International Journal of Medical Arts

Volume 4, Issue 7, July 2022

https://ijma.journals.ekb.eg/

Print ISSN: 2636-4174

Online ISSN: 2682-3780

Available online at Journal Website
https://ijma.journals.ekb.eg/
Main Subject [Internal Medicine]

Original Article

Study of the Role of Nailfold Capillaroscopy in the Evaluation of Patients with Interstitial Lung Diseases

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Article information

Received: 05-09-2022

Accepted: 26-09-2022

DOI: 10.21608/IJMA.2022.160690.1508

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Citation: Abd-Elmaksoud HA, Darwish KM, Abdelaty MH, Abas AS, Abd-El-Naser WS. Study of the Role of Nailfold Capillaroscopy in the Evaluation of Patients with Interstitial Lung Diseases. IJMA 2022 July; 4 [7]: 2522-2527. doi: 10.21608/IJMA.2022.160690.1508.

ABSTRACT

Background: Interstitial lung disease [ILD] is one of the most prevalent respiratory symptoms of connective tissue diseases [CTDs], leading to significant morbidity and death. Nailfold capillaroscopy [NFC] is the best tool for analysing microvascular disorders in CTDs since capillaroscopic alterations in the nailfold are well documented in several CTDs.

The Aim of the work: To assess the value of Nailfold capillaroscopy examination in patients with ILD.

Patients and methods: This study involved 100 patients aged between 18 and 90 years diagnosed with ILD divided into three groups; group [I] involved 30 patients with rheumatoid arthritis [RA] associated with ILD, group [II] involved 30 patients with systemic sclerosis [SSc] associated with ILD, and group [III] included 40 patients with idiopathic ILD. In all patients, NFC was performed with clinical and laboratory assessment.

Results: According to nailfold capillaroscopic findings, patients with normal nailfold capillaroscopy were found only in idiopathic ILD. CTD-ILD group has a significantly lower mean capillary density than idiopathic ILD [p= <0.05]. Also, RA-ILD, IPF, and SSC-ILD subgroups had more severe abnormalities in capillaroscopy. The RA-ILD subgroup's capillary density was significantly lower than that of the idiopathic ILD only group. Furthermore, we found that [SSc-ILD] group had the lowest significant capillary number [ranged from 4-9/mm] & the highest significant capillary width [ranged from 29-76/µm] and the shortest significant capillary length [ranged from 75-256/µm] in comparison to the other groups.

Conclusion: We can conclude that SSc-ILD patients had more severe nailfold-capillaroscopic abnormalities than both RA-ILD and idiopathic ILD groups. Assessment of Nail should be considered during ILD examination for early detection of Nailfold abnormality to improve prognosis of the disease.

Keywords: Nailfold Capillaroscopy; Interstitial Lung Diseases; Connective tissue diseases.

INTRODUCTION

Interstitial lung disease [ILD] is defined by lung parenchymal inflammation and fibrosis. A significant proportion of patients with fibrotic ILD have a loss in pulmonary function, as well as worsening symptoms, a poor response to therapy, and a lower quality of life. Idiopathic pulmonary fibrosis [IPF] is the most prevalent, serious, and progressive variant of idiopathic interstitial pneumonia [ILD]; nevertheless, other ILD subtypes show a progressive fibrosing pattern as well [1].

Connective tissue diseases [CTDs] are a set of autoimmune diseases that share certain pathogenesis, such as autoimmunity and immune-mediated organ failure, but also have distinct characteristics. Interstitial lung disease [ILD] is one of the most prevalent respiratory symptoms of CTDs, lead to significant morbidity and death [2].

Nailfold capillaroscopy [NFC] is the best tool for analyzing microvascular disorders in CTDs since capillaroscopic alterations in the nailfold are well documented in several CTDs. It is often used to distinguish between primary and secondary Raynaud's phenomenon, as well as to diagnose scleroderma-spectrum illnesses such as systemic sclerosis [SSc], dermato-myositis [DM], un-differentiated CTD, and mixed CTD [3]. Other chronic autoimmune rheumatic disorders, such as systemic lupus erythematosus [SLE], Sjogren's syndrome, rheumatoid arthritis, and antiphospholipid syndrome, may also show NFC alterations [4]. However, the relation between lung involvement and nailfold changes are still unknown. Our study rational was to evaluate the value of Nailfold capillaroscopy in patients with ILD examination.

PATIENTS AND METHODS

A prospective cohort study carried out at Chest and Rheumatology Departments, Al-Azhar Assiut University Hospital in the period from January 2021 to October 2021. This study involved 100 patients, 69 males and 31 females aged between 18 and 90 years diagnosed as Idiopathic ILD clinically [dyspnea, chronic cough] and radiologically by High-resolution CT [HRCT] chest and divided into three groups:

Group [I]: Thirty patients with RA associated with ILD fulfilling the American Colleague of Rheumatology / European league against Rheumatism [ACR/EULAR] 2010 classification criteria.

Group [II]: Thirty patients with SSc associated with ILD who satisfied the ACR\EULAR 2013 criteria.

Group [III]: Included 40 patients with idiopathic ILD who satisfied the Official ATS/ERS/JRS/ALAT 2018 Clinical Practice Guideline.

Patients with peripheral microangiopathies, e.g. diabetes, hypertension, receiving vasoactive drugs, e.g. prostacyclin, with respiratory failure as hypoxia increase microvascular damage were excluded.

All patients subjected to history taking, clinical assessment, pulmonary function tests, imaging [chest x-ray [PA] and HRCT chest] and laboratory investigation [CBC, E.S.R using western green tubes method, C.R.P using latex agglutination test aspartate transaminase, Rheumatoid factor [RF], Serum Anti-Cyclic Citrullinated Peptide by ELISA, Anti-Nuclear Antibodies [ANA] by IF and Anti dsDNA antibody by ELISA].

A Nailfold capillaroscopy was done for all patients prior to enrollment in the trial; using [Micro Viewer Capillaroscopy VER2.2a STR and Science Company-USA] field capillary microscopy at a magnification of 100 [Figure 1]. A bifocal stereomicroscope was used to check eight digits [excluding the thumbs]. To promote skin transparency, immersion oil was administered, and the whole nailfold region, including the margins, was evaluated. Enlargement of capillary loops [giant capillaries; absolute number > 3], presence of bushy capillaries [> 1], and avