and vasculitis through the exposure of immunostimulatory proteins and autoantigens. (13)

In some patients with SLE, particularly those with central nervous system involvement, inflammatory vascular injury may result from complement activation despite the absence of immune complex deposition. This mechanism is referred to as the Shwartzman phenomenon. Vasculitic manifestations in SLE may also develop secondary to medications or infections. Drugs such as penicillin and allopurinol may function as haptens by binding to autoantigens and initiating immune responses that produce inflammatory vascular lesions. Infection-associated vasculitis may arise either from direct microbial invasion of the vessel wall or from deposition of immune complexes containing microbial antigens and their corresponding antibodies. This mechanism has

been particularly described in hepatitis C virus infection associated with cryoglobulinemia. (14)

Nailfold capillaroscopy

Capillaroscopy is a non-invasive imaging modality used to evaluate the microcirculation and is primarily employed to distinguish Raynaud's phenomenon (RP) from other disorders. Several optical devices are available for performing this examination; however, only dermatoscopy and videocapillaroscopy have demonstrated satisfactory reliability **(Figure 2).** At present, image analysis software is available exclusively for videocapillaroscopes, allowing a standardized method of image assessment for research applications. The handheld videocapillaroscope offers additional practical advantages, as it is easy to master and can be used in a wide range of clinical settings, including the assessment of patients with flexion contractures. (15)

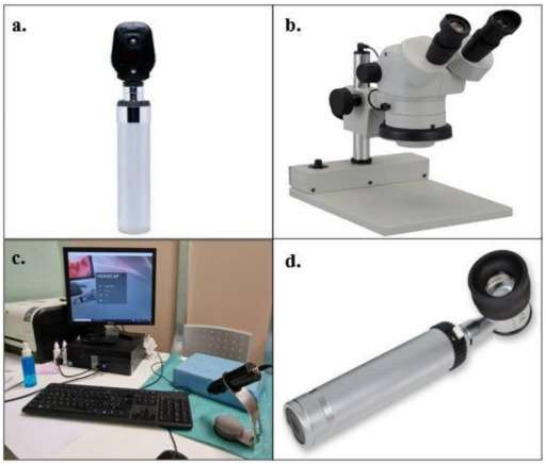

Figure 2: imaging modalities used for the assessment of nailfold microvascular morphology. (a) Ophthalmoscope. (b) Stereomicroscope adapted for nailfold capillaroscopy. (c) Nailfold videocapillaroscopy (NVC) system. (d) Dermatoscope. [16]

- **Nailfold videocapillaroscopy technique and image acquisition (17)**

Nailfold videocapillaroscopy (NVC) is a non-invasive imaging modality that enables direct visualization of the nailfold microcirculation. It is currently regarded as the gold standard for the evaluation of peripheral microvascular abnormalities in connective tissue diseases. Based on the recommendations of the EULAR Study Group on Microcirculation in Rheumatic Diseases and the Scleroderma Clinical Trials Consortium (SCTC), NVC should be performed using a videocapillaroscope with high-resolution digital imaging at ×200 magnification, as this configuration provides optimal assessment of capillary morphology and overall architecture.

For optimal image acquisition, patients should undergo acclimatization in a temperature-controlled environment (20–22°C) for approximately 15 minutes before the examination. A drop of immersion oil is then applied to improve epidermal transparency. The nailfolds of the second through fifth fingers are subsequently examined while avoiding excessive pressure from the probe, as compression may artificially distort the morphology of the capillary loops.

The acquired images are evaluated according to standardized qualitative and quantitative parameters. Qualitative analysis includes assessment of capillary morphology, giant capillaries, microhemorrhages, avascular areas, and neoangiogenesis. Quantitative analysis, on the other hand, mainly involves measurement of capillary density together with other morphometric variables. Standardized image acquisition and interpretation are essential for improving reproducibility, minimizing interobserver variability, and facilitating comparisons among different clinical studies.

