Autoimmunity Reviews 21 (2022) 103087

Contents lists available at ScienceDirect

Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev

Review

Standardised interpretation of capillaroscopy in autoimmune idiopathic inflammatory myopathies: A structured review on behalf of the EULAR study group on microcirculation in Rheumatic Diseases

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ARTICLE INFO

Keywords:
Idiopathic inflammatory myopathies
Dermatomyositis
Microcirculation
Nailfold videocapillaroscopy
EULAR study group on microcirculation in rheumatic diseases
Systematic literature review

ABSTRACT

Objective: We conducted a systematic review, on behalf of the EULAR Study Group on Microcirculation in Rheumatic Diseases (EULAR SG MC/RD), to investigate the value of nailfold videocapillaroscopy (NVC) in idiopathic inflammatory myopathies (IIM).

Methods: Three electronic databases were systematically searched to find all relevant manuscripts reporting NVC outcomes in IIM patients. Articles were assessed based on study design, population, NVC methodology and description of NVC results. To allow comparison between the articles, all NVC results were interpreted according to standardised capillaroscopic terminology, as previously consented by the EULAR SG MC/RD and the Scleroderma Clinical Trials Consortium (SCTC) Group on Capillaroscopy.

Results: Of the 653 identified records; five were retained after critical appraisal on title, abstract and manuscript level. A marked difference in NVC was observed between (juvenile) dermatomyositis [(j)DM] *versus* polymyositis, healthy controls and systemic sclerosis patients. In addition, reduced capillary density and scleroderma pattern seem to be associated with active disease in (j)DM, while immunosuppressive treatment appears to reduce NVC abnormalities.

Conclusion: This is the first systematic review investigating NVC in IIM, interpreting the results according to an international consented standardised manner, as proposed by the EULAR SG MC/RD and SCTC Group on Capillaroscopy. We can conclude that NVC presents a promising asset in the diagnosis of (j)DM. Moreover, NVC could be a biomarker for organ involvement and follow-up. Large multicentre prospective standardised studies are further needed to definitely describe associations with clinical and laboratory parameters in the different IIM subtypes.

Abbreviations: ACR, American College of Rheumatology; ANA, anti-nuclear antibodies; ASS, anti-synthetase syndrome; DM, dermatomyositis; EULAR, European League Against Rheumatism; EULAR SG MC/RD, EULAR Study Group on Microcirculation in Rheumatic Diseases; HC, healthy controls; HRCT, high-resolution computed tomography; IIM, idiopathic inflammatory myopathies; ILD, interstitial lung disease; jDM, juvenile DM; MAA, myositis-associated autoantibodies; MSA, myositis-specific autoantibodies; NVC, nailfold videocapillaroscopy; OM, overlap myositis; PM, polymyositis; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses; RP, Raynaud's phenomenon; SCTC, Scleroderma Clinical Trials Consortium; SSc, systemic sclerosis.

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https://doi.org/10.1016/j.autrev.2022.103087
Received 1 March 2022; Accepted 5 April 2022
Available online 12 April 2022

1. Introduction

The idiopathic inflammatory myopathies (IIM) are a group of rare inflammatory diseases hallmarked by muscle inflammation, with or without extramuscular manifestations [1]. In recent years, the IIM landscape has evolved enormously, largely thanks to the identification of myositis-specific autoantibodies (MSA) and myositis-associated autoantibodies (MAA) [2]. These autoantibodies correlate with various clinical manifestations (*e.g.* the presence of anti-MDA5 antibodies is associated with rapidly progressive interstitial lung disease [ILD], whereas anti-TIF-1-γ antibodies are linked with cancer associated dermatomyositis [DM]). As a result, new IIM subtypes, such as anti-synthetase syndrome (ASS), have been proposed [3–5]. The IIM are now classified into five subtypes: DM, polymyositis (PM), overlap myositis (OM), including ASS, immune-mediated necrotizing myopathy, and sporadic inclusion body myositis. Over the years, classification criteria have been developed to classify these complex diseases. In 1975, Bohan and Peter published their proposal for the classification of PM and DM. According to these criteria, PM can be considered in patients with muscle weakness, elevated muscle enzymes, suggestive electromyographic and histopathological features. The additional presence of specific skin lesions leads to a classification of DM (Fig. A.1.) [6,7]. In 2017, the European League Against Rheumatism and American College of Rheumatology (EULAR/ACR) presented the first validated classification criteria for IIM. These criteria use a number of clinical and laboratory variables and allow for subclassification into the most frequent IIM subgroups [8,9].

By visualising the distal nailfold capillaries, nailfold video-capillaroscopy (NVC) is frequently used to differentiate between primary and secondary Raynaud's phenomenon (RP) due to scleroderma spectrum diseases. NVC plays an important role in the daily management of SSc [10,11]. Not only is it included in the 2013 ACR/EULAR classification criteria, NVC characteristics have also shown to be predictive for future organ involvement in patients with SSc [12–17]. To date, there are few NVC studies in IIM patients using a consensus-based evaluation. The principal aim of this manuscript is to critically review the literature on IIM and NVC, and to report the results standardisedly by using the consensual reporting framework of the EULAR Study Group on Microcirculation in Rheumatic Diseases (EULAR SG MC/RD) and the Scleroderma Clinical Trials Consortium (SCTC) Group on Capillaroscopy [16].

2. Methods

2.1. Research strategy (supplementary file 1)

The databases of PubMed, Web of Science and EMBASE were systematically searched according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 guidelines [18]. Records published before July 1st 2021 were included in the search. Only articles in English were withheld. All unique records were screened based on study design, population and NVC methodology. Only if the majority of studied patients met the Bohan and Peter criteria or the 2017 EULAR/ACR Classification Criteria for IIM, the study was considered eligible [6,7,9]. Furthermore, we wished to exclusively retain studies performing standardised NVC, as previously described by the EULAR SG MC/RD and SCTC Group on Capillaroscopy [16]. Throughout literature multiple NVC devices with different techniques and magnifications as well as different definitions to describe NVC alterations have been used. However, these variables indisputably implicate difficulties in comparing NVC manuscripts. When evaluating different NVC studies, it is thus important to take into account the used NVC device, image acquisition and examination method [19]. Currently, evaluation of all fingers except for the thumbs, with a magnification of 200 fold, is accepted as gold standard [16,20,21]. All manuscripts using other magnifications were excluded.

2.2. Quality assessment (supplementary file 2)

There are no standardised tools for assessing the methodological quality of NVC studies. We therefore adapted the assessment process used by Melsens et al. [22]. This tool was developed using the most recent recommendations consented by the EULAR SG MC/RD and SCTC Group on standardised capillaroscopy and the Consensus-based Standards for the selection of health Measurement Instruments- Outcome Measures in Rheumatology Clinical Trials good methods checklist [16,23].

2.3. Data abstraction

In order to enable a comparison between the retained articles, all quantitative, semi-quantitative and qualitative NVC results were interpreted following standardised capillaroscopic terminology [16]. If a certain NVC parameter was not clearly defined in the manuscript, it was not retained for analysis.

