



Correlations between skin blood perfusion values and nailfold capillaroscopy scores in systemic sclerosis patients



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ABSTRACT

Objectives: To correlate blood perfusion (BP) values assessed by laser speckle contrast analysis (LASCA) in selected skin areas of hands and face with nailfold capillary damage scores in systemic sclerosis (SSc) patients.

Methods: Seventy SSc patients (mean SSc duration 6 ± 5 years) and 70 volunteer healthy subjects were enrolled after informed consent. LASCA was performed at different areas of the face (forehead, tip of nose, zygomas and perioral region) and at dorsal and volar regions of hands. Microvascular damage was assessed and scored by nailfold videocapillaroscopy (NVC) and the microangiopathy evolution score (MES) was calculated.

Results: SSc patients showed a significantly lower BP than healthy subjects at fingertips, periungual areas and palm of hands ($p < 0.0001$), but not at the level of face and dorsum of hands. A gradual decrease of BP at fingertips, periungual and palm areas, was found in SSc patients with progressive severity of NVC patterns of microangiopathy (“early”, “active”, or “late”) ($p < 0.01$). A negative correlation was observed between MES and BP values, as well as between loss of capillaries and BP, at the same areas ($p < 0.001$ and $p < 0.01$, respectively). Patients with diffuse cutaneous SSc (dcSSc) showed lower BP than those with limited cutaneous SSc ($p < 0.04$).

Conclusions: LASCA detects a significant reduction of BP only in those areas usually affected by Raynaud’s phenomenon (fingertips, periungual and palm areas), especially in dcSSc patients, and BP values significantly correlate with the nailfold capillaroscopy scores of microangiopathy.

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Introduction

Systemic sclerosis (SSc) is characterized by early impairment of the microvascular system and decreased peripheral blood perfusion together with progressive tissue fibrosis (Cutolo et al., 2010a,b; Herrick, 2008; Rosato et al., 2011).

Nailfold videocapillaroscopy (NVC) is a safe and validated technique to assess and quantify morphological capillary alterations, while laser speckle contrast analysis (LASCA) is a non-invasive method to evaluate and quantify blood perfusion (BP) at different skin sites, especially in SSc patients (Smith et al., 2010; Sulli et al., 2014a; Ruaro et al., 2014). Compared to the limits of the contact and single point technique Laser Doppler flowmetry, LASCA allows analysis of BP on different and larger skin areas of the body, with a more reproducible and safer non-contact approach (i.e. face or legs) (Ruaro et al., 2014). Furthermore, LASCA is less prone to movement artifacts.

Limited information is available about BP at specific body sites in SSc, like either dorsum of hands or face, usually spared by Raynaud’s

phenomenon, with the exception of nose (Cutolo et al., 2010b; Rosato et al., 2011; Ruaro et al., 2014; Murray et al., 2006). The aim of this study was to assess by LASCA the BP in different skin areas of hands and face in SSc patients, and to search for correlations with nailfold capillary damage extent as detected by NVC.

Patients and methods

During their regular followup, seventy consecutive SSc patients (mean age 63 ± 12 SD years, 63 women and 7 men, mean Raynaud’s phenomenon duration 12 ± 11 years, mean SSc duration 6 ± 5 years), according to the new ACR/EULAR criteria and 70 healthy subjects (mean age 63 ± 15 years, 62 women and 8 men), were enrolled and after informed consent (van den Hoogen et al., 2013).

Assessments were carried out after a treatment-free period of at least one month from prostanoids, calcium channel blockers, ACE-inhibitors and endothelin-1 receptor antagonists, in order to avoid the vasodilatory effects of treatments. All SSc patients at the time of analysis were taking aspirin, as a practice in our center.

Complete medical history and clinical examination were recorded, including the detection of either limited (lcSSc), or diffuse (dcSSc) skin involvement. Patients with diabetes, arterial hypertension, or other vascular diseases that could potentially interfere with peripheral

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blood perfusion were excluded. Patients were asked not to either drink coffee or smoke the day of the assessment.

Laser speckle contrast analysis (LASCA)

BP was analyzed by LASCA (Pericam PSI, Perimed, Jarfalla, Sweden) in SSc patients and healthy subjects (Ruaro et al., 2014). The principle of LASCA is that when laser light illuminates a tissue, it forms a speckle pattern. Any such changes in the speckle pattern are recorded by a detector camera and analyzed by software. If the illuminated area is static, then the speckle pattern is stationary. When there is movement in the area, such as red blood cells in tissue, the speckle pattern will change over time and appear blurred. The level of blurring (contrast) is analyzed and interpreted as blood perfusion.

Technical parameters e.g. working distance (14.3–14.8 cm), point density (1386×1036), frame rate resolution (10 images/s), as well as the width and height of the measurement area ($12.5 \times 14/15$ cm) were standardized for all subject evaluations. All subjects stayed in the waiting room for 30 min at 22–23 °C before all the assessments. BP was registered at the level of whole face and dorsal and volar aspects of hands for 30 s, and the values were recorded as perfusion units (PU).

