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Microvascular abnormalities between anti-TIF1-γ-associated dermatomyositis with and without malignancy

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Abstract

Background Dermatomyositis (DM) is an immune-mediated myopathy characterized by proximal muscle weakness, inflammation, and cutaneous manifestations. Up to 25% of DM patients have an associated malignancy. Those with cancer-associated DM often face worse prognoses, poorer treatment responses, and reduced survival rates. Interestingly, anti TIF1γ-positive DM patients are notably at increased risk for malignancy, yet the underlying mechanisms and clinical correlation remain poorly understood. Nailfold video capillaroscopy (NVC) is a safe, non-invasive method for assessing vascular abnormalities, previously explored in various DM subsets but not specifically in anti TIF1γ-positive DM patients with malignancy. This study aims to characterize NVC findings in anti-TIF1γ-positive DM and assess their clinical relevance, particularly in malignancy-associated cases.

Methods A retrospective review at Mayo Clinic, Jacksonville from January 1st, 2010 to May 16th, 2024 was conducted. 19 cases with anti TIF1γ-positive DM and 18 idiopathic inflammatory myopathy controls were included.

Results We observed anti TIF1γ-positive DM cases to have significantly increased capillary density loss and higher microhemorrhages ($p = 0.057$). Cases also had higher frequencies of dilated capillaries, capillary ramifications, and capillary disorganization. Although no statistically significant differences in NVC pattern were identified in cancer vs. non-cancer anti TIF1γ-positive DM, there were greater hemorrhages and ramifications noted in the cancer anti TIF1γ-positive subset.

Conclusion This study investigated NVC differences among anti TIF1γ-positive DM with malignancies versus idiopathic inflammatory myopathy controls. Our findings indicate promising microvascular differences with a potential for predicting cancer development that warrant further exploration in larger studies.

Clinical trial number Not applicable.

Highlights

- Up to 25% of DM patients have malignancies and worse prognoses.
- Anti TIF1γ-positive DM is associated with malignancies, but this relationship is poorly understood.
- NVC may be useful in clinically characterizing anti TIF1γ-positive DM, including cancer subsets.

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- NVC shows differences between Anti TIF-DM including malignancy associated cases.
- These findings may aid diagnosis and management of these patients.

Keywords Dermatomyositis (DM), Anti-transcription intermediary factor-1gamma (TIF), Nailfold video capillaroscopy (NVC), Malignancy, Cancer, Myositis-specific autoantibody (MSA), Idiopathic inflammatory myopathy (IIM)

Introduction

Dermatomyositis (DM), an immune-mediated myopathy characterized by proximal muscle weakness, inflammation, and various cutaneous manifestations, is classified as one of the idiopathic inflammatory myopathies (IIM) [1]. DM is a rare condition, typically affecting individuals aged between 40 and 50 years, with an incidence of about 10 per 1,000,000 people [2]. DM mortality rate is about 10% and is highest in the first year of diagnosis, while 34% of survivors have some form of mild-to-moderate disability [3]. A significant amount of DM patients (nearly 25%) have an underlying malignancy (a five-to-seven-fold increase compared to that of the general population) [4]. DM-associated cancer has significant prognosis implications, as these patients exhibit poorer responses to treatment and decreased survival rates compared to their counterparts without an underlying malignancy [5]. Ultimately, DM pathophysiology, particularly for cancer-associated DM, is not fully understood, warranting further research to better risk-stratify and prognosticate disease course for these patients.

Nailfold video capillaroscopy (NVC) has emerged as a safe, inexpensive, non-invasive technique that allows for a real-time assessment of vascular abnormalities, providing quick and objective data with high inter-reader reliability among users [6–7]. NVC is widely used in rheumatology clinics for systemic sclerosis (SSc), where distinct capillaroscopy phenotypes facilitate disease diagnosis and prognostication, subsequently allowing for monitoring of disease activity [8–9]. These findings have since also been applied to IIM [10, 11], [12]. One study reported an association between NVC findings and disease activity in DM patients [11]. A separate study observed distinct capillaroscopy features, such as vascular array disorganization, capillary loss, and enlarged capillaries, to be more prevalent in DM patients than those with polymyositis (PM) [13], while another study observed a higher frequency of giant capillaries in DM compared to that of antisynthetase syndrome and immune-mediated necrotizing myopathy [12]. These results are promising so that DM patients have characteristic NVC findings which can potentially be used to monitor disease activity, however, the literature on NVC findings among individual subsets of DM, and particularly those with associated malignancy, remains limited.

A variety of serum autoantibodies, referred to as myositis-specific autoantibodies (MSAs), anti-melanoma differentiation-associated gene 5 (MDA5), and anti-transcription intermediary factor-1gamma (TIF) are well-known to be associated with DM while anti-aminoacyl-tRNA synthetase (ARS) is associated with anti-synthetase syndrome. Clinically, MSA identification in DM patients is critical as each is associated with specific clinical features that can affect prognosis [14]. Interestingly, anti TIF1γ-positive DM has been observed to have an increased risk for underlying malignancy, which has been reported to vary from 15–27% [15, 16]. However, anti TIF1γ-positive DM remains poorly understood regarding definitive clinical characteristics and response to traditional therapies (e.g., systemic glucocorticoids or immunosuppressants). Prior studies have observed NVC differences among the various subsets of MSA-associated DM [14, 17]. Interestingly, one study observed significantly increased enlarged capillaries and greater capillary loss with anti TIF1γ-positive autoantibodie [18], suggesting that NVC may have prognostication benefits in this setting.