Qualitative assessment of images: Following review of the 32 (or 16) stored images, the examiner performs an overall qualitative evaluation. Based on these findings, the capillaroscopic pattern is classified as either a scleroderma pattern or a non-scleroderma pattern. (18)

Nailfold capillaroscopy assessment parameters and scoring systems

Nailfold capillaroscopy evaluation has been standardized through several scoring methods, including the template described by Hosking et al. (2013) (19), which was developed according to the European League Against Rheumatism (EULAR) recommendations published in 2008 (20) **(Figure 3).** Using this method, each nailfold image is generally divided into four adjacent 1-mm fields, followed by systematic assessment of the principal capillaroscopic abnormalities. (21)

The initial step involves assessment of capillary morphology by identifying the predominant capillary configuration. Capillaries may be categorized as tortuous, characterized by bending without crossing of the afferent and efferent limbs; crossed, in which the two limbs intersect; or elongated, when the capillary length exceeds 300 µm. Capillary density is subsequently

evaluated and represents one of the most important quantitative parameters. Under normal conditions, capillary density ranges from 9 to 13 capillaries/mm, and the average density is usually determined from multiple examined digits to improve measurement reliability.

Microhemorrhages are identified as red or brown hemosiderin deposits located distal to the capillary row and are considered evidence of microvascular injury. Giant capillaries are defined as homogeneously enlarged capillary loops with an apical diameter of ≥50 µm and represent a characteristic feature of specific microangiopathic disorders. Conversely, neoangiogenesis is recognized by the presence of bushy, markedly irregular capillaries exhibiting considerable variation in both size and morphology, together with disruption of the normal capillary architecture.

Assessment also includes the identification of avascular areas, which are defined by an intercapillary distance of ≥500 µm and reflect significant capillary loss, making them an important indicator of disease progression. In addition, evaluation of the visibility of the venous plexus at the base of the nailfold may provide supplementary information regarding underlying microvascular abnormalities.

Quantitative morphometric evaluation includes measurements of capillary length, width, and apical loop diameter. Capillary length is determined from the apex of the loop to the point where it disappears into the dermis and normally ranges between 200 and 300 µm in healthy individuals. Capillary width is measured as the maximum transverse dimension of the capillary loop and is generally less than 50–60 µm. The apical (loop) diameter, measured at the curved apex of the capillary, is normally ≤20 µm under physiological conditions.

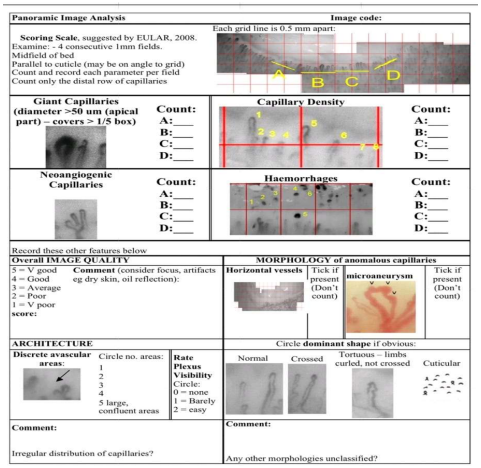

Figure 3: The template for assessment of nailfold capillaroscopy image designed by Hosking and colleagues in 2013 based on EULAR Guidelines (2008) [18].

Standardized definitions of nailfold capillaroscopy abnormalities (22)

To improve the reproducibility of NVC assessment and facilitate comparison between studies, the EULAR Study Group on Microcirculation in Rheumatic Diseases, in collaboration with the Scleroderma Clinical Trials Consortium (SCTC), developed standardized definitions for capillaroscopic abnormalities. These recommendations aimed to reduce the variability caused by the use of different terminologies and subjective descriptions of microvascular changes.

According to the standardized definitions, NVC abnormalities are evaluated through several domains, including capillary density, capillary dimensions, morphology, hemorrhages, and neoangiogenesis. Giant capillaries are defined as uniformly enlarged capillary loops with an apical diameter ≥50 µm, while microhemorrhages represent small extravasated blood deposits adjacent to capillary loops. Avascular areas indicate significant capillary loss and are defined as intercapillary spaces wider than 500 µm. Neoangiogenesis is characterized by irregular, bushy, or ramified capillary formations reflecting attempts of vascular regeneration after microvascular injury.

The updated EULAR 2020 terminology introduced more precise morphological descriptions compared with earlier classifications. Previously used broad terms such as “ramifications” or “bushy capillaries” were replaced by more standardized descriptions of abnormal capillary morphology, improving interobserver agreement. Moreover, capillary abnormalities were classified into two major categories: non-scleroderma pattern and scleroderma pattern. The latter is further divided into early, active, and late stages according to the sequential progression of giant capillaries, hemorrhages, capillary loss, and neoangiogenesis.

