

Nailfold Capillaroscopy Findings in Rheumatoid Arthritis Patients and its Correlation to Teatment Response

Original Article

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ABSTRACT

Background: Nailfold capillaroscopy (NFC) is a non-invasive method to assess microvascular change.

Aim: Evaluate NFC abnormalities in RA patients and assess the correlation between NFC findings and therapeutic responses in patients receiving biologics versus conventional synthetic DMARDs (csDMARDs).

Methods: In this prospective study, 76 RA patients were divided into two groups: Group I (biologics) and Group II (csDMARDs). Capillaroscopic parameters, disease activity scores (DAS-28), and laboratory markers were assessed at baseline and after 6 months. NFC findings, including capillary number, width, length, shape abnormalities, and density scores, were analyzed before and after treatment.

Results: At baseline, both groups demonstrated common NFC abnormalities, such as tortuous, meandering, dilated capillaries and avascular areas. Tortuous capillaries were observed in 100%), meandering capillaries (34.2%), and dilated capillaries (25%) while microhemorrhages were rare (2.6%). Sub-papillary venous plexus (SPVP) visibility and normal U-shaped architecture were uncommon (11.8% and 19.7%, respectively). After 6 months, significant improvements in capillary number and width were reported, particularly in Group I. Group I demonstrated a greater reduction in capillary width ($p<0.001$). In Group I, etanercept led to the most significant increase in capillary number, while Baricitinib resulted in the lowest capillary width.

Conclusion: NFC effectively assesses microvascular involvement and monitors therapeutic response in RA. At baseline, RA patients commonly exhibited NFC findings such as tortuous, meandering, and dilated capillaries. Biologic therapies showed greater improvement in capillary parameters compared to csDMARDs. NFC may aid in selecting the most appropriate therapy, particularly in cases with significant microvascular involvement.

Key Words: Biologics, csDMARDs, nailfold capillaroscopy, rheumatoid arthritis.

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INTRODUCTION

Rheumatoid arthritis (RA) is a systemic autoimmune disorder contributing to articular destruction and vascular damage, affecting both macrovascular and microvascular systems. Microvascular involvement can be observed early in the disease, even before macrovascular damage occurs. A serious complication of RA is rheumatoid vasculitis, which can develop in advanced stages^[1].

Rheumatoid arthritis arises from the interaction between genetic predisposition and environmental factors. An initial triggering event leads to an inflammatory

autoimmune response that targets not only the synovial joints but also the blood vessels^[2].

In rheumatoid arthritis, Tumor necrosis factor-alpha (TNF- α) is recognized as a key pro-inflammatory cytokine, with elevated levels often observed in the serum of affected individuals. The primary cells involved in TNF- α production are T helper cells 1 (Th1) and macrophages. This cytokine plays a crucial role in activating fibroblasts, promoting epidermal hyperplasia, and facilitating the recruitment of other inflammatory cells^[3]. It also contributes to processes such as angiogenesis and the activation of osteoclasts. Additionally, interleukin-6 (IL-6) and interleukin-1 (IL-1) are significant contributors to joint degradation.

The cytokines induce fibroblasts to secrete enzymes like cathepsins and matrix metalloproteinases (MMPs), which break down key components of the extracellular matrix, including collagen and proteoglycans^[4].

Several therapeutic strategies are available to improve the clinical outcomes of RA. Disease-modifying anti-rheumatic drugs (DMARDs) are typically the first-line treatment for early-stage disease, but as RA progresses, more aggressive therapies may be required to prevent long-term disability^[5]. Biologic therapies have shown a significant impact on controlling disease activity and preventing joint destruction. However, issues related to cost and safety continue to be important considerations^[6,7].

Nailfold capillaroscopy (NFC) is a simple, widely used method to examine microvascular changes. It allows for the evaluation of peripheral microangiopathy by assessing nail fold capillary morphology^[8,9]. NFC detects early signs of microangiopathy, differentiates various disease stages, and provides insights into disease severity and prognosis^[10,11]. The most commonly observed capillaroscopic changes in RA patients include elongated capillaries, prominent subpapillary plexus, and dilated capillaries^[12]. Our study aimed to further investigate these changes and compare responses between biological and csDMARD treatments.

PATIENTS AND METHODS

Study Design

This prospective observational study examined nailfold capillaroscopic abnormalities in RA patients and their response to treatment. The data were collected between July and January 2024. Written informed consent was obtained from all patients prior to their participation in the study. The study was approved by the Medical Ethics Committee of the Faculty of Medicine (FWA000017585) [R161/2024].

Subjects

The study involved 76 RA patients (mean age: 47.89 ± 6.83 years in Group I, 48.11 ± 7.12 years in Group II), diagnosed based on the 2010 ACR/EULAR criteria. Patients were enrolled in the Rheumatology and Rheumatology Rehabilitation outpatient clinics. The patients were grouped into two categories:

Group 1: Patients receiving biological therapy
Group 2: Patients receiving cs DMARD therapy

Inclusion Criteria:

-Diagnosed with RA based on the 2010 ACR/EULAR criteria^[13].

