Capillaroscopic Skin Ulcers Risk Index (CSURI) calculated with different videocapillaroscopy devices: how its predictive values change

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Abstract

Introduction. Digital ulcers (DU) occur in about 50% of systemic sclerosis (SSc) patients. Scleroderma DU are responsible for chronic pain and disability with the need of systemic and local treatments. Recently, capillaroscopic skin ulcer risk index (CSURI) has been validated as useful tool in predicting the appearance of new scleroderma ulcers and/or persistence of non-healing lesions, within 3 months from capillaroscopy evaluation.

Objectives. Since the image length of 1.57 mm might represent a critical factor for CSURI calculation, the present study aimed to evaluate the reliability of CSURI using three different videocapillaroscopy devices with distinct image widths.

Methods. One hundred and seventy-six unselected SSc patients were consecutively enrolled for the study during a six-month period, using three different capillaroscopy devices (image widths of 1.33, 1.57, and 1.70 mm).

Results. After a three-month-follow-up new DU or persisting non-healing ulcers were observed in 46/176 patients (26.1%). The receiver operating characteristic curve analysis for CSURI showed an area under curve respectively of 0.705 for the image width of 1.33 mm, 0.786 for the image of 1.70 mm, and 0.888 for the image width of 1.57 mm.

Conclusions. The good sensitivity, specificity and positive predictive value of CSURI was confirmed in the whole patients’ series, as well as in the three subgroups on different image widths obtained with various available devices. In addition, the negative predictive value of the capillaroscopic index remained very high regardless of the picture length adopted.

Introduction

Digital ulcers (DU) occur in about 50% of systemic sclerosis (SSc) patients (1, 2). Scleroderma DU are responsible for chronic pain and disability with the need of systemic and local treatments; consequently, their impact on quality of life is often very detrimental (3). The identification of patients with high risk to develop this manifestation could be very helpful to adopt more aggressive prevention strategies; however, risk factors for the appearance of DU in SSc patients and the better strategies to monitor the therapy efficacy are not definitely established (4-7).

Recently, our group proposed a quantitative scoring method named capillaroscopic skin ulcer risk index (CSURI) able to identify SSc patients at high risk for complicating DU (8). This method has been subsequently validated on larger patient population in a multicentre study (9). CSURI makes it possible to predict the appearance of new ulcers and/or persistence of non-healing ulcers, within the first 3 months from capillaroscopic evaluation, with a sensitivity and a specificity of 92.98% and 81.4%, respectively, at the cut-off value of 2.96 (7).

To increase interobserver agreement, all measures necessary to the CSURI calculation were performed on the entire width of capillaroscopic image; the CSURI formula included the total number of capillaries (N), the number of megacapillaries (M), and the maximum diameter of megacapillary (D). Since the M/N ratio represents a relevant parameter, the image dimension of 1.57 mm in our validation study (9) might represent a critical factor in the CSURI calculation; therefore, the predictive value of this index could be influenced by the variability of image
Various capillaroscopic devices and digital ulcers’ risk / M. Sebastiani et al.

The present study aimed to evaluate the reliability of CSURI calculated using three different videocapillaroscopy devices with distinct image widths.

Patients and methods

One hundred and seventy-six unselected SSc patients (male/female 17/150, limited/diffuse cutaneous SSc 136/40, mean age 56.6 years ± 14.4 SD, mean SSc duration 98 months ± 88.6 SD; detailed clinico-demographic features are reported in Table I) from 4 Italian Rheumatologic Centres (Rheumatology Unit of the Universities of Rome, Modena and Reggio Emilia, Bari, and Ferrara) were consecutively enrolled for the study during a six-month period; patients undergoing bosentan treatment were invariably excluded (9). All patients met the preliminary American College of Rheumatology classification criteria for SSc (11). After capillaroscopic evaluation of the whole nailfold from 2nd through 5th fingers of both hands, the CSURI was calculated according to the formula D•M/N^2, choosing only the image with the lowest N and, secondarily, with the highest M among all saved images, as previously described (8, 9).

In agreement, the adopted parameters were defined as follows:

N: all the capillaries detectable in the entire distal front line, including capillaries placed at different levels; namely, by counting all the capillaries that one can see from the top of the picture. In the case of a ramified capillary, which occupies more than one dermal papilla, it corresponds to the number of papillae. A ramified giant capillary is considered as one in the megacapillary count and as two or more in the total capillary count, according to the number of occupied papillae;

M: a capillary with a homogeneously enlarged loop with a diameter of 50 μm or greater;

D: the largest distal row giant capillary diameter present in a capillaroscopic image, except at the level of a microaneurysm.

The 176 CSURI determinations were performed, with the same magnification of 200x, using three different capillaroscopy devices: Blue Vision, PBS software; Alphadoc-Standard, Milan (group 1, University of Rome, 36 patients); Videocap software 9.07; DS Medica, Milan, Italy (group 2, University of Modena and Reggio Emilia, 66 patients), and Videocap software 3.0; DS Medica, Milan, Italy (Group 3, Universities of Bari and Ferrara, 74 patients). Clinical and therapeutic features of the 3 groups were comparable (Table I), and all images were evaluated by an operator from every centre and CSURI was collegially calculated.

Ulcers were defined as loss of surface epithelialisation and did not include fissures or cracks in the skin or areas of calcium extrusion from calcinosis cutis. Only ulcers at or distal to the proximal interphalangeal joint were scored (12).