The association between NVC findings in anti TIF1γ-positive DM patients with associated malignancy, to our knowledge, has not been described in detail in current literature, warranting additional studies to further investigate changes in capillary architecture among these patients. The present study sought to address such gaps in the literature – the primary objective of this study was to characterize and describe distinct NVC findings amongst patients with anti TIF1γ-positive compared to patients with idiopathic inflammatory patients, with secondary objectives of identifying any clinically significant NVC features that can facilitate disease course prognostication and evaluating any correlating NVC features with cancer. We hypothesized that NVC differences between groups would facilitate future diagnosis, prognostic information, and response to therapies.

Materials and methods

Patient characteristics

A single-institution retrospective chart review of all patients with anti TIF1γ-positive at Mayo Clinic, Jacksonville, FL from January 1st, 2010 to May 16th, 2024 who had NVC performed was conducted. Adult patients ≥ 18 years of age were included – 21 patients with TIF-positive DM were identified and NVC was performed on 19 cases. Controls ($n = 18$ from another research study) included TIF-negative patients who had positive serologies for other myositis antibodies (jo1, pl-7, pl-12, EJ, OJ, pm-scl, Ku, RNP U1/U2/U3). MDA-5 was excluded due

to its distinctly different clinical picture and more severe prognosis, while NXP-2 was excluded due to its higher association with cancer (such that the anti TIF1γ-positive DM malignancy association could be uniquely assessed). Immunoprecipitation technique was used for antibody identification. Clinical information was retrospectively collected via chart review of patient medical charts. Variables recorded included demographics, clinical features, serologies and laboratory data, imaging and biopsy studies, comorbidities, last follow-up, treatment interventions, and NVC findings. The study was approved by the Mayo Clinic Institutional Review Board.

NVC characteristics

We assessed NVC findings using the Optilia Video Capillaroscopy system (magnification of 200x; analyzed via Optipix software). NVC was performed on all eight nail beds using the 2nd-5th digits of both hands. NVC findings, such as capillary number, morphology, density, organization, micro-hemorrhages, and ramifications, were compared amongst anti TIF1γ-positive DM patients with cancer and idiopathic inflammatory myopathies controls. In this study, only baseline NVC scores were obtained (longitudinal values were not tracked). Capillaroscopy parameters included capillary density, dimension, morphology, and hemorrhage. Density was considered abnormal if there were fewer than 7 capillaries per 1-mm field. Abnormal dimension was defined as greater than 20 μm as enlarged and greater than 50 μm as giant. Morphology was considered abnormal if capillaries did not exhibit the characteristic hairpin loop shape. A semi-quantitative scoring system well described by Cutolo et al. was used and scoring was reviewed by at least two trained providers or researchers [19].

Statistical analysis

Continuous variables were summarized with the sample median and interquartile range, while categorical variables were summarized with numbers and percentages. Jitter plots were used to display the distribution of NVC scores graphically. Multivariable linear regression was used to estimate the difference in mean NVC scores between anti TIF1γ-positive cases and controls; 95% confidence intervals (CI) were also reported. The multivariable models were adjusted for age and sex. P-values less than 0.05 were considered statistically significant, and all statistical tests were two-sided. Descriptive statistics for cases were used to report clinical characteristics, serologies and markers, imaging and biopsy findings, and treatments. Single-variable linear regression was used to explore associations of characteristics with NVC scores in cases. Statistical analyses were performed using R Statistical Software (version 4.2.2; R Foundation for Statistical Computing, Vienna, Austria). An additional subgroup analysis between cancer and non-cancer anti TIF-positive DM cases was conducted.

Table 1 Patient characteristics

Variable	*N*	TIF-γ DM (*N* = 19)	Controls (*N* = 18)
Age (years)	37	56 (48, 63)	60 (58, 66)
Sex	37		
Male		1 (5%)	8 (44%)
Female		18 (95%)	10 (56%)
Race	19		
White		19 (100%)	18 (100%)

The sample median (Q1, Q3) is given for continuous variables, while categorical variables are reported as frequency (percentage)

Results

Demographics

The baseline characteristics of the 19 anti TIF1γ-positive cases and the 18 controls are summarized in Table 1. The mean age was 56 and 60 for cases and controls, respectively. Most cases ($n = 18$; 95%) and controls ($n = 10$; 56%) were female, and all cases ($n = 19$; 100%) were Caucasian.

Clinical characteristics

Of relevance, not every case had documented testing for every clinical variable (if missing, the sample size, n, is specified in parentheses). Descriptive statistics summarizing clinical characteristics for cases are summarized in Table 2. Cases commonly reported muscle weakness ($n = 13$; 68%) and skin rash ($n = 15$; 79%), while less commonly reporting pulmonary involvement ($n = 7$; 37%), inflammatory arthritis ($n = 6$; 32%), dysphagia ($n = 5$; 26%), weight loss ($n = 5$; 26%), fatigue ($n = 4$; 21%), and fever ($n = 3$; 16%). Manifestations with mechanic's hands, gastrointestinal involvement, and arthralgias were rare (each $n = 1$; 5%). Descriptive statistics summarizing serologies and markers for cases are summarized in Table 3. Cases had a median CRP, ESR, aldolase, and CK of 4 mg/L, 10 mm/hr, 4.9 u/L, and 93 u/L, respectively. Cases commonly had positive ANA ($n = 15/18$; 83%) and TIF-1 gamma ($n = 19$; 100%), while less commonly having positive RF ($n = 2/13$; 15%), SSA/RO ($n = 4/18$; 22%), scl70 ($n = 3/16$; 19%), and U1RNP ($n = 2/14$; 14%). Descriptive statistics summarizing imaging, biopsy, and other clinical findings for cases are summarized in Table 4. Two cases ($n = 2/2$; 100%) had positive MRI findings. Most skin biopsy findings indicated interface dermatitis ($n = 12/19$; 63%). Cases had a median FVC% predicted and DLCO% predicted of 90 and 83.5, respectively. 5 patients (26.3%) had associated malignancy, which included rectal cancer, non-Hodgkin's lymphoma, extra-nodal marginal B cell lymphoma, Hodgkin's lymphoma, and breast cancer.