Patients in Group I (biologic therapy) had initially received csDMARDs but transitioned to biologics due to failure of response or disease progression. Group II included patients who remained on csDMARDs throughout the study. NFC parameters, disease activity scores (DAS-28), and laboratory markers were assessed at baseline and after 6 months of treatment in both groups to assess microvascular changes associated with each therapeutic strategy. Group I continued biologic therapy exclusively for the entire six-month study period (Adalimumab, etanercept, and baricitinib).

Exclusion Criteria: Patients with coronary arterial diseases, cerebrovascular diseases, and peripheral vascular disorders. Patients with diabetes mellitus, hypertension, smoking history, or alcohol consumption. Patients with ongoing or previous trauma to the fingers (e.g., professional injury, obvious trauma, or cosmetic methods). Patients presented with other connective tissue diseases or any occlusive vascular disorders.

Methods

Clinical Assessment:

Medical history was obtained, focusing on disease onset and treatment history. Clinical examination, including both general and local assessments.

Disease Activity Assessment: Disease activity was evaluated by the Disease Activity Score in 28 joints (DAS28-ESR).

Laboratory investigations:

- Blood specimens were collected for the following tests:
- Complete Blood Count (CBC) with differential using automated technology.
- Erythrocyte Sedimentation Rate (ESR): Measured by the Wintergreen method and recorded in mm/hr, with the first-hour reading obtained.
- C-reactive Protein (CRP): Measured by automated ELISA or nephelometric methods.
- Rheumatoid Factor (RF): Assessed by ELISA.
- Cyclic Citrullinated Peptide Antibodies (Anti-CCP): Measured by ELISA.

Nailfold Capillaroscopy(NFC)

NFC was carried out for all patients by an experienced rheumatologist in the technique, NFC was performed using an XW 880 USB digital microscope with $\times 400$

magnification. The microscope included an 8-inch LCD screen and a 0.38-megapixel camera (Hefei Golden Brains Optical Instrument Co., China). In the beginning, patients rested for 20 minutes in a place with a temperature range of 20°C to 24°C. Both middle and ring fingers from each hand were assessed for any abnormalities associated with nailfold capillaroscopy (NFC) in rheumatoid arthritis (RA) patients. A small amount of immersion oil was applied to the nail fold area to enhance visibility. Measurements included capillary density (capillaries per 1 mm), capillary length ($\geq 300 \mu\text{m}$ = elongated), capillary width (20–50 μm = dilated, $>50 \mu\text{m}$ = giant), capillary shape, hemorrhages, capillary configuration (capillary shape), and the occurrence or not of hemorrhages. Measurements were taken over a 1-mm area per finger, analyzing the middle and ring fingers of both hands^[14,15].

Statistical analysis

Data analysis was performed using SPSS (Statistical Package for the Social Sciences) version 28. Categorical variables were presented as absolute frequencies and analyzed using the chi-square test or Fisher's exact test, as appropriate. The chi-square test for trend was applied to compare ordinal data between two groups.

The Shapiro-Wilk test was used to assess normality and check assumptions for parametric tests. Quantitative data were compared between two groups using the independent samples t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. To compare within the same group across two-time points, the paired samples t-test was used for normally distributed data, while the Wilcoxon signed-rank test was used for non-normally distributed or ordinal data. Statistical significance was set at $P < 0.05$, with $P \leq 0.001$ indicating a highly significant difference.

RESULTS

We analyzed data from patients both at baseline and after a 6-month follow-up period of treatment. Demographics and disease characteristics and laboratory data:

The study included 76 patients with rheumatoid arthritis, with 34 females and 4 males in group I, while all patients in group II were females, their mean age was 47.89 ± 6.83 and 48.11 ± 7.12 in group I and group II sequentially. On the other hand, there was no significant difference between the two groups regarding gender and age, as shown (Table 1).

Table 1: Comparison between the studied groups regarding demographic data.

	Group I N=38 (%)	Group II N=38 (%)	χ^2	P
Gender:				
Female	34 (89.5)	38 (100%)	Fisher	0.115
Male	4 (10.5%)	0 (0%)		
	Mean $\pm$ SD	Mean $\pm$ SD	t	P
Age (year)	47.89 ± 6.83	48.11 ± 7.12	-0.132	0.896

χ^2 Chi square test Z Mann Whitney test t independent sample t test.

Among patients who received biological treatment (group I); 20 patients received Adalimumab (52.6%), 12 patients received etanercept (31.6%), and six patients received baricitinib (15.8%). Among patients who received cs DMARDs (group II), 24 patients received methotrexate (63.2%), 24 patients received hydroquinone (63.2%), 26 patients received leflunomide (68.4%), and eight patients received sulphasalazine (21.1%)

At baseline, both Group I and Group II exhibited moderate disease activity, as reflected by identical DAS-28 scores of 5.6 (5.6 – 6.3) for Group I and 5.6 (5.6 – 6.1) for Group II. Group II showed a slightly higher ESR (49.5 vs. 45) and a significantly higher CRP (12.2 vs. 6). However, both groups had elevated Rheumatoid Factor (RF) levels

(137.5 vs. 130). Anti-CCP levels were also slightly higher in Group I (45 vs. 34.2). Despite these differences, both groups had comparable disease activity and inflammation at baseline, setting a similar starting point for treatment (Table 2)

