Clinical Applications of Nailfold Capillaroscopy in Different Rheumatic Diseases

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Abstract

Microvascular involvement in systemic inflammatory diseases has been well known more than one hundred years. Abnormal microangiopathy of nailfold often occurs in systemic rheumatic diseases, especially in scleroderma, Raynaud's phenomenon and related conditions.Nailfold capillaroscopy uses a lens that allows analysis of the capillary morphology and microcirculation of nailfold. Recently, the video-base or computer-base system of capillaroscopy is developed and it is used as a noninvasive, simple, repeatable, highly sensitive and inexpensive method of evaluating microvascular abnormalities in rheumatic diseases.This review stresses the importance and advantages of NFC for investigating microvascular morphological patterns and their clinical correlations in rheumatic diseases. (J Intern Med Taiwan 2009; 20: 238-247)

Key Words：Nailfold capillaroscopy, Raynaud's phenomenon, Systemic sclerosis

Introduction

Microvascular involvement in systemic inflammatory diseases has been well known since the 19th century. Abnormal microangiopathy of nailfold often occurs in systemic rheumatic diseases, especially in scleroderma and related conditions. Nailfold capillaroscopy (NFC) uses a lens that allows analysis of the capillary morphology and microcirculation of nailfold. It is used as a noninvasive, simple, repeatable, highly sensitive and inexpensive method of evaluating microvascular abnormalities in rheumatic diseases[1].

The main feature of capillaroscopy that is of interest to the rheumatologist is the detection of early microvascular changes that can occur in some inflammatory connective tissue diseases. The most important and well-defined capillary abnormalities detectable by capillaroscopy have been reported in patients with systemic sclerosis (SSc). These features have recently been suggested as the new additional criteria in the American College of Rheumatology preliminary classification system for SSc[2,3]. In addition, other connective tissue diseases such as dermatomyositis (DM), mixed connective

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tissue disease (MCTD), and CREST syndrome are shown to have characteristic capillaroscopy patterns, which are valuable for diagnosis[4-6]. This review stresses the importance and advantages of NFC for investigating microvascular morphological patterns and their clinical correlations in rheumatic diseases.

History of NFC

Capillaroscopy is a useful and direct tool for observing the microvasculature. Several methods, including viewing by magnifying glass, ophthalmoscopy, dermatoscopy and wide-field capillary microscopy, have been applied before capillaroscopy. In 1663, Johan Christophorous Kolhaus was the first to use a primitive microscope to observe the small blood vessels surrounding the nails. Subsequent researchers used optical magnifying systems to study capillaries at different body sites such as the conjunctiva, lips, malleoli, nailfolds and fingertips in humans[7,8]. The first morphological study of microcirculation was performed by Giovanni Rasori (1766-1873), who used a magnifying glass to describe the close relationship between conjunctival inflammation and the presence of an "inextricable knot of capillary loops." In 1901, Hutchinson was able to distinguish primary Raynaud's phenomenon (RP) from secondary RP[9].

Since then, many investigators have used NFC for studying several diseases in the early 20th century[10,11]. They used microscopes with 100-300x magnification power, which could provide detailed images of a few capillary loops in a limited microscopic field. In 1911, Lombard discovered that placing a drop of immersion oil on periungual skin capillaries enabled easy observation of human capillaries[12]; this finding influenced Weiss[13] who standardized capillaroscopic techniques and produced the first images of capillaries by using a primordial camera. In 1925, by following the technique of Weiss, Brown and O'Leary used capillaroscopic analysis to show the abnormalities of the microvasculature in RP of SSc[14], and these findings linked NFC and rheumatic diseases.

In 1939, Müller[15] published a large volume of color capillaroscopic atlas. However, due to the great morphological variability of individual capillary loops and the lack of healthy controls in most studies, the narrow field approach became highly subjective, and the results were not reproducible. Therefore, the NFC technique became less popular and was neglected for several decades. In the mid-20th century, the NFC technique was reexamined when Maricq[16] recognized and established the advantages of using panoramic capillaroscopy for the diagnosis of connective tissue diseases. By describing the morphological details of individual losing loops and abnormal assemblage of the capillaries, Maricq directed attention away from the wide and subtle morphological variability of individual loops and toward the recognition of the microvascular landscape. Shortly thereafter, a new technique using fluorescent tracers for capillary videomicroscopy was introduced by Bollinger in 1979[17]. In this technique, a 20% solution of sodium fluorescein is administered by bolus injection into the antecubital vein that enables the dye to reach the capillaries. By using this technique, transcapillary and interstitial diffusion of the dye can be visualized. Bollinger et al[17]. revealed that enhanced transcapillary passage of dye with the loss of the pericapillary diffusion barrier can be distinguished by RP. More recently, in 2000, the Italian physician Cutolo et al[18]. further refined the findings of Maricq by defining 3 major nailfold videocapillaroscopic (NVC) patterns as early, active and late stages. These stages were used to assess the appearance and progression of sclerodermic microangiopathy.

