Assessment of morphology and distribution of capillaries in patients with SSc and healthy individuals in nailfold capillaroscopy

Ocena morfologii i dystrybucji naczyń włosowatych w kapilaroskopii wału paznokciowego u chorych na twardzinę układową i zdrowych osób

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ABSTRACT

Introduction: Systemic sclerosis (SSc) is a connective tissue disease characterized by vascular damage and immunological abnormalities leading to fibrosis that can damage multiple organs. The pathogenesis is complex and still poorly understood. However impaired angiogenesis in SSc has a major role in tissue injury and sequelae fibrosis. Nailfold capillaroscopy (NC)/nailfold videocapillaroscopy (NVC) is a safe and non-invasive method used to investigate microvascular changes in the peripheral circulation and it is a method of great diagnostic value in diagnosing and monitoring the patients with SSc. Typical microvascular alterations, called scleroderma pattern characterized by giant capillaries, haemorrhages and successive loss of capillaries, are observed at NC/NVC in a significant percentage of SSc patients, hence our interest was focused on the assessment of NVC in patients with systemic sclerosis (SSc).

Material and methods: Thirty patients with SSc according to the ACR and EULAR criteria and healthy volunteers underwent NVC assessment. Nailfold capillaroscopy was performed by a videocapillaroscope and the picture of the capillaries at the hands were documented and evaluated.

Results: NVC disturbed patterns were significantly prominent in SSc patients (p < 0.05) compared to the healthy control group. A normal capillaroscopic pattern was not observed in patients with SSc. The number of loops/mm was significantly lower in SSc group (p < 0.05) and was 4.28 capillaries/mm (min.1/mm; max. 10/mm). We did not notice significant difference in frequency of mega-capillaries (lcSSc/dcSSc: 41%/29%, p > 0.05) and avascular areas (lcSSc/dcSSc: 64%/57%, p > 0.05) between limited (lSSc) and diffuse (dSSc) SSc.

Conclusions: Severe capillary damage is characteristic for SSc patients therefore NVC seems to be useful for selection of patients developing SSc.

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and prognosis of future development of rheumatic diseases. NVC is mostly used in SSc diagnosis and observation as capillaroscopic changes are observed in over 90% of patients [5, 6] (Fig. 1, 2, 3).

The aim of the study was to assess capillaroscopic changes in the investigated group of patients with SSc.

**MATERIAL AND METHODS**

The study was carried out on 30 patients with SSc (7 patients with dSSc and 23 with lSSc) and 15 healthy volunteers. All patients fulfilled SSc criteria according to ACR and EULAR (2013) [2, 7]. The mean age of first clinical symptoms was 40 years. The mean time of Reynaud phenomenon was 13.5 years, the minimum time from developing Reynaud phenomenon to the investigation was 3 years, the maximum 35 years.

At the time of investigation, the patients with ISSc were given vasodilators (pentoxifylline) and/or calcium channel antagonists and/or angiotensin receptor antagonists and vitamin E. Periodically, pentoxifylline and dextran infusions were administered. Patients with SSc also continued earlier instituted or modified, according to clinical indications, immunosuppressive treatment (low doses of corticosteroids — prednisone 0.5 mg/kg body mass/daily and/or methotrexate up to 15 mg/weekly).

Microcirculation in the investigated patients was assessed with the use of the optical microscope OPTEK MC-980. [objective: achromatic 4X/0.10; condenser 1/3"CMOS; resolution: 380 TVL (Television Lines), automatic white balance; video exit; 1Vp-p/75Ω.NTSC/PAL; power: 220V/110V; output: 9V; shifting table (size: 130 mm × 118 mm; shift range: 64 mm × 28 mm]; light source: LED.

Layout and number of capillaries were assessed by capillaroscopic examination.

The study Nr. KE/3139/15 & RNN/218/09/KE was approved by Bioethical Committee, Medical University, Lodz.

Clinical data were transcribed to a Microsoft Office Excel spreadsheet and then analyzed statistically with the use of standard procedures. For statistical analysis STATISTICA v.10 was used. Differences and relationships p < 0.05 were considered statistically significant.

**RESULTS**

In capillaroscopic examination, the mean number of capillaries per 1 mm was 8.5 (min. 7/mm; max. 10/mm) in healthy individuals. A proper capillary loop resembled U letter and consisted of an ascending arm (arterial), ~10.45 µm in diameter and was narrower than a descending arm (venous), ~12.76 µm in diameter. The ratio of an ascending arm width to descending one was smaller than 2:1 (Tab. 1).