When comparing the two studied groups following treatment, the DAS-28, and ESR were significantly lower in Group I compared to Group II. Rheumatoid factor (RF) decreased in Group I ($p = 0.012$), while

no significant change was observed in Group II ($p = 0.056$). Anti-cyclic citrullinated peptide (Anti-CCP) levels exhibited a significant decrease in Group I ($p = 0.003$). (Table 2)

Table 2: Comparison between the studied groups regarding disease activity score and laboratory data at baseline and after treatment.

variable	Group I (n=38)	Group II (n=38)	t	P
	Mean $\pm$ SD	Mean $\pm$ SD		
Disease duration (years)	8.2 $\pm$ 3.6 (2-14)	8.6 $\pm$ 4.1 (2-14)	0.452	0.652
DAS-28	5.6(5.6 – 6.3)	5.6(5.6 – 6.1)	-0.554	0.58
Baseline	2.6(2.3 – 4.4)	4.1(2.3 – 4.7)	-3.792	<0.001**
After				
p [¥]	<0.001**	<0.001**		
Hemoglobin				
Baseline	11.61 $\pm$ 0.75	11.32 $\pm$ 0.82	1.537	0.129
After	11.52 $\pm$ 1.32	11.39 $\pm$ 1.09	-2.39	0.119
p [¥]	0.0621	0.814		
	Median (IQR)	Median (IQR)	Z	P
WBCs				
Baseline	7.4(4.6 – 8.7)	7.4(6.25 – 7.8)	-0.011	0.992
After	6(4.3 – 7.8)	5.5(4.7 – 8.2)	-1.65	0.099
p [¥]	<0.001**	0.055		
Platelet count Baseline				
After	239(169 – 280)	217.5(190 – 297)	-0.849	0.396
	210(165 – 220)	210(178 – 231.25)	-0.905	0.365
p [¥]	0.001**	0.034*		
ESR				
Baseline	45(42 – 54)	49.5(45 – 67.5)	-1.898	0.058
After	20(12 – 40)	35(24.25 – 62)	-3.297	<0.001**
p [¥]	<0.001**	0.01*		
CRP				
Baseline	6(6 – 18.4)	12.2(6 – 23.8)	-1.038	0.299
After	6(2.2 – 16.8)	7(6 – 9.9)		
p [¥]	0.255	0.039*		
RF				
Baseline	137.5(130 – 147.7)	130(130 – 145)	1.563	0.118
After	50(16.08 – 130)	50(18 – 130)	0.321	0.748
p [¥]	0.012*	0.056		
Anti-CCP Baseline				
After	45(20 – 58.4)	34.2(23 – 37.6)	-0.138	0.89
	34.2(23 – 53)	25(9 – 58)	-1.801	0.072
p [¥]	0.003*	0.96		

DAS-28: disease activity score-28; WBC: white blood cells; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; RF: rheumatoid factor; Anti-CCP: Anti-cyclic citrullinated peptide; Z Mann Whitney test; t independent sample t test; §Paired sample t test; ¥Wilcoxon signed rank test; $p < 0.05$: statistically significant.

NFC finding in Rheumatoid arthritis patients:

Baseline capillaroscopic findings in RA patients revealed that tortuous capillaries were the most common

abnormality (100%), followed by meandering capillaries (34.2%), crossing dilated capillaries (25%), and the subpapillary venous plexus, which was observed in only 11.8% of cases (Table 3).

Table 3: Capillary microscopy findings before treatment.

	Mean $\pm$ SD/n	Range%/
Capillary number/mm	7.09 $\pm$ 1.35	1 – 12
Capillary width	62.99 $\pm$ 19.08	40 – 83
Capillary length	201.40 $\pm$ 62.11	89-340
Capillary shape		
Tortuous	76	100 %
Meandering	26	34.2%
U-shape	15	19.7%
	14	18.4 %
Crossing	19	25 %
Dilated		
Subpapillary plexus		
Present	9	11.8%
Pericapillary edema		
Present	9	11.8%
Capillary hemorrhage		
Present	2	2.6%
Avascular zone score Zero	76	100%
Capillary density score		
Zero	12	15.7%
One	35	46
Two	29	38.1

Comparison between group I and group 2 regarding after-treatment capillaroscopic parameters.

Significant increase in capillary number and reduction in capillary width in both groups ($p < 0.001$), with a

more pronounced capillary width reduction in Group I ($p < 0.001$) (Table 4). Subpapillary plexus and pericapillary edema, present in 11.8% of patients pre-treatment, were completely absent post-treatment in both groups.