In systemic sclerosis, this classification allows recognition of the typical scleroderma pattern; however, in SLE, no disease-specific capillaroscopic pattern has been established. Therefore, NVC evaluation in SLE mainly focuses on the presence and severity of individual microvascular abnormalities and their possible association with disease activity, organ involvement, and cumulative vascular damage.

- **Nailfold capillaroscopy in SLE**

A systematic review performed by the EULAR Study Group on Microcirculation in Rheumatic Diseases evaluated 40 studies investigating NVC findings in patients with SLE. Compared with healthy individuals, patients with SLE showed a higher frequency of capillary dilatation, abnormal capillary morphology, and microhemorrhages. Moreover, both non-specific and scleroderma-like capillaroscopic patterns were reported more commonly in the SLE population. Several capillaroscopic abnormalities were found to correlate with clinical variables, with the overall NVC score showing an association with disease activity, particularly through the presence of abnormal capillary morphology and microhemorrhages. Nevertheless, the available evidence remains insufficient to establish consistent relationships with specific clinical manifestations or laboratory parameters. (23) **(figure 4)**

Current evidence regarding NVC characteristics in SLE remains limited because most published studies have included relatively small patient cohorts and have used heterogeneous methodologies, making direct comparison of findings difficult. In addition, inconsistent results have been reported concerning nailfold capillary density and morphometric measurements in patients with SLE. The lack of a characteristic SLE-specific capillaroscopic pattern may reflect the marked heterogeneity of disease phenotypes and the diversity of mechanisms responsible for microvascular involvement, particularly when compared with other connective tissue diseases (CTDs). To overcome these limitations, an ongoing international multicenter study has been initiated to develop standardized capillaroscopic definitions and to clarify the associations between NVC parameters and the clinical and serological characteristics of SLE. (24)

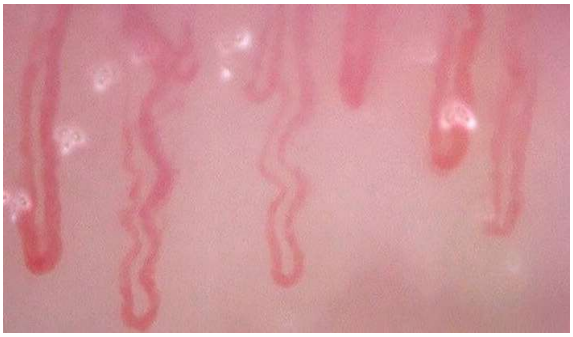

Figure 4: NFC (×500): SLE: Non-specific pattern (personal collection

Assessment of the microvascular involvement in SLE

- **Vascular involvement in SLE: micro- and macrovascular**

Vascular involvement represents one of the most serious manifestations of SLE and contributes substantially to disease-related morbidity and mortality. Both large and small blood vessels may be affected, with vascular abnormalities occurring either as vasculopathy, which is characterized by non-inflammatory vascular injury, or as vasculitis, which involves inflammatory lesions accompanied by leukocytic infiltration and fibrinoid necrosis of the vessel wall. Large- and medium-vessel involvement has been associated with accelerated atherosclerosis, thrombosis related to antiphospholipid syndrome, and vasculitis involving the visceral, coronary, and cerebral arteries. In addition, microvascular manifestations may include cutaneous vasculitis, livedo reticularis, lupus nephritis, pulmonary and intestinal vasculitis, as well as pulmonary hypertension. (4)

Nailfold Capillaroscopic Findings and Their Association with Clinical and Laboratory Parameters in SLE

Inflammatory mediators released during SLE contribute to vascular endothelial injury, which subsequently promotes neovascularization. Considerable efforts have been directed toward identifying a characteristic microcirculatory pattern in SLE using NFC to facilitate early diagnosis and improve prognostic assessment. However, no disease-specific capillaroscopic pattern has yet been established. The most frequently reported findings include tortuous capillaries with increased capillary diameter and length. Other non-specific abnormalities commonly observed are irregular capillary morphology, increased tortuosity, and microhemorrhages. A scleroderma-like capillaroscopic pattern has been reported only in a small proportion of patients, with a prevalence ranging from 2% to 15%. (25)

Several capillaroscopic patterns have been described in patients with SLE, with five distinct NFC models reported in the literature**. Granier et al. (26)** were the first to describe one of these patterns in 1986, which was characterized by tortuous and meandering capillaries, elongated capillary loops, and a prominent subpapillary venous plexus, reflecting an increase in capillary loop length. (26)

In 2013, **Lambova et al.** (27) proposed an "SLE-type pattern" characterized by elongated and

tortuous capillaries, capillary dilatation, and a prominent subpapillary plexus. They also reported additional capillaroscopic features associated with SLE, including the presence of capillary loops, variability in capillary loop length, altered visibility of the venular plexus, and blood sludging within the capillaries. Subsequently, **Bărbulescu et al.** (28) described a comparable capillaroscopic pattern consisting of elongated tortuous capillaries, dilated capillaries, and a prominent subpapillary plexus.