Table 2 Clinical characteristics

Variable	*N*	TIF positive DM (*N* = 19)
Constitutional symptoms		
Fever	19	3 (16%)
Weight loss	19	5 (26%)
Night sweats	19	2 (11%)
Fatigue	19	4 (21%)
Rheumatologic symptoms		
Inflammatory arthritis	19	6 (32%)
Raynaud's phenomenon	19	9 (47%)
Muscle weakness	19	13 (68%)
Dysphagia	19	5 (26%)
Skin rash	19	19 (100%)
Inflammatory eye disease	19	0 (0%)
Nerve involvement	19	2 (11%)
Pulmonary involvement	19	7 (37%)
Mechanic hands	19	1 (5%)
GI involvement	19	1 (5%)
Renal involvement	19	0 (0%)
Cardiac involvement	19	0 (0%)
Arthralgia (not inflammatory arthritis)	19	1 (5%)
Manual muscle strength		
Upper extremity	19	
0		0 (0%)
1		0 (0%)
2		0 (0%)
3		1 (5%)
4		4 (21%)
5		14 (74%)
Lower extremity	19	
0		0 (0%)
1		0 (0%)
2		0 (0%)
3		1 (5%)
4		5 (26%)
5		13 (68%)

The sample median (Q1, Q3) is given for continuous variables, while categorical and ordinal variables are reported as frequency (percentage)

Table 3 Serologies and markers

Variable	*N*	TIF positive DM (*N* = 19)
Inflammatory markers		
CRP (mg/L)	18	4.0 (2.9, 10.2)
ESR (mm/1H)	19	10.0 (5.0, 24.5)
Serologies		
ANA+	18	15 (83%)
RF+	13	2 (15%)
CCP+	13	1 (8%)
dsDNA+	18	1 (6%)
ENA panel		
SSA/RO+	18	4 (22%)
SSB/La+	18	1 (6%)
Sm ab+	18	0 (0%)
RNP+	18	1 (6%)
SCL70+	16	3 (19%)
centromere+	16	0 (0%)
Myomarker panel 3		
JO-1+	19	0 (0%)
MI-2+	19	0 (0%)
PL-7+	18	0 (0%)
PL-12+	19	0 (0%)
EJ+	19	0 (0%)
OJ+	19	2 (11%)
SRP+	18	1 (6%)
MDA-5+	19	0 (0%)
TIF-1 Gamma+	19	19 (100%)
Ku+	14	0 (0%)
anti-pm/scl+	17	1 (6%)
U1RNP+	14	2 (14%)
U2 SN RNP+	8	0 (0%)
Fibrillarin U3+	10	0 (0%)
SSA-52D+	11	4 (36%)
CMP		
Aldolase (u/L)	17	4.9 (3.8, 5.5)
CK (u/L)	19	93.0 (51.0, 153.5)

The sample median (Q1, Q3) is given for continuous variables, while categorical and ordinal variables are reported as frequency (percentage)

NVC findings

NVC results in anti TIF1γ-positive cases compared to controls are summarized in Table 5. Capillaroscopy density loss was significantly higher in cases (median 2.1) versus controls (median 0.3) (adjusted difference 0.8; 95% CI 0.0-1.5; $p = 0.047$). Microhemorrhages were found to trend towards significance in cases (median 0.5) than in controls (median 0.1) (adjusted difference 0.5; 95% CI 0.0–1.0; $p = 0.057$). Dilated capillaries (median 1.2 versus 0.9; $p = 0.25$), capillary ramifications (median 1.0 versus 0.3; $p = 0.50$), and capillary disorganization (median 0.5 versus 0.0; $p = 0.36$) were all more likely to be present in cases than controls, however, p-values were not significant. There was no difference in the presence of giant capillaries in cases (median 0.4) versus controls (median 0.4) (adjusted difference −0.3; 95% CI -0.9-0.3; $p = 0.28$).

Figure 1 Panels A-D depict abnormal NVC findings in cases. On single-variable linear regression, there was no association of the magnitude of CRP and aldolase doubling in predicting an increase in any of the assessed NVC findings (Table 6). Notably, an increase in ESR had a significant correlation with dilated capillaries [95% CI (0.08, 1.07), $p = 0.025$], and CK doubling and association with dilated capillaries was noted to trend towards statistical significance. Anti TIF1γ-positive DM subset with cancer had higher NVC scores of capillary microhemorrhages and ramifications compared to patients without cancer (Table 7). Non-cancer anti TIF1γ-positive DM patients had more enlarged (> 20 but < 50 microns) and giant (> 50 microns) capillaries with higher disorganization. A

Table 4 Imaging, biopsy, and other clinical findings

Variable	*N*	Overall (*N* = 19)
MRI positive findings	2	2 (100%)
Muscle biopsy findings		
Polymoysitis	19	0 (0%)
DM	19	1 (5%)
MHC	19	0 (0%)
Complements deposition	19	0 (0%)
Myopathic features	19	2 (11%)
Others	19	0 (0%)
Skin biopsy findings		
Interface dermatitis	19	12 (63%)
Perivascular infiltrate	19	4 (21%)
Mucin deposition	19	8 (42%)
Normal	19	1 (5%)
PFT		
FVC	10	3.1 (2.3, 3.6)
FVC%	10	90.0 (86.0, 97.5)
DLCO	10	15.3 (13.8, 18.7)
DLCO%	10	83.5 (71.5, 88.0)
SPO2 at rest	10	98.0 (97.0, 98.0)
SPO2 at exertion	10	96.0 (95.2, 96.0)
EMG findings		
Fibrillation potential w/irritative insertional activity	19	5 (26%)
High frequency repetitive discharges	19	1 (5%)
Polyphasic potentials of short duration and low amplitude	19	4 (21%)
Neuropathy	19	0 (0%)
Non-diagnostic	19	5 (26%)
Chest findings		
NSIP	19	2 (11%)
UIP	19	0 (0%)
LIP	19	0 (0%)
DIP	19	0 (0%)
DAD	19	0 (0%)
NSIP w/ OP overlap	19	0 (0%)
Normal	19	7 (37%)
Other	19	3 (16%)

