CAPILLAROSCOPY IN PATIENTS WITH EXPOSURE TO RISK FACTORS IN THE WORK ENVIRONMENT AND RHEUMATIC DISEASES

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Abstract. *Capillaroscopy is a non-invasive method for assessing microcirculation that provides important information about the condition of capillaries and the pericapillary space. The method is valuable for the diagnosis and monitoring of various diseases with manifestations of Raynaud's phenomenon (RP), such as systemic connective tissue diseases, diabetes, hypertension, occupational diseases, and other conditions that lead to microcirculation disorders. It plays an extremely important role in the early diagnosis and prognosis of these diseases, helping to detect both functional and structural changes in the capillary network, even in cases in the absence of many characteristic clinical symptoms. Raynaud's phenomenon is a disease characterized by reversible attacks of vasospasm leading to impaired peripheral circulation. It can be primary (idiopathic) or secondary (associated with other diseases). Capillaroscopy is the gold standard in rheumatology practice for differentiating primary from secondary Raynaud's phenomenon and has been included in the EULAR/ACR classification criteria for systemic sclerosis (SSc) since 2013. In primary RP, functional disorders of the capillaries are observed, without structural changes, while in secondary RP, which is associated with systemic, general or occupational diseases, it leads to various structural changes with characteristic signs of microangiopathy. The method has not only diagnostic, but also prognostic value in systemic sclerosis, lupus erythematosus, dermatomyositis, etc. Specific capillaroscopic patterns are observed – "scleroderma" and "scleroderma-like", and non-specific changes can also be detected in the early stages of the disease. In recent years, there has been an increase in publications reporting data on various capillaroscopic findings in patients with vibration disease (VD). It is a specific occupational disease caused by prolonged exposure to vibrations, which leads to microcirculatory and peripheral nerve damage, including Raynaud's phenomenon. Studies have shown that capillaroscopy provides important information about the state of microcirculation in patients with occupationally induced microangiopathy, and more specifically in cases of exposure to local and general vibrations. The method can be used for diagnosis and monitoring of these diseases, helping to detect abnormal capillaroscopic findings, including elongated capillaries, hemorrhages, and avascular zones. Capillaroscopy, as a non-invasive method, is effective for diagnosing and monitoring the progression of diseases and can be used in combination with other functional studies to better assess the patient's condition.*

Key words: *capillaroscopy, occupational diseases, rheumatic diseases*

Introduction

Nail fold capillaroscopy (NFC) is a non-invasive method included in the 2013 EULAR/ACR classification criteria for systemic sclerosis and is the "gold standard" in rheumatology practice for differentiating primary from secondary Raynaud's phenomenon (RP). RP is a vascular clinical syndrome characterized by vasoconstriction following vascular exposure or states of anxiety and stress. Capillaroscopic changes that develop following occupational risk factors (cold exposure, vibrations, toxic substances) are still scarcely and poorly defined. Of interest is microangiopathy in "occupational Raynaud's phenomenon". Dystonias with observation of spastic/dilated/crossed capillaries, aneurysmal dilations, pericapillary edema, hemorrhages, avascular zones, and reduced capillary count have been reported in patients with vibration disease (VD). At present, there is a lack of sufficient data on capillaroscopic changes in VD, but in recent years, it has been suggested that the absence of giant capillaries seems to differentiate microangiopathy in occupational exposure from the "scleroderma-like" pattern in rheumatology practice. Further studies in this direction are needed.

Methods

Publications published in global databases were reviewed – PubMed, Scopus, Google Scholar, and those that met the criteria set by keywords were

selected: Raynaud's phenomenon, capillaroscopy, vibration disease, occupational diseases, systemic sclerosis, rheumatic diseases. 65 publications were selected, of which 21 were excluded due to lack of full text or non-compliance with the inclusion criteria. Fig. 1 presents the selection of publications.