Using NFC to evaluate patients with SLE**, Shirani and Barahimi** (28) reported a high frequency of several capillaroscopic abnormalities. These findings included microvascular structural abnormalities (37.5%), reduced capillary density (78.6%), enlarged capillary loops (32.1%), microhemorrhages (16.1%), and neoangiogenesis (25.0%). The study also demonstrated a positive association between disease duration and the occurrence of microhemorrhages. Furthermore, patients with SLE had significantly lower mean capillary density and significantly greater capillary loop width than healthy controls.

SLE clinical manifestations from a microvascular perspective

1) Cutaneous involvement in SLE

Cutaneous manifestations are observed in approximately 85–90% of patients with SLE and include RP, livedo reticularis, and cutaneous vasculitis. The reported prevalence of RP ranges from 10% to 45%, and its clinical course is generally benign. Although RP may lead to digital microinfarctions and ulceration, progression to tissue necrosis is uncommon. The development of RP has been attributed to endothelial dysfunction together with abnormal adrenergic vascular responses. Secondary RP is typically associated with elongated and tortuous capillaries on capillaroscopic examination. Patients with SLE who develop RP are also at an increased risk of PAH. Indeed, PAH was reported in 81% of patients with RP compared with 56% of those without RP, highlighting RP as an important clinical indicator for identifying patients at increased risk of PAH. (30)

In a study by **Zhao T et al.** (31) involving 85 patients with SLE, RP was present in 31.7% of the study population. NFC examination demonstrated a normal capillaroscopic pattern in 15.3% of patients, whereas 75.3% exhibited a non-specific pattern and 9.4% showed a scleroderma pattern. Capillary dilatation was detected in 81.5% of patients with RP compared with only 14% of those without RP ($p < 0.005$).

Among patients with SLE and RP, enlarged capillaries and microhemorrhages represented the most frequent NFC abnormalities. Similarly, **Shenavandeh and Habibi** (32) reported minor capillaroscopic abnormalities in 30.6% of patients and major abnormalities in 63.9%. Their findings also demonstrated an association between active cutaneous involvement and disturbed capillary distribution.

Pavlov-Dolijanovic et al. (33) evaluated 79 patients with SLE, including 44 patients with RP and 35 without RP. They reported that central nervous system involvement and peripheral neuropathy occurred significantly more frequently in patients with RP, whereas secondary Sjögren's syndrome was more prevalent among those without RP. NFC examination further showed that enlarged capillaries, avascular areas, capillary hemorrhages, and granular blood flow were significantly more common in patients with RP than in those without RP. In addition, a scleroderma-like capillaroscopic pattern was observed more frequently in the RP group.

Livedo reticularis has been reported in approximately 14–48% of patients with SLE and is thought to result from spasm of the dermal arterioles together with swelling of the cutaneous venules. Cutaneous vasculitis occurs in 19–28% of patients and usually manifests as leukocytoclastic vasculitis caused by immune complex deposition within the small vessels of the dermis and/or subcutaneous tissue. All affected patients demonstrated either a non-specific or a scleroderma-like pattern on NFC. (4)

2) Pulmonary involvement in SLE (interstitial lung disease; PAH)

Nailfold capillary density has been proposed as a potential surrogate marker of alveolar capillary density, particularly in patients with SLE, in whom impairment of gas exchange may result from a reduction in alveolar capillary networks. PAH occurs in approximately 30% of adults with autoimmune rheumatic diseases, while its reported prevalence among patients with SLE ranges from 0.5% to 14%, depending on the diagnostic approach employed. Accumulating evidence supports an association between nailfold capillaroscopic abnormalities and both the presence and severity of PAH, suggesting that microvascular alterations may contribute to its development and pathogenesis. (34)

Donnarumma et al. (35) demonstrated that a scleroderma capillaroscopic pattern was identified in 56.3% of patients with SLE and PAH, compared with 15.9% of patients with SLE without

PAH (p = 0.002). In the univariate analysis, both RP and a scleroderma-like capillaroscopic pattern were significantly associated with PAH. However, after multivariate analysis, the scleroderma capillaroscopic pattern remained the only independent variable significantly associated with an increased risk of PAH.