Firstly, in quantitative assessment, the capillary density, capillary dimension, capillary morphology and microhaemorrhages are documented per unit of 1 linear millimetre (mm). "Normal" mean capillary density is considered ≥7 capillaries per linear mm in adults [16]. It has been suggested that the capillary density in children is lower, and increases with age (5–9 per linear mm) [24]. Other terms such as "capillary loss" or "avascular areas" are also used to document capillary density. "Capillary loss" is defined as a lower density than what is considered normal. "Avascular areas" are characterised by the absence of consecutive capillaries [16]. A "normal" capillary dimension refers to a diameter of ±20 μm (μm), whereas giants are normally shaped capillaries with an apical diameter of ≥50 μm. Capillaries with an diameter of 20-50 μm are called dilated capillaries and can be homogeneous or irregularly enlarged [16]. Concerning morphology, a "normal" shape is the hairpin, tortuous shape or (single/double) crossing of the limbs, on the condition that the tip of the capillary is convex. All other capillaries should be considered as non-specific abnormalities [16]. This classification into normal or abnormal capillary morphology has proven to show an excellent reliability [16,25,26]. Microhaemorrhages are characterised by dark masses of haemosiderin deposits [16]. An often-used semi-quantitative scoring method categorises the number of capillaroscopic characteristics *versus* the total number of capillaries found in that linear mm in a score (0 = no changes, 1 = ≤ 33% of capillary alterations/reduction, 2 = 33–66% of capillary alterations/reduction, 3 = ≥66% of capillary alterations/reduction, per linear mm) [27,28]. Thirdly, in qualitative NVC assessment, images are classified into different patterns. Initially, an image can be classified into scleroderma-pattern *versus* non-scleroderma pattern [29]. Additionally, a scleroderma pattern can be subclassified in early, active and late scleroderma pattern [16,30]. The "scleroderma-like" pattern is defined as a capillary pattern showing mixed microvascular markers of the scleroderma capillary patterns, but not fully fitting the definition for the single early, active or late scleroderma pattern (see Fig. A.2. for examples) [27].

2.4. Association of NVC findings and disease/laboratory parameters

Hypothesised associations between NVC and clinical or laboratory parameters were noted. If a particular association was found in none, one or two or more of the studies, it was considered non-conclusive, suggestive or conclusive, respectively. If studies showed opposite results, the association was considered non-conclusive.

3. Results

3.1. Search process and quality assessment

A total of 653 records has been identified in the PubMed, EMBASE and Web Of Science databases (138, 377, 138, respectively). After critical elimination, 42 articles remained for full-text review, leading to five retained articles (supplementary file 1). No studies were excluded based on quality (supplementary file 2). Three of the final articles report results from an adult IIM population, whereas two manuscripts study juvenile DM (jDM) patients [31,32]. Supplementary file 3 provides an overview of the study design, population and methodology of the retained manuscripts.

3.2. Capillaroscopic parameters (Table A.1, A.2. and A.3.)

3.2.1. (Semi-) quantitative capillaroscopic parameters (supplementary file 4)

3.2.1.1. Capillary density. Manfredi et al. studied capillary density in a semi-quantitative way, by determining a mean density score (0 = ≥7, 1 = 4–6, 2 = ≤3 capillaries/mm). Investigating an adult population, they found a significant lower density score in DM patients (0.96) compared to healthy controls with primary Raynaud's phenomenon (HC; 0.00; $p \leq 0.001$) and PM patients (0.04; $p \leq 0.001$). They also found a lower mean density in DM patients with disease duration ≤6 months compared to patients with longer disease duration ($p = 0.039$) [33]. The 2016 study from the same group examined DM and SSc patients and revealed a lower density in SSc *versus* DM (mean density score: 1.26 *vs.* 0.93; $p = 0.048$). Importantly, the SSc group deliberately included 30 patients with early, 30 with active and 30 with late scleroderma pattern. When the entire DM group was compared separately with each subgroup of SSc patients with different scleroderma patterns, the DM patients showed significantly more capillary loss than patients with an early scleroderma pattern ($p = 0.018$). In contrast, they presented less capillary loss than patients with active and late scleroderma patterns ($p = 0.027$ and < 0.001, respectively) [34].

Barth et al. described capillary density in a quantitative way in a juvenile cohort. A significantly lower density was found in jDM patients compared to HC (6.4 ± 2.1/mm *vs.* 7.6 ± 0.8/mm; $p < 0.01$), which persisted after controlling for age. When classifying the jDM patients into active and inactive disease, a significantly lower capillary density was found in the group with active disease (5.9 ± 2.3/mm *vs.* 7.0 ± 1.7/mm; $p = 0.031$) [32].

3.2.1.2. Capillary dimension. More dilations were seen in DM patients (69%) compared to PM patients (17.4%; $p \leq 0.001$) and HC (17%; $p \leq 0.001$). Giants were present in 60–65.5% of DM patients, but absent in PM patients and HC [33,34]. Compared with SSc patients, a lower prevalence of giants was seen in DM patients ($p \leq 0.001$). On the other hand, a significantly higher number of abnormal shaped capillaries with an apical diameter of ≥50 μm was seen in patients with DM compared to SSc patients ($p \leq 0.001$) [34]. Giants were significantly more frequent ($p = 0.027$) in DM patients with shorter disease duration (≤6 months) than in DM patients with longer disease duration (85.7% *vs.* 46.7%) [33].

In another study, Manfredi et al. saw a significant decrease of the number of abnormal shaped capillaries with an apical diameter of ≥50 μm after 30-month follow up in DM patients ($p = 0.018$). The number of giants tended to decrease as well, without reaching statistical significance ($p = 0.058$). In SSc, contrastingly, the number of giants was much more stable. [34].

In jDM patients more dilations (33% *vs.* 11%; $p < 0.01$) and giants (9 *vs.* 0%; $p < 0.01$) were noted compared to a HC group. In addition, active jDM patients seemed to present with giants more often than inactive jDM patients. However, this difference failed to be significant [32].

3.2.1.3. Capillary morphology. A significantly higher ratio of abnormal shapes was found in DM patients (>55%) compared to HC (9.4%; $p \leq 0.001$), PM patients (8.7%; $p \leq 0.001$) and SSc patients (34.1%, $p = 0.042$) [33,34]. The presence of abnormal shapes increased significantly after 30 months of follow-up ($p = 0.022$) [34].

3.2.1.4. Microhaemorrhages. Compared to PM patients and HC, more microhaemorrhages were seen in DM patients ($p \leq 0.001$). There was no significant difference between PM patients and HC [33]. When comparing DM to SSc, the presence of microhaemorrhages was similar at baseline evaluation. At 30 months, there were less microhaemorrhages in DM patients, however, without reaching statistical significance [34].

Significantly more microhaemorrhages were seen in jDM patients than in HC ($p < 0.01$). There was no significant difference between active and inactive disease [32].

3.2.2. Qualitative capillaroscopic parameters (supplementary file 5)

Manfredi et al. and Kubo et al. used standardised definitions for scleroderma (early, active and late) and scleroderma-like pattern [16,27,33,35]. Manfredi et al. revealed a scleroderma pattern in 69% of DM and 0% of PM patients and controls. The presence of a scleroderma pattern was more common in DM patients with a shorter disease duration (<6 months), although the difference between groups was not significant ($p = 0.063$) [33]. Kubo et al. found a scleroderma pattern and scleroderma-like pattern in 32.6% and 32.7% of DM and 5.6% and 22.2% of PM patients, respectively. The IIM patients presented with an early scleroderma pattern more frequently than with an active or late scleroderma pattern (15.7%, 7.1% and 2.9%, respectively). An early and active scleroderma pattern was significantly more prevalent in the SSc group, while the scleroderma-like pattern was more common in the IIM group [35].

