Sirs.

CSURI is a capillaroscopic index that is able to identify scleroderma (SSc) patients at high risk for new or non-healing digital ulcers (DU) in the next three months (1). CSURI has been validated, only in patients not treated with bosentan in a large multicentre study in 2011 (1). Bosentan is an endothelin receptor antagonist and at present it is the only drug approved to reduce the number of new scleroderma DU in secondary prevention (2-3).

The aim of the present study was to evaluate the predictive value of CSURI in SSc patients assuming bosentan for the secondary prevention of DU.

Seventy-six consecutive SSc patients treated with bosentan 125 mg bid were enrolled in a multicentre study (female/male 4.4:1; mean age 56.4±13.6 years; diffuse/limited cutaneous subset 30/44) and undergone nailfold videocapillaroscopy (NVC). Fifty-eight patients were also treated with monthly intravenous prostanooids; no patient was taking therapies remained unchanged for the complete duration of the study. All the patients had a history of at least one DU during the previous year, and 26 patients (30.3%) showed ongoing DU. The CSURI was calculated according to previously published methods (1).

Three months after NVC, 36 patients showed DU (18 non-healing ulcers and 18 new DU), with no differences regarding the ongoing therapies. Receiver operator characteristic curve, performed to analyse the prognostic accuracy of CSURI, is reported in Figure 1. The area under the curve was 0.69 (95%-CI 0.57-0.79; p=0.0019) and, at the validated cut-off value of 2.96, sensitivity was 86.1%, specificity 60.0%, positive and negative likelihood ratio 2.15 and 0.23, while negative and positive predictive values were 82.1% and 64.6%, respectively. These patients were compared with a control group of 76 subjects with similar DU history (at least one DU in the last year, 30 of them with active DU; female/male 7:4:1; mean age 51.6±14.7 years; diffuse/limited cutaneous subset 26/50; 73.7% treated with intravenous prostanooids, and 26.3% with calcium channel blockers), but never treated with bosentan. In this group, CSURI showed a sensitivity of 95.2% and a specificity of 67.6%, positive and negative likelihood ratios were 2.94 and 0.07, respectively, while negative and positive predictive values were 96.5% and 65.4%.

CSURI showed a lower negative predictive value in the bosentan group when compared with the control group, while the positive predictive value was similar (1). This discrepancy cannot be clarified by the results of our study. Endothelin-1 is a potent vasoconstrictor that can also affect pro-fibrotic cytokines (4-6) which are closely involved in the pathogenesis of SSc peripheral microangiopathy. However, the latter is sustained by a multifactorial process, only partially known, involving a complex cytokine-cell network. In this context, in some subjects, bosentan could interfere with vessel morphological parameters included in CSURI calculation and reduce the incidence of new DU with different mechanisms (1).

Some authors have observed a general improvement of the NVC pattern in SSc patients treated with bosentan (7-9). These findings are in agreement with our study, although CSURI is calculated by considering the “worst” capillaroscopic image (1). Moreover, the longer period of observation of the other studies should more significantly influence the observed changes in NVC parameters (7-9).

In previous studies (1,10), CSURI was proposed for the screening of SSc patients at risk to develop DU. Therefore, in patients already treated with bosentan the role in primary DU prevention cannot be applicable, and CSURI could play a role in monitoring patients with recurrent DU, regardless of the ongoing specific vasoactive treatments. Drug management based on both clinical features and CSURI could be worthy of further study; therefore, only prospective clinical trials could clarify the correct role of NVC in the prognostic evaluation of scleroderma DU undergoing vasoactive treatments.

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