Table 4: Comparison between the studied groups regarding capillary morphology baseline and after treatment:

	Group I (n=38)	Group II (n=38)	t	p
	Mean ± SD	Mean ± SD		
Capillary number/mm				
Baseline	7.21 ± 1.3	6.97 ± 1.4	0.764	0.448
After	8.74 ± 1.43	8.63 ± 1.0	0.373	0.711
p [‡]	<0.001**	<0.001**		
Capillary width				
Baseline	60.95 ± 19.76	65.03 ± 18.41	-0.931	0.355
After	31.45 ± 1.32	11.39 ± 1.09	-3.887	<0.001**
p [‡]	<0.001**	<0.001**		
Capillary length				
Baseline	214 ± 52.4	221 ± 61.3	0.535	0.594
After	201 ± 45.2	212 ± 52.7	0.977	0.331
p [‡]	0.250	0.494		
Capillary shape				
Baseline				
Tortious	38 (100%)	38 (100%)	Fisher	0.262
Meandering	11 (28.9%)	15 (39.5%)	15.683	<0.001**
U shaped	5 (13.2%)	10 (26.3%)	0.592	0.442
Crossing	12 (31.6%)	10 (23.7%)	0	>0.999
Dilated	11 (28.9%)	8 (21.1%)	Fisher	0.005*
After				
Tortious	32 (82.4%)	36 (94.7%)	0	>0.999
Meandering	0 (0%)	13 (34.2%)	0.935	0.333
U shaped	5 (13.2%)	9 (23.7%)	2.077	0.15
Crossing	0 (0%)	0 (0%)	1.401	0.237
Dilated	0 (0%)	6 (15.8%)	1.894	0.169
p [‡]	0.461	0.918		
Subpapillary plexus				
Baseline				
Absent	32 (84.2%)	35 (92.1%)	Fisher	0.48
Present	6 (15.8%)	3 (7.9%)		
After				
Absent	38 (100%)	38 (100%)	-	-
p [‡]	0.014*	0.083		
Pericapillary edema				
Baseline Absent	32 (84.2%)	35 (92.1%)	Fisher	0.48
Present	6 (15.8%)	3 (7.9%)	-	-
After				
Absent	38 (100%)	38 (100%)	-	-
p [‡]	0.014*	0.083		

Capillary hemorrhage				
Baseline Absent				
Present	38 (100%)	36 (94.7%)	Fisher	0.493
	0 (0%)	2 (5.3%)		
After				
Absent	38 (100%)	38 (100%)	-	-
p [‡]	>0.999	0.157		
Avascular zone score				
Baseline				
Zero	38 (100%)	38 (100%)	-	-
After				
Zero	38 (100%)	38 (100%)	-	-
Capillary density score				
Baseline				
Zero	38 (100%)	38 (100%)	-	-
After				
Zero	6 (15.8%)	6 (15.8%)	2.149 [∞]	0.143
One	22 (57.9%)	13 (34.2%)		
Two	10 (26.3%)	19 (50%)		
p [‡]	<0.001**	<0.001**		

Z Mann Whitney test t independent sample t test ** $p < 0.001$ is statistically highly significant * $p < 0.05$ is statistically significant §Paired sample t test ¶Wilcoxon signed rank test

Capillary hemorrhage, initially observed in 2.6% of patients, was absent after treatment. Avascular zone scores remained at zero in all participants before and after treatment. The capillary density score showed a shift toward normalization, with significant improvements in both groups ($p < 0.001$).

A comparison of various biological treatments in

Group 1 was conducted based on nail fold capillaroscopic parameters:

Patients receiving etanercept had the highest mean capillary number ($p < 0.001$), while those receiving Baricitinib showed the lowest capillary width ($p = 0.008$) and capillary shape abnormalities ($p < 0.001$). (Table 5)

Table 5: Comparison between the studied groups with different biological therapy regarding capillary morphology after treatment:

	Adalimumab (n=20) Mean $\pm$ SD	Etanercept N=12 (%) Mean $\pm$ SD	Baricitinib (n=6) Mean $\pm$ SD	F	P
Capillary number/mm	6.5 $\pm$ 0.51	8.5 $\pm$ 1.57	7.0 $\pm$ 0	16.579	<0.001**
Bonferroni	P ₁ <0.001**	P ₂ 0.01*	P ₃ 0.807		
Capillary width	67.5 $\pm$ 17.63	60.5 $\pm$ 21.41	40.0 $\pm$ 0.0	5.585	0.008*
Bonferroni	P ₁ 0.857	P ₂ 0.079	P ₃ 0.006*	χ^2	
Capillary shape	5 (25%)	6 (50%)	0 (0%)	39.272	<0.001**
Tortious	0 (0%)	6 (50%)	0 (0%)		
Meandering U shaped	5 (25%)	0 (0%)	6 (100%)		
Crossing	5 (25%)	0 (0%)	0 (0%)		
Dilated	5 (25%)	0 (0%)	0 (0%)		
p	P ₁ <0.001**	P ₂ <0.001**	P ₃ <0.001**		
Subpapillary plexus Absent	20 (100%)	10 (100%)	6 (100%)	-	-
Pericapillary edema Absent	20 (100%)	10 (100%)	6 (100%)	-	-
Capillary hemorrhage Absent	20 (100%)	10 (100%)	6 (100%)	-	-
Avascular zone score Zero	20 (100%)	10 (100%)	6 (100%)	-	-
Capillary density score					
Zero	0 (0%)	6 (50%)	0 (0%)	24.182 ∞	<0.001**
One	10 (50%)	6 (50%)	6 (100%)		
Two	10 (50%)	0 (0%)	0 (0%)		
p	P ₁ <0.001**	P ₂ 0.039*	P ₃ 0.03*		

F One way ANOVA test * $p < 0.05$ is statistically significant ** $p \leq 0.001$ is statistically highly significant χ^2 Chi square test p for Chi square test p1 difference between Adalimumab and etanercept p2 difference between etanercept and Baricitinib p3 difference between Adalimumab and Baricitinib



Fig 1: Post biological treatment nail fold capillaroscopy: hairpin capillaries, increase in capillary density, reduction of capillary width.