A simple history of nailfold capillaroscope is shown in Table 1. Nailfold capillaroscopic analysis

was mainly developed at the end of the last century, and the most recent development is computer-based nailfold video capillaroscopy system, which can record images, enhance image quality, and show real-time blood flow and velocity. In addition, laser Doppler imaging (LDI) is a relativity new method for measuring the microcirculation of peripheral perfusion[19]. The NFC and LDI can be used together to detect secondary RP or in distinguishing whether the reduced blood flow is due to primary/secondary autoimmune diseases. The technique is now recognized as a safe, noninvasive, and repeatable method of microvascular investigation[20].

Standard technique for capillaroscope operation

The study of NFC in patients with rheumatic disorders analyzes the nailfold skin. This is because in this area, the major axis of the capillaries is parallel to the skin surface, whereas in other skin areas, the capillaries run perpendicular to the skin surface. Ideally, patients should be seated indoors for at least 15 minutes and allowed to acclimatize to a room temperature of 20℃-24℃ before the examination. After depositing a drop of immersion oil on the nailfold bed to improve resolution, all nailfolds in each finger should be examined. Cedar oil is the preferable to immersion oil due to its higher viscosity. The quantity of oil must be adequate to avoid abnormal light reflex.

The nailfold capillaries of the fourth and fifth fingers of the nondominant hand are tested to achieve the best visibility. The skin in these areas is more transparent than that in other fingers. Fingers affected by recent trauma are not analyzed. Generally, NFC is performed using an NVC with changeable lenses that provide magnifications of 100x and 200x. Even minimal pressure on the nailfold should be avoided when using contact optical probes because it can compromise the vessels. In addition, a cold light source can prevent vasodilatation[1,21].

Table 1. A simple history of nailfold capillaroscope for diagnosing rheumatic diseases

● Johan Christophorous Kolhaus	1663	Used primitive microscope firstly
● Giovanni Rasori (1766–1837)		First noted the relationship between inflammation and capillary abnormality
● Brown and O'Leary	1925	Abnormal microvasculature of scleroderma
● Müller	1939	Large capillaroscopic atlas
● Hildegard Maricq	1977	Recognition of the microvascular landscape
● Alfred Bollinger	1979	Pioneer of fluorescence videomicroscopy
● Maurizio Cutolo	2000	Capillaroscopic training course

Capillaroscopic microvascular morphology

During capillaroscopic examination, the following microvascular morphology should be observed and documented: tortuosity, loop size, density, angiogenesis, capillary loss, microbleeding, subpapillary venous plexus, and architectural structure[1,18,21,22].

Tortuosity

In a healthy subject, capillary morphology is "reverse U-shaped" or "hairpin-like" in appearance. Tortuosity is usually a physiological variation that refers to an irregular or undulating appearance with single/multiple crossover looking like "treble clef" loop, "antler" loop, "trefoil" loop, or "glomerule" loop. Tortuosity has limited diagnostic value but may indicate angiogenesis in some diseases[23].

Loop size

The length of the nailfold capillaries is rather variable, and the measurement is further complicated by differences in skin transparency. The capillary length of the fourth and fifth fingers is always longer than that of the other fingers[21]. The average length is 475 μm, and a length exceeding 700 μm is defined as loop elongation[21].

The diameter of the afferent limb capillary can vary from 6 to 19 μm (mean value: 11 $\pm$ 3 μm) and the diameter of the efferent limb is 8-20 μm

(mean value: 12 ± 3 μm)[20]. The efferent (or venous) limb is usually of greater diameter than the afferent (or arterial) limb, but the venous limb: arterial limb diameter ratio does not exceed 2:1[21].

A definite abnormally large capillary loop is characterized by a 4-fold increase in the size or capillary diameter exceeding 20 μm. Enlarged capillaries may exhibit homogeneous or heterogeneous (or irregular) enlargement in the afferent and efferent limbs. Additionally, capillaries with a 10-fold larger diameter than the normal range or more than 50 μm are referred to as giant capillaries or megacapillaries (Figure 1). The presence of homogeneously and/or irregularly enlarged microvascular loops is one of the earliest and most striking features of secondary RP.

