Diagnostic value of nailfold capillaroscopy to systemic sclerosis with Raynaud’s phenomenon: a preliminary study

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Objective: To analyze the sensitivity, specificity, positive predictive value, and negative predictive value of nailfold capillaroscopy to systemic sclerosis with Raynaud’s phenomenon.

Methods: The database of the National Taiwan University Hospital was searched for patients with Raynaud’s phenomenon who had been given a nailfold capillaroscopy examination between 2007 and 2008. The medical records were reviewed.

Results: The medical records of a total of 33 patients were obtained from the database and the sensitivity and specificity of a scleroderma pattern for systemic sclerosis were 84.62% and 75%, respectively. The positive predictive value and negative predictive value of a scleroderma pattern for systemic sclerosis were 68.75% and 88.24%, respectively.

Conclusion: This study is unique in measuring semi-quantitative and qualitative parameters of the nailfold vasculature for systemic sclerosis. The sensitivity, specificity, positive predictive value, and negative predictive value of scleroderma pattern for systemic sclerosis are demonstrated.

Key words: Nailfold capillaroscopy, Raynaud’s phenomenon, sensitivity, specificity, systemic sclerosis

Introduction

Raynaud’s phenomenon (RP) is one of the early clinical manifestations of diffuse connective tissue diseases (DCTD), such as systemic sclerosis (SSc), mixed connective tissue disease (MCTD), systemic lupus erythematosus (SLE), and dermatomyositis (DM)/polymyositis (PM), and nailfold capillaroscopy (NC) enables an in vivo assessment of the morphology of cutaneous capillaries, and has been used for evaluating patients with RP [1]. NC distinguishes primary and secondary RP due to, connective tissue diseases (CTD) [1].

A typical normal NC pattern demonstrates hairpin capillaries, arranged in parallel with each other. In 1973, Maricq et al. recognized massive capillary dilatation in scleroderma-dermatomyositis [2], and in 1980, they identified “scleroderma spectrum disorders”, including classic scleroderma, MCTD and DM, because of their indistinguishable NC findings [3]. In 1996, Kabasakal et al. described and quantified the morphological characteristics of different forms of CTD, thus enhancing the value of NC [4], and in 2000, Cutolo et al. classified NC patterns of scleroderma into 3 major patterns, namely “early”, “active” and “late” [5], which are now considered to be useful in assessing the appearance and progression of sclerodermic micro-angiopathy [5].
detection of mega-capillaries in patients with RP has a good predictive value for the subsequent development of a scleroderma spectrum disorder [6], and Blockmans et al. studied the predictive value of NC in the diagnosis of CTD [7], concluding the sensitivity of the presence of mega-capillaries in different forms of CTD as follows: diffuse systemic sclerosis: 100%, limited cutaneous systemic sclerosis: 73%, MCTD: 56%, and DM: 86%.

The positive predictive value (PPV) of the presence of mega-capillaries for a scleroderma spectrum disorder (SSD) was 63.5% and the negative predictive value (NPV) of a normal capillaroscopy was 96.7%. It was, thus, concluded that NC can be utilized to rule out SSD [7].

However, so far, no study has illustrated the sensitivity, specificity, positive predictive value, and negative predictive value of scleroderma pattern (by the classification of Cutolo et al.) for systemic sclerosis. Therefore we addressed this issue in a retrospective study.

Materials and Methods

 Patients and subjects

The database of National Taiwan University Hospital was searched for patients who had received an NC examination between 2007 and 2008 and, after a careful review of the medical records, patients without RP were excluded. Finally, 33 patients were recruited for this study, and they were examined by physicians blind to the clinical information.

 Clinical and laboratory data collection

Clinical data relating to RP was obtained from the medical records, including the duration of RP, NC patterns, age, gender, laboratory data at NC examination, patients’ final diagnosis, and associated clinical conditions (such as smoking, diabetes…).

