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# CAPILLAROSCOPY AS A PROGNOSTIC TOOL FOR THE DEVELOPMENT OF CONNECTIVE TISSUE DISEASE IN PATIENTS WITH RAYNAUD'S PHENOMENON

# KAPILAROSKOPIJA KAO PROGNOSTIČKO ORUĐE RAZVOJA BOLESTI VEZIVNOG TKIVA U BOLESNIKA S RAYNAUDOVIM FENOMENOM

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Nailfold capillaroscopy (NC) is a non-invasive, useful, easy to perform and repeate imaging method for the in vivo observation of small blood vesels in the skin, and analysis of microvascular abnormalities in rheumatic diseases (1,2,3). Major role of NC in rheumatic diseases is to predict the future development of the connective tissue disease (CTD) in subjects with Raynaud's phenomenon (RP (4,5,6,7,8,9).

Raynaud's phenomenon (RP) is condition resulting in episodic discoloration of the fingers and/or the toes triggered by cold or emotional stress. Abnormal spasm of the blood vessels causes a diminished blood supply to the local tissues and results in paleness, followed by cyanosis and hyperemia of the digits. RP can be of unknown cause ("primary" RP), or connected to a number of different diseases ("secondary" RP), among which are some connective tissue diseases (CTDs). Associated connective tissue disease (CTD) could develop in 3%, up to 49% of patients with RP during the follow up (5). Early detection of CTD in subjects with RP is crucial for early treatment. Nailfold capillaroscopy (NC) is considered one of the very important methods to screen subjects with RP for future development of CTD (4,5,6,7,8,9). It is proven to be helpful in the early differential diagnosis of RP (4,5,6,7,8,9), but additional long-term follow up studies assessing the validity of NC in predicting the development of CTD in subjects with RP are still needed.

Typical NC microangiopathy changes, named "Scleroderma Pattern" (reduced number of capillary loops with so-called avascular areas, irregularly enlarged and giant capillaries, sometimes combined with microbleeding and ramified capillaries) could be seen in vast majority of patients with Systemic Sclerosis and scleroderma related disorders (8,10,11). The extent of NC abnormalities can correlate with pulmonary hypertension (11). Scleroderma pattern (SD pattern) of microangiopathy, seen by NC in subjects with RP, could predict future development of CTD (5,8,9).

We have been following group of 3035 pts with RP (2702 female and 333 male) patients (pts) with RP (12,13), assessing the prognostic value of SD pattern of NC microangiopathy for the development of CTD. If a patient with RP developed CTD during the follow up period of at least 1 year, we have been taking in to analysis only his NC examination finding from the examination that took place at least 6 months before the CTD was diagnosed.

At the end of 1-10 years follow-up period, 1129/3035 (37,2%) pts had secondary RP, and among them 11 different CTDs were recorded. During the follow up 363 (11.96%) pts have been diagnosed as having undifferentiated CTD (UCTD, 263 (8.66%) pts had systemic sclerosis (SSc), 143 (4.4%) pts had systemic lupus erythematosus (SEL), 106 (3,5%) pts had rheumatoid arthritis (RA), 102 (3.4%) pts had Sjögren's syndrome (SS), 61 (2,01%) pts had overlap syndrome (OS) with some signs of SSc. Rare diseases in this large group of patients with RP (less than 1% of pts in each group) were systemic vasculitides, polymyositis/dermatomyositis (PM/DM), mixed connective tissue disease (MCTD), primary antiphospholipid syndrome (APs), psoriatic arthritis (PsA) and ankylosing spondilitis.

All pts with PsA, APs, and about 90% of pts with primary RP (94%), RA (93%), UCTD (91%), SEL (90%), systemic vasculitides (90%), SS (89%) had normal or nonspecific NC finding. On the contrary, almost all (246/263 - 94%) pts with SSc had SD pattern of microangiopathy. Less frequently, SD pattern of capillary changes were found in 28/61 (46%) pts with OS, 9/24

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(37%) pts with MCTD, 7/26 (27%) pts with PM/DM. All these NC findings have been recorded at least 6 months before the patient full-filed the criteria for the diagnosis of UCTD of particular CTD.

SD pattern of NC finding significantly correlated with future development of SSc in subjects with primary RP ($p<0,001$ - $\chi^2$ test) with Sensitivity 94%, Specificity 92%, Positive Predictive Value 52%, Negative Predictive Value 99%, and Odds Ratio (OR) 163. Beside extremely high OR for the future development of SSc in subjects with RP having SD pattern of NC finding, OR higher than 1 was also calculated for pts with OS and signs of SSc (OR 4,83), pts with MCTD (OR 3,30) and pts with PM/DM (OR 2,02).

Our prospective study of 3035 pts with RP showed high rate of development of CTD (37,2% of pts) during the follow up period of 1-10 years. Eleventh different CTDs were developed during the follow up period, most frequently being the systemic sclerosis. Normal capillaries or nonspecific capillary changes were predominantly seen in patients with primary RP, and in pts who developed UCTD, Sjögren's syndrome, SEL, RA, Systemic vasculitides, Psoriatic arthritis, and primary antiphospholipid syndrome.

SD pattern of capillary changes found during the examination of patients with RP as only detectable medical problem, was highly significant prognostic factor for future development of SSc, and less significant for future development of overlap syndrome with signs of SSc, PM/DM and MCTD.

Nailfold capillaroscopy is a useful method for detection of patients with high risk of future development of systemic sclerosis and overlap syndromes with signs of systemic sclerosis.


## Keywords

capillaroscopy, connective tissue disease, Raynaud's phenomenon


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