Capillaroscopy: Importance and application in the diagnosis of microcirculatory disorders

Capillaroscopy is a proven, rapid, accessible, safe, reliable, and non-invasive method for qualitative and quantitative assessment of skin microcirculation, which provides valuable information about the condition of capillaries and the pericapillary space [4, 7, 8]. The method is used to diagnose a number of diseases, including Raynaud's phenomenon (RP), connective tissue diseases (scleroderma, systemic lupus erythematosus, dermatomyositis), diabetes mellitus, arterial hypertension, polyneuropathies, and vibration disease [2, 3, 4, 7, 8, 14, 29, 31, 32, 36]. Capillaroscopy plays an important role not only in early diagnosis but also in the prognosis of these diseases, providing data on functional and structural changes in the capillary network [2, 4, 7, 8, 14, 29].

Capillary Examination: Technique and Conditions

Digital videocapillaroscopes with magnifications from 50x to 1000x are used to examine capillaries, with 200x magnification being most commonly used in clinical practice [8, 29]. The procedure is performed on the eponychium of fingers II-V of the hands at a room temperature of 21-24°C after the patient has been acclimatized for 15-20 minutes. Visibility of the capillaries is improved by using immersion oil [2, 4, 8, 14, 32]. It is important that the patient has not had cosmetic procedures (manicure) in the last 15-30 days, and has not consumed coffee or tobacco prior to the test, as these factors can lead to false-positive results. [2, 4, 8]

Raynaud's phenomenon: Primary vs. Secondary

Raynaud's phenomenon (RP) is a common pathological condition characterized by impaired peripheral circulation, in which attacks of vasospastic ischemia are reversible [4, 5, 8, 11, 12, 16, 23, 31, 34, 36, 44]. This condition is divided into primary (idiopathic) and secondary Raynaud's phenomenon. The primary phenomenon affects mainly young women and has a favorable prognosis, while the secondary phenomenon is associated with other diseases such as scleroderma, systemic lupus erythematosus, dermatomyositis, and vibration disease [4, 5, 8, 9, 11, 12, 16, 31, 34, 36, 44]. Etiological factors that provoke the phenomenon include cold exposure, stress, medications (beta-blockers, vinblastine, amphetamine, etc.), smoking, vibrations, family history, as well as existing connective tissue and arterial diseases [8, 31, 34, 36].

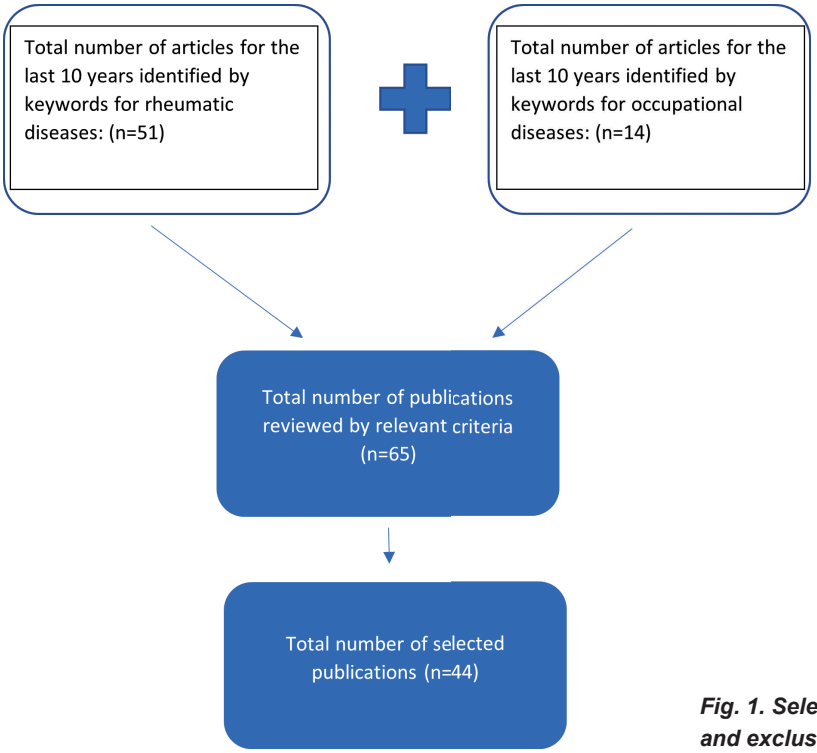


Fig. 1. Selection of publications based on inclusion and exclusion criteria

Vascular disorders – structural and functional (endothelial defects), neurogenic disorders (impaired balance between vasoconstriction and vasodilation), as well as intravascular abnormalities, especially in patients with scleroderma, play a leading role in the pathogenesis of RP [8, 31].