Density

At the nailfold, each dermal papilla has 1 to 3 capillaries. Nine to 13 capillaries per millimeter or 10 to 30 capillaries per square millimeter are visible.

Angiogenesis

The features of capillary neoformation may be heterogeneous. Highly tortuous and arborized capillary loop clusters, often surrounded by a dropout of normal capillary loops, are a characteristic feature of angiogenesis and are indicated by the following: (1) extremely tortuous, branching, "bushy" and "coiled" capillaries (2) more than 4 capillaries within a dermal papilla (3) extremely elongated loops; and (4) thin, branching, and interconnected capillaries. These morphological features of capillary neoformation may be observed in patients with secondary RP, particularly related to SSc or DM[24,25].

Loss of capillaries (avascular areas)

A decreased number of loops (<30 over 5 mm length in the distal row of the nailfold) or loss of capillaries in a field of at least 500 μm should be considered an avascular area. This pattern is highly characteristic of SSc. Loss of capillaries may be related to tissue hypoxia. Avascular areas also have prognostic value because they have been reported to be associated with more progressive diseases[26].

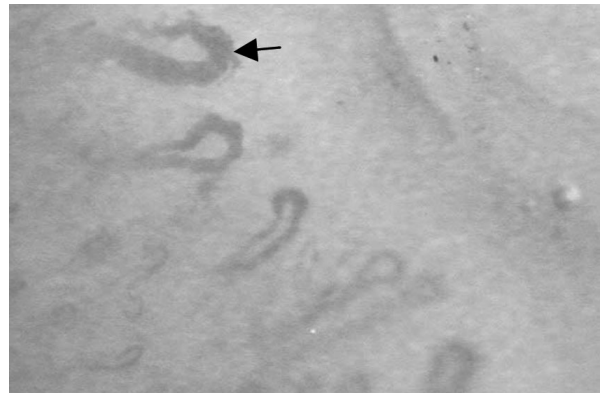

Fig.1. Microscopic image of nailfold of a scleroderma patient showing megacapillary (arrow) and irregular capillary orientation.

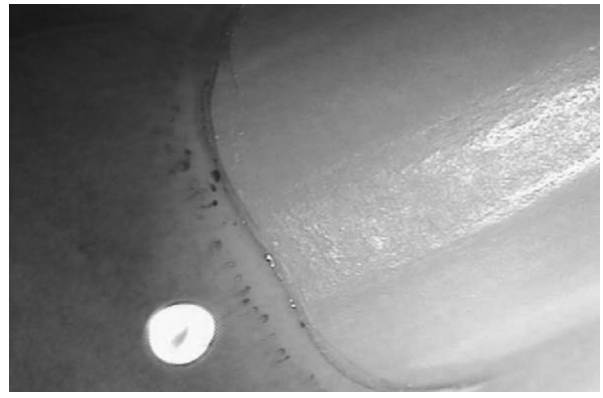

Fig.2. Presence of microhemorrhage and enlarged capillary loops visible in low-power field (10X). An artificial light reflex is noted near the nailfold.

Microbleeding and capillary thrombosis

Microbleeding (or microhemorrhage) is also associated with early vascular damage and it appears as an easily detectable dark spot. Traumatic bleeding should be excluded. Microbleeding may also be related to capillary thrombosis that can occur in some rheumatic disorders, including SSc and antiphospholipid syndrome (APS)[27]. Capillary thrombosis may be misinterpreted as microbleeding. A prominent feature of thrombosis is the shape of the dark area, which mirrors that of the capillary loop (Figure 2).

Subpapillary venous plexus

The deep arterial plexus connects with superficial vessels and finally with terminal arterioles, which begin the afferent limb of the capillary loops. These loops continue perpendicularly into the dermal papilla. The efferent limb merges with the superficial subpapillary venous plexus and intercommunicates with deep venous plexuses. Only the subpapillary venous plexus and the capillaries in the dermal papillae are visible by NFC[22]. The plexus is also subject to the level of skin transparency and the major axis, which is generally perpendicular to that of the capillaries (Figure 3). The subpapillary venous plexus is visible in approximately one-third of healthy humans[21].

