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Short-term follow-up of digital ulcers by laser speckle contrast analysis in systemic sclerosis patients

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ABSTRACT

Objective: To monitor in systemic sclerosis (SSc) the evolution of digital ulcer (DU) status by analysing blood perfusion (BP) using laser speckle contrast analysis (LASCA).
Methods: Hand BP was recorded by LASCA in twenty SSc patients with recent onset fingertip DUs before and after 10 days of local/systemic treatment. Regions of interest (ROIs) to analyse BP were created al the level of ulcer, peri-ulcer, periungual and fingertip areas. Visual analogue pain scale (VAS) was also administered to patients before and after follow-up.
Results: A statistically significant increase of BP was observed from T0 to T1 in the ROIs created at the level of the ulcer area ($p < 0.0001$), as well as a significant decrease of BP was observed in the peri-ulcer area ($p < 0.0001$). A statistically significant decrease of both ulcer size ($p < 0.0001$) and VAS ($p = 0.001$) was observed, whereas no significant variation of both periungual and fingertip BP was detected.
Conclusions: LASCA may safely monitor DU evolution in SSc patients, by evaluating its blood perfusion and area during standard treatment. This may be useful to monitor DU evolution during treatment in clinical trials.

Introduction

Systemic sclerosis (SSc) is a rare connective tissue disease characterized by immune system activation, microangiopathy and progressive fibrosis of the skin and internal organs. Typical skin SSc clinical aspects include nailfold microvascular alterations and reduction of peripheral blood perfusion, resulting in increased incidence of digital ulcers (DUs) that appear in 36–58% of SSc patients during the course of the disease (Cutolo et al., 2010a,b; Rosato et al., 2011; Walker et al., 2007; Steen et al., 2009). Their management may be both systemic and/or local (Steen et al., 2009; Guillevin et al., 2013; Korn et al., 2004; Kowal-Bielecka et al., 2009). The visual analogue pain scale (VAS) has been adopted among the methods to subjectively assess the severity of DUs and their negative effect on the quality of life (Steen et al., 2009; Guillevin et al., 2013; Korn et al., 2004; Kowal-Bielecka et al., 2009).

No past studies have directly evaluated the DU status by measuring their diameter and the VAS, together with local blood perfusion, in particular using laser speckle contrast analysis (LASCA), a non-contact and safe technique already validated in SSc (Steen et al., 2009; Guillevin et al., 2013; Korn et al., 2004; Kowal-Bielecka et al., 2009; Ruaro et al., 2014).

Therefore, present study investigates the evolution of DU area and its blood perfusion (BP) by LASCA, during combination of standard systemic treatment and local medications.

Methods

Twenty SSc patients (mean age 63 ± 12 years, mean disease duration 7 ± 6 years) affected by fingertip DUs of recent onset (mean DU duration 12 ± 7 days) were enrolled after written informed consent to enter the study. All patients were recruited from the Rheumatologic Unit for the Diagnosis and Management of Vascular and Connective Tissue Diseases at the University of Genova. Patients met the ACR/EULAR criteria for SSc (van den Hoogen et al., 2013).

Laser speckle contrast analysis (LASCA)

BP was registered by LASCA device (Pericam PSI, Perimed, Jarfalla, Sweden) in SSc patients at the level of dorsal and palmar regions of the hand, as previously reported (Ruaro et al., 2014; Sulli et al., 2014; Della Rossa et al., 2013). In a second time, to study local BP inside specific areas, different regions of interest (ROIs) were created at the level of ulcer area (Fig. 1C, D: white circles), peri-ulcer area (Fig. 1C, D: area between blue and white circles), as well as periungual and fingertip areas (Fig. 1A, B: white circles), reporting the average BP values as perfusion units (PU).

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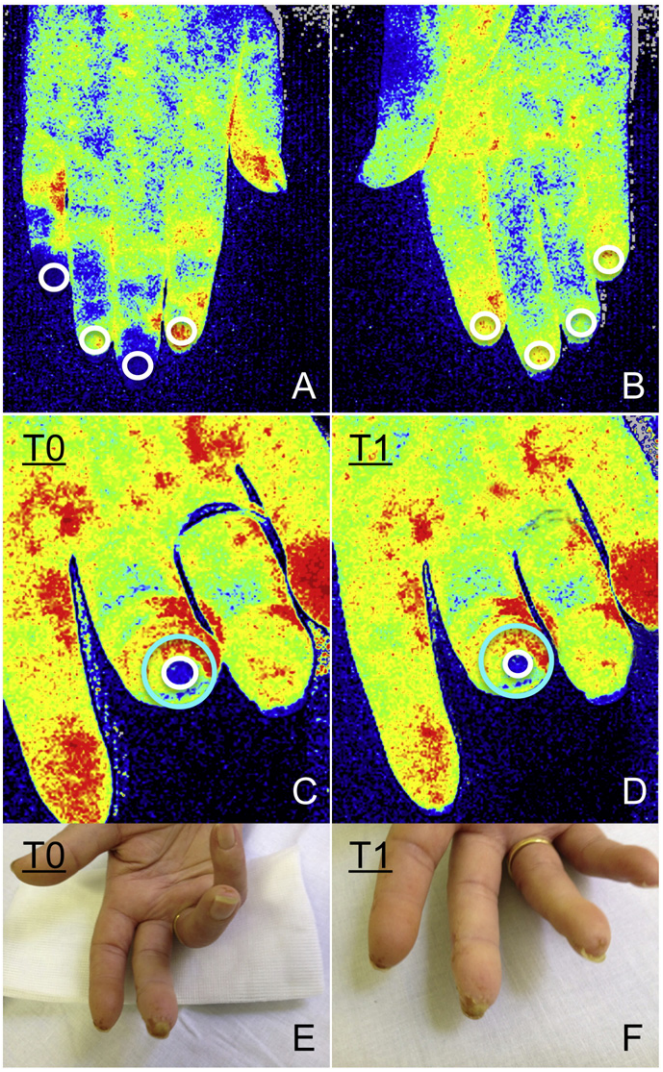