Remarkably, after a one-year follow-up and treatment with immunosuppressive therapy, scleroderma (−like) pattern disappeared in more than half of the IIM patients (55.7% at baseline *vs.* 25% at follow-up; $p < 0.001$). This decrease was not seen in the SSc group [35].

Barth et al. also describe scleroderma patterns. However, the definition used for early scleroderma pattern was not compatible with the present consented standard [16]. On the other hand, active and late scleroderma pattern were defined in line with the present consented EULAR study group on microcirculation consensus definition. A significant higher prevalence of these patterns was found in jDM patients compared to HC ($p < 0.01$). In addition, the prevalence of a late scleroderma pattern was higher in active *vs.* inactive disease ($p < 0.05$). [32].

3.3. Association between NVC findings, clinical and laboratory parameters (Table A.4)

Two studies showed significantly more capillary loss in DM patients with shorter disease duration, while one of them also found significantly more giants [32,33]. Contrastingly, Kubo et al. observed no significant difference in disease duration when comparing patients with and without scleroderma (−like) pattern. However, they did notice a significant decrease in NVC abnormalities after one year with treatment with immunosuppressive therapies [35]. Barth et al. found a weak correlation between lower capillary density and active global disease ($p < 0.05$, $r < 0.5$), active skin disease ($p < 0.05$, $r < 0.5$) and muscle

weakness ($p < 0.05$, $r < 0.5$). They also found a higher prevalence of scleroderma pattern in patients with high total disease activity ($p < 0.05$) [31,32]. Similarly, Kubo et al. observed a scleroderma (−like) pattern more often in patients with active DM skin lesions such as Gottron papules and heliotropic rash ($p = 0.004$, $p = 0.003$). While searching for a relationship between NVC patterns and skin histopathology, they found scleroderma (−like) pattern to be associated with more severe perivascular lymphocytic infiltration, suggesting a possible correlation [35]. Manfredi et al. on the other hand found no association with skin disease [33]. Two studies did not find an association between NVC abnormalities and muscle weakness, myalgia or muscle enzymes [33,35]. Moreover there was no significant relation with the level of creatine kinase or acute phase proteins [32,33,35]. Barth et al. described a weak correlation ($r < 0.4$) between capillary density and forced vital capacity and signs of airway disease on high-resolution computed tomography (HRCT) [31]. No significant association was found between NVC parameters and ILD or internal malignancies [31,33,35]. Three studies observed no significant association between NVC alterations and RP [33–35]. Manfredi et al. found no association between capillaroscopic findings and autoantibodies (antinuclear autoantibodies, anti-Jo-1, anti-SSA), whereas Kubo et al. found the scleroderma (−like) pattern to be present more often in patients with anti-MDA5 and anti-TIF1γ antibodies and significantly less in patients with anti-synthetase antibodies [34,35]. One study found a clear decrease of NVC abnormalities after one year of immunosuppressive therapy (*e.g.* cyclophosphamide) [35]. No association with vasomodulatory therapy was found [34].

4. Discussion

With this review we provide for the first time an overview of the available NVC studies in IIM that implement standardised image acquisition and report with a uniform standardised interpretation according to by the EULAR Study Group on Microcirculation in Rheumatic Diseases and Scleroderma Clinical Trials Consortium (SCTC) Group on Capillaroscopy [16].

These studies indicate that NVC can be a valuable tool in the management of IIM.

Firstly, NVC characteristics differ between DM and SSc and healthy controls, but also between different IIM subsets. Two studies described a significant difference in NVC findings between DM and SSc patients [34,35]. DM patients seem to have less capillary loss than SSc patients in general. When specifically comparing DM to SSc patients with early, active or late scleroderma patterns, DM patients presented with significantly more capillary loss only than SSc patients with an early scleroderma pattern [34]. Noteworthy is also that the presence of scleroderma-like patterns seems to be discriminatory between IIM patients and SSc patients (respectively present in 30% *vs.* 0%) [35].

In conjunction with this, NVC shows also clear differences between (j)DM patients and HC / PM, demonstrated by a significantly lower capillary density and higher prevalence of dilations, giants and scleroderma pattern in DM and jDM patients [32,33]. No differences were found between PM patients and HC [33]. Since vasculopathy is thought to play an important role in the pathogenesis of (j)DM, and not in PM, this finding is not surprising and underlines the potential value of NVC as an additional asset in the diagnosis of DM [36–41]. Remarkably, Kubo et al. and Manfredi et al. showed contrasting results regarding the presence of scleroderma (−like) patterns in PM patients (28% *vs.* 0%). This could potentially be explained by the heterogeneity in applied classification criteria, being the 2017 EULAR/ACR Classification Criteria and the Bohan & Peter criteria, respectively [33,35]. When using the former criteria, ASS patients are more likely to be diagnosed and subsequently subcategorised as PM, as the presence of anti-Jo-1 antibodies is an important criterion. Thus, higher prevalence of ASS patients is expected in the PM subgroup [41]. It can be hypothesised that ASS patients show more NVC alterations than PM patients, given the fact that, similar to DM, vasculopathy plays a role in the pathophysiology of ASS [3,42]. This hypothesis was confirmed by two recent retrospective studies, showing a high prevalence of scleroderma (−like) pattern in ASS patients [42,43]. These contrasting results underscore the importance of future prospective NVC studies that will compare and truly respect the different IIM subtypes.

Secondly, this review describes suggestive correlations between NVC findings and disease activity. In SSc, disease severity and the risk of organ involvement are clearly associated with progressive loss of capillaries and more severe capillaroscopy patterns [10,11,13,14,44,45]. In IIM, studies are scarcer and the evidence is less demonstrable. Interestingly, one study in jDM found a lower capillary density and higher prevalence of active and late scleroderma patterns significantly correlated with active disease, both with global disease activity and with muscle impairment [32]. One study also found a significant correlation between scleroderma pattern and more severe perivascular lymphocytic infiltration on skin biopsy [35]. Data on clinical skin involvement, however, were conflicting [33,35]. Although pulmonary disease and concurrent malignancies are important complications in IIM, these features were hardly investigated in the retained manuscripts, leading to inconclusive associations [31–33,35,46,47]. An interesting retrospective study by Wakura et al. did describe a significant correlation between capillary loss and the extent of lung fibrosis on HRCT in DM patients with anti-MDA5 and antisynthetase antibodies. Furthermore, a moderate correlation was observed between giants and ground glass opacities on HRCT. Finally, there were significantly more microhaemorrhages and abnormal shapes present in the group that died due to ILD compared to the group that survived [47]. Given the impact of these disease manifestations, further investigation of a possible role for NVC as a predictive biomarker for lung disease or underlying malignancy is warranted, with interpretation through internationally consented standardised definitions [26,48]. No associations between NVC and Raynaud's phenomenon, CRP and muscle enzymes were observed [32–34,40].