3) Lupus nephritis

In patients with lupus nephritis, **Shenavandeh and Habibi** (32) reported no significant association between nailfold capillaroscopic abnormalities and renal involvement, except for the presence of elongated capillary loops. In contrast, **Ragab et al.** (36) demonstrated a statistically significant positive correlation between meandering capillaries and 24-hour urinary protein excretion. This association may reflect a common vascular pathological process affecting both renal vessels and the nailfold microcirculation. Furthermore**, Kabasakal et al.** (37) showed that renal vascular lesions are related to SLE severity. Collectively, all available studies have demonstrated the presence of capillaroscopic abnormalities in patients with LN. The discrepancies among reported findings may be explained by differences in patient selection criteria, including variations in the methods used for identifying renal involvement, whether through renal histopathological evaluation or urine and blood-based assessments.

- **4) Serology and SLE activity**

NFC abnormalities have been reported in up to 36% of patients with SLE and are associated with the presence of anti-U1 ribonucleoprotein (U1RNP) autoantibodies. Positivity for RNP antibodies has been linked to reduced capillary density and more pronounced abnormalities on NFC examination. Although capillaroscopic patterns may differ between patients with low and high disease activity, no significant differences have been demonstrated regarding the presence of anti-double-stranded DNA antibodies, anti-Smith antibodies, or complement protein levels. (38)

Kuryliszyn-Moskal A et al. (39) investigated the relationship between NFC findings, serum endothelial activation markers, and disease activity in 80 patients with SLE. Among these patients, 33 (41.25%) showed normal or mild capillaroscopic abnormalities, whereas 47 (58.75%) demonstrated moderate to severe changes. An NFC score >1 was associated with internal organ involvement, with significant differences in endothelial activation markers observed between patients with SLE and the control group. Additionally, the severity of NFC abnormalities showed a positive correlation with the SLEDAI score.

Zhao et al. (31) reported that microhemorrhages occurred more frequently among patients with active SLE compared with those with inactive disease. Similarly, **Shenavandeh and Habibi** (32) found minor NFC abnormalities in 30.6% of patients and major abnormalities in 63.9%. They also demonstrated that increased disease activity was associated with more severe capillaroscopic changes. Patients with active SLE had a higher frequency of microhemorrhages, while those with active cutaneous involvement more commonly exhibited disturbed capillary distribution patterns. Conversely, subtle capillaroscopic abnormalities were less frequently observed in patients without active skin manifestations.

Nasser et al. (40) identified a significant association between the NFC score and disease activity assessed by the SLEDAI scale. They reported increased levels of interferon I and interleukin-17A in patients with active SLE. These inflammatory mediators are also involved in vascular injury, which can be evaluated using NFC.

Patients with SLE have an increased susceptibility to premature and accelerated atherosclerosis. **Farouk et al.** (41) demonstrated that abnormal capillary characteristics, including reduced density and disorganized architecture, are associated with atherosclerotic changes. Previous research has also shown significant differences in NFC abnormalities between patients with SLE and healthy individuals.

Furthermore, previous studies have suggested possible associations between specific medications, hypocomplementemia, and LN with alterations in nailfold microvascular findings among patients with SLE. Capillaroscopy may also provide additional value in predicting internal organ involvement in patients with lupus. (42)

Conclusion

SLE is an autoimmune inflammatory disorder in which persistent immune activation and inflammation contribute to endothelial injury and subsequent vascular alterations. These microvascular changes can be detected and evaluated using NFC. Although no disease-specific capillaroscopic pattern has been identified in patients with SLE, available studies have demonstrated an association between NFC scores and disease activity. Furthermore, significant differences in capillaroscopic abnormalities have been reported between patients with SLE and

healthy individuals. Current evidence suggests that changes in capillaroscopic patterns may reflect vascular involvement affecting different organs. Therefore, the detection of NFC abnormalities in patients with SLE should prompt assessment for possible involvement of other organ systems, including nephritis and pulmonary hypertension. Due to the considerable heterogeneity of capillaroscopic findings among patients with SLE, further multicenter studies are required to better define NFC patterns and determine their relationship with clinical and laboratory characteristics.

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