The sample median (Q1, Q3) is given for continuous variables, while categorical and ordinal variables are reported as frequency (percentage)

subgroup analysis between cancer and non-cancer anti TIF1γ-positive DM was conducted and no statistically significant differences among NVC scores were observed (Table 7). Figure 2 depicts a jitter plot representation of NVC scores in cases versus control.

Discussion

The present study enhances understanding of NVC findings in the context of anti TIF1γ-positive DM and malignancy. 26.3% of anti TIF1γ-positive DM patients had an associated malignancy, which is consistent with reported malignancy rates in this subset [16], with 0% cancer occurrence in the control group. We observed cases to have significantly higher capillary density loss and higher microhemorrhages (trending towards significance) compared to controls. Additionally, cases were more likely to have higher frequencies of dilated capillaries, capillary ramifications, and capillary disorganization. Overall, our results suggest that NVC findings can facilitate the diagnosis of anti TIF1γ-positive DM patients while also identifying distinct NVC patterns in patients with associated malignancy, which can guide prognosis and management discussions.

The efficacy of NVC in SSc is widely reported, and studies involving NVC in IIM have steadily been increasing. Prior literature commonly utilizes the term "SSc-like pattern" to describe NVC findings in patients with IIM, which refers to specific nail fold microvascular abnormalities, such as enlarged capillaries, microhemorrhages, capillary loss, and capillary ramification and disorganization [20–21]. Such terminology has also been used in IIM, including antisynthetase syndrome and dermatomyositis [11, 22], overall highlighting its widespread, practical use in rheumatology. The literature on NVC findings assessed by varying MSA expression remains limited, however, prior reports have suggested that different MSA-expressing IIM have separate, unique characteristics. One study of antisynthetase syndrome ($n = 190$) observed NVC findings in 62% of cases, with an SSc-like pattern in 35% of patients. The authors also suggested that an SSc-like NVC pattern was associated with anti-Jo-1 expression [22]. However, a separate study observed

Table 5 Nailfold videocapillaroscopy results

Nailfold videocapillaroscopy scores	TIF-γ DM (*N* = 19)	Controls (*N* = 18)	Adj. Difference (95% CI)	*P*-value
Capillaroscopy density	2.1 (1.3, 2.3)	0.3 (0.0, 1.0)	0.8 (0.0, 1.5)	0.047
Giant capillaries	0.4 (0.0, 1.0)	0.4 (0.0, 1.0)	-0.3 (-0.9, 0.3)	0.28
Micro hemorrhages	0.5 (0.3, 1.2)	0.1 (0.0, 0.4)	0.5 (-0.0, 1.0)	0.057
Dilated capillaries	1.2 (0.3, 2.1)	0.9 (0.1, 1.1)	0.4 (-0.3, 1.0)	0.25
Capillaries ramifications	1.0 (0.1, 1.4)	0.3 (0.0, 1.1)	0.2 (-0.3, 0.7)	0.50
Capillaries disorganization	0.5 (0.2, 1.7)	0.0 (0.0, 0.3)	0.3 (-0.4, 1.0)	0.36

Median (Q1, Q3) scores are shown separately for each group. The adjusted difference (TIF-γ DM vs. controls) in NVC scores and corresponding 95% confidence intervals were estimated from linear regression models adjusting for age and sex