 Nailfold capillaroscopy techniques

An observation of nailfold capillaries was performed on all patients by an in vivo NC (Fig. 1). Each patient stayed inside the examination room for a minimum of 15 minutes before the nailfold was examined and the room temperature was 23-25°C. The epithelium was made transparent by adding a drop of immersion oil, and images were generated by lens providing a magnification of ×200, and a charged-coupled device (CCD) camera giving high-resolution images of 752 × 582 pixels. The capillaries in the distal row were observed, and a 1 mm graticule was imaged along with each finger to allow for quantification of the capillary density and width (CapiScope, KK Research Technology LTD UK). At least 4 fingers on each hand were examined, and a minimum of 4 photo-micrographs were taken of each patient. All capillary examinations were performed by clinicians to whom the clinical information of each individual not to be provided.

 Vascular loops were estimated to be of normal width (<25 µm) [4], widened (>50 µm) [6], or giant (>125 µm). Distinctive morphological alterations were recorded along with their average count, and these were classified as few (<4 altered capillaries/mm), moderate (4–6 altered capillaries/mm), or frequent (>6 altered capillaries/mm) [8]. The nailfold bleeding/finger was classified as grade 1 (punctate hemorrhages >2/finger), grade 2 (punctate hemorrhages >2/finger), or grade 3 (confluent areas of hemorrhage) [4], and the avascularity of the capillary bed was classified as grade 1 (≤2 discrete areas of vascular deletion), grade 2 (>2 discrete areas of vascular deletion), or grade 3 (large avascular areas) [4]. These morphological descriptions and quantifications were adapted from two previous studies conducted by Kabasakal et al. [4] and Dolezalova et al. [9].

Interpretation of the nailfold capillaroscopy findings

A typical normal NC pattern shows hairpin capillaries, arranged parallel with each other, and the “early scleroderma pattern (Scl-early)” is defined by a few (<4 altered capillaries/mm) giant capillaries, a few capillary hemorrhages (grade 1), relatively well-preserved capillary distribution without obvious loss of capillaries [5]. The “active scleroderma pattern (Scl-active)” is defined by frequent (>6 altered capillaries/mm) giant capillaries, frequent capillary hemorrhages (grade 1), relatively well-preserved capillary distribution without obvious loss of capillaries [5]. The “active scleroderma pattern (Scl-active)” is defined by frequent (>6 altered capillaries/mm) giant capillaries, frequent capillary hemorrhages (grade 2 or 3), a moderate loss (20-30%) of capillaries (grade 2), mild disorganization of the capillary architecture, and absent or mildly ramified capillaries.
The “late scleroderma pattern (Scl-late)” is defined by an irregular enlargement of the capillaries, few or absent giant capillaries and hemorrhages, severe loss (50-70%) of capillaries with extensive avascular areas (grade 3), disorganization of the normal capillary array, and ramified/bushy capillaries [5] (Fig. 2).

**Statistical analysis**

The results were expressed as means ± standard deviation (SD), and the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of scleroderma pattern for SSc, were calculated.

**Results**

**Demographics and clinical characteristics of patients**

The data of a total of 33 patients with RP was analyzed, 13 of whom had been diagnosed with SSc and 20 with non-scleroderma. The non-scleroderma diagnoses included SLE, PM/DM, MCTD, primary Sjögren’s syndrome, anti-phospholipid syndrome (APS), undifferentiated connective tissue disease (UCTD), and a number of other diagnoses. A summary of the demographic details and clinical characteristics of these patients is shown in Table 1.

**Table 2. Capillaroscopic patterns and corresponding clinical diagnoses**

<table>
<thead>
<tr>
<th>NC pattern</th>
<th>SSc (n = 10)</th>
<th>Non-scleroderma* (n = 20)</th>
<th>Total numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scleroderma</td>
<td>11</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td>Early</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Active</td>
<td>7</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Late</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Not Scleroderma</td>
<td>2</td>
<td>15</td>
<td>17</td>
</tr>
</tbody>
</table>

Abbreviations: NC = nailfold capillaroscopy
*The non-scleroderma diagnoses included SLE, PM/DM, MCTD, primary Sjögren’s syndrome, APS, UCTD, and a number of other diagnoses.
Table 3. Sensitivity, specificity, PPV, and NPV of scleroderma pattern for SSc

