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POSSIBILITIES OF NAILFOLD CAPILLAROSCOPY IN THE DIFFERENTIAL DIAGNOSIS OF IMMUNO-INFLAMMATORY AND RHEUMATOLOGICAL DISEASES

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◆ This article considers capillaroscopic changes in the patients with systemic sclerosis compared to the patients with a group of rheumatological diseases (rheumatoid arthritis, polymyositis, osteoarthritis) and the patients with idiopathic pulmonary hypertension. All the patients diagnosed with systemic sclerosis according to nailfold capillaroscopy had a characteristic combination of capillary disorders (Raynaud's syndrome): the expansion of all three segments of the capillary loop, the "loss" of capillaries, and the destruction of the nail fold. In the comparison groups, the capillaroscopic picture was represented by single pathological changes that did not add up to the pathognomonic scleroderma patterns, with the exception of the groups with dermato/polymyositis, where 2 patients had significant Raynaud's syndrome. There were also significant differences in the density of the capillaries in the patients with systemic sclerosis in comparison with the other groups.

◆ **Keywords:** capillaroscopy; systemic sclerosis; rheumatoid arthritis; polymyositis; osteoarthritis; pulmonary arterial hypertension.

ВОЗМОЖНОСТИ КАПИЛЛЯРОСКОПИИ НОГТЕВОГО ЛОЖА В ДИФФЕРЕНЦИАЛЬНОЙ ДИАГНОСТИКЕ ИММУНОВОСПАЛИТЕЛЬНЫХ И РЕВМАТОЛОГИЧЕСКИХ ЗАБОЛЕВАНИЙ

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◆ В данной статье проведено сравнение капилляроскопических изменений ногтевого ложа у пациентов с системной склеродермией, у пациентов с ревматологическими заболеваниями (ревматоидным артритом, полимиозитом, остеоартритом), а также с идиопатической легочной гипертензией. У всех пациентов с диагнозом системной склеродермии по данным капилляроскопии ногтевого ложа обнаружена характерная комбинация капиллярных нарушений — расширение всех трех сегментов капиллярной петли, «потеря»

капилляров и разрушение ногтевого капиллярного ложа, характерная для синдрома Рейно. У пациентов в группах сравнения капилляроскопическая картина была представлена единичными патологическими изменениями капилляров, не складывающимися в патогномоничные склеродермические паттерны, за исключением группы с дермато/полимиозитом, где у 2 пациентов диагностирован достоверный синдром Рейно. Наблюдались также достоверные различия в плотности капиллярной сети у больных системной склеродермией по сравнению с больными других групп.

◆ **Ключевые слова:** капилляроскопия; системная склеродермия; ревматоидный артрит; полимиозит; остеоартрит; легочная артериальная гипертензия.

Introduction

Capillaroscopic analysis of the microvasculature was established in 1939 when Muller published various color capillaroscopic images. In the following decades, capillaroscopy method gained importance in the diagnosis of Raynaud's syndrome and associated pathological conditions since Maricq and LeRoy published in 1973 the first study to describe specific capillaroscopic patterns in systemic sclerosis (SS) [1].

In 1976, the same authors noted a continuous change in the nature of the capillary blood flow during cold exposure in both primary and secondary Raynaud's syndrome. Detailed studies by Bollinger, Grassi, Carpentier, and Herrick (1980–1990) contributed to the further use of nailfold capillaroscopy (NFC) in the diagnosis of rheumatological diseases [2–4].

In 2000, Cutolo et al. identified three main NFC patterns, namely, early, active, and late, to identify and assess the progression of microangiopathy in SS and created a qualitative and semi-quantitative assessment system of the recorded alterations [5, 6]. Since 2004, the European League Against Rheumatism (EULAR) has held annual training courses on NFC, which indicates an increased interest and the need to master this technique. In addition, capillaroscopy was included in the 2013 American College of Rheumatology (ACR)/EULAR criteria for diagnosis of SS.

This study aimed to compare capillaroscopic changes in the nail bed in SS and in rheumatological diseases (such as rheumatoid arthritis, polymyositis, and osteoarthritis) and idiopathic pulmonary hypertension.

Materials and methods

The SS group included 68 patients. The 1980 APA classification criteria were used to verify the diagnosis. Of the 68 patients, 32 had a diffuse form and 36 had a limited form. The median age was 50.2 [42.0–60.0] years, and the median disease duration was 7 [3.0–9.0] years. Most of the patients were women (98%).