Fig 2: Pre-treatment nail fold capillaroscopy for a patient in Group I showing tortuous, crossing, increased capillaries width, low capillary density, microhaemorrhage.

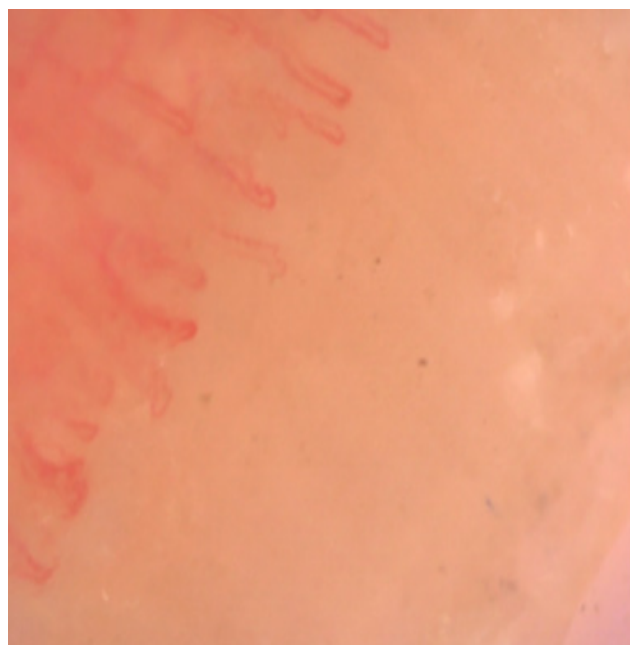


Fig 3: Pre-treatment nail fold capillaroscopy for a patient in group II showing tortuous, meandering, increased capillary width.

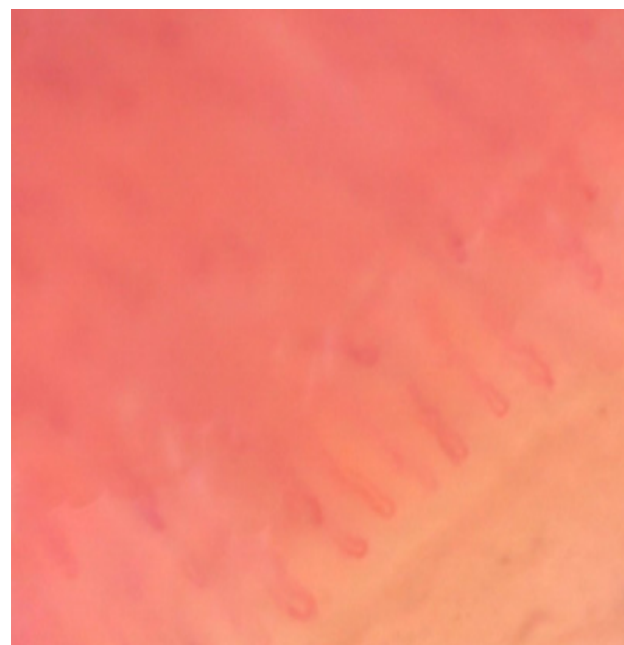


Fig 4: Post-DMARDs treatment nail fold capillaroscopy: crossing tortuous capillaries, reduced capillary width.

Overall, the study showed significant improvements in capillary morphology. Disease activity, and inflammatory markers following treatment, with notable differences among the biological therapies.

DISCUSSION

Rheumatoid arthritis (RA) is a long-term inflammatory autoimmune disorder with a predicted frequency of 1%^[16]. The pharmacological treatment of RA was traditionally centered around the utilization of corticosteroids and conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), for instance, methotrexate (MTX). Meanwhile, the introduction of biologic DMARDs (bDMARDs) has noteworthy transformed the treatment approach for RA patients^[17].

Our findings underscore the value of NFC in assessing RA-related microvascular involvement and treatment response. Both treatment groups exhibited reductions in DAS-28 and inflammatory markers (ESR), supporting the efficacy of csDMARDs and biologics in controlling RA. Group I demonstrated a more profound reduction in disease activity, consistent with previous research highlighting the superiority of biologics^[18,19].

Tortuous capillaries were the most frequent abnormality (100%), followed by meandering capillaries (34.2%) and crossing dilated capillaries (25%). Subpapillary venous plexus was observed in only 11.8% of cases. These results align with previous NFC studies in RA.^[20,21] In contrast, some studies have reported that there are no specific NFC findings exclusive to rheumatoid arthritis (RA) patients^[22,23].

In both groups, capillary width significantly decreased after treatment, while capillary number increased, indicating an overall enhancement in the microvascular environment. Notably, Group I exhibited a more pronounced reduction in capillary width compared to Group II, highlighting the superior efficacy of biological agents in alleviating vascular abnormalities. These results are consistent with prior research by *Caraba et al.*^[19], who reported a significant increase in capillary number following anti-TNF therapy. Similarly, *Anghel et al.*^[24] documented improvements in the avascular area score, along with a reduction in the occurrence of giant and dilated capillaries in patients with rheumatoid arthritis after six months of anti-TNF treatment. However, this study did not include a comparative analysis of treatment responses between (csDMARDs) and biologic DMARDs, limiting the assessment of their relative efficacy.