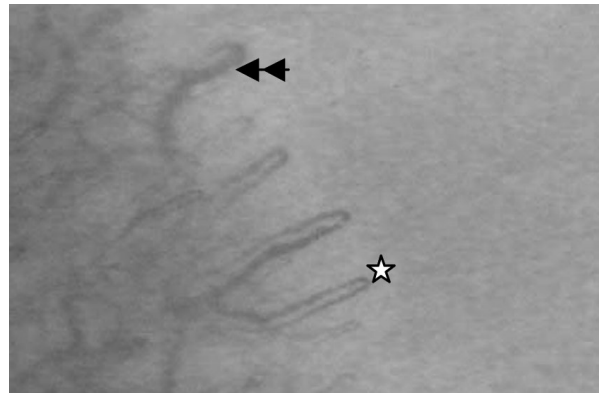

Fig.3. Capillary morphological anomalies with subpapillary venous plexus and homogeneously dilated efferent limb (arrow). Normal (typical) capillary loop looks hairpin (star).

Architectural structure

A major change in the architecture of the capillary network is the microvascular involvement of scleroderma. The following characteristics of NFC contribute to the alteration altering of the normal architecture[28]:

—capillaries not in one row as normal

—small areas (<500 μm) with missing capillaries next to the areas with clusters of capillaries

—altered capillary distribution

—heterogeneity of loop shapes

—irregular capillary orientation

Capillaroscopy in Rheumatic Diseases

Capillary changes observed by NFC have been well documented in several rheumatic disorders, particularly in RP, SSc, and SSc-like diseases (Table 2). Meli et al.[28] reported 308 RP patients without serological findings or clinical signs of connective tissue disease (CTD) but with pathological NFC features indicating CTD. Follow-up data were available for 133 patients. In these patients, the presence of giant capillaries, avascular fields, or irregular NFC architecture was predictive of the development of a CTD, mainly scleroderma, CREST (calcinosis, RP, esophageal dysmotility, sclerodactyly, and telangiectases) syndrome, and MCTD. In another follow-up study assessing the prognostic value of capillaroscopy findings for the development of connective tissue disease in children and adolescents with RP, a group of 250 patients (mean age, 15 years) was followed up for 1 to 6 years after their first capillaroscopy. Capillary changes were classified into 3 types: normal, nonspecific, or sclerodermatous. Children and adolescents who developed scleroderma spectrum disorders displayed sclerodermatous type of capillary changes 6 months before expressing the disease: this indicates that this capillary change in children and adolescents with RP is highly correlated with further development of scleroderma spectrum disorders[29]. Therefore, NFC is an effective technique for prognosis and prediction of RP[28-30].

In 1981, H. R. Maricq[25] first described SSc pattern as enlargement of capillary loops, loss of capillaries, disruption of capillary bed and distortion and budding of capillary or hemorrhage. Later, giant capillaries and loss of capillaries were included as SSc patterns, which exhibited 80% and 89% diagnostic sensitivity and specificity, respectively[31]. In addition, in a recent European study of

Table 2. Summary of the frequencies of capillaroscopic patterns in rheumatic diseases reported in previous studies#

	Long loop	Tortuosity	Enlarged loop	Giant loop	Avascular area	Micro hemorrhage	Angio genesis	Subpapillary venous plexus
Health subject	–/+	+	+	–	–	–/+	+	++
Primary RP	+	++	–/+	–	–	–/+	+	–/+
SSc	++	+	+++	+++	+++	++	++	+
SLE	+++	+	++	+	+	+	++	++
RA	++	+	+	–	–	+	–/+	++
PM	+	+	+	++	++	+	–/+	+
DM	+	+	+++	+++	+++	+	+	+
MCTD	+	++	+++	+++	+	+	+	+
Sjögren's syndrome	+	++	++	–/+	–	+	+	++
Cryo globulinemia	?	?	?	–/+	–/+	++	+++	++
APS	–/+	+	+	–/+	–/+	+++	+	+

RP, Raynaud's phenomenon; SSc, systemic sclerosis; SLE, systemic lupus erythematosus; RA, rheumatic arthritis; PM, polymyositis; DM, dermatomyositis; MCTD, mixed connective tissue disease; APS, antiphospholipid syndrome.

*Frequency: -, 0%; -/+, 0-10%; +,10-30%; ++, 30-50%; +++, >50%; ?, no data.

Reference: 1,3,4,5,6,18,22,23,25,28,32,36,38,40,41,43-46.