In SSc patients, the mean number of capillaries per 1 mm was 4.28 (min. 1/mm; max. 10/mm), which was
Table 1. Assessment of morphology and distribution of capillaries in the investigated groups

<table>
<thead>
<tr>
<th>Investigated groups</th>
<th>SSc</th>
<th>lSSc</th>
<th>dSSc</th>
<th>control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ascending limb of capillary loop</strong></td>
<td><strong>x</strong></td>
<td><strong>min. – max.</strong></td>
<td><strong>SD</strong></td>
<td><strong>x</strong></td>
</tr>
<tr>
<td>X</td>
<td>38.13</td>
<td>11–88 P &lt; 0.05</td>
<td>11.83</td>
<td>20.17</td>
</tr>
<tr>
<td>SD</td>
<td>40.89</td>
<td>20.83</td>
<td>10.45</td>
<td>7.7–11</td>
</tr>
<tr>
<td>SD</td>
<td>11–88 P &lt; 0.05</td>
<td>31–55 P &lt; 0.05</td>
<td>22.08</td>
<td>31.43</td>
</tr>
<tr>
<td>SD</td>
<td>11–55 P &lt; 0.05</td>
<td>11–88 P &lt; 0.05</td>
<td>4.57</td>
<td>31.43</td>
</tr>
<tr>
<td><strong>Descending limb of the capillary loop</strong></td>
<td><strong>x</strong></td>
<td><strong>min. – max.</strong></td>
<td><strong>SD</strong></td>
<td><strong>x</strong></td>
</tr>
<tr>
<td>X</td>
<td>39.97</td>
<td>11–110 P &lt; 0.05</td>
<td>21.52</td>
<td>4.57</td>
</tr>
<tr>
<td>SD</td>
<td>42.57</td>
<td>22.08</td>
<td>10.45</td>
<td>8–50</td>
</tr>
<tr>
<td>SD</td>
<td>31–55 P &lt; 0.05</td>
<td>11–110 P &lt; 0.05</td>
<td>4.8</td>
<td>12.76</td>
</tr>
<tr>
<td>SD</td>
<td>7–16.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Number of capillaries/mm</strong></td>
<td><strong>x</strong></td>
<td><strong>min. – max.</strong></td>
<td><strong>SD</strong></td>
<td><strong>x</strong></td>
</tr>
<tr>
<td>X</td>
<td>4.28</td>
<td>1–10 P &lt; 0.05</td>
<td>1.76</td>
<td>1.40</td>
</tr>
<tr>
<td>SD</td>
<td>4.18</td>
<td>1–10 P &lt; 0.05</td>
<td>1.40</td>
<td>1.04</td>
</tr>
<tr>
<td>SD</td>
<td>4.57</td>
<td>2–6 P &lt; 0.05</td>
<td>1.40</td>
<td>1.04</td>
</tr>
<tr>
<td>SD</td>
<td>8–50</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

X — mean; SD — standard deviation; *statistical significance p < 0.05

Control group:ascular areas present in 53% of the patients with ISSc and 29% of dSSc patients; capillary hemorrhage — 64% and 57%, respectively; megacapillaries — 41% and 29%; lengthening of capillaries — 35% and 57%; bushy capillaries — 48% and 43%, respectively. However, the results of statistical analysis did not show relationship between the observed deviations in capillaroscopic picture and type of systemic sclerosis (ISSc vs dSSc) (p > 0.05).

**DISCUSSION**

At the end of the last century there was a great advancement in understanding vascular disorders in the development of many diseases. As the microvasculopathy in the course of SSc are not fully understood, the research is being carried out. Capillaroscopic examination to assess blood vessels is considered an important element of diagnosing SSc patients [5, 6, 8] and also in monitoring the course of SSc [9, 10].

In the investigated group of SSc patients, deviations from the norm were found in all patients, however, there were no statistically significant differences between patients with lSSc and those with dSSc. The obtained data are in accordance with the subject literature, a characteristic capillaroscopic picture is observed in 85 to 100% patients [9,11] and depends on duration of the disease, so proper vascular pattern in SSc patients by ACR and EULAR was not observed.

Rapid development of vascular disorders is observed mostly in the first years of the disease [5, 12]. Lovy et al. found relationship between duration of SSc and progressive vascular loss [13], which proves the need to monitor the disease with the use of capillaroscopy. Also layout of capillary size in the controls in capillaroscopic image was in accordance with that described by Michalska-Jakubus et al. [8].

No statistical significance was found between the observed disorders such as vascular loss, mega-capillaries or capillary lengthening between lSSc patients and those with dSSc, which confirms an open question if ISSc and dSSc are separate diseases or phenotypes of the same disease.

Vascular disorders at the cellular scale may cause different organ changes in the course the disease [14, 15]. One of the first symptoms of SSc development is Raynaud’s phenomenon. Secondary symptoms like skin and internal organ changes develop. Non-healing ulcers, pulmonary hypertension, coronary heart disease, disorders in respiratory, urinary and digestive systems appear. Interestingly, Sato et al. [16] found positive correlation between vascular loss, number of capillaries < 8/mm and involvement of more than three organs.

To sum up, the obtained data confirm significant differences in between SSc patients and the healthy controls in capillaroscopic image. It must be stressed that monitoring of vascular changes may determine further organ diagnosis and treatment in the course of SSc but further studies are needed.

**Conflict of interest statement**

No disclosures.

**REFERENCES**