In our study, Group I exhibited a significant reduction in meandering and dilated capillaries following treatment compared to Group II, while no notable changes were observed in the presence of tortuous capillaries. These findings align with those of *Anghel et al.*^[24], who observed significant improvements in capillaroscopic abnormalities after 12 months of anti-TNF- α therapy. These improvements included increased capillary density and reductions in dilated, giant, and elongated capillaries, as well as neoangiogenesis. However, similar to our results, *Anghel et al.*^[24] did not observe significant changes in other parameters, such as tortuous, crossed, or bushy capillaries.

Within Group I, the post-hoc analysis of different biological agents revealed variations in their effects on capillary characteristics. Patients receiving etanercept

demonstrated a more pronounced increase in capillary number compared to those treated with Adalimumab or Baricitinib, suggesting that etanercept may have a greater role in promoting microvascular repair and improving capillary density in RA patients.

Conversely, Baricitinib resulted in the most significant reduction in capillary width, indicating its potential effectiveness in reducing capillary dilation associated with severe inflammation.

The results are consistent with previous studies, which observed that treatment involving the JAK inhibitor led to a significant reduction in venous limb length, apical width, and capillary length. Additionally, there was an increase in the number of ramified capillaries. These alterations in microvascular capillaroscopic variables were noted from baseline to three months of therapy^[25].

Our study included rheumatoid arthritis patients who had been initially treated with csDMARDs before transitioning to biologics (Group I) and those who remained on csDMARDs (Group II). This design allows us to assess NFC changes in response to biologic therapy after csDMARD exposure, providing insights into treatment-related vascular improvements. The observed improvements in capillary number

and width, particularly in biologic-treated patients, suggest a more pronounced effect on microvascular repair compared to csDMARDs alone.

The study's novelty lies in its direct comparison of NFC changes before and after biological versus csDMARD therapy. Within biologic treatments, etanercept demonstrated the most significant increase in capillary number, while Baricitinib showed the greatest reduction in capillary width. These insights may guide personalized treatment approaches for RA patients with microvascular involvement.

CONCLUSION

This study highlights NFC's utility in monitoring microvascular changes in RA and suggests that biologic therapies provide superior vascular improvements compared to csDMARDs. These findings underline the importance of personalized therapy selection, allowing for treatment strategies tailored to individual patients' vascular involvement and disease severity. Personalized therapy selection based on NFC findings may enhance treatment efficacy and disease management.

LIMITATIONS AND FUTURE DIRECTIONS

The small sample size and the fact that it was a single-center study may limit the generalizability of the findings.

- Post-hoc analysis of different biologics on NFC changes
- Future studies should examine long-term outcomes and integrate NFC findings with clinical disease progression

ABBREVIATIONS

RA: Rheumatoid arthritis

NFC: Nailfold capillaroscopy conventional synthetic DMARDs csDMARDs

TN F- α : Tumor necrosis factor-alpha

IL-6: Interleukin-6

IL-1: Interleukin-1

MMPs: Matrix metalloproteinases

DAS28-ESR: Disease Activity Score in 28 joints.

CRP: -C-reactive Protein

RF: Rheumatoid Factor

Anti-CCP: Cyclic Citrullinated Peptide Antibodies

DECLARATIONS

ETHICAL CONSIDERATIONS

Written informed consent was obtained from all patients prior to their participation in the study. Consent for publication:

CONSENT TO PARTICIPATE

Not applicable.

DATA AVAILABILITY

Not applicable

CONFLICT OF INTEREST

None declared Funding: No external funding.

AUTHOR CONTRIBUTIONS

S. M. integrated and evaluated the data. O.A clarified the data. A.R. participated in drafting the manuscript. R.M. reviewed it critically to ensure key insights were addressed. All authors agreed to submit the work to the current journal, Accepted responsibility for the version to be published, and are accountable for the overall accuracy and integrity of the study.