Thirdly, since the importance of autoantibodies is rapidly increasing in IIM, this review also evaluated potential associations between NVC parameters and myositis specific antibodies. However, the search for correlation between NVC alterations and MSA was rather limited in the retained studies. This is not unexpected since detection of MSA was historically confined to research laboratories, the routine measurement of most MSA being considerably novel [2]. One study in our review observed a striking association between the presence of anti-TIF1 and anti-MDA5 antibodies and NVC scleroderma spectrum abnormalities. Contrastingly, prevalence of anti-synthetase antibodies was significantly lower in patients with NVC scleroderma spectrum abnormalities [35]. Some recent retrospective studies also investigated correlations with MSA, but mostly found conflicting results [42,47,48]. Larger prospective studies are necessary to make conclusive statements about correlations between MSA and NVC alterations.

Finally, in contrast to the slowly progressive NVC alterations in SSc patients, NVC seems to display a more changeable and even reversible pattern in IIM patients [34,49]. In relation to this, some authors found a clear association between disease duration and NVC abnormalities in DM patients, with an increase in nailfold capillaroscopic density and a reduction of giant capillaries over time [32,33]. Similarly, De Angelis et al. found a significant turnover of microhaemorrhages and abnormal shapes in DM patients compared to more stable NVC findings in SSc patients after 4, 8 and 12 weeks ($p = 0.001$–0.044) [34,49]. Only two of the retained studies examined the effect of therapy on the NVC

alterations in IIM patients [34,35]. One of them observed a striking decrease in NVC abnormalities after one year of immunosuppressive therapy, with disappearance of scleroderma spectrum abnormalities in more than half of the patients [35]. The other one on the other hand, found no association with vasomodulary therapy [34]. When searching the available literature, few studies investigated a possible effect. In 2011, Schmeling found a decrease in capillary loss after immunosuppressive treatment in 28 jDM patients [50]. Mugii et al. also found favourbale changes in NVC abnormalities after immunosuppressive treatment, with reduction of dilated capillaries, haemorrhages and capillary loss [51]. In SSc, vasomodulatory therapy has been associated with fewer capillary alterations, making it a plausible marker for disease control [52–54]. An association with therapy in IIM should certainly be further investigated, as it would implement a new and non-invasive parameter for follow-up in therapeutic trials.

Recently, IIM classification has progressed from a clinicopathological approach with only two subsets (DM and PM), towards a clinicoseropathological approach with multiple subsets, linked to specific autoantibodies [1,2,55]. This evolution impedes easy comparison between studies, and the use of different classification criteria could explain several inconsistences that were encountered in this review. Future research on NVC in IIM should therefore take this evolution into consideration and focus on a standardised NVC evaluation in all IIM subsets [16].

The limited number of studies retained in this review and the heterogeneity in patients and parameters investigated may have hampered further the finding of additional conclusive associations between NVC and clinical and laboratory parameters.

5. Conclusion

This first systematic review on capillaroscopy in IIM supports the use of NVC as an additional asset in the diagnosis and follow-up of DM. NVC could be a biomarker for evaluating disease activity and response on therapy, making it a potential new parameter for follow-up in therapeutic trials. The marked differences between DM and PM patients, along with the apparent lack of studies considering the other subtypes, highlight the need for future prospective NVC studies comparing the different IIM subtypes. Large multicentre prospective standardised NVC studies are needed to further investigate associations between NVC parameters and MSA, disease activity, organ involvement and response to therapy.

Funding statement

Vanessa Smith is a Senior Clinical Investigator of the Research Foundation – Flanders (Belgium) (FWO) [1.8.029.20 N]. The FWO was not involved in study design, collection, analysis and interpretation of data, writing of the report, nor in the decision to submit the manuscript for publication.

Vanessa Smith is supported by an unrestricted educational chair on systemic sclerosis of Janssen-Cilag NV. Janssen-Cilag NV was not involved in study design, collection, analysis and interpretation of data, writing of the report, nor in the decision to submit the manuscript for publication.

Data availability statement

Data sharing is not applicable to this article as no new data were created or analysed.

Statement of author contribution

Yves Piette: Ideation of the study, substantial contributions to the design of the study, acquisition of data, analysis and interpretation of data, drafting of the article, critical revision of the intellectual content, final approval of the version to be published.

Valerie Reynaert: Substantial contributions to the design of the study, acquisition of data, analysis and interpretation of data, drafting of the article, critical revision of the intellectual content, final approval of the version to be published.

Amber Vanhaecke: Acquisition of data, analysis and interpretation of data, critical revision of the intellectual content, final approval of the version to be published.

Carolien Bonroy: Critical revision of the intellectual content, final approval of the version to be published.

Jan Gutermuth: Critical revision of the intellectual content, final approval of the version to be published.

Alberto Sulli: Ideation of the study, critical revision of the intellectual content, final approval of the version to be published.

Maurizio Cutolo: Ideation of the study, critical revision of the intellectual content, final approval of the version to be published.

Vanessa Smith: Ideation of the study, substantial contributions to the design of the study, acquisition of data, analysis and interpretation of data, drafting of the article, critical revision of the intellectual content, final approval of the version to be published.

Submission Declaration

We confirm that this work is original and has not been published elsewhere.

Informed consent

Written informed consent was obtained from the patients in this manuscript.

Declaration of Competing Interest

Vanessa Smith reports a relationship with Boehringer-Ingelheim Pharma GmbH&Co that includes: speaking and lecture fees. Vanessa Smith reports a relationship with Janssen-Cilag NV that includes: speaking and lecture fees. Vanessa Smith reports a relationship with UCB Biopharma SPRL that includes: speaking and lecture fees. Vanessa Smith reports a relationship with Boehringer Ingelheim Pharma GmbH and Co that includes: consulting or advisory. Vanessa Smith reports a relationship with Boehringer Ingelheim Pharma GmbH and Co that includes: funding grants. Vanessa Smith reports a relationship with Janssen-Cilag NV that includes: funding grants. M. Cutolo, co-author, is member of the editorial board of Autoimmunity Reviews

Acknowledgements

The Ghent University Hospital is member of the European Reference Network on Rare and Complex Connective Tissue and Musculoskeletal Diseases (ERN ReCONNET), of the Flemish Network on rare connective tissue diseases (VNZZ) as well as Centre of Excellence for Imaging of EULAR. We would like to thank all collaborators of the EULAR Study Group on Microcirculation in Rheumatic Diseases (EULAR SG MC/RD). In particular we would like to express our gratitude to Prof. A. Herrick for her continuous efforts in this study group and for her contributions to this manuscript.