The clinical picture of Raynaud's phenomenon is characterized by triphasic changes in the color of the fingers (and less commonly the toes) caused by vasospasm. Initially, there is a bluish discoloration of the distal phalanges of the fingers (vasoconstrictive phase), followed by cyanosis (due to tissue hypoxia), and finally postischemic erythema upon warming (reperfusion phase) [4, 5, 8, 9, 11, 12, 31, 44]. The reduced blood supply and subsequent restoration of blood flow can result in tingling, numbness, clumsiness, burning pain, swelling, and other symptoms [5, 8, 12, 34].

Raynaud's phenomenon and capillaroscopy

Capillaroscopy is a valuable diagnostic tool for differentiating primary from secondary Raynaud's phenomenon [2, 4, 6, 7, 8, 11, 14, 29, 31, 36]. Approximately 20% of patients with primary Raynaud's phenomenon develop secondary Raynaud's phenomenon within 10 years [8, 11, 14]. Capillaroscopy findings in Raynaud's phenomenon are classified into several main types:

1. **Raynaud's phenomenon type** – In this type, a normal number of properly arranged capillaries with varying degrees of spasticity and/or dilatation (functional disorders) are observed. Structural changes in the capillaries, such as thinning, hemorrhages, and thrombosis, are absent. This type is characteristic of primary Raynaud's phenomenon [8, 31, 36].

2. **Scleroderma type** – It is observed in over 95% of patients with systemic sclerosis [4, 8] and includes a combination of dilation of the three segments of capillary loops, loss of capillaries, disorganization of the capillary network, and numerous branched and tortuous capillaries. It is characterized by hemorrhages, avascular zones, and neoangiogenesis. Cutulo et al. provide a very precise definition of the different types of scleroderma capillaroscopic appearance (the so-called early, active, and late types). The appearance is pathognomonic for systemic sclerosis [4, 7, 8, 14, 32]. It is characterized by a reduced number of capillaries, irregular arrangement, focal thinning, avascular zones, the presence of giant and dilated capillaries, hemorrhages and/or thrombosis, extravasations, and neoangiogenesis. Enlarged capillary loops are the most characteristic and earliest manifestation of secondary Raynaud's phenomenon in collagen diseases [1, 4, 7, 8, 14, 27, 31, 32, 36].

3. **Scleroderma-like type** – Includes components of the "scleroderma type", but with differences in the distribution, shape, number and size of the capillaries. Polymorphic megacapillaries (branched, bushy, arborescent, corkscrew, crossed, tortuous, folded, branched, elongated, curved, dilated), hemorrhages, ectasias, avascular zones, sludge phenomenon are observed [7, 8, 14, 30, 36]. The changes are characteristic of dermatomyositis, mixed connective tissue disease, undifferentiated connective tissue disease, and systemic lupus erythematosus. In lupus erythematosus, corkscrew capillaries with abnormal morphology and hemorrhages may also be observed [6, 8, 14]. A "comb-like" pattern of hemorrhages is seen in patients with antiphospholipid syndrome (APS) [7].

Stoyneva examined 95 patients with Raynaud's phenomenon (35 with primary and 60 with secondary) by capillaroscopy. The cause of the secondary Raynaud's phenomenon in 35 of them was systemic sclerosis, and in 25, systemic lupus erythematosus. Various functional and/or structural changes in capillary morphology have been identified during the study. In patients with primary Raynaud's phenomenon, pronounced spasm of the capillary loops is detected [36].