The comparison groups were as follows:

1. Thirteen patients (11 women and 2 men) with idiopathic pulmonary hypertension, with median age of 51 [33.0–60.0] years and median disease duration of 12.6 [6.4–18.5] months.
2. Twenty patients (18 women and 2 men) with rheumatoid arthritis diagnosed based on the 2010 EULAR criteria, with median age of 62.5 [44.0–78.0] years and median disease duration of 18.2 [8.0–24.5] months.
3. Twenty patients with primary generalized osteoarthritis (16 women and 4 men), with median age of 59.5 [44.0–82.0] years and median disease duration of 15.4 [12.2–18.4] months.
4. Twelve patients (all women) with primary dermatomyositis/polymyositis (diagnosed based on the criteria developed by Bohan and Peter in 1975). The median age was 55.3 [29.0–71.0] years, and the median disease duration was 20.4 [16.3–25.7] months.

NFC was performed using a DigiMicro Lab 5.0 digital microscope. Lesions of the microvasculature were assessed according to the proportions of the parameters of sclerodermic patterns (such as giant capillaries, "loss" of capillaries, microhemorrhages, and capillary branching). Three main patterns are generally accepted in the standards of capillaroscopic research technique, namely, early, active, and late (Figs. 1–4).

The experiment was performed using immersion oil applied to the base of the nail bed of the phalanges of fingers II–V of both hands. Parameters such as morphology, architecture, and capillary density were evaluated. When the number of pathologically altered capillaries correlated with the number of capillaries along 1 mm in the distal row of the nail bed, a semi-quantitative assessment of morphological changes was also performed. The average value for each

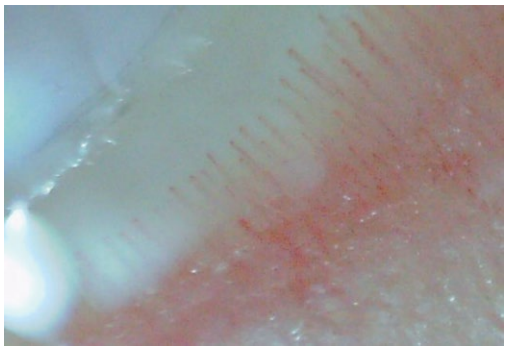

Fig. 1. Normal structure of capillaroscopic pattern. Homogeneous structure of the capillaries, their parallelism. Capillary density is more than 7 capillaries per 1 mm^2

Рис. 1. Нормальная структура капилляроскопического паттерна. Однородная структура капилляров, их параллельность. Плотность на 1 мм^2 более 7 капилляров

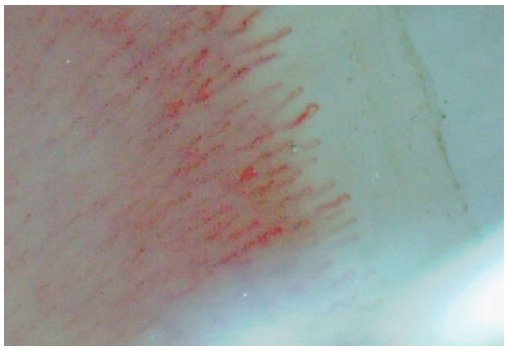

Fig. 2. "Early" pattern. The capillaries with dilated ascending and descending loops, marked loss of parallelism. Capillary density is normal: more than 7 capillaries per 1 mm^2

Рис. 2. «Ранний» паттерн. Капилляры с расширенными восходящими и нисходящими петлями, отмечается потеря параллельности. Плотность нормальная, более 7 капилляров на 1 мм^2

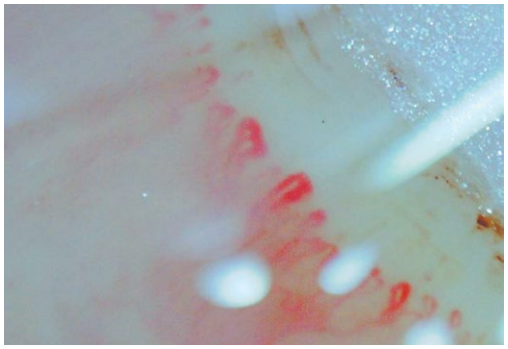

Fig. 3. "Active" pattern. The dilated capillaries with a more than three-fold increase in the diameter (giant capillaries). Non-parallelism is more expressed than in the "early" pattern. Capillary density is less than 7 capillaries per 1 mm^2