Appendix A

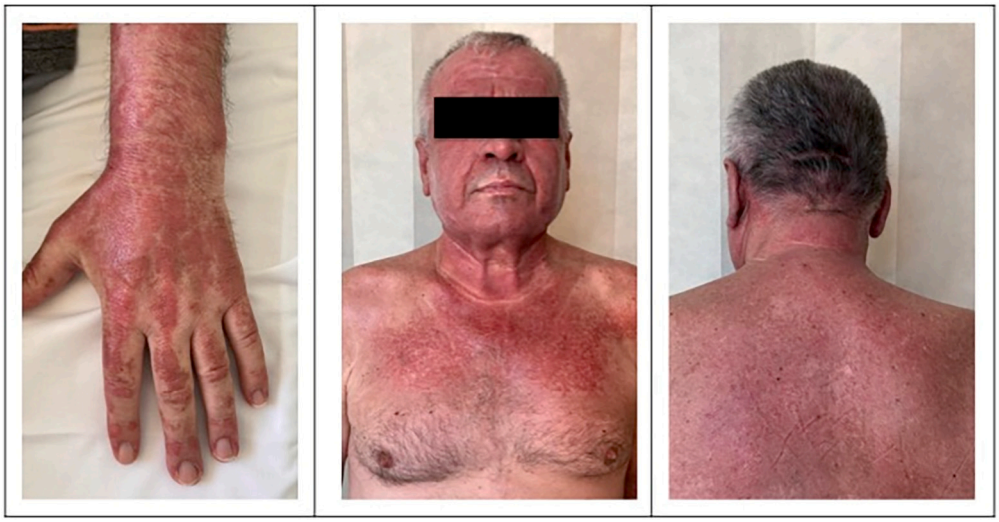


Fig. A.1. Typical skin lesions in a patient with dermatomyositis and anti-TIF1γ antibodies.
Left panel: Gottron's sign on the dorsum of the hand and fingers.
Middle panel: V-sign on the chest and malar/facial erythema.
Right panel: scalp erythema and shawl sign on upper back.

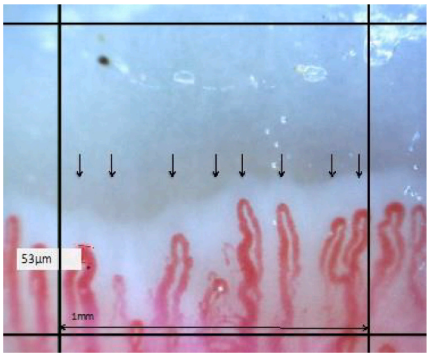
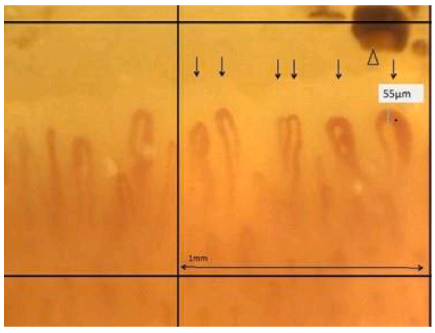
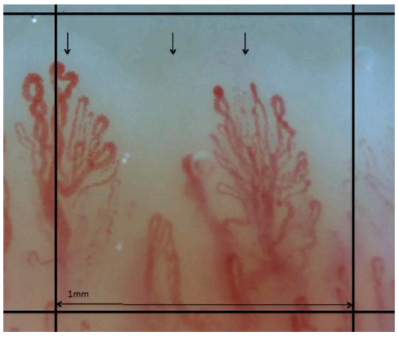
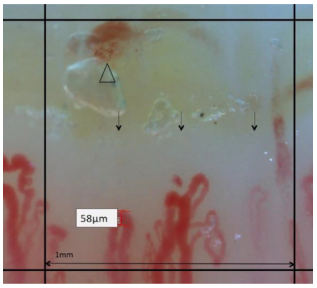
Scleroderma pattern [a]	
Early: The early scleroderma pattern contains few giant capillaries, some haemorrhages and normal density.	 **Capillaroscopic characteristics:** *Density: 8 capillaries in 1 linear mm (↓)* *Dimension: Presence of giant (*)* *Morphology: Some abnormally shaped capillaries* *Haemorrhages: None* *Pattern: Early scleroderma pattern*
Active: The active scleroderma pattern is defined as frequent giant capillaries, frequent haemorrhages and moderate loss of capillaries.	 **Capillaroscopic characteristics:** *Density: 6 capillaries in 1 linear mm (↓)* *Dimension: Presence of giant (*)* *Morphology: Predominantly normal* *Haemorrhages: Present (Δ)* *Pattern: Active scleroderma pattern*
Late: The late scleroderma pattern involves irregular enlargement of capillaries and no giants. There is a severe loss of capillaries and presence of multiple abnormally shaped capillaries.	 **Capillaroscopic characteristics:** *Density: 3 capillaries in 1 linear mm (↓)* *Dimension: No giants* *Morphology: Multiple abnormally shaped capillaries* *Haemorrhages: None* *Pattern: Late scleroderma pattern*

Fig. A.2. Qualitative NVC assessment.
a: Scleroderma pattern as consented by the EULAR SG MC/RD and the SCTC Group on Capillaroscopy (16, 30). b: A pattern that is often mentioned when assessing NVC in patients with DM, is the 'scleroderma-like' pattern (27). c: Capillaroscopic images (Videocapillaroscope, DS Medica, 200×), showing 'scleroderma-like' patterns.

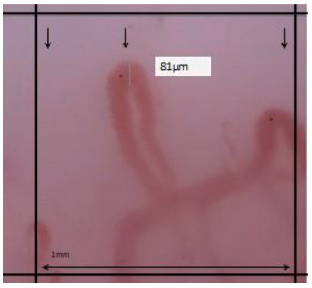
Scleroderma-like pattern [b]

The 'scleroderma-like' pattern is defined as a capillary pattern showing mixed microvascular markers of the scleroderma capillary patterns, but not fully fitting the definition for the single early, active or late scleroderma pattern (27).

Examples [c]



Capillaroscopic characteristics:
Density: 3 capillaries in 1 linear mm (↓)
Dimension: Presence of irregularly dilated capillaries and giants (*)
Morphology: Abnormally shaped capillaries
Haemorrhages: Present (Δ)
Pattern: combination of severely reduced number of capillaries, haemorrhages, giants and abnormally shaped capillaries is not expected in a scleroderma pattern, hence this is called scleroderma-like.



Capillaroscopic characteristics:
Density: 3 capillaries in 1 linear mm (↓)
Dimension: Presence of giants (*)
Morphology: Predominantly normal
Haemorrhages: None
Pattern: presence of giants in a situation of severely reduced number of capillaries. This is not expected in a scleroderma pattern, hence this is called scleroderma-like.

Fig. A.2. (*continued*).

Table A.1
Significance of NVC parameters in IIM *vs.* HC.

DM COMPARED TO HC					
Quantitative & Semi-quantitative	**Parameters**		**Significant**	**Not significant**	**Conclusion**
	Density	Mean density	1 study (32)	0 studies	**More capillary loss in (j)DM *vs.* HC**
		Avascularity	1 study (33)	0 studies	
		Mean density score	1 study (33)	0 studies	
	Dimension	Dilated capillaries	2 studies (32,33)	0 studies	**More dilated capillaries in (j)DM *vs.* HC**
		Dilated capillaries [a]	1 study (33)		
		Giants	2 studies (32, 33)	0 studies	**More giants in in (j)DM *vs.* HC**
		Giants [a]	1 study (33)		
	Morphology	Abnormal morphology	1 study (33)	0 studies	*More abnormal capillaries in DM vs. HC*
		Abnormal morphology [a]	1 study (33)		
	Microhaemorrhages	Microhaemorrhages	0 studies	1 study (33)	Microhaemorrhages: non-conclusive
		Microhaemorrhages [a]	1 study (33)	0 studies	
Qualitative	Scleroderma pattern		2 studies (32, 33)	0 studies	**More scleroderma pattern (j)DM *vs.* HC**
PM COMPARED TO HC					
Quantitative & Semi-quantitative	**Parameters**		**Significant**	**Not significant**	**Conclusion**
	Mean density score		0 studies	1 study (33)	*No significant difference*
	Dimension	Dilated capillaries	0 studies	1 study (33)	*No significant difference*
		Dilated capillaries [a]	0 studies		
		Giants	0 studies	1 study (33)	*No significant difference*
		Giants [a]	0 studies		
	Morphology	Abnormal morphology	0 studies	1 study (33)	*No significant difference*
		Abnormal morphology [a]	0 studies		
	Microhaemorrhages	Microhaemorrhages	0 studies	1 study (33)	*No significant difference*
		Microhaemorrhages [a]	0 studies	1 study (33)	
Qualitative	Scleroderma pattern		0 studies	1 study (33)	*No significant difference*