Capillaroscopy in rheumatology practice

In patients with scleroderma, capillaroscopy shows a specific pattern called the "scleroderma type." This includes dilation of capillary loops (arterial, intermediate, and venous segments), the presence of giant capillaries, capillary loss, disorganization of the capillary network, and numerous branched and tortuous capillaries, hemorrhages, and avascular areas. These findings are characteristic of systemic sclerosis and are used as one of the European League Against Rheumatism (EULAR) criteria for early diagnosis of this disease [2, 4, 6, 7, 8, 14, 30, 32, 36]. Similar findings are seen in other connective tissue diseases, including systemic lupus erythematosus and dermatomyositis, and these abnormalities are referred to as "scleroderma-like type" [2, 4, 6, 7, 8, 14, 36].

Microcirculatory disorders in Vibration disease

Vibration disease (VD) is a specific occupational disease, caused by chronic exposure to combined adverse production factors – general and local vibrations, tool kickback, excessive noise levels, unfavorable microclimate and cold exposure, forced working

posture, monotonous movements, heavy physical labor, static load and psycho-emotional stress, toxic noxious substances [3, 8, 12, 35]. It leads to vascular, nervous, and musculoskeletal damage, with the majority of patients developing microcirculatory and peripheral nerve disorders, including Raynaud's phenomenon, numbness, pain, and skin ulcers [3, 8, 12, 35, 38]. Workers using vibrating tools frequently develop Raynaud's phenomenon, with between 40-60% reporting vibration-induced whiteness of the fingers [9, 12]. Capillaroscopy is a valuable tool for diagnosing and monitoring microcirculatory disorders associated with vibration exposure, although the findings are not yet well defined. Studies are heterogeneous and report the presence of spastic, atonic, dilated and crossed capillaries, tortuous capillaries (20%), elongated capillaries (30%), aneurysmal dilations, pericapillary edema, hemorrhages, ectasias, avascular zones, neoangiogenesis and/or reduced total capillary number [12, 35], disorganization of the capillary network (50%), and visible subpapillary plexus (40%) [7, 8, 12, 14, 24, 36]. According to some authors, capillaroscopy may show "nonspecific changes" or "nonspecific abnormal videocapillaroscopy patterns" in patients with vibration disease [3, 8, 10, 12, 22, 24, 26, 28, 35, 37, 38].

Studies on microcirculatory disorders in occupational exposure and their diagnosis by capillaroscopy

Localized vibrations, vinyl chloride, and work at low temperatures are considered etiological factors in occupational Raynaud's phenomenon. Occupational exposure to localized vibrations is mainly associated with activities involving the use of power tools such as hammers, crushers, polishers, grinders, drills, lawn mowers, countersinks, and chainsaws [5, 35]. Vinyl chloride is a volatile substance that is rapidly absorbed through the lungs and metabolized by the liver. The end product of vinyl chloride polymerization is polyvinyl chloride (PVC), which is widely used in the plastics industry [5]. Vinyl chloride disease causes acroosteolysis, hepatopathy, neuropathy, thrombocytopenia, skin lesions, and vascular changes in the RP type [5, 35]. Since 1979, vinyl chloride has been considered by the International Agency for Research on Cancer (IARC) to be a proven human carcinogen (Group 1) [5, 33, 43]. Cold is a triggering and aggravating factor for Raynaud's phenomenon of any etiology. According to the literature review, the incidence of RP in VD varies in different studies from (0.6-83.5%); cold has not been considered as an isolated risk factor in any article, and vinyl chloride has not been discussed in any study [5].

A single publication describes bilateral nonspecific capillaroscopic changes (dilation of capillaries, no megacapillaries, rare tortuosity of capillaries, several small traumatic hemorrhages and pericapillary edema, with normal density and no avascular zones) in occupational exposure to organic solvents (xylene and acetone), with capillaroscopic changes improving one year after cessation of contact with organic solvents [44].