Рис. 3. «Активный» паттерн. Расширенные капилляры с увеличением диаметра более чем в 3 раза от нормы (гигантские капилляры). Непараллельность выражена больше, чем при «раннем» паттерне. Плотность капилляров менее 7 на 1 мм^2

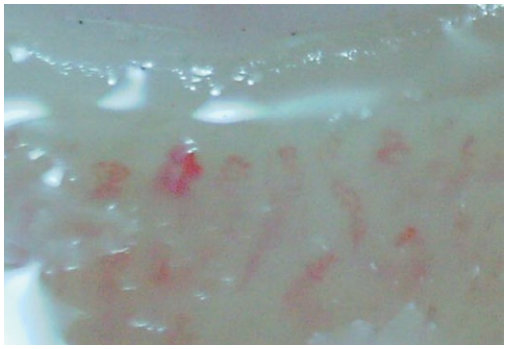

Fig. 4. "Late" pattern. A rapid decrease in density of the capillaries, complete destruction of the capillary structure, the signs of neoangiogenesis

Рис. 4. «Поздний» паттерн. Резкое снижение плотности капилляров, полное разрушение структуры капилляров, признаки неоангиогенеза

capillaroscopic parameter was calculated by analyzing at least two fields in the middle area of the nail bed of each finger. The average values of each of these eight fingers were added and then divided by eight. The resulting index for each capillaroscopic parameter was analyzed according to the system presented in Fig. 5 (0–3 points).

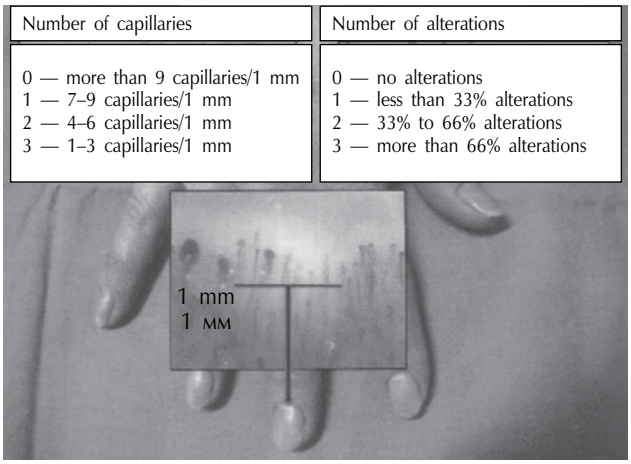

Fig. 5. Semi-quantitative assessment of capillaroscopic changes

Рис. 5. Полуколичественная оценка капилляроскопических изменений

Results

In all patients with SS, the NFC revealed a characteristic pathognomonic combination of capillary disorders in the nail bed, namely, dilatation of all three segments of the capillary loop,

Sensitivity and specificity of various elements of the capillaroscopic pattern in the patients with systemic scleroderma of different duration

Чувствительность и специфичность различных элементов капилляроскопического паттерна у больных системной склеродермией с различной длительностью заболевания

Systemic sclerosis	Early pattern		Active pattern		Late pattern	
	Sensitivity, %	Specificity, %	Sensitivity, %	Specificity, %	Sensitivity, %	Specificity, %
Early form	100	66,67	100	100	–	–
Active form	100	100	94,4	100	100	100
Late form	50	100	100	100	100	100

"loss" of capillaries, and destruction of the nail capillary bed. Many branched capillaries were also recorded. According to the proportions of the parameters of the scleroderma pattern (i.e., giant capillaries, "loss" of capillaries, microhemorrhages, and branching of the capillaries), one of three main patterns (i.e., early, active, and late) was identified in all subjects. The ratios of these patterns were 10%, 45%, and 45%, respectively.

The distribution of patterns depending on the disease duration was established. Table presents the sensitivity and specificity of various elements of the capillaroscopic patterns in patients with varying disease durations.

In the comparison groups, the capillaroscopic pattern was represented by single pathological changes in the capillaries that did not indicate pathognomonic sclerodermic patterns, except for the group with dermatomyositis/polymyositis where significant Raynaud's syndrome was diagnosed in two patients (Figs. 6–9).

In 13 patients with idiopathic pulmonary hypertension, NFC revealed capillary dilatation ($n = 7$) and pathological tortuosity and microhemorrhages ($n = 4$) in all study fields. These abnormalities may be associated with microangiopathy that occurs with endothelial dysfunction or damage due to an imbalance between vasodilation and vasoconstriction.

In 20 patients with osteoarthritis, NFC showed dilatation and pathological tortuosity of the capillaries ($n = 2$ each) in all study fields. These abnormalities are clinically insignificant and may be caused by angiopathy in nodular osteoarthritis.