NFC in 447 patients with CTD and Raynaud's disease, 14 of the 16 (87.5%) patients with diffuse cutaneous SSc and 53 of the 86 (61.6%) patients with limited cutaneous SSc exhibited the SSc capillary pattern. Nine of the 65 (13.8%) cases with undifferentiated connective tissue disease (UCTD) and 24 of the 186 (12.9%) cases with RP also presented the same pattern. Four of the 47 (8.5%) patients with SLE, 7 of the 26 (26.9%) patients with dermatomyositis/polymyositis, and none of the patients with rheumatoid arthritis or Sjögren's syndrome (SS) exhibited the SSc capillary pattern[6]. These findings suggest that the "SSc pattern" is often present in SSc and dermato/polymyositis. Another study that evaluated the association of capillaroscopic alterations with pulmonary disease activity in SSc indicated that the severity of NFC abnormalities is associated with lung disease activity in SSc, particularly when the disease duration is relatively short[32]. Additionally, a case report study of long-term treatment of SSc patients with cyclosporin A (CsA) revealed progressive improvement in capillary lesions during the first 2 years of CsA therapy[33]. Therefore, NFC seems to be a useful tool for the early selection of candidates who develop SSc spectrum disorders associated with disease severity.

A consistent pattern of DM has been reported[34,35]. This pattern, which is somewhat similar to the SSc pattern, includes the presence of 2 or more of the following characteristics in at least 2 nailfolds: large capillary loops, loss of capillaries, disorganization of capillary distribution, "budding" ("bushy") capillaries, twisted enlarged capillaries and capillary haemorrhages[36]. Enlarged capillary loops are more common in patients with DM (56%) than in those with PM (21%)[37]. Avascular lesions occur in both PM and DM but are more prevalent and more severe in patients with DM. With regard to severity, nailfold capillary abnormalities reveal no correlation with active myositis or residual muscle weakness [37].

Characteristic SLE patterns are less consistent. These findings, which include meandering capillary loops, prominent sub-papillary venous plexus and extremely long capillary loops (>750 μm) are

more acceptable and reported more frequently by investigators[16,37]. Additionally, the presence of avascular areas and enlarged or giant loops in SLE, are associated with the presence of RP and anti-U1-RNP antibodies alone or in combination[36]. Moreover, NFC changes in SLE correlate with disease activity or systemic manifestation[39-41].

Microvascular alterations caused by APS have been observed. Cutolo et al. reported symmetrical hemorrhage in a nailfold analysis, particularly in patients showing serum IgG and IgM anticardiolipin antibodies[27]. However, a subsequent case-control study revealed no specific NFC pattern in patients with anticardiolipin antibodies[42]. A recent study of primary APS patients in Brazil confirmed the alteration of nailfold capillary morphology, but these changes could not be correlated with impaired functional capillary density and blood flow velocity[43].

Capillaroscopic changes have also been observed in primary SS[44]. Forty SS patients, including 14 without RP, 16 with RP and 10 with anticentromere antibodies (ACA), were evaluated by NFC. Capillaroscopic abnormalities in SS ranged from nonspecific findings (crossed capillaries) to more specific findings (confluent hemorrhages and hemorrhages) or SSc-type findings. SS patients with RP presented with capillary abnormalities more frequently than patients without RP. Most (80%) SS patients with ACA showed SSc pattern, and this finding was considerable as overlapping presentation of autoimmune diseases. NFC is a simple noninvasive method for evaluating microvascular abnormalities in SS patients, especially in those with RP and ACA. However, another study reported different NFC findings in SS patients who did not show SSc pattern[6].

In rheumatoid arthritis (RA) patients, elongated and tiny capillaries and tortuosity are the primary abnormal patterns in NFC. Subpapillary venous plexus is another typical finding, especially in patients with positive antinuclear antibody[45].

In addition to the above mentioned studies, we also revealed the frequencies of capillaroscopic

Table 3. Frequencies of capillaroscopic patterns in rheumatic diseases with RP in authors' hospital

	Long loop(%)	Tortuosity (%)	Enlarged loop (%)	Giant loop (%)	Avascular area (%)	Micro hemorrhage (%)	Angio genesis (%)	Subpapillary venous plexus (%)	Thickening skin (%)
SLE (No. = 11)	9%	91%	72.7%	9%	18%	64%	27%	45%	0%
RA (No. = 4)	0%	100%	75%	25%	0%	0%	75%	50%	0%
Sjögren's syndrome (No. = 4)	50%	25%	50%	25%	0%	25%	25%	50%	25%
SSc (No. = 8)	13%	75%	63%	38%	63%	63%	63%	13%	38%
PM/DM (No. = 0)	0%	0%	0%	0%	0%	0%	0%	0%	0%
MCTD (No. = 3)	0%	100%	67%	33%	0%	67%	0%	0%	33%
UCTD (No. = 17)	12%	65%	65%	18%	12%	29%	18%	24%	53%
Primary RP (No. = 16)	19%	94%	44%	0%	6%	25%	25%	19%	44%
Cryo globulinemia (No. = 16)	19%	81%	50%	13%	13%	19%	19%	31%	50%
APS (No. = 2)	0%	100%	50%	0%	0%	50%	0%	0%	50%

UCTD: undifferentiated connective tissue disease.