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REFERENCE

1. Bocci, E.B.; Monache, F.D.; Angrisani, M.C.C.; Gerli, R (2005). Recent views on the pathogenesis of cardiovascular damage associated with rheumatoid arthritis. *Recenti. Prog. Med.* 2005, 96, 65–69.
2. Padjen I, Gabay C, and Aletaha D (2018). Pathogenesis and clinical aspects of rheumatoid arthritis. In: Bijlsma J, Hachula E, editors. *Textbook on Rheumatic Disease*. 3rd ed. London: BMJ Publishing Group Ltd; 2018; 237-275
3. Armaka M, Apostolaki M, Jacques P *et al.* (2008). Mesenchymal cell targeting by TNF as a common pathogenic principle in chronic inflammatory joint and intestinal diseases. *J Exp Med* 2008;205:331–7.
4. Goldring, S.R.; Gravalles, E.M (2000). Pathogenesis of bone erosions in rheumatoid arthritis. *Curr. Opin. Rheumatol.* 2000, 12, 195–199.
5. Chauhan K, Jandu JS, Goyal A, Bansal P, Al-Dhahir MA (2021). *StatPearls* [Internet] Treasure Island (FL): Stat Pearls Publishing; 2021. Rheumatoid arthritis.
6. Kondo N, Kuroda T, Kobayashi D(2021). Cytokines networks in the pathogenesis of rheumatoid arthritis. *Int J Mol Sci.* 2021;22(20):10922. doi: 10.3390/ijms222010922. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
7. Sokolova MV, Schett G, Steffen U (2022). Autoantibodies in rheumatoid arthritis: historical background and novel findings. *Clin Rev Allergy Immunol.* 2022;63(2):138–151. doi: 10.1007/s12016-021-08890-1.
8. Errichetti E, Stinco G(2015). The practical usefulness of dermoscopy in general dermatology. *G Ital Dermatol Venereol* 2015;150:533–46.
9. Cutolo M, Pizzorni C, Tuccio M, Burroni A, Craviotto C, Basso M, *et al.* (2004). Nail fold videocapillaroscopic patterns and serum autoantibodies in systemic sclerosis. *Rheumatol Oxford* 2004;43:719–26.
10. Fink C, Kilian S, Bertlich L, Hoxha E, Bardehle F, Enk A, *et al.* (2018). Evaluation of capillary pathologies by nailfold capillaroscopy in patients with psoriasis vulgaris: study protocol for a prospective, controlled exploratory study. *BMJ Open* 2018;8(8):021595.
11. Shenavandeh S, Tarakemeh T, Sarvestani EK, Nazarinia MA (2017). Serum vascular endothelial growth factor (VEGF), soluble VEGF receptor-1 (sVEGFR-1) and VEGFR-2 in systemic sclerosis patients: relation to clinical manifestations and capillaroscopy findings. *Egypt Rheumatol* 2017;39(1):19–24.
12. Lambova SN, Müller-Ladner U(2012). Capillaroscopic pattern in inflammatory arthritis. *Microvasc Res.* 2012 May;83(3):318–22. doi: 10.1016/j.mvr.2012.03.002. Epub 2012 Mar 9. PMID: 22426123; PMCID: PMC3332153.
13. Aletaha, D., Neogi, T., Silman, A. J., Funovits, J., Felson, D. T., Bingham, C. O. 3rd, Birnbaum, N. S., Burmester, G. R., Bykerk, V. P., Cohen, M. D., Combe, B., Costenbader, K. H., Dougados, M., Emery, P., Ferraccioli, G., Hazes, J. M., Hobbs, K., Huizinga, T. W., Kavanaugh, A., Kay, J., Kvien, T. K., Laing, T., Mease, P., Ménard, H. A., Moreland, L. W., Naden, R. L., Pincus, T., Smolen, J. S., Stanislawski-Biernat, E., Symmons, D., Tak, P. P., Upchurch, K. S., Vencovsky, J., Wolfe, F., Hawker, G. (2010) rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Annals of Rheumatic Diseases*, 2010, 69(9), 1580–1588. <https://doi.org/10.1136/ard.2010.138461>
14. Manfredi A, Sebastiani M, Cassone G, Pipitone N, Giuggioli D, Colaci M *et al.* (2015). Nailfold capillaroscopic changes in dermatomyositis and polymyositis. *Clin Rheumatol* 2015, 34:279–28
15. Cutolo M, Sulli A, Smith V(2015). How to perform and interpret capillaroscopy. *Best Pract Res Clin Rheumatol*, 2013,27:237–248 18.
16. Tornero Molina J, Hernández-Cruz B, Corominas H(2023). Initial Treatment with Biological Therapy in Rheumatoid Arthritis. *J Clin Med.* 2023 Dec 21;13(1):48. doi: 10.3390/jcm13010048. PMID: 38202055; PMCID: PMC10779475.