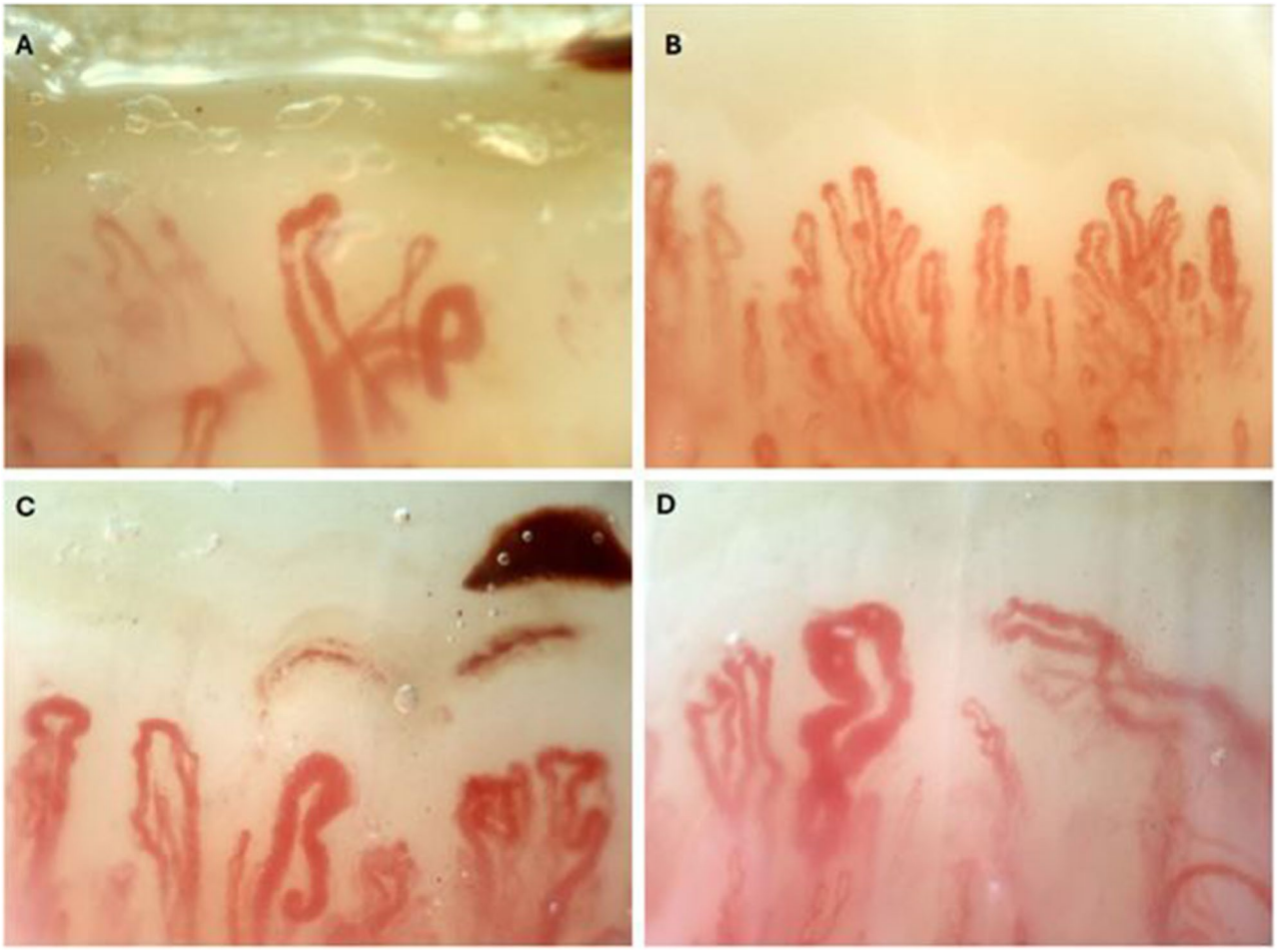

Fig. 1 (**A**) Ramification and microhemorrhage (x200). (**B**) Ramification and enlarged capillary > 20 microns (x200). (**C**) Giant capillary, ramification, and microhemorrhages (x200). (**D**) Giant capillary > 50 microns (x200)

Table 6 Single variable linear regression exploring associations of characteristics with nailfold videocapillaroscopy scores in patients with TIF-γ DM (updated)

Variable	Estimated difference in mean NVC scores (95% CI)					
	Capillaroscopy density	Giant capillaries	Micro hemorrhages	Dilated capillaries	Capillaries ramifications	Capillaries disorganization
CRP (1-unit increase), mg/L	-0.03 (-0.11, 0.05)	-0.02 (-0.08, 0.05)	-0.03 (-0.10, 0.04)	-0.03 (-0.12, 0.05)	0.02 (-0.05, 0.08)	-0.04 (-0.12, 0.04)
ESR (1-unit increase on cube-root scale), mm/1H	0.07 (-0.47, 0.62)	0.14 (-0.27, 0.54)	0.00 (-0.44, 0.45)	0.58 (0.08, 1.07)	0.06 (-0.36, 0.47)	-0.13 (-0.67, 0.41)
CK (doubling), u/L	0.01 (-0.44, 0.46)	-0.06 (-0.40, 0.28)	-0.26 (-0.60, 0.08)	0.42 (0.00, 0.85)	-0.14 (-0.47, 0.20)	-0.16 (-0.60, 0.29)
Aldolase (doubling), u/L	-0.10 (-1.06, 0.87)	-0.33 (-1.05, 0.38)	-0.14 (-0.91, 0.63)	0.16 (-0.74, 1.07)	0.03 (-0.71, 0.77)	-0.35 (-1.28, 0.59)

no association between anti-Jo-1 positivity and NVC capillary findings [23], highlighting inconsistencies in the literature among IIM MSA subtypes and warranting additional research to further elucidate such discordance. Our study provides additional insight into this gap, highlighting that anti TIF1γ-positive DM patients were more likely to have an SSc-like pattern versus idiopathic inflammatory myopathies controls.

Prior studies have also observed the presence of NVC findings (e.g., reduced capillaries) to be significantly higher in IIM patients expressing anti-MDA5 and anti TIF1γ antibodies compared with those expressing anti-ARS antibodies [18, 24], further highlighting that MSA subtypes should be considered when assessing NVC findings. These results are consistent with our findings, in which statistically significant increased capillary density loss was observed in anti TIF1γ-positive DM cases. Although cancer anti TIF1γ-positive DM patients had higher hemorrhages and ramifications and lower enlarged and giant capillaries with disorganization than

Table 7 Subgroup analysis of nailfold videocapillaroscopy results between Cancer and Non-Cancer TIF-positive dermatomyositis

Nailfold videocapillaroscopy scores	Associated cancer +TIF-gamma dermatomyositis patients (*N* = 5)	Non-cancer TIF-gamma dermatomyositis patients (*N* = 14)	Adj. Difference (95% CI)	*P*-value
Capillaroscopy density	2.1 (0.0, 2.1)	2.2 (1.8, 2.3)	-0.5 (-1.6, 0.6)	0.34
Giant capillaries	0.1 (0.0, 0.4)	0.5 (0.1, 1.2)	-0.3 (-1.1, 0.5)	0.42
Micro hemorrhages	0.8 (0.5, 1.3)	0.5 (0.3, 1.0)	0.1 (-0.8, 0.9)	0.84
Dilated capillaries	0.4 (0.3, 2.0)	1.3 (0.3, 2.1)	-0.2 (-1.4, 1.0)	0.71
Capillaries ramifications	1.4 (0.9, 1.5)	0.9 (0.0, 1.1)	0.3 (-0.5, 1.1)	0.48
Capillaries disorganization	0.4 (0.0, 0.5)	1.0 (0.3, 1.9)	-0.6 (-1.7, 0.5)	0.24