Fig. 1. Distribution of regions of interest (ROIs) (white circles) created in order to evaluate blood perfusion (BP) by LASCA at the level of periungual (A) and fingertip areas (B) in a SSc patients (values quantified as perfusion units, see Table 2). LASCA images (3rd finger) of active ulcer (C, D, white circle) and peri-ulcer areas (C, D, area between blue and white circles), before (T0, C) and after ten days of medication (T1, D), at the level of the fingertips in a SSc patient (see Methods section for further details). Pictures E and F show ulcer status before (T0) and after (T1) local medication (3rd finger) of the same patient. Scan image: Blue colour = low BP, yellow colour = intermediate BP, red colour = higher BP (values quantified as perfusion units, see Table 2).

Care was taken when drawing the ROIs around the DU areas, by following faithfully the DU outline. The ROI to delimit the peri-ulcer area was chosen by drawing an area of 5 mm around the ulcer area (Fig. 1C, D: blue circles), and assessing the perfusion in the area between ulcer and peri-ulcer boundaries (Fig. 1C, D: area between blue and white circles). DU areas, calculated by LASCA, were recorded as square millimetres (mm^2). Direct measure on ulcer diameter was not assessed to avoid the risk of contamination of the lesions.

To evaluate the average BP from either periungual or fingertip areas, BP was calculated by summing the perfusion values of the ROIs of fingers from 2nd to 5th, and then dividing the total value by the number of fingers, as previously reported (9,11). LASCA was performed before (T0) and after 10 days of local dressing (T1). In particular, LASCA was performed 20 min after dressing removing, just before the medication.

The patients waited in an adjoined waiting room (at an average temperature of 23 °C) for at least 30 min before the assessment, and examinations were always carried out by the same operator in all SSc patients.

Treatments and local medication of digital ulcers (DUs)

Patients continued their on-going systemic treatments including vasodilator drugs, endothelin receptor antagonists (ERA) and immunosuppressive drugs, when indicated.

Patients were not taking calcium channel blockers, and they were prostacyclin analogue free from at least two months before entry the study; furthermore, prostacyclins were not started until the end of the study. Clinical characteristics and treatments for patients are reported in Table 1.

Concerning local medications, always performed by same nurse, the ulcers were cleaned with warm saline irrigation to remove any debris tissue, before applying a local standard hydrocolloid dressing. This type of dressing is of carboxymethylcellulose and other hydrocolloids, adherent substances or hydroactive compounds, providing absorption capacity (Chung, 2007; Guillén-Solà et al., 2013). Non-adherent gauze on above reported hydrocolloid dressings was applied in order to retain the medication, and all the package was renewed every 2 days.

Patients did not modify their diet before and during the study, they did not perform any further treatment in addition to local medication made by nurse, and the patients were given the information by the nurse to protect the medication during their normal daily activity.

Visual analogue pain scale (VAS)

VAS (cm 0–10) was administered to patients before and 10 days after local medication. The patients marked on the line from 0 ("no pain") to 10 ("worst imaginable pain") the intensity of DU pain that they felt (Steen et al., 2009; Wewers and Cowe, 1999).

Statistical analysis

Statistical analysis was carried out by nonparametric tests. The Wilcoxon signed rank test was employed to compare paired group of variables, and the Spearman rank correlation test was used to search for any relationships between variables, along with linear regression tests. Any p value lower than 0.05 was considered statistically significant. The results are reported as median and interquartile range [IQR].

Table 1
Patients' clinical and laboratory characteristics.

	Total SSC patients
Number	20
Age (years ± SD)	63 ± 12
Sex (female/male)	20/0
SSc duration (years ± SD)	8 ± 4
Raynaud's duration (years ± SD)	16 ± 4
NVC pattern (early/active/late)	1/9/10
ANA indirect immunofluorescence pattern (centromeric/speckled/homogeneous/nucleolar)	13/6/0/1
Specific autoantibody positivity (ACA/Scl70)	13/6
Skin involvement (limited/diffuse)	11/9
Gastrointestinal involvement (yes/no)	1/19
Lung involvement (yes/no)	2/18
Pulmonary arterial hypertension (yes/no)	2/18
Heart involvement (yes/no)	1/19
Renal involvement (yes/no)	2/18
Digital ulcers (yes/no)	20/0
Systemic treatment (cardioaspirin, PPI, anti-hypertension drugs, cyclosporine, MTX, ERA)	19/19/5/4/4/1

SSc: systemic sclerosis. NVC: nailfold videocapillaroscopy. ANA: anti-nuclear antibodies. ACA: anti-centromere antibodies. Scl-70: anti-topoisomerase antibodies. PPI: proton pump inhibitors. MTX: methotrexate. ERA: endothelin receptor antagonists.