17. **Kerschbaumer A, Sepriano A, Smolen JS, van der Heijde D, Dougados M, van Vollenhoven R, *et al.* (2020).** Efficacy of pharmacological treatment in rheumatoid arthritis: a systematic literature research informing the 2019 update of the EULAR recommendations for management of rheumatoid arthritis. *Ann Rheum Dis.* 2020 Jun;79(6):744-759. doi:10.1136/annrheumdis-2019-216656. Epub 2020 Feb 7. PMID: 32033937; PMCID: PMC7286044.
18. **Sun X, Li R, Cai Y, Al-Herz A, Lahiri M, Choudhury MR *et al.* (2021).** Clinical remission of rheumatoid arthritis in a multicenter real-world study in Asia-Pacific region. *Lancet Reg Health West Pac.* 2021 Aug 12;15:100240. doi: 10.1016/j.lanwpc.2021.100240. PMID: 34528015; PMCID: PMC8365438.
19. **Caraba A, Stancu O, Crişan V, Georgescu D (2024).** Anti TNF-Alpha Treatment Improves Microvascular Endothelial Dysfunction in Rheumatoid Arthritis Patients. *Int J Mol Sci.* 2024 Sep 14;25(18):9925. doi: 10.3390/ijms25189925. PMID: 39337413; PMCID: PMC11432218.
20. **Lin KM, Cheng TT, Chen CJ.** Clinical applications of nailfold capillaroscopy in different rheumatic diseases. *J Intern Med.* 2009;20:238–47.
21. **Rajaei A, Dehghan P, Amiri A (2017).** Nailfold capillaroscopy in 430 patients with rheumatoid arthritis. *Caspian J Intern Med.* 2017 Fall;8(4):269-274. doi: 10.22088/cjim.8.4.269. PMID: 29201317; PMCID: PMC5686305.
22. **Khalil, W. E., Mahmoud, S. A., & Elabd, H (2022).** Nailfold capillaroscopic patterns in rheumatoid arthritis patients. *JRAM* 2022; 3 (2): 169-177.
23. **Adel M. Ali, Sherin M. Hamza, Fatma M. Aboud, Nouran M. El-Shahat (2019).** Nailfold capillaroscopic changes in Egyptian patients with psoriatic arthritis in comparison to rheumatoid arthritis, *The Egyptian Rheumatologist*, Volume 41, Issue 4, 2019, Pages 303-307, ISSN 1110-1164.
24. **Anghel D, Sîrbu CA, Petrache OG, Opriş-Belinski D, Negru MM, Bojincă VC, Pleşa CF, Ioniţă Radu F (2023).** Nailfold Videocapillaroscopy in Patients with Rheumatoid Arthritis and Psoriatic Arthropathy on ANTI-TNF-ALPHA Therapy. *Diagnostics (Basel).* 2023 Jun 15;13(12):2079. doi: 10.3390/diagnostics13122079. PMID: 37370974; PMCID: PMC10296951.
25. **Anyfanti, P., Angeloudi, E., Dara, A., Pagkopoulou, E., Moysidou, G.-S., Deuteraiou.** Non-Invasive Assessment of Micro- and Macrovascular Function after Initiation of JAK Inhibitors in Patients with Rheumatoid Arthritis. *Diagnostics*, 2024,14(8),834.

نتائج تنظير الشعيرات الدموية في طيات الأظافر لدى مرضى التهاب المفاصل الروماتويدي وارتباطها باستجابة العلاج

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المقدمة: يُعد تنظير الشعيرات الدموية في طيات الأظافر (NFC) طريقة غير جراحية لتقييم التغيرات الدقيقة في الأوعية الدموية. **الهدف:** تقييم تشوهات NFC لدى مرضى التهاب المفاصل الروماتويدي، وتقييم العلاقة بين نتائج NFC والاستجابات العلاجية لدى المرضى الذين يتلقون أدوية بيولوجية مقارنةً بأدوية الروماتيزم المعدلة للمرض الاصطناعية التقليدية (csDMARDs).

الطريقة: في هذه الدراسة الاستشراكية، قُسم ٧٦ مريضاً بالتهاب المفاصل الروماتويدي إلى مجموعتين: المجموعة الأولى (أدوية بيولوجية) والمجموعة الثانية (csDMARDs). قُيِّمت معايير تنظير الشعيرات الدموية، ودرجات نشاط المرض (DAS-28)، والعلامات المخبرية في بداية الدراسة وبعد ٦ أشهر. حُلِّلت نتائج NFC، بما في ذلك عدد الشعيرات الدموية، وعرضها، وتشوهات شكلها، ودرجات كثافتها، قبل العلاج وبعده.

النتائج: في بداية الدراسة، أظهرت كلتا المجموعتين تشوهات NFC شائعة، مثل الشعيرات الدموية المتعرجة والمتعرجة والمتوسعة والمناطق اللاوعائية. لوحظت الشعيرات الدموية المتعرجة في ١٠٠٪ والشعيرات الدموية المتعرجة (٣٤،٢٪) والشعيرات الدموية المتوسعة (٢٥٪) بينما كانت النزيفات الدقيقة نادرة (٢،٦٪). كانت رؤية الضفيرة الوريدية تحت الحليمية (SPVP) والبنية الطبيعية على شكل حرف U غير شائعة (١١،٨٪ و ١٩،٧٪ على التوالي). بعد ٦ أشهر، تم الإبلاغ عن تحسينات كبيرة في عدد الشعيرات الدموية وعرضها، وخاصة في المجموعة الأولى. أظهرت المجموعة الأولى انخفاضاً أكبر في عرض الشعيرات الدموية ($p < 0.001$). في المجموعة الأولى، أدى سيكيوكينوماب إلى أكبر زيادة في عدد الشعيرات الدموية، بينما أدى باريستينيب إلى أقل عرض للشعيرات الدموية.

الخلاصة: يقيم NFC بشكل فعال مشاركة الأوعية الدموية الدقيقة ويراقب الاستجابة العلاجية في التهاب المفاصل الروماتويدي. في البداية، أظهر مرضى التهاب المفاصل الروماتويدي عادةً نتائج NFC مثل الشعيرات الدموية المتعرجة والمتعرجة والمتوسعة. أظهرت العلاجات البيولوجية تحسناً أكبر في معايير الشعيرات الدموية مقارنةً بأدوية الروماتيزم المعدلة للمرض (csDMARDs). قد يساعد العلاج بالخلايا الجذعية (NFC) في اختيار العلاج الأنسب، خاصةً في الحالات التي يكون فيها تأثير الأوعية الدموية الدقيقة كبيراً.