In 20 patients with rheumatoid arthritis, NFC revealed capillary dilatation ($n = 3$) and

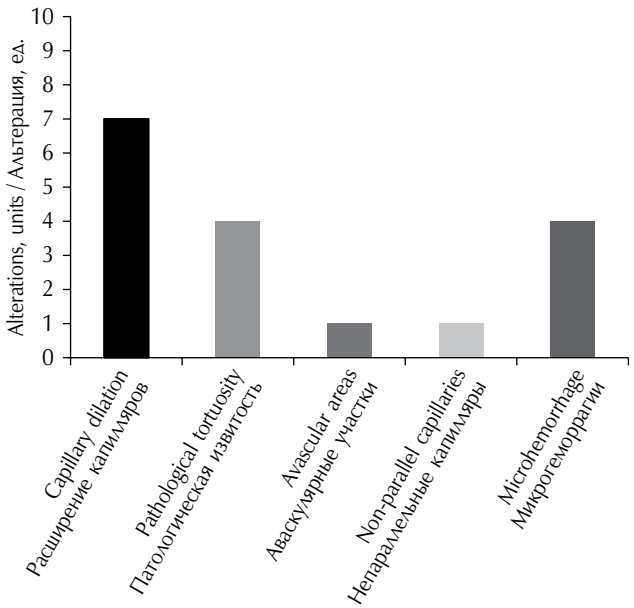

Fig. 6. Pathological changes of the capillary bed in the group of patients with idiopathic pulmonary hypertension

Рис. 6. Патологические изменения капиллярного русла в группе пациентов с идиопатической легочной гипертензией

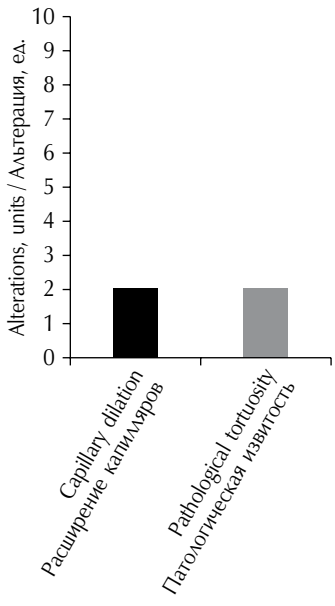

Fig. 7. Pathological changes of the capillary bed in the group of patients with osteoarthritis

Рис. 7. Патологические изменения капиллярного русла в группе пациентов с остеоартритом

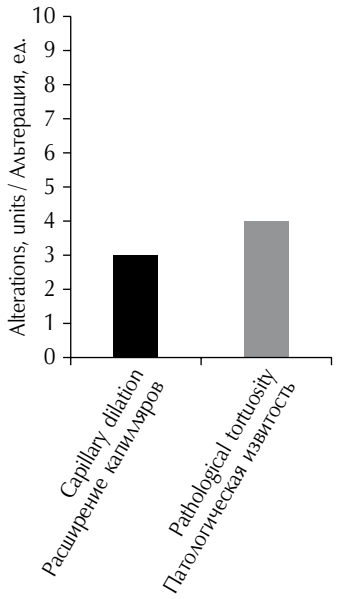

Fig. 8. Pathological changes of the capillary bed in the group of patients with rheumatoid arthritis

Рис. 8. Патологические изменения капиллярного русла в группе пациентов с ревматоидным артритом

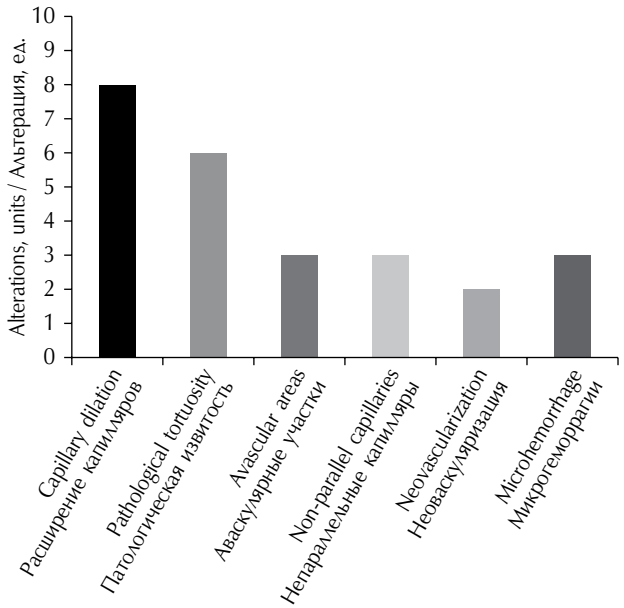

Fig. 9. Pathological changes of the capillary bed in the group of patients with dermato/polymyositis

Рис. 9. Патологические изменения капиллярного русла в группе пациентов с дермато/полимиозитом

pathological tortuosity (n = 4) in all study fields. These abnormalities are clinically insignificant and may be associated with the initial manifestations of digital vasculitis.