A study by Littleford et al. (1997) evaluated microvascular abnormalities in 10 patients with vibration-induced whiteness of the fingers. The mean age of the patients was 29-70 years, with a mean duration of disease of 11.8 years. Capillaroscopy shows mild to moderate damage, such as capillary loss (70% of patients), disorganization of the capillary network (50%), tortuous and elongated capillaries (20% and 30%, respectively), and a visible subpapillary plexus (40%). This study confirmed that dilated capillaries are not found in patients with VD, which distinguishes these findings from those in progressive systemic sclerosis. The finding is defined as "abnormal capillary morphology" that does not meet the criteria for "scleroderma" and "scleroderma-like" type capillaroscopy [12, 24].

A study by Hiroshi et al. (2004) in 294 workers exposed to vibration showed that 90.8% of patients with VD had Raynaud's phenomenon. Capillaroscopic findings included a semicolon- or comma-shaped appearance of the capillaries, decreased tonicity and dilation in 40 patients, indistinct capillaries (edema, sclerosis) and hemorrhages in 42 patients, and the presence of only a few visible capillaries in 16 patients [10, 12]. These results highlight the diagnostic value of capillaroscopy as a noninvasive method for assessing microcirculation, especially when compared to other tests such as arteriography and cold provocation test.

Sakaguchi et al. (2011) proposed a morphological classification of capillaroscopic changes in workers exposed to vibration. Their study found that patients with longer exposure to vibration had slower mean blood flow velocity (83.5%) compared to patients with short exposure (67%), suggesting that morphological changes in capillaries are associated with damage to the capillary wall due to long-term vibration stimulation [12, 26]. Despite the small number of patients studied, the study again highlights the importance of capillaroscopy in addition to other functional studies for assessing microcirculation in patients with VD. It should be noted, however, that

in this study, capillaroscopy was not performed according to standard requirements (it was performed on only one finger of the dominant hand).

A 2012 South Korean study also confirmed abnormal capillary findings in workers exposed to vibration [12, 22]. Unfortunately, the results of this study are conflicting, as abnormal capillaroscopic findings were observed in both groups. The exposed group had a higher number of crossed and enlarged capillaries, more avascular zones, smaller venous arm size, smaller overall width, and longer capillary length compared to controls. Tortuous, bushy, tortuous, and branched capillaries were more common in the control group.

Stoyneva's two key research projects, conducted in 2014 and 2015-2017, focus on peripheral vascular and microcirculatory disorders in patients with vibration disease from local vibration exposure. The first study in 2014 included 30 patients and 30 healthy individuals (controls). The results showed that spastic capillaries, capillary dilation, crossed capillaries, aneurysms, and pericapillary edema predominated in patients with VD. In addition, skin perfusion and finger temperature values of patients were significantly lower than those of controls. In 36.7% of patients, there was no venoarteriolar reflex response, confirming the existence of significant microcirculatory disorders [8, 12, 37].

Stoyneva's next study, conducted between 2015-2017, included 125 men aged 51.3 ± 13.1 years with hand-arm vibration syndrome and a length of work experience between 6 and 18 years. The studies were performed using distal Doppler sonography, laser Doppler flowmetry, and videocapillaroscopy. The results showed that the majority of patients (46%) were in the first to second stage of VD, while 41% were in the primary second stage. A small percentage of patients (13%) reached the second to third stage of the disease. Regarding capillaroscopic changes, 30% of patients have dystonic capillaries, 45% have spastic capillaries, and 22% show structural changes such as aneurysms, missing capillary loops, and hemorrhages in the eponychium. In addition, angiospastic changes in the distal peripheral vessels and microcirculation of the fingers predominate. All these findings indicate a direct correlation between functional and structural changes in capillaries and the stage of the disease [8, 12, 38].

Stoyneva's research demonstrates that capillaroscopy, laser Doppler flowmetry, and infrared thermography provide comprehensive information about microcirculation and vasomotor function in patients with vibration disease. These methods not only contribute to the accurate diagnosis of the condition, but also play a key role in determining the prognosis and treatment approach for patients with hand-arm vibration syndrome.

A study by Chen et al. (2016) in 113 miners showed significant capillaroscopic differences between groups with chronic vibration exposure (HAVS group) and those without clinical manifestations of VD. The changes included hemorrhages (65.7%), dilated capillaries (60%), and avascular zones (74.3%), which were associated with the clinical manifestations of vibration-induced finger whitening [3, 8, 12]. The results confirm the importance of capillaroscopy in the diagnosis and prevention of permanent damage to the microcirculation in patients with VD.

