Concise report

Systemic sclerosis patients with and without pulmonary arterial hypertension: a nailfold capillaroscopy study

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Abstract

Objective. Pulmonary arterial hypertension (PAH) is a complication of SSc due to increased vascular resistance, and abnormal vascularity is a well-known feature of the disease as shown by nailfold videocapillaroscopy (NVC). This study investigated for specific NVC changes in SSc patients with and without PAH to assess any useful difference.

Methods. Twenty-four SSc patients, 12 with PAH and 12 without, entered the study. Evidence of PAH was defined as increased systolic pulmonary artery pressure (PAP) (>35 mmHg), indirectly assessed by echocardiography and confirmed by right heart catheterization (mPAP >25 mmHg). NVC was performed, and a semi-quantitative rating scale, a rating system for avascular areas and a specific NVC pattern evaluation, namely early, active and late, were used.

Results. An NVC score >1 was more frequently found in patients with PAH than those without, 11 cases (92%) vs 5 cases (42%) (P=0.03); an avascular areas grade >1 was present in 10 (83%) and 2 (17%) cases, respectively (P=0.003); and a more severe NC pattern (active/late) was described in 11 (92%) and 5 (42%) patients, respectively (P=0.03). When we compared the mPAP with NVC parameters, we found significant correlations between mPAP values and the NVC score (P<0.005) and with the avascular areas score (P<0.001).

Conclusion. Our results underline the relevance of early microvascular assessment in patients at risk of developing a severe complication such as PAH that can amplify the systemic microvascular impairment in SSc. More severe NVC abnormalities should lead to strict cardiopulmonary surveillance and a complete NVC study is indicated.

Key words: nailfold videocapillaroscopy, systemic sclerosis, pulmonary arterial hypertension.

Introduction

Pulmonary arterial hypertension (PAH) is considered a severe complication with a negative prognostic value that occurs in 10–15% of SSc patients [1]. PAH is characterized by increased pulmonary vascular resistance due to remodelling and occlusion of pulmonary arterioles with consequent elevation of the mean pulmonary artery pressure (PAP) >25 mmHg at rest or >30 mmHg during exercise, in the absence of elevated pulmonary capillary wedge pressure, evaluated by right heart catheterization (RHC) [2]. The presence of abnormal vascularity is a well-known feature of SSc, and these patients show progressive capillary abnormalities on nailfold videocapillaroscopy (NVC), a useful instrument able to identify significant structural changes [3].

Many authors have shown significant association between NVC abnormalities and organ involvement, and more severe capillaroscopy findings correlate with the...
extension and severity of clinical manifestations [4]. In SSc, a reduction of the capillary density, but not the capillary loop dimension, seems to be associated with PAH and correlates with its severity, suggesting that either systemic microvascular changes play a part in the development of PAH or PAH itself contributes to the systemic microvascular changes [5]. The aim of our study was to investigate for specific NVC abnormalities in SSc patients with and without PAH, trying to assess any significant differences to identify those cases with a worse prognosis due to the presence of PAH.

**Patients and methods**

We evaluated 12 consecutive SSc patients diagnosed according to ACR criteria [6], all suffering from PAH diagnosed by echocardiography and confirmed by RHC [2]. They were all females, mean age 66 years (range 50–75 years) and mean disease duration 236 months (range 4–696 months). Two were diffuse and 10 were limited forms.

We then identified 12 SSc patients without PAH matchable for sex (all females) mean age [63 years (range 47–79 years)], mean disease duration [161 months (range 84–502 months)] and the extent of cutaneous involvement (2 with diffuse and 10 with limited forms).

All patients, after giving informed consent, had a clinical, laboratory and instrumental assessment. Their organ system involvement was defined as previously described [7]. The modified Rodnan skin score (mRSS) [8], presence/absence of RP, digital pitting scars, telangectasia and calcinosis were evaluated.

Clinical evidence of isolated PAH was first defined as increased systolic PAP (≥35 mmHg) by echocardiography in the absence of severe pulmonary interstitial fibrosis and then confirmed by RHC (mPAP > 25 mmHg). In patients without PAH, mean PAP was estimated by means of the formula validated by Chemla et al. [9]: mPAP = 2 + (0.61 x systolic PAP). Approval for the study was obtained from the local ethics committee (Azienda Policlinico Umberto I, Rome).

**Nailfold videocapillaroscopy**

NVC was carried out using a videocapillaroscope with a probe (magnification ×200). All the images were registered and collected using a dedicated software system (Blu Vision). NVC was performed according to the standard method [10].

The following parameters were considered, according to previous classifications: the presence of enlarged and giant capillaries, haemorrhages, loss of capillaries (avascularity), disorganization of the vascular array, ramified/bushy capillaries and sludging of blood. A semi-quantitative rating scale was adopted to score these changes: score 0 = no changes; 1 = few (<4) alterations; 2 = some (between 4 and 6) alterations; 3 = frequent (6 or more) alterations per linear millimetre. The mean score for each subject was obtained from the analysis of all fingers [3, 11].

The rating system for avascular areas (avascularity of the capillary bed) was classified as follows: grade 0 = no obvious avascular areas; grade 1 = mild (one or two discrete areas of vascular deletion); grade 2 = moderate (more than two discrete areas of vascular deletion); grade 3 = severe (the presence of large, confluent avascular areas) [12].