Median (Q1, Q3) scores are shown separately for each group. The adjusted difference (Cancer patients vs. Non-cancer patients) in NVC scores and corresponding 95% confidence intervals were estimated from linear regression models adjusting for age

non-cancer anti TIF1γ-positive DM controls, these findings were not statistically significant. Our study is unique in that additional subgroup analysis between cancer and non-cancer anti TIF1γ-positive DM yielded no statistically significant differences, although our data is limited by the small sample size ($n = 5$ for cancer association). Although NVC changes have been reported to be associated with disease activity, such as improvement in hemorrhages with treatment in anti TIF1γ-positive DM with persistence of density loss and enlargements, the association of features with malignancy has not been studied [25].

As such, the present study is the first to compare NVC findings in anti-TIF1-γ-positive DM patients with malignancy versus those without malignancy, suggesting that NVC findings can be interpreted both by MSA subtypes and distinct NVC findings should be considered in underlying malignancy association. NVC findings may have different clinical relevance based on the MSA subtype, which should be accounted for in prognosis and management discussions.

While our study assessed baseline NVC results in cases and controls, prior studies have evaluated long-term NVC changes in SSc and IIM patients across disease courses, a clinically relevant topic in rheumatologic management. Prior SSc literature has suggested NVC findings are chronically progressive and irreversible [20–21], while several studies in IIM have suggested that NVC findings are reversible and correlate with disease activity and response to treatment [11, 24, 26]. Temporal data regarding NVC findings have also been studied in DM patients, however there are inconsistencies in the literature. One study observed anti-MDA5 DM patients to have reversible NVC findings with treatment [26], while a separate study observed no statistically significant differences in NVC findings after three years of follow-up [23]. Interestingly, Mugii et al. assessed the longitudinal course of NVC findings in IIM patients expressing anti-MDA5, anti TIF1γ, and anti-ARS antibodies, demonstrating that NVC findings differed for each MSA [19]. They observed that, while microhemorrhages improved for all three groups, enlarged and reduced capillaries were only significantly improved in patients expressing anti-MDA5 antibodies, further highlighting that nuanced differences exist among MSA subtypes in assessing longitudinal NVC findings. The present study did not assess NVC scores longitudinally, and to our knowledge, no such studies exist in the literature assessing longitudinal NVC findings in anti TIF1γ-positive DM patients with associated malignancy, posing a highly clinically relevant direction for future rheumatologic research.

Our study has several limitations. Given its retrospective nature, additional prospective studies are warranted to confirm our results. Our sample size was small and included only Caucasian patients, limiting the generalizability of our results. Additionally, several NVC variables were trending towards significance, and a larger sample size would have greater power in elucidating underlying significant differences. The present study only assessed baseline NVC characteristics, as such, longitudinal data are absent which would have greater clinical relevance in identifying temporal relationships among our groups. Effects of long term immunosuppressive therapy on evolution of microvascular abnormalities may also be a potential confounding factor as evidenced in a prior study by Sugimoto et al. [27]. Future, larger, prospective studies accounting for such limitations are warranted to confirm our findings and provide additional insight into the clinical utility of NVC in anti TIF1γ-positive DM patients with underlying malignancy.

Conclusion

In conclusion, our study is the first to assess NVC differences among anti TIF1γ-positive DM patients with a subset of patients with associated malignancies versus idiopathic inflammatory myopathy controls. We observed anti TIF1γ-positive DM cases to have significantly increased capillary density loss and higher microhemorrhages (trending towards significance) on NVC when compared to controls. Cases were also observed