After scan acquisition, regions of interest (ROI) were created at the central area of fingertips and periungual areas from fingers II to V bilaterally, palm and dorsum of both hands, as well as at the level of the face (forehead, tip of nose, zygomas and perioral region) (see Fig. 1 for ROI areas). The ROIs created at the level of periungual areas include a portion of nail and a portion of periungual skin, in order to evaluate blood perfusion in the same area where nailfold capillaroscopy is performed.

The amplitude of the ROI area may be easily reproduced in order to quantitate blood perfusion inside similar areas in all subjects;

furthermore, the assessment of mean BP of a large area by LASCA highly reduces the variability and errors linked to repeated measurements.

The average BP from either fingertips or periungual areas was calculated by summing the perfusion values of 8 fingers together and then dividing the final value by the number of fingers. Likewise, the average BP from palm, dorsum of hands, and zygomas was calculated by summing the perfusion values of the two sides (right and left) together and then dividing the final value by two. The same operator (BR) performed the examination in all SSc patients and healthy subjects, blind to NVC examination. There was a 95% reproducibility of the LASCA assessment by evaluating the same patients two consecutive times, and drawing new ROIs on the body areas.

Nailfold videocapillaroscopy (NVC)

NVC was performed in each patient to assess morphological microvascular damage using a videocapillaroscopy optical probe, equipped with a $200\times$ contact lens, connected to an image analysis software (Videocap, DS Medica, Milan, Italy).

The same operator (CP) performed the NVC examination in all SSc patients the same day of LASCA examination (blind to its results), according to previously published methods (Cutolo et al., 2010a; Smith et al., 2010; Sulli et al., 2012). Each capillary abnormality (including number of capillaries and angiogenic vessels) was scored by a validated semi-quantitative rating scale by considering the average of the eight fingers, and the appropriate NVC pattern of microangiopathy was assigned to the SSc patients on the basis of their nailfold capillary abnormalities: “early” NVC pattern (21 patients), “active” NVC pattern (21 patients) or “late” NVC pattern (28 patients) (Smith et al., 2010; Sulli et al., 2008, 2012). The microangiopathy evolution score (MES), sum of three scores for loss of capillaries, disorganization of the microvascular array and capillary ramifications (range 0–9), was

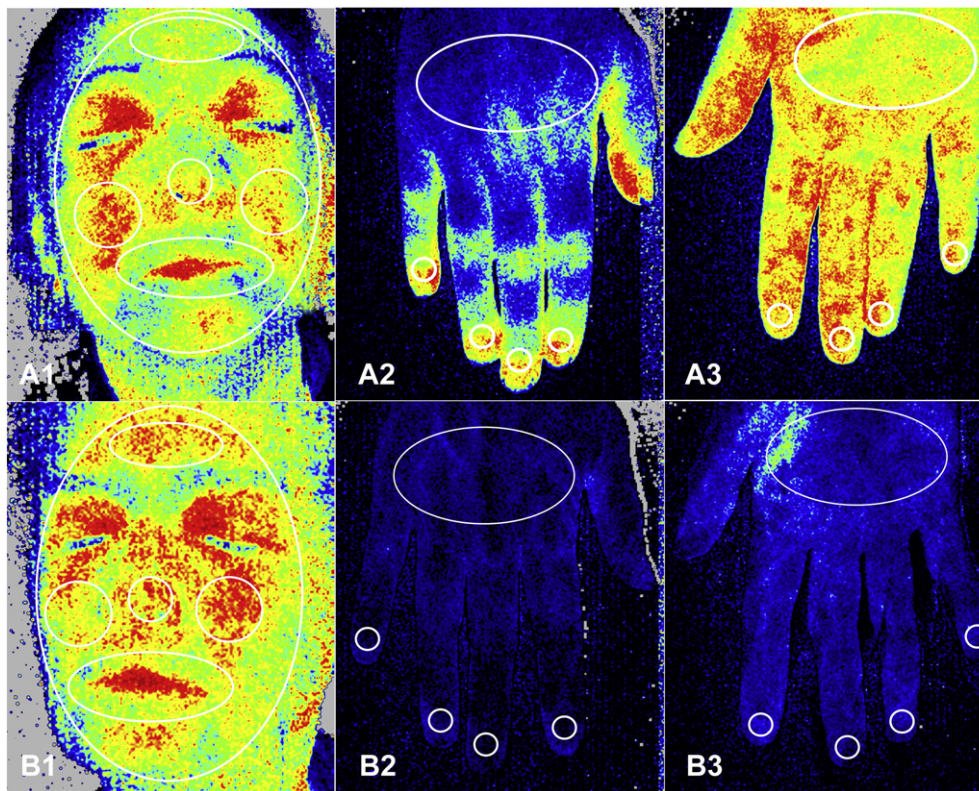


Fig. 1. Laser speckle contrast analysis (LASCA) images of healthy subject (A) and systemic sclerosis patient (B) showing the regions of interest (ROI – white circles) created at the level of whole face, forehead, tip of nose, zygomas, perioral region, dorsum, periungual areas, palm and fingertips to evaluate blood perfusion. A1, B1 face; A2, B2 dorsum of hand; A3, B3 palm of hand.

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