<table>
<thead>
<tr>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>84.62</td>
<td>75</td>
<td>68.75</td>
<td>88.24</td>
</tr>
</tbody>
</table>

Abbreviations: SSc = systemic sclerosis; PPV = positive predictive value; NPV = negative predictive value

Discussion

Our study is unique in measuring the semi-quantitative and qualitative parameters of the nailfold vasculature for systemic sclerosis. This morphological description and quantification were modified from two previous studies conducted by Kabasakal et al. [4] and Dolezalova et al. [9]. These parameters are advantageous for the classification of a specific nailfold capillaroscopic pattern. The definition and classification of a scleroderma pattern were adapted from previous research conducted by Cutolo [5]. Although several studies have shown a good predictive value [7,10] and prognostic role [6,11] of NC in patients with RP over the past three decades, these focused mainly on morphological (such as giant loops or micro-hemorrhages…) and quantitative changes (such as area of vascularity or number of mega-capillaries…) of connective tissue diseases.

In 1980, Mariq et al. attempted to determine the specificity of a “scleroderma pattern”. However, they discovered that this pattern could also be seen in related disorders, such as MCTD, and dermatomyositis but rarely in SLE (only 1 of 60 patients studied) [3]. Due to their indistinguishable NC findings, they suggested “scleroderma spectrum disorders”, including classic scleroderma, MCTD, and dermatomyositis [3]. The sensitivity of a “scleroderma pattern” for SSc was 82% [3]. However, the specificity of a “scleroderma pattern” was undetermined, since there was no definite classification and quantification of the nailfold capillaroscopic pattern.

In 1996, Kabasakal et al. described and quantified the morphological characteristics of different forms of CTD [4]. In addition, in the year 2000, Cutolo et al. re-classified NC patterns of scleroderma into three major patterns, namely “early”, “active” and “late” [5]. However, no study was conducted to demonstrate the sensitivity and specificity of scleroderma patterns for SSc, and our study is the first one to address this issue. The sensitivity and specificity of a scleroderma pattern for SSc were found to be 84.62% and 75%, respectively.

In 1996, Blockmans et al. suggested the sensitivity of the presence of mega-capillaries for different forms of CTD was as follows: diffuse systemic sclerosis: 100%, limited cutaneous systemic sclerosis: 73%, MCTD: 56%, and DM: 86% [7]. They reported the single parameter (mega-capillaries) of the nailfold vasculature with high sensitivity and high NPV (96.7%). However, the PPV of the presence of mega-capillaries for a scleroderma spectrum disorder (SSD) was low (63.5%) [7]. Our research addressed the scleroderma patterns for SSc, and demonstrated a superior specificity, and the overall sensitivity of the three scleroderma patterns for SSc was also high (84.62%). The PPV and NPV of the scleroderma pattern for SSc were 68.75% and 88.24%, respectively.

The limitation of our study is the relatively low case numbers of SSc, which could potentially cause an inaccurate statistical evaluation. With higher case numbers, such a calculation would be more reliable and thus, we hope to investigate more cases in future studies.

In conclusion, our results demonstrate the usefulness of semi-quantitative parameters for the classification of a scleroderma pattern, as well as confirm the high diagnostic value of NC in SSc.

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Reference


甲褶鏡應用於全身性硬化症合併雷諾氏現象的診斷價值—初步研究報告

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目的：研究甲褶鏡用於全身性硬化症診斷上的敏感性、特異性、陽性預測值、以及陰性預測值。方法：我們搜尋台大醫院資料庫中，從西元2007年到2008年中，有雷諾式現象並接受甲褶鏡檢查的病例，分析其在全身性硬化症的診斷經驗。結果：33位病患符合有雷諾式現象並接受甲褶鏡檢查的病例進行分析研究。甲褶鏡用於全身性硬化症診斷上的敏感性為84.62%；特異性為75%；陽性預測值為68.75%；陰性預測值為88.24%。結論：臨床上有雷諾式現象的病例，使用甲褶鏡檢查，其在全身性硬化症上的診斷價值相當高。

關鍵詞：甲褶鏡、雷諾式現象、敏感性、特異性、全身性硬化症