a: Capillary parameter was measured with a semi-quantitative score with a scale of 0 to 3 (0 = no changes, 1 = ≤ 33% of capillary alterations/reduction, 2 = 33–66% of capillary alterations/reduction, 3 = ≥66% of capillary alterations/reduction, per linear mm).
Only studies reporting clear NVC alterations are mentioned in this table. Conclusive results are written in bold; suggestive results are written in italics. Significance is set at p value < 0,05.
DM: dermatomyositis; jDM: juvenile dermatomyositis; HC: healthy controls; IIM: idiopathic inflammatory myopathies; PM: polymyositis.

Table A.2
Significance of NVC parameters in DM *vs.* PM.

DM COMPARED TO PM					
Quantitative & Semi-quantitative	**Parameters**		**Significant**	**Not significant**	**Conclusion**
	Density	Avascularity (33) Mean density score	1 study (32)	0 studies	*More capillary loss in DM vs. PM*
	Dimension	Dilated capillaries Dilated capillaries [a]	1 study (33)	0 studies	*More dilated capillaries in DM vs. PM*
		Giants Giants [a]	1 study (33)	0 studies	*More giants in DM vs. PM*
	Morphology	Abnormal morphology Abnormal morphology [a]	1 study (33)	0 studies	*More abnormal capillaries in DM vs. PM*
	Microhaemorrhages	Microhaemorrhages Microhaemorrhages [a]	1 study (33)	0 studies	*More microhaemorrhages in DM vs. PM*
Qualitative	Scleroderma pattern		1 study (33)	0 studies	*More scleroderma pattern in DM vs. PM*

a: Capillary parameter was measured with a semi-quantitative score with a scale of 0 to 3 (0 = no changes, 1 = ≤ 33% of capillary alterations/reduction, 2 = 33–66% of capillary alterations/reduction, 3 = ≥66% of capillary alterations/reduction, per linear mm).
Only studies reporting clear NVC alterations are mentioned in this table. Conclusive results are written in bold; suggestive results are written in italics. Significance is set at p-value < 0,05.
DM: dermatomyositis; PM: polymyositis.

Table A.3
Significance of NVC parameters in IIM *vs.* SSc.

IIM COMPARED TO SSC					
Quantitative & Semi-quantitative	**Parameters**		**Significant**	**Not significant**	**Conclusion**
	Mean density score		1 study (34)	0 studies	*Less capillary loss in DM vs. SSc*
	Dimension	Irregularly dilated capillaries	1 study (34)	0 studies	*More abnormal shaped capillaries with an apical diameter of ≥ 50 μm in DM vs. SSc*
		Giants	1 study (34)	0 studies	Giants: non conclusive
		Giants [a]	0 studies	1 study (34)	
	Morphology	Abnormal morphology Abnormal morphology [a]	1 study (34)	0 studies	*More abnormal capillaries in DM vs. SSc*
	Microhaemorrhages	Microhaemorrhages Microhaemorrhages [a]	0 studies	1 study (34)	*No significant difference*
Qualitative	Scleroderma pattern	Scleroderma pattern	1 study (35)	0 studies	*Less scleroderma pattern in IIM vs. SSc*
		Early scleroderma	1 study (35)	0 studies	*Less early scleroderma pattern in IIM vs. SSc*
		Active scleroderma	1 study (35)	0 studies	*Less active scleroderma pattern in IIM vs. SSc*
		Late scleroderma	0 studies	1 study (35)	*No significant difference*
		Scleroderma-like	1 study (35)	0 studies	*More scleroderma-like pattern in IIM vs. SSc*

a: Capillary parameter was measured with a semi-quantitative score with a scale of 0 to 3 (0 = no changes, 1 = ≤ 33% of capillary alterations/reduction, 2 = 33–66% of capillary alterations/reduction, 3 = ≥66% of capillary alterations/reduction, per linear mm).
Only studies reporting clear NVC alterations are mentioned in this table. Conclusive results are written in bold; suggestive results are written in italics. Significance is set at p-value < 0,05.
DM: dermatomyositis; IIM: idiopathic inflammatory myopathies; SSc: systemic sclerosis.

Table A.4
Association between NVC findings, clinical and laboratory parameters.

			Significant	Not significant	Conclusion
CLINICAL	Disease duration		2 studies (32, 33)	1 study (35)	Non-conclusive
	Raynaud's phenomenon		0 studies	3 studies (33–35)	**No significant association**
	Skin involvement [a]		1 study (35)	1 study (33)	Non-conclusive
	Muscle	Muscle weakness	1 study (32)	2 studies (33, 35)	Non-conclusive
		Myalgia	0 studies	1 study (35)	*No significant association*
	Arthritis		0 studies	1 study (35)	*No significant association*
	Total disease activity (32)		1 study (32)	0 studies	*Higher prevalence of low capillary density and scleroderma pattern with active disease in jDM*
	Pulmonary dysfunction	PFT abnormalities	1 study (31)	1 study (35) (adult)	Non-conclusive
		Airway disease on HRCT	1 study (31)	0 studies	*Higher prevalence of low capillary density when signs of airway disease on HRCT in jDM*
		ILD	0 studies	3 studies (32, 33, 35)	**No significant association**
	Internal malignancy		0 studies	1 study (35)	*No significant association*
	Calcium channel blocker therapy		0 studies	1 study(34)	*No significant association*
	Immunosuppressive treatment [b]		1 study (35)	0 studies	*Significant decrease of NVC abnormalities after immunosuppressive therapy*
LABORATORY	Antibodies	ANA	0 studies	3 studies (33–35)	**No significant association**
		Anti-Jo-1	0 studies	1 study (34)	*No significant association*
		Anti-ARS	1 study (35)	0 studies	*Lower prevalence of scleroderma (like) pattern*
		Anti-MDA5	1 study (35)	0 studies	*Higher prevalence of scleroderma (like) pattern*
		Anti-TIF1γ	1 study (35)	0 studies	*Higher prevalence of scleroderma (like) pattern*
		Anti-Mi2	0 studies	1 study (35)	*No significant association*
		Anti-SSA	0 studies	1 study (34)	*No significant association*
	Acute phase proteins (ESR or CRP)		0 studies	3 studies (32, 33, 35)	**No significant association**
	Levels of muscle enzymes (CK)		0 studies	2 studies (33, 35)	**No significant association**
	Skin pathology		1 study (35)	0 studies	*More NVC abnormalities when severe perivascular lymphocytic infiltration*

a: Such as Gottron's sign/papules, heliotropic rash, palmar papules; b: Cyclophosphamide, calcineurin inhibitors, oral glucocorticoids.
Conclusive associations are written in bold; suggestive associations are written in italics. Significance was set at p value $< 0,05$.
ANA: anti-nuclear antibodies; Anti-ARS: anti-aminoacyl tRNA synthetase antibodies; CK: creatine kinase; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; HRCT: high-resolution computed tomography; ILD: interstitial lung disease; jDM: juvenile dermatomyositis; PFT: Pulmonary function test.