In 12 patients with primary dermatomyositis/polymyositis, NFC revealed capillary dilatation (n = 8) and pathological tortuosity (n = 6) in all study fields. Three alterations of each type, namely, non-parallel capillaries, microhemorrhages, and avascular areas, were detected. Capillary dilatation, pathological tortuosity, microhemorrhages, non-parallel capillaries, and avascular areas in two patients formed a pathognomonic presentation caused by Raynaud's syndrome, which is detected in this rheumatological disease. In other patients, the alterations were clinically insignificant.

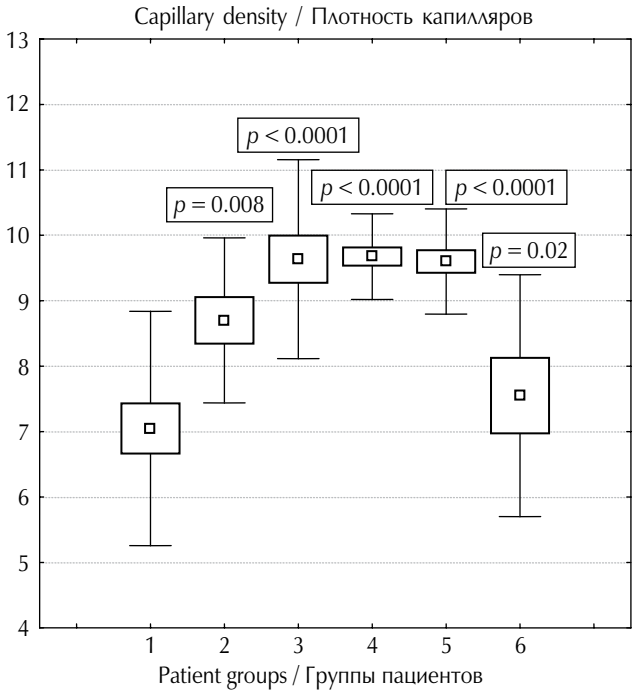

Fig. 10. Comparison of capillary density in different groups (□ — mean; ▭ — mean error; ⌶ — mean deviation, p — relative to the group with systemic scleroderma). The patient groups: 1 — with systemic scleroderma; 2 — with idiopathic pulmonary hypertension; 3 — control group; 4 — with osteoarthritis; 5 — with rheumatoid arthritis; 6 — with dermato/polymyositis

Рис. 10. Сравнение плотности капилляров в разных группах (□ — среднее; ▭ — средняя ошибка; ⌶ — среднее отклонение, p — относительно группы пациентов с системной склеродермией). Группы пациентов: 1 — с системной склеродермией; 2 — с идиопатической легочной гипертензией, 3 — группа контроля; 4 — с остеоартритом; 5 — с ревматоидным артритом; 6 — с дермато/полимиозитом

Compared with the patients in the comparison groups, patients with SS showed a decrease capillary density ($p = 0.0003$) (Fig. 10).

Discussion

In this study, specific changes in the capillary network (i.e., capillaroscopic patterns) were found in the group of patients with SS. Moreover, significant differences were found in the capillary network density in patients with SS when compared with the patients of the comparison groups ($p = 0.0003$). This confirms the high diagnostic value of NFC. In 2001, LeRoy and Medsger proposed the criteria for the early diagnosis of SS with Raynaud's syndrome as the only major clinical manifestation that were included in the ACR/EULAR criteria in 2013. These criteria are SS-specific autoantibodies and specific sclerodermic abnormalities detected by capillaroscopy.

Conclusions

The results of this study suggest that NFC is the safest, most atraumatic, and easy-to-perform technique of microvasculature morphological examination in patients with Raynaud's syndrome. NFC is characterized by high diagnostic specificity and sensitivity in the measures for the differential diagnosis of SS and other rheumatic and immunoinflammatory diseases. The capillary density in patients with SS was significantly lower than those of patients of the comparison groups ($p = 0.0003$).

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