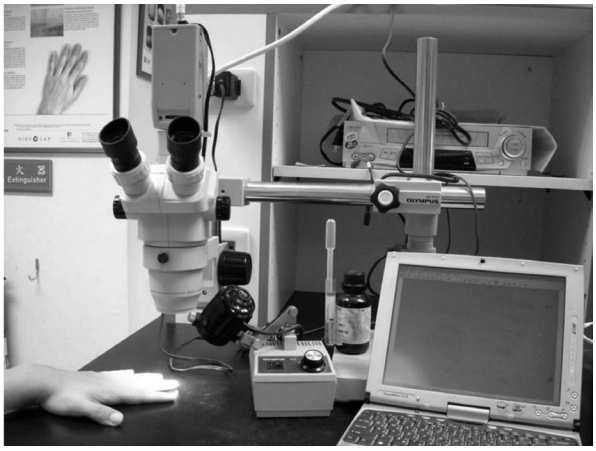

Fig.4. The present nailfold capillaroscope in authors' hospital (Olympus SZ-ZTU1).

patterns in rheumatic diseases with RP in our hospital (Table 3). We studied 97 patients, including 17 males and 80 females, who were underwent nailfold capillaroscopic examination (figure 4) during 2005-2008. Indications of NFC in these patients were RP (91), digital ulcer (4) and disease follow-up (2). Clinical diagnosis were SLE (11), RA (4), SSc (8), SS (4), MCTD (3), UCTD (17), primary RP (16), cryoglobulinemia (16), APS (2), and other diseases, including adrenal adenoma (1), palindromic rheumatism (2), peripheral arterial occlusive disease (4), cryofibrinogenemia (2), pulmonary hypertension (1), and psoriatic arthritis (1). Although, the frequencies of capillaroscopic patterns in rheumatic diseases with RP in our hospital differed from those reported in previous studies (Table 2), we suggest that further well-designed NFC studies are required.

Conclusions

Although NFC lacks specificity, it is a noninvasive, easy, repeatable, safe, and inexpensive method of evaluating microvascular abnormalities in rheumatic diseases. This method is indicated not only for distinguishing between primary and secondary RP but also for adjuvant diagnosis of rheumatic diseases. For the follow-up of disease processes, NFC also enables survey of digital ulceration or ischemic changes, as well as assessment of disease severity. Additionally, improved methods of reading NFC enable the investigation of clinical correlations and the extent of organ involvement, prognosis, change of disease, and therapeutic response.

References

1. Cutolo M, Pizzorni C, Sulli A. Capillaroscopy. Best Pract Res Clin Rheumatol 2005; 19: 437-52.
2. Lonzetti LS, Joyal F, Raynauld JP, et al. Updating the American College of Rheumatology preliminary classification criteria for systemic sclerosis: addition of severe nailfold capillaroscopy abnormalities markedly increases the sensitivity for limited scleroderma [letter]. Arthritis Rheum 2001; 44: 735-6.
3. Bukhari M, Hollis S, Moore T, Jayson MI, Herrick AL. Quantitation of microcirculatory abnormalities in patients with primary Raynaud's phenomenon and systemic sclerosis by video capillaroscopy. Rheumatology (Oxford) 2000; 39: 506-12.
4. Kabasakal Y, Elvins DM, Ring EF, McHugh NJ. Quantitative nailfold capillaroscopy findings in a population with connective tissue disease and in normal healthy controls. Ann Rheum Dis 1996; 55: 507-12.
5. Sarrat P. Periungual capillaroscopy in children with scleroderma and dermatomyositis. J Mal Vasc 1983; 8: 175-7.
6. Nagy Z, Czirjak L. Nailfold digital capillaroscopy in 447 patients with connective tissue disease and Raynaud's disease. J Eur Acad Dermatol Venereol 2004; 18: 62-8.
7. Callender CL. Photomicrographic studies of morphology of surface capillaries in health and disease. JAMA 1925; 84: 352-56.
8. Duryee AW, Wright IS. Study of human capillaries. Am J Med Sci 1933; 185: 664-73.
9. Hutchinson H. Raynaud's phenomenon. Presse Med 1901; 71: 403-5.
10. Leader SD. Capillary microscopy in children. Am J Dis Child 1932; 44: 403-16.
11. Müller O. Pathologie des Capillaries humains. J Physiol Pathol Gen 1941; 38: 52-62.
12. Lombard WP. The blood pressure in the arterioles, capillaries, and small veins of the human skin. Am J Physiol 1911; 29: 355-62.
13. Weiss W. Demonstration von Hautkapillarveraenderungen bei akuter Nephritis. Med Bl Landerver 1916; LXXXVI: 383.
14. Brown GE, O'Leary PA. Skin capillaries in scleroderma. Arch Intern Med 1925; 36: 73-88.
15. Müller O. Die feinsten blutgefäessen des menschen. Stuttgart: E. Enke Verlag; 1939.
16. Maricq HR, LeRoy EC. Patterns of finger capillary abnormalities in connective tissue disease by "wide-field" microscopy. Arthritis Rheum 1973; 16: 619-28.