Appendix B. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.autrev.2022.103087.

References

[1] Betteridge Z, McHugh N. Myositis-specific autoantibodies: an important tool to support diagnosis of myositis. J Intern Med 2016;280(1):8–23.
[2] Damoiseaux J, Vulsteke JB, Tseng CW, Platteel ACM, Piette Y, Shovman O, et al. Autoantibodies in idiopathic inflammatory myopathies: clinical associations and laboratory evaluation by mono- and multispecific immunoassays. Autoimmun Rev 2019;18(3):293–305.
[3] Mandel DE, Malemud CJ, Askari AD. Idiopathic inflammatory myopathies: a review of the classification and impact of pathogenesis. Int J Mol Sci 2017;18(5).
[4] Mariampillai K, Granger B, Amelin D, Guiguet M, Hachulla E, Maurier F, et al. Development of a new classification system for idiopathic inflammatory myopathies based on clinical manifestations and myositis-specific autoantibodies. JAMA Neurol 2018;75(12):1528–37.
[5] Vencovsky J, Alexanderson H, Lundberg IE. Idiopathic inflammatory myopathies. Rheum Dis Clin N Am 2019;45(4):569–81.
[6] Bohan A, Peter JB. Polymyositis and dermatomyositis (first of two parts). N Engl J Med 1975;292(7):344–7.
[7] Bohan A, Peter JB. Polymyositis and dermatomyositis (second of two parts). N Engl J Med 1975;292(8):403–7.
[8] Bottai M, Tjarnlund A, Santoni G, Werth VP, Pilkington C, de Visser M, et al. EULAR/ACR classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups: a methodology report. RMD Open 2017;3(2):e000507.
[9] Lundberg IE, Tjärnlund A, Bottai M, Werth VP, Pilkington C, de Visser M, et al. 2017 European league against rheumatism/American College of Rheumatology Classification Criteria for Adult and Juvenile Idiopathic Inflammatory Myopathies and Their Major Subgroups. Arthritis & Rheumatology (Hoboken, NJ) 2017;69(12):2271–82.
[10] Smith V, Scire CA, Talarico R, Airo P, Alexander T, Allanore Y, et al. Systemic sclerosis: state of the art on clinical practice guidelines. RMD Open 2018;4(Suppl. 1):e000782.
[11] Vanhaecke A, Cutolo M, Distler O, Riccieri V, Allanore Y, Denton CP, et al. Nailfold capillaroscopy in SSc: Innocent bystander or promising biomarker for novel severe organ involvement/progression? Rheumatology (Oxford, England) 2022. https://academic.oup.com/rheumatology/advance-article/doi/10.1093/rheumatology/keac079/6530300.
[12] Avouac J, Lepri G, Smith V, Toniolo E, Hurabielle C, Vallet A, et al. Sequential nailfold videocapillaroscopy examinations have responsiveness to detect organ progression in systemic sclerosis. Semin Arthritis Rheum 2017;47(1):86–94.
[13] Smith V, Decuman S, Sulli A, Bonroy C, Piettte Y, Deschepper E, et al. Do worsening scleroderma capillaroscopic patterns predict future severe organ involvement? A pilot study. Ann Rheum Dis 2012;71(10):1636–9.
[14] Sulli A, Paolino S, Pizzorni C, Ferrari G, Pacini G, Pesce G, et al. Progression of nailfold capillaroscopic patterns and correlation with organ involvement in systemic sclerosis: a 12 year study. Rheumatology (Oxford) 2020;59(5):1051–8.
[15] Cutolo M, Herrick AL, Distler O, Becker MO, Beltran E, Carpentier P, et al. Nailfold Videocapillaroscopic features and other clinical risk factors for digital ulcers in systemic sclerosis: a multicenter, prospective cohort study. Arthritis & Rheumatology (Hoboken, NJ) 2016;68(10):2527–39.
[16] Smith V, Herrick AL, Ingegnoli F, Damjanov N, De Angelis R, Denton CP, et al. Standardisation of nailfold capillaroscopy for the assessment of patients with Raynaud's phenomenon and systemic sclerosis. Autoimmun Rev 2020;19(3):102458.
[17] van den Hoogen F, Khanna D, Fransen J, Johnson SR, Baron M, Tyndall A, et al. 2013 classification criteria for systemic sclerosis: an American college of rheumatology/European league against rheumatism collaborative initiative. Ann Rheum Dis 2013;72(11):1747–55.
[18] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ (Clinical research ed) 2021;372:n71.
[19] Ingegnoli F, Herrick AL, Schioppo T, Bartoli F, Ughi N, Pauling JD, et al. Reporting items for capillaroscopy in clinical research on musculoskeletal diseases: A systematic review and international Delphi consensus. Rheumatology (Oxford, England) 2020;60(3):1410–8.
[20] Cutolo M, Sulli A, Smith V. How to perform and interpret capillaroscopy. Best Pract Res Clin Rheumatol 2013;27(2):237–48.
[21] Dinsdale G, Roberts C, Moore T, Manning J, Berks M, Allen J, et al. Nailfold capillaroscopy-how many fingers should be examined to detect abnormality? Rheumatology (Oxford) 2019;58(2):284–8.
[22] Melsens K, Leone MC, Paolino S, Elewaut D, Gerli R, Vanhaecke A, et al. Nailfold capillaroscopy in Sjögren's syndrome: a systematic literature review and standardised interpretation. Clin Exp Rheumatol 2020;38(Suppl 126(4)):150–7.
[23] Boers Jr MK, Tugwell P. Appendix B: The COSMIN-OMERACT Good Methods Checklist adapted for OMERACT Filter 2.1 Instrument Selection needs. In: The OMERACT handbook 20.12.2017 ed. Ottowa, ON, Canada; 2017. p. 20.

