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Review

The role of nail-videocapillaroscopy in early diagnosis of scleroderma

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ABSTRACT

Raynaud's phenomenon (RP) is a clinical sign of precocious abnormal microcirculation and can be considered a major risk factor for the development of connective tissue disease, especially systemic sclerosis (SSc). Nailfold videocapillaroscopy is the most valuable tool for the early diagnosis of SSc and related disorders. It allows classification of capillary abnormalities. Scoring capillaroscopic alterations, which change significantly during patient follow-up, should be systematically used in order to monitor microangiopathy. The effectiveness of the nailfold videocapillaroscopy in allowing an early diagnosis of SSc and monitoring the progression of the disease, and its predictive value of clinical complications make it a powerful tool for clinical evaluation and research.

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1. Introduction

Although the structural vascular disease in scleroderma is patent, the nature of endothelial injury is still elusive, yet markers of endothelial activation and injury continue to be proposed. However, the assessment of microvascular function by laboratory methods is not specific or sensitive [1].

Despite a large prevalence in the general population [2], Raynaud's phenomenon remains a typical manifestation of vascular involvement in scleroderma. It is characterized by intense vasospasm of the digital arteries under cold exposure or emotional stress, which leads to

characteristic color changes in the skin of the fingers, which is the expression of the imbalance between vasoconstrictor and vasodilator factors [3]. It may be primary or secondary to an underlying condition, especially immune-mediated diseases [4]. Physical examination, nailfold capillaroscopy and immunological tests can distinguish primary from secondary forms.

Capillaroscopy is an imaging technique, which is used in medicine since 1823, when Purkinje described skin capillaries by observing the nail-bed with a magnifying glass. One century later (1911), it was discovered that, using a drop of immersion oil, capillaries became visible for examination by microscope. More recently, Maricq and Le Roy described the specific capillaroscopic pattern in systemic sclerosis.

Nowadays, thanks to its greater magnification (from $50 \times$ to $1000 \times$), the digital videocapillaroscopy, which consists of a microscope assembled with a digital videocamera, represents the gold standard for

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assessing or measuring capillaroscopic parameters. Furthermore, nailfold capillaroscopy is a non-invasive, inexpensive, easy to repeat imaging technique, which is of considerable importance for the evaluation of microcirculation in vivo [5].

2. Capillaroscopic technique

In order to evaluate capillaries a drop of cedar oil has to be placed on the finger nailfold. A precise morphologic evaluation may be obtained by examining the fourth and the fifth finger of both hands due to the high transparency of the skin in these areas [5,6]. However, all fingers from second to fifth should be examined, since early capillary alterations may be on occasionally present in only a few digits. Each patient should stay inside the examination room, at a temperature of 23–25 °C, for 10–15 min before the nailfold is examined.

The images are generated by lens providing a magnification \times 200, and a charged-coupled device (CCD) camera giving high-resolution images (752 \times 582 pixels). Only the capillaries in the distal row are observed. A 1 mm grid is used to quantify capillary density and width. Usually 4 fingers on each hand are examined, and at least 8 photo-micrographs are taken of each patient [7].

The following parameters are routinely evaluated: capillary distribution and width, presence of dilated and giant capillaries, loss of capillaries, presence of hemorrhages and signs of neoangiogenesis (meandering and ramified capillaries) [8–16]. Generally speaking, a capillaroscopic feature is considered an abnormal finding if changes are observed in at least two fingers [5,6].

3. Clinical implications

Capillaroscopy is of crucial importance for the differentiation of primary and secondary RP in rheumatic diseases, and also in differentiation between different forms of connective tissue diseases as well as for their early diagnosis [17].

The detection of abnormal capillaroscopic patterns has high positive predictive value for the development of systemic rheumatic disease [18].

The most specific pattern is the so called "scleroderma pattern", which is characterized by the presence of giant capillaries, hemorrhages, avascular areas and neoangiogenesis. It is found in more than 90% of patients with overt SSc. Similar changes, called "scleroderma-like patterns", are found in patients with dermatomyositis, mixed connective tissue disease, undifferentiated connective tissue disease and overlap syndromes [6,9,10,16]. Absence of abnormal capillaroscopic findings can be regarded as a diagnostic criterion for primary RP.

3.1. Normal pattern

In normal conditions, the microvascular pattern is characterized by a regular array of microvessels with large intra/interindividual variability [19]. Usually, capillaries show a perpendicular disposition to the nailfold edge, with a capillary diameter lower than 20 μm , and at least 9 capillaries per linear millimeter are present.

3.2. Primary RP

The suggested criteria for primary RP include symmetric attacks, absence of tissue necrosis or ulceration or gangrene, absence of a secondary cause, negative tests for antinuclear antibodies and normal erythrocyte sedimentation rate. Nailfold capillaries are usually normal-shaped and no specific alterations are present [20].

A diagnosis of primary RP means that no underlying disease has yet been identified, but it is difficult to predict if and when it may become secondary RP [21–24]. Therefore, a follow-up nailfold capillaroscopic analysis is recommended to be performed every 6 months [9,10].

Women are 4–20 times more likely than men to develop primary RP. A presentation with symmetrical vasospastic attacks and a benign course without skin lesions is typical [25,26]. The onset of the disease is usually at puberty and is more frequent in certain families [5].

3.3. Secondary RP

Secondary RP includes a wide spectrum of diseases ranging from peripheral artery disorders and connective tissue diseases (CTDs) to paraneoplastic syndromes [27,28]. Onset age, which is older than primary PR, clinical signs of autoimmune disease, trophic alterations of the fingers [29,30], positive autoantibodies [5] and abnormal capillaroscopic findings are suggestive features of secondary RP.

As calculated by meta-analysis, a secondary disorder develops in 12.6% of patients with presumed primary RP. Other studies reported that 15–20% of patients initially diagnosed as affected by primary RP transitioned to secondary RP over a mean follow-up of 2 years [31,32].

Notably, RP is the first manifestation in about 90% of patients with SSc [24.33–36].

The microvascular damage in SSc [37] is mainly characterized by increasing structural alterations of the capillaries with progressive decrease in their density [38]. Blood flow is also altered, with an average slowing of flow and increased periods of stasis [19]. Nagy et al. found specific abnormalities in 87.5% of patients with diffuse and in 61.6% with limited form of SSc [5] by evaluating advanced capillary changes. Conversely, by assessing both early and advanced capillary

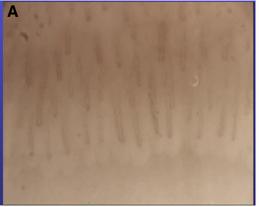




Fig. 1. A. Normal nailfold capillaroscopic pattern showing regular disposition of the capillary loops along the nail bed. B. Scleroderma pattern early. The arrow indicates a single giant capillary.

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