Letters to the Editors

Reproducibility of digital arterial obstructive disease diagnosis using laser Doppler flowmetry in systemic sclerosis

Sirs,

Systemic sclerosis (SSc) is a connective tissue disease characterised by vascular hyper-reactivity and remodelling, immune dysregulation, and fibrosis of the skin and viscera (1). Digital ulcers (DUs) related to digital obstructive arterial disease (DOAD) are frequent in patients with SSc (2).

DOAD can be diagnosed by Laser Doppler Flowmetry (LDF) with a heating box (Fig. 1, Panel 1) with high sensitivity 93% (95% confidence interval, 85%-97%) and specificity 96% (95% confidence interval, 90%-99%) but the interday reproducibility is still unknown. Therefore, our aim was to assess the interday reproducibility of the LDF to diagnose DOAD in SSc patients.

From November 2017 to September 2018, SSc patients fulfilling 2013 ACR/EULAR classification criteria for SSc (3), were prospectively enrolled in the "Reprolaser Study" in the Vascular Medicine Department at Rennes University Hospital. Patients were also sub-classified in limited cutaneous SSc (lcSSc) and diffuse cutaneous SSc (dcSSc) according to Leroy's classification⁴. In this study rules of ethics were followed for all patients in accordance with the Declaration of Helsinki of 2008. All patients provided informed written consent. The study was approved by the "Comité de Protection des Personnes Sud Mediterranée" and registered with the American National Institutes of Health database under reference No. NCT03264820. Patients performed two visits within 15 days apart. Patients had the same treatment between the two visits. A post warming Skin Blood Flow of ≤206 arbitrary units measured with LDF was used to define a finger with DOAD (5). The reproducibility was assessed by the interday agreement using the kappa coefficient with 95% confidence interval. The Landis and Koch interpretation of k values was used: 0.21-0.40: fair; 0.41–0.60: moderate, 0.61-0.80: substantial; >0.80: almost perfect (6). A pvalue <0.05 was considered as statistically significant.

Sixteen patients were included: 8 with dc-SSc and 8 with lcSSc. The general characteristics of the patients are presented in Figure 1, Panel 2. Eight patients had a medical history of DUs and none of them had active DUs. The mean modified Rodnan skin score was 8 ± 8 . The prevalence of DOAD in this population was 60%. The mean duration between the visit 1 and 2 was 9 ± 5 days. The interday agreement for the all digits was substantial with a k value equal to 0.80[95% CI 0.70-0.89]. Only one patient had pain in the heating box that did not disturb the measurement.

This study demonstrates that the interday

reproducibility of the LDF is substantial in SSc patients (6). Ruaro et al. has shown that the intraday reproducibility for LDF to assess blood flow perfusion performed twice within one hour in both patients and controls by the same operator was 88% for LDF (ICC 0.88, 95% CI 0.83-0.91) (7). Our results are closed to these while our SSc patients were evaluated with 15 days apart. Moreover, it has been shown that vascular response to heating seems primarily localised to the fingers (8) and SSc patients with a decreased blood flow perfusion could be partially reversible by local skin heating (9). Here, hand warming using a heating box allowed us to confirm the diagnosis of DOAD by LDF in SSc patients (5). Further, this study demonstrated that in patients with SSc, LDF assessment is safe, with only one patient having increased pain that did not disturb the measurement. However, the substantial reproducibility found in this study cannot be extrapolated to other patient conditions. Finally, the present results suggest that LDF could be used to evaluate the severity of digital vasculopathy and to assess the risk of digital complication such as DUs. Further longitudinal studies will be necessary to address these questions in the future.

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Panel 1: Laser Doppler Flowmetry (LDF) measurement in the heating box was performed on the pulp finger using a single-point LDF probe on each digit (Probe 457 with a fiber separation of 0.25 mm and wavelength of 780 nm; Perimed, Jarfalla, Sweden) connected to a Perimed PF 5010 LDPM unit. The hands were placed inside the warming box for 15 minutes. After 15 minutes, single-point LDF measurements (probe heated to 44.0° C) of each digit were repeated while the hands remained inside the heating box.

Patients Characteristics	n=16
General Datas	
Limited Cutaneous Systemic Sclerosis (lcSSc) [n (%)]	8 (50%)
Diffuse Cutaneous Systemic Sclerosis (lcSSc) [n (%)]	8 (50%)
Age (years) [mean \pm sd]	63±1
Male [n (%)]	6 (38%)
BMI (Kg/m2) [mean \pm sd]	24±4
Cardiovascular Risk Factors	
Arterial Hypertension [n (%)]	5 (31%)
Smoke [n (%)]	0 (0%)
Diabetes Mellitus [n (%)]	3 (19%)
Dyslipidemia [n (%)]	5 (31%
Hands Abnormalities and Rodnan Score	
Raynaud's Phenomenon [n (%)]	16 (100%)
Pitting Scars [n (%)]	8 (50%)
Sclerodactyly [n (%)]	15 (94%)
Pterygium Inversus Unguis [n (%)]	8 (50%)
Telangiectasia [n (%)]	11 (69%)
Modified Rodnan Skin Score (/51) [mean \pm sd]	8±3
Active Digital Ulcers [n (%)]	0 (0%
Auto-Antibodies	
Anti-Nuclear [n (%)]	16 (100%)
Anti-Centromere [n (%)]	8 (8%)
Anti Scl-70 [n (%)]	8 (8%)
Vasoactive Treatment	
Calcium-Channel Blockers [n (%)]	11 (69%)
Endothelin Receptor Antagonists [n (%)]	1 (6%)

Panel 2: Patients Characteristics of the REPROLASER Study

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