[24] Dolezalova P, Young SP, Bacon PA, Southwood TR. Nailfold capillary microscopy in healthy children and in childhood rheumatic diseases: a prospective single blind observational study. Ann Rheum Dis 2003;62(5):444–9.
[25] Cutolo M, Melsens K, Herrick AL, Foeldvari I, Deschepper E, De Keyser F, et al. Reliability of simple capillaroscopic definitions in describing capillary morphology in rheumatic diseases. Rheumatology (Oxford) 2018;57(4):757–9.
[26] Smith V, Beeckman S, Herrick AL, Decuman S, Deschepper E, De Keyser F, et al. An EULAR study group pilot study on reliability of simple capillaroscopic definitions to describe capillary morphology in rheumatic diseases. Rheumatology (Oxford) 2016;55(5):883–90.
[27] Smith V, Pizzorni C, De Keyser F, Decuman S, Van Praet JT, Deschepper E, et al. Reliability of the qualitative and semiquantitative nailfold videocapillaroscopy assessment in a systemic sclerosis cohort: a two-centre study. Ann Rheum Dis 2010;69(6):1092–6.
[28] Sulli A, Secchi ME, Pizzorni C, Cutolo M. Scoring the nailfold microvascular changes during the capillaroscopic analysis in systemic sclerosis patients. Ann Rheum Dis 2008;67(6):885–7.
[29] Smith V, Vanhaecke A, Herrick AL, Distler O, Guerra MG, Denton CP, et al. Fast track algorithm: how to differentiate a "scleroderma pattern" from a "non-scleroderma pattern". Autoimmun Rev 2019;18(11):102394.
[30] Cutolo M, Sulli A, Pizzorni C, Accardo S. Nailfold videocapillaroscopy assessment of microvascular damage in systemic sclerosis. J Rheumatol 2000;27(1):155–60.
[31] Barth Z, Schwartz T, Flatø B, Aaløkken TM, Koller A, Lund MB, et al. Association between nailfold capillary density and pulmonary and cardiac involvement in medium to longstanding juvenile dermatomyositis. Arthritis Care Res 2019;71(4):492–7.
[32] Barth Z, Witczak BN, Flatø B, Koller A, Sjaastad I, Sanner H. Assessment of microvascular abnormalities by nailfold capillaroscopy in juvenile dermatomyositis after medium- to long-term followup. Arthritis Care Res 2018;70(5):768–76.
[33] Manfredi A, Sebastiani M, Cassone G, Pipitone N, Giuggioli D, Colaci M, et al. Nailfold capillaroscopic changes in dermatomyositis and polymyositis. Clin Rheumatol 2015;34(2):279–84.
[34] Manfredi A, Sebastiani M, Campomori F, Pipitone N, Giuggioli D, Colaci M, et al. Nailfold Videocapillaroscopy alterations in dermatomyositis and systemic sclerosis: toward identification of a specific pattern. J Rheumatol 2016;43(8):1575–80.
[35] Kubo S, Todoroki Y, Nakayamada S, Nakano K, Satoh M, Nawata A, et al. Significance of nailfold videocapillaroscopy in patients with idiopathic inflammatory myopathies. Rheumatology (Oxford) 2019;58(1):120–30.
[36] Dalakas MC. Inflammatory muscle diseases. N Engl J Med 2015;372(18):1734–47.
[37] Ernste FC, Reed AM. Idiopathic inflammatory myopathies: current trends in pathogenesis, clinical features, and up-to-date treatment recommendations. Mayo Clin Proc 2013;88(1):83–105.
[38] Feldman BM, Rider LG, Reed AM, Pachman LM. Juvenile dermatomyositis and other idiopathic inflammatory myopathies of childhood. Lancet (London, England) 2008;371(9631):2201–12.
[39] Mostmans Y, Cutolo M, Giddelo C, Decuman S, Melsens K, Declercq H, et al. The role of endothelial cells in the vasculopathy of systemic sclerosis: a systematic review. Autoimmun Rev 2017;16(8):774–86.
[40] Mercer LK, Moore TL, Chinoy H, Murray AK, Vail A, Cooper RG, et al. Quantitative nailfold video capillaroscopy in patients with idiopathic inflammatory myopathy. Rheumatology (Oxford) 2010;49(9):1699–705.
[41] Leclair V, Lundberg IE. New myositis classification criteria-what we have learned since Bohan and Peter. Curr Rheumatol Rep 2018;20(4):18.
[42] Sebastiani M, Triantafyllias K, Manfredi A, González-Gay MA, Palmou-Fontana N, Cassone G, et al. Nailfold capillaroscopy characteristics of antisynthetase syndrome and possible clinical associations: results of a multicenter international study. J Rheumatol 2019;46(3):279–84.
[43] Bernardino V, Rodrigues A, Lladó A, Panarra A. Nailfold capillaroscopy and autoimmune connective tissue diseases in patients from a Portuguese nailfold capillaroscopy clinic. Rheumatol Int 2020;40(2):295–301.
[44] Smith V, Vanhaecke A, Guerra MG, Melsens K, Vandecasteele E, Paolino S, et al. May capillaroscopy be a candidate tool in future algorithms for SSC-ILD: are we looking for the holy grail? A systematic review. Autoimmun Rev 2020;19(9):102619.
[45] Sulli A, Pizzorni C, Smith V, Zampogna G, Ravera F, Cutolo M. Timing of transition between capillaroscopic patterns in systemic sclerosis. Arthritis Rheum 2012;64(3):821–5.
[46] Marie I. Morbidity and mortality in adult polymyositis and dermatomyositis. Curr Rheumatol Rep 2012;14(3):275–85.
[47] Wakura R, Matsuda S, Kotani T, Shoda T, Takeuchi T. The comparison of nailfold videocapillaroscopy findings between anti-melanoma differentiation-associated gene 5 antibody and anti-aminoacyl tRNA synthetase antibody in patients with dermatomyositis complicated by interstitial lung disease. Sci Rep 2020;10(1):15692.
[48] Pizzorni C, Cutolo M, Sulli A, Ruaro B, Trombetta AC, Ferrari G, et al. Long-term follow-up of nailfold videocapillaroscopic changes in dermatomyositis versus systemic sclerosis patients. Clin Rheumatol 2018;37(10):2723–9.
[49] De Angelis R, Cutolo M, Gutierrez M, Bertolazzi C, Salaffi F, Grassi W. Different microvascular involvement in dermatomyositis and systemic sclerosis. A preliminary study by a tight videocapillaroscopic assessment. Clin Exp Rheumatol 2012;30(2 Suppl 71):S67–70.
[50] Schmeling H, Stephens S, Goia C, Manlhiot C, Schneider R, Luthra S, et al. Nailfold capillary density is importantly associated over time with muscle and skin disease activity in juvenile dermatomyositis. Rheumatology (Oxford) 2011;50(5):885–93.
[51] Mugii N, Hasegawa M, Matsushita T, Hamaguchi Y, Horie S, Yahata T, et al. Association between nail-fold capillary findings and disease activity in dermatomyositis. Rheumatology (Oxford) 2011;50(6):1091–8.
[52] Bellando-Randone S, Lepri G, Bruni C, Blagojevic J, Radicati A, Cometi L, et al. Combination therapy with Bosentan and sildenafil improves Raynaud's phenomenon and fosters the recovery of microvascular involvement in systemic sclerosis. Clin Rheumatol 2016;35(1):127–32.
[53] Cestelli V, Manfredi A, Sebastiani M, Praino E, Cannarile F, Giuggioli D, et al. Effect of treatment with iloprost with or without bosentan on nailfold videocapillaroscopic alterations in patients with systemic sclerosis. Mod Rheumatol 2017;27(1):110–4.
[54] Trombetta AC, Pizzorni C, Ruaro B, Paolino S, Sulli A, Smith V, et al. Effects of Longterm treatment with Bosentan and Iloprost on Nailfold absolute capillary number, fingertip blood perfusion, and clinical status in systemic sclerosis. J Rheumatol 2016;43(11):2033–41.
[55] Baig S, Paik JJ. Inflammatory muscle disease - an update. Best Pract Res Clin Rheumatol 2020;34(1):101484.