17.Bollinger A, Jäger K, Roten A, Timeus C, Mahler F. Diffusion, pericapillary distribution and clearance of Na-fluorescein in the human nailfold. Pflugers Arch 1979; 382: 137-43.
18.Cutolo M, Sulli A, Pizzorni C, Accardo S. Nailfold videocapillaroscopy assessment of microvascular damage in systemic sclerosis. J Rheumatol 2000; 27: 155-60.
19.Szabo N, Csiki Z, Szanto A, Danko K, Szodoray P, Zeher M. Functional and morphological evaluation of hand microcirculation with nailfold capillaroscopy and laser Doppler imaging in Raynaud's and Sjögren's syndrome and poly/dermatomyositis. Scand J Rheumatol 2008; 37: 23-9.
20.Anderson ME, Allen PD, Moore T, Hillier V, Taylor CJ, Herrick AL. Computerized nailfold video capillaroscopy--a new tool for assessment of Raynaud's phenomenon. J Rheumatol 2005; 32: 841-8.
21.Grassi W. Basic findings in capillaroscopy. Grassi W, Del Medico P. Atlas of capillaroscopy. 1st Ed, Italy, EDRA, 2004; 10-25.
22.Andrade LE, Gabriel Junior A, Assad RL, Ferrari AJ, Atra E. Panoramic nailfold capillaroscopy: a new reading method and normal range. Semin Arthritis Rheum 1990; 20: 21-31.
23.Hern S, Mortimer PS. In vivo quantification of microvessels in clinically uninvolved psoriatic skin and in normal skin. Br J Dermatol 2007; 156: 1224-9.
24.Leteurtre E, Hachulla E, Janin A, Hatron PY, Brouillard M, Devulder B. Vascular manifestations of dermatomyositis and polymyositis. Clinical, capillaroscopic and histological aspects. Rev Med Interne 1994; 15: 800-7.
25.Maricq HR. Wide-field capillary microscopy. Arthritis Rheum 1981; 24: 1159-65.
26.Chen ZY, Silver RM, Ainsworth SK, Dobson RL, Rust P, Maricq HR. Association between fluorescent antinuclear antibodies, capillary patterns, and clinical features in scleroderma spectrum disorders. Am J Med 1984; 77: 812-22.
27.Sulli A, Pizzorni C, Cutolo M. Nailfold videocapillaroscopy abnormalities in patients with antiphospholipid antibodies. J Rheumatol 2000; 27: 1574-6.
28.Meli M, Gitzelmann G, Koppensteiner R, Amann-Vesti BR. Predictive value of nailfold capillaroscopy in patients with Raynaud's phenomenon. Clin Rheumatol 2006; 25: 153-8.
29.Pavlov-Dolijanovic S, Damjanov N, Ostojic P, et al. The prognostic value of nailfold capillary changes for the development of connective tissue disease in children and adolescents with primary raynaud phenomenon: a follow-up study of 250 patients. Pediatr Dermatol 2006; 23: 437-42.
30.Ingegnoli F, Boracchi P, Gualtierotti R, et al. Prognostic model based on nailfold capillaroscopy for identifying Raynaud's phenomenon patients at high risk for the development of a scleroderma spectrum disorder: PRINCE (prognostic index for nailfold capillaroscopic examination). Arthritis Rheum 2008; 58: 2174-82.
31.McGill NW, Gow PJ. Nailfold capillaroscopy: a blinded study of its discriminatory value in scleroderma, systemic lupus erythematosus, and rheumatoid arthritis. Aust N Z J Med 1986; 16: 457-60.