In 2020, Maria Maddalena Sirufo et al. reported a case of a 16-year-old girl, a professional shooter, who complained of pain and swelling in her right arm that worsened after training or competition. Magnetic resonance imaging and Doppler sonography of the hands and upper limbs were performed, but no pathological changes were found. However, capillaroscopy revealed pericapillary edema and morphological changes of the capillaries in the right hand, with irregular arrangement of the capillaries, ectasias, branched capillaries, "sludge" phenomenon, microhemorrhages, and dilated capillaries. According to the authors, these changes are related to muscle strain, repetitive movements, and local vibrations during archery. The patient was advised to change her shooting posture and undertake hand relaxation exercises, as well as to have annual follow-up with capillaroscopy [8, 12, 28].

Most studies have included small numbers of patients. Some studies have reported only a reduced number of capillaries and/or abnormal vasospasm (of the digital artery) in response to cold (disappearance of capillaries, disappearance of reactive hyperemia, and appearance of pericapillary edema) in loggers [12, 25, 39, 40].

Conclusion

Capillaroscopy provides valuable information about morphological and functional changes in the microcirculation associated with various diseases with manifestations of Raynaud's phenomenon. Thanks to this study, early vascular disorders can be detected, the disease can be predicted, and its development monitored. Early detection of microcirculatory changes by capillaroscopy can be crucial for choosing a therapeutic strategy and improving the quality of life of patients. In rheumatology practice, capillaroscopy findings are standardized, while in patients with oc-

Table 1. Presents the main capillaroscopic characteristics in rheumatological and occupational diseases

Characteristics	Rheumatological diseases				Occupational diseases		
RP frequency %	MCTD (50-85%)	UCTD (50-80%)	SLE (2-15%)	DM (20%)	RA (3-17%)	APS (34%	VD (0,6- 83,5%)*
Atonic capillaries			Yes 36				Yes 2, 8, 12, 38
Dystonic capillaries			Yes 36				Yes 8, 12, 38
Spastic capillaries			Yes 36				Yes 2, 8, 12, 37, 38
Dilated capillaries	Yes 20	Yes 19, 32	Yes 14, 16, 17, 20, 21	Yes 13, 32	Yes 16	Yes 7, 20	Yes 2, 3, 8, 10, 12, 28, 37
Giant capillaries	Yes 20	Yes 19, 32	Yes 17, 20, 36	Yes 4, 13, 14, 30, 32		Yes 7, 20	No 2, 24
Enlarged capillaries		Yes 19	Yes 4,1 4,16, 17, 20, 21	Yes 20	Yes 16, 20	Yes 7, 20	Yes 12, 22, 24
Tortuouse capillaries	Yes 20	Yes 19	Yes 4, 14, 17, 20, 21, 36	Yes 30	Yes 4, 20	Yes 7, 20	Yes 12, 24
Crossed capillaries	Yes 20						Yes 2, 8, 12, 22
Branched capillaries		Yes 19		Yes 4, 13, 30			Yes 2, 8, 28
Bushy capillaries			Yes 36				
Atypically shaped capillaries			Yes 36		Yes 16		
Aneurysmal dilations							Yes 2, 8, 12, 37, 38
Capillary loss							Yes 12, 24

cupational exposure, variability of the findings is observed. All studies in the field of occupational pathology emphasize the importance of capillaroscopy as a non-invasive method for the diagnosis and prevention of vascular and nerve damage. Standardization of capillaroscopic findings in occupational pathology is difficult due to the varying duration and intensity of exposure and the impact of a combination of occupational risk factors in the work environment. Further studies are needed in this direction. Early diagnosis and monitoring of capillary changes are essential for the prevention of trophic disorders, for improving the prognosis and quality of life of patients, and for preserving their working capacity.

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Постъпил за печат: 24.07.2025 г.

Submitted: 24.07.2025

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