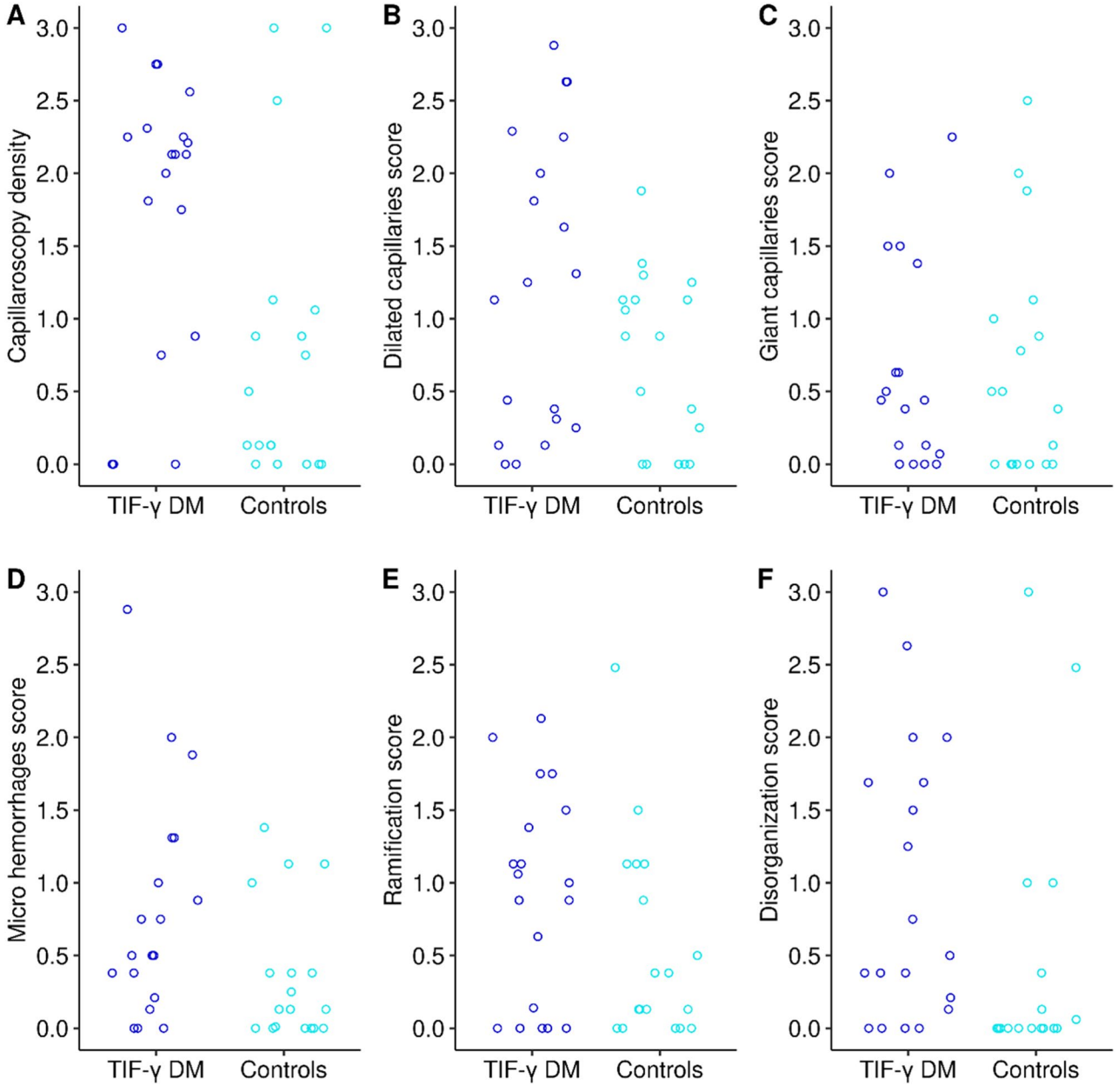

Fig. 2 Jitter plot representation of nailfold video capillaroscopy scores (**A**) Capillary Density (**B**) Dilated capillaries (**C**) Giant capillaries. (**D**) Microhemorrhages (**E**) Ramification (**F**) Disorganization

to have higher frequencies of dilated capillaries, capillary ramifications, and capillary disorganization. Although no statistically significant differences in NVC pattern were identified in cancer vs. non-cancer anti TIF1γ-positive DM, there were greater hemorrhages and ramifications noted in the cancer- anti TIF1γ-positive subset. Such NVC differences between cancer and non-cancer DM are promising, indicating the presence of microvascular differences with a potential for predicting cancer development that needs to be further investigated in future, larger studies (especially in the context of MSA subtype).

Abbreviations

DM	Dermatomyositis
IIM	Idiopathic inflammatory myopathy
MSA	Myositis–specific autoantibody
PM	Polymyositis
NVC	Nailfold video capillaroscopy
SSc	Systemic sclerosis
ARS	Anti–aminoacyl–tRNA synthetase
MDA5	Anti–melanoma differentiation–associated gene 5
TIF	Anti–transcription intermediary factor–1gamma

Author contributions

SM performed literature review, data collection, and edited/revised the manuscript. JP performed literature review and prepared the manuscript. MS and MDM helped with literature review and data collection. EC and BW

helped with statistical methodology and analysis. FB conceptualized the project idea and FB, BW and VM finalized approval of the manuscript draft.

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Data availability
Data is provided within the manuscript.