Finally, patients were distributed into a proper NVC pattern: (i) early (few giant capillaries, few haemorrhages, relatively preserved capillary distribution, no evident loss of capillaries); (ii) active (frequent giant capillaries, frequent haemorrhages, moderate loss of capillaries with some avascular areas, mild disorganization of the capillary architecture, absent or some ramified capillaries); (iii) late (irregular enlargement of the capillaries, few or absent giant capillaries, absence of haemorrhages, severe loss of capillaries with large avascular areas, severe disorganization of the normal capillary array, frequent ramified/bushy capillaries) [11].

ANAs including ACAs were detected by indirect immunofluorescence on the HEp-2 cell line (binding site); antibodies against topoisomerase I (anti-Scl70) were measured by ELISA (Diamedix, Miami, FL). ESR, CRP, C3 and C4 complement fractions, full blood count and renal function were also evaluated.

**Statistical analysis**

Categorical variables were analysed by χ² test or Fisher’s exact test and differences between the means were determined using the Mann–Whitney test for unpaired samples; Spearman’s rank correlation test was used to analyse correlations between mean PAP values and NVC features. P values < 0.05 were considered statistically significant.

**Results**

We did not find any significant difference concerning age or disease duration. All patients reported having RP. The mean mRSS value was 13 in those patients with PAH and 10 in those without PAH. Digital ulcers were present in 2/12 (17%) and 3/12 (25%), respectively. ACAs were found in 5/12 (42%) and 8/12 (67%) while anti-topoisomerase-1 antibodies were present in 1/12 (8%) and 2/12 (17%), respectively. A significantly higher ESR (>30 mm/h) was found in patients with PAH compared with those without (P < 0.03).

An NC score >1 was more frequently found in patients with PAH [11 cases (92%)], than in those without PAH [5 cases (42%)] (P = 0.03); an avascular areas grade >1 was present in 10 (83%) and 2 (17%) cases with and without PAH, respectively (P = 0.003); and a more severe NC pattern (active/late) was described in 11 (92%) and 5 (42%) patients, respectively, showing a statistically significant difference between the two groups (P = 0.03). Fig. 1 shows the NVC features of SSc patients with and without PAH.

When we compared the mean PAP, evaluated by haemodynamics or estimated by echocardiography in the subgroup without pulmonary hypertension, with the main capillaroscopy parameters of all the SSc patients we found significant correlations between pulmonary pressure values and the NVC score (P < 0.005) as well as with the avascular areas score (P < 0.001) (Fig. 2).
Discussion

NVC is a useful examination for evaluating microvascular changes in the peripheral circulation, thus it has a relevant role for the diagnosis of SSc, where the classic changes are giant capillaries and decreased capillary density with capillary dropout [3, 10]. NVC also seems to be helpful in identifying those SSc patients at risk for PAH in a very early phase of the disease [13]. The main data concern capillary density, resulting in a significant reduction in patients with or without PAH, but with a more severe loss in those with PAH [5, 13]. The hypothesis is that structural changes in the microcirculation, as shown by NVC, may be related to those vascular abnormalities presenting in pulmonary circulation. The common loss of capillaries at nailfold and pulmonary bed may be a similar pathway, although the greater loss of capillaries may be due to PAH itself, a condition able to amplify the reduction of vascularity. Thus NVC findings seem to reflect what happens in the pulmonary circulation of SSc patients, whereas a reduced number of capillaries may represent a marker of disease severity [14].

In contrast, a low prevalence of NVC changes is described in idiopathic PAH compared with SSc patients, substantially consistent with those of healthy subjects [5]. Thus, while SSc with PAH and idiopathic PAH share the same pulmonary vessel abnormalities, there is no evidence for scleroderma-like nailfold changes in the digital bed of patients with idiopathic PAH. It seems that something different happens at least in the nailfold capillaries of PAH patients with or without SSc [15].

Moreover, other authors have shown that more severe NVC abnormalities are associated with the presence of PAH in SSc and also with higher pulmonary vascular resistances, ECG abnormalities, reduced vital capacity and reduced DLco [16], thus more severe systemic involvement together with more severe NVC findings.
In the present study we investigated specific and detailed NVC changes using a semi-quantitative rating scale, the rating system for avascular areas and a specific NVC pattern evaluation. For each of these items we detected a clear association between more severe scores and the presence and severity of PAH, while we were unable to correlate PAH with other clinical or laboratory findings, with the exception of ESR values, thus sustaining a major sensitivity for NVC that leads us to underline the relevance of early microvascular assessment in those SSc patients at risk of developing a severe complication such as PAH. The hypothesis is that this relevant vascular complication can somehow amplify the systemic microvascular impairment constantly detectable in SSc. In our opinion, a correct approach to SSc patients should always include a complete NVC study in order to identify early those cases who may possibly develop a complication such as PAH.

**Rheumatology key messages**
- NVC is useful to assess the risk of developing PAH in SSc.
- Severe nailfold capillaroscopy changes are associated with PAH in SSc.

**Disclosure statement:** The authors have declared no conflicts of interest.

**References**