A receiver operating characteristic (ROC) curve analysis was performed to

### Table I. Predictive value of CSURI with different capillaroscopic devices.

<table>
<thead>
<tr>
<th>SSc patients (no.)</th>
<th>Image width</th>
<th>M/F</th>
<th>Cutaneous SSc subtypes (L/D)</th>
<th>Mean age (years±SD)</th>
<th>DU at baseline</th>
<th>DU after 3 months*</th>
<th>AUC</th>
<th>CSURI cut-off</th>
<th>specificity</th>
<th>sensitivity</th>
<th>positive predictive value</th>
<th>negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (36)</td>
<td>1.33</td>
<td>7/29</td>
<td>20/16</td>
<td>54.5 ± 14.4</td>
<td>5</td>
<td>9</td>
<td>0.705</td>
<td>3.81</td>
<td>55.6</td>
<td>88.9</td>
<td>40%</td>
<td>93%</td>
</tr>
<tr>
<td>Group 2 (66)</td>
<td>1.57</td>
<td>7/59</td>
<td>49/17</td>
<td>53.5 ± 14.5</td>
<td>11</td>
<td>16</td>
<td>0.888</td>
<td>2.96</td>
<td>78.0</td>
<td>93.7</td>
<td>61%</td>
<td>98%</td>
</tr>
<tr>
<td>Group 3 (74)</td>
<td>1.70</td>
<td>5/69</td>
<td>64/10</td>
<td>58.5 ± 14.4</td>
<td>17</td>
<td>21</td>
<td>0.786</td>
<td>2.13</td>
<td>72.2</td>
<td>90.0</td>
<td>56%</td>
<td>95%</td>
</tr>
</tbody>
</table>

*cumulative number of new DU and/or non-healing DU present at the time of capillaroscopy examination (baseline).

AUC: area under the receiver receiver operating characteristic curve.

![Fig. 1. The receiver operating characteristic (ROC) curve analysis for CSURI calculated in group 1, 2, and 3, using three different capillaroscopies characterised by distinct image width (1.33, 1.57, and 1.70 mm, respectively). Both sensitivity and specificity of CSURI were significant in the three patients’ groups.](image-url)
obtain the predictive accuracy of CSURI with regards to new ulcer development.

Results
Demographic and clinical features of patients included in group 1, 2, and 3 were comparable with regards to the patients’ mean age and male/female ratio, disease duration, cutaneous subsets, and previous history of DU. At the time of capillaroscopy examination, 22/176 enrolled patients presented DU. All patients underwent videocapillaroscopy at baseline; three months later they were investigated for the development or persistence of DU. In particular, new DU or persisting non-healing ulcers were observed in 46/176 patients (26.1%); namely, 9/36 (25%) in group 1, 16/76 (21%) in group 2, and 21/74 (28.4%) in group 3.

The receiver operating characteristic (ROC) curve analysis for CSURI (Fig. 1) calculated in group 1 (1.33 mm image width) showed an area under curve (AUC) of 0.705 (95% CI 0.552 to 0.861) for new ulcer appearance or non-healing ulcers, with a specificity of 55.56% (95% CI 35.3–74.5) and a sensitivity of 88.89% (95% CI 51.7–98.2), at the cut-off value of 3.81 (the positive and negative likelihood ratios were 2.00 and 0.2, respectively); while, the ROC curve calculated in group 2 (image width of 1.57 mm) showed an AUC of 0.888 (95%CI 0.786 to 0.952) for new ulcer appearance or non-healing ulcers, with specificity and sensitivity of 78% (95% CI 64–88.5) and 93.7% (95% CI 69.7–99.5) respectively, at the cut-off value of 2.96 (the positive and negative likelihood ratios were 4.26 and 0.08 respectively); finally, the ROC curve calculated in group 3 (image width of 1.70 mm) showed an AUC of 0.786 (95%CI 0.675-0.873) for new ulcer appearance or non-healing ulcers, with specificity and sensitivity of 72.2% (95 CI 58.4–83.5) and 90.00% (95% CI 68.3–98.5) respectively, at the cut-off value of 2.13 (the positive and negative likelihood ratios were 3.24 and 0.14 respectively). On the whole, negative predictive value of CSURI appeared to be very high; only few patients who developed DU were incorrectly classified using the score (from 2 to 7%).

Discussion
The use of nailfold capillaroscopy is worldwide accepted in the differential diagnosis of Raynaud’s phenomenon (13, 14). The present study confirmed the good sensitivity, specificity and predictive value of CSURI on the appearance of new ulcers and/or persistence of non-healing ulcers within the first 3 months from capillaroscopy evaluation (7). Moreover, the predictive value of CSURI was also confirmed when the index was calculated on different image widths obtained with various available devices; interestingly, the negative predictive value of the capillaroscopic index remained very high regardless of the picture length adopted. A limit of this study is the impossibility to study the same patients with the 3 different devices; however, the collegial calculation of CSURI should allow a good reproducibility of the results.

The prominent role of M/N ratio for the CSURI calculation has been clearly demonstrated in our previous studies (6, 7); thus, it is supposable that the width of the capillaroscopic image might represent a critical point. The results of our comparative study suggest that CSURI could be able to identify patients at higher risk to developing DU, with high sensitivity and specificity, despite the use of different videocapillaroscopy devices. However, the lower positive predictive value observed with the image width of 1.33 mm suggests that a wider picture length, possibly in the range of 1.57–1.70 mm, should appreciably increase both specificity and sensitivity of the CSURI.

Technical characteristics of commonly used videocapillaroscopy devices are quite dissimilar; they provide images of different, often no modifiable width. Therefore, to optimise the CSURI calculation it should be really helpful to dispose of software with specific function to choose the optimal field width.

References