Declarations

Ethics approval and consent to participate
The present study was approved by the Mayo Clinic Institutional Review Board (IRB number 19-012625). Human Ethics and Consent to Participate declarations: All participants consented to participate in the study. The research was conducted in accordance with the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. Baig S, Paik JJ. Inflammatory muscle disease - An update. Best Pract Res Clin Rheumatol. 2020;34(1):101484.
2. Bendewald MJ, Wetter DA, Li X, Davis MD. Incidence of dermatomyositis and clinically amyopathic dermatomyositis: a population-based study in olmsted County, Minnesota. Arch Dermatol. 2010;146(1):26–30.
3. Bronner IM, van der Meulen MF, de Visser M, Kalmijn S, van Venrooij WJ, Voskuyl AE, Dinant HJ, Linssen WH, Wokke JH, Hoogendijk JE. Long-term outcome in polymyositis and dermatomyositis. Ann Rheum Dis. 2006;65(11):1456–61.
4. Zahr ZA, Baer AN. Malignancy in myositis. Curr Rheumatol Rep. 2011;13(3):208–15.
5. Liu Y, Xu L, Wu H, Zhao N, Tang Y, Li X, Liang Y. Characteristics and predictors of malignancy in dermatomyositis: analysis of 239 patients from Northern China. Oncol Lett. 2018;16(5):5960–8.
6. Hofstee HM, Serné EH, Roberts C, Hesselstrand R, Scheja A, Moore TL, et al. A multicentre study on the reliability of qualitative and quantitative nail-fold videocapillaroscopy assessment. Rheumatology (Oxford). 2012;51:749–55.
7. Rodriguez-Reyna TS, Bertolazzi C, Vargas-Guerrero A, Gutiérrez M, Hernández-Molina G, Audisio M, et al. Can nailfold videocapillaroscopy images be interpreted reliably by different observers? Results of an inter-reader and intra-reader exercise among rheumatologists with different experience in this field. Clin Rheumatol. 2019;38:205–10.
8. Araújo FC, Rocha ML. Nailfold capillaroscopy: from the early ages to the early diagnosis of systemic sclerosis. ARP Rheumatol. 2022;1:188–9.
9. Johnson D, van Eeden C, Moazab N, Redmond D, Phan C, Keeling S, et al. Nailfold capillaroscopy abnormalities correlate with disease activity in adult dermatomyositis. Front Med (Lausanne). 2021;8:708432.
10. Ganczarczyk ML, Lee P, Armstrong SK. Nailfold capillary microscopy in polymyositis and dermatomyositis. Arthritis Rheum. 1988;31(1):116–9.
11. Mugii N, Hasegawa M, Matsushita T, Hamaguchi Y, Horie S, Yahata T, Inoue K, Someya F, Fujimoto M, Takehara K. Association between nail-fold capillary findings and disease activity in dermatomyositis. Rheumatology (Oxford). 2011;50(6):1091–8.
12. Soubrier C, Seguier J, Di Costanzo MP, Ebbo M, Bernit E, Jean E, Veit V, Swiader L, Salort-Campana E, Attarian S, De Paula AM, Kaplanski G, Durand JM, Harlé JR, Schleinitz N. Nailfold videocapillaroscopy alterations in dermatomyositis, antisynthetase syndrome, overlap myositis, and immune-mediated necrotizing myopathy. Clin Rheumatol. 2019;38(12):3451–8.
13. Manfredi A, Sebastiani M, Cassone G, Pipitone N, Giuggioli D, Colaci M, Salvarani C, Ferri C. Nailfold capillaroscopic changes in dermatomyositis and polymyositis. Clin Rheumatol. 2015;34(2):279–84.
14. Fujimoto M, Watanabe R, Ishitsuka Y, Okiyama N. Recent advances in dermatomyositis-specific autoantibodies. Curr Opin Rheumatol. 2016;28(6):636–44.
15. Chinoy H, Fertig N, Oddis CV, Ollier WE, Cooper RG. The diagnostic utility of myositis autoantibody testing for predicting the risk of cancer-associated myositis. Ann Rheum Dis. 2007;66(10):1345–9.
16. Khanna U, Galimberti F, Li Y, Fernandez AP. Dermatomyositis and malignancy: should all patients with dermatomyositis undergo malignancy screening? Ann Transl Med. 2021;9(5):432.
17. 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.
18. Mugii N, Hamaguchi Y, Horii M, Fushida N, Ikeda T, Oishi K, Yahata T, Someya F, Matsushita T. Longitudinal changes in nailfold videocapillaroscopy findings differ by myositis-specific autoantibody in idiopathic inflammatory myopathy. Rheumatology (Oxford). 2023;62(3):1326–34.
19. Cutolo M. Atlas of capillaroscopy in rheumatic diseases. Milan: Elsevier; 2015.
20. Cutolo M, Sulli A, Pizzorni C, Accardo S. Nailfold videocapillaroscopy assessment of microvascular damage in systemic sclerosis. J Rheumatol. 2000;27(1):155–60.
21. Manfredi A, Sebastiani M, Campomori F, Pipitone N, Giuggioli D, Colaci M, Praino E, Ferri C. Nailfold videocapillaroscopy alterations in dermatomyositis and systemic sclerosis: toward identification of a specific pattern. J Rheumatol. 2016;43(8):1575–80.
22. Sebastiani M, Triantafyllias K, Manfredi A, González-Gay MA, Palmou-Fontana N, Cassone G, Drott U, Delbrück C, Rojas-Serrano J, Bertolazzi C, Nuño L, Giannini M, Iannone F, Vicente EF, Castañeda S, Selva-O'Callaghan A, Trallero Araguas E, Emmi G, Iuliano A, Bauhammer J, Miehle N, Parisi S, Cavagna L, Codullo V, Montecucco C, Lopez-Longo FJ, Martínez-Barrio J, Nieto-González JC, Vichi S, Confalonieri M, Tomietto P, Bergner R, Sulli A, Bonella F, Furini F, Scirè CA, Bortoluzzi A, Specker C, Barsotti S, Neri R, Mosca M, Caproni M, Weinmann-Menke J, Schwarting A, Smith V, Cutolo M. American and European network of antisynthetase syndrome collaborative group. Nailfold capillaroscopy characteristics of antisynthetase syndrome and possible clinical associations: results of a multicenter international study. J Rheumatol. 2019;46(3):279–84.
23. Pizzorni C, Cutolo M, Sulli A, Ruaro B, Trombetta AC, Ferrari G, Pesce G, Smith V, Paolino S. Long-term follow-up of nailfold videocapillaroscopic changes in dermatomyositis versus systemic sclerosis patients. Clin Rheumatol. 2018;37(10):2723–9.
24. Kubo S, Todoroki Y, Nakayamada S, Nakano K, Satoh M, Nawata A, Satoh Y, Miyagawa I, Saito K, Smith V, Cutolo M, Tanaka Y. Significance of nailfold videocapillaroscopy in patients with idiopathic inflammatory myopathies. Rheumatology (Oxford). 2019;58(1):120–30.
25. Mugii N, Hamaguchi Y, Fushida N, Horii M, Kitano T, Fujii K, Sawada K, Oishi K, Maeda S, Matsushita T. Early improvement of nailfold videocapillaroscopy abnormalities in dermatomyositis patients with anti-NXP-2 antibody. J Cutan Immunol Allergy. 2023;6(6):245–8.
26. Hamaguchi Y, Mugii N, Matsushita T, Takehara K. Long-term changes in nail fold capillary abnormalities and serum fibroblast growth factor 23 levels in dermatomyositis patients with anti-melanoma differentiating antigen 5 antibody. J Dermatol. 2021;48(1):106–9. https://doi.org/10.1111/1346-8138.15589. Epub 2020 Sep 9. PMID: 32902854.
27. Sugimoto T, et al. Nailfold capillaries and myositis-specific antibodies in anti-melanoma differentiation-associated gene 5 antibody-positive dermatomyositis. Rheumatology (Oxford). 2022;61(5):2006–15.

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