32.Bredemeier M, Xavier RM, Capobianco KG, et al. Nailfold capillary microscopy can suggest pulmonary disease activity in systemic sclerosis. J Rheumatol 2004; 31: 286-94.
33.Filaci G, Cutolo M, Basso M, et al. Long-term treatment of patients affected by systemic sclerosis with cyclosporin A. Rheumatology (Oxford) 2001; 40: 1431-2.
34.Klyscz T, Bogenschutz O, Junger M, Rassner G. Microangiopathic changes and functional disorders of nail fold capillaries in dermatomyositis. Hautarzt 1996; 47: 289-93.
35.Ganczarczyk ML, Lee P, Armstrong SK. Nailfold capillary microscopy in polymyositis and dermatomyositis. Arthritis Rheum 1988; 31: 116-9.
36.Bergman R, Sharony L, Schapira D, et al. The handheld dermatoscope as a nail-fold capillaroscopic instrument. Arch Dermatol 2003; 139: 1027-30.
37.Granier F, Vayssairat M, Priollet P, Housset E. Nailfold capillary microscopy in mixed connective tissue disease. Arthritis Rheum 1986; 29: 189-95.
38.Furtado RN, Pucinelli ML, Cristo VV, Andrade LE, Sato EI. Scleroderma-like nailfold capillaroscopic abnormalities are associated with anti-U1-RNP antibodies and Raynaud's phenomenon in SLE patients. Lupus 2002; 11: 35-41.
39.Riccieri V, Spadaro A, Ceccarelli F, Scrivo R, Germano V, Valesini G. Nailfold capillaroscopy changes in systemic lupus erythematosus: correlations with disease activity and autoantibody profile. Lupus 2005; 14: 521-5.
40.Ingegnoli F, Zeni S, Meani L, Soldi A, Lurati A, Fantini F. Evaluation of nailfold videocapillaroscopic abnormalities in patients with systemic lupus erythematosus. J Clin Rheumatol 2005; 11: 295-8.
41.Kuryliszyn-Moskal A, Klimiuk PA, Sierakowski S, Ciolkiewicz M. Vascular endothelial growth factor in systemic lupus erythematosus: relationship to disease activity, systemic organ manifestation, and nailfold capillaroscopic abnormalities. Arch Immunol Ther Exp 2007; 55: 179-85.
42.Vayssairat M, Abuaf N, Deschamps A, et al. Nailfold capillary microscopy in patients with anticardiolipin antibodies: a case-control study. Dermatology 1997; 194: 36-40.
43.Vaz JL, Dancour MA, Bottino DA, Bouskela E. Nailfold videocapillaroscopy in primary antiphospholipid syndrome (PAPS). Rheumatology 2004; 43: 1025-7.
44.Tektonidou M, Kaskani E, Skopouli FN, Moutsopoulos HM. Microvascular abnormalities in Sjogren's syndrome: nailfold capillaroscopy. Rheumatology 1999; 38: 826-30.
45.Altomonte L, Zoli A, Galossi A, et al. Microvascular capillaroscopic abnormalities in rheumatoid arthritis patients. Clin Exp Rheumatol 1995; 13: 83-6.
46.Rossi D, Mansouri M, Baldovino S, et al. Nail fold videocapillaroscopy in mixed cryoglobulinaemia. Nephrol Dial Transplant 2004; 19: 2245-9.

甲褶微血管顯微鏡（甲褶鏡）在風濕性疾病的應用與角色

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摘　要

末梢血管病變和全身性發炎疾病的關係密不可分。其中屬於風濕性疾病的雷諾氏症和硬皮症的微血管變化更是明顯異常。而甲褶鏡是一種用顯微放大原理來觀察手指末端微血管變化的一種檢查方式。它對於評估風濕病的微循環可以是非侵入性、方便、簡單、可重覆以及高敏感度的一種檢查。借藉由輔以新式影像攝影系統，甲褶鏡更容易及清楚的分析微血管變化。目前，對用在鑑別原發性或次發性雷諾氏症、硬皮症、皮肌炎的輔助診斷和全身性紅斑狼瘡的疾病活性變化等都有一定價值。因此本文藉由文獻回顧來分析微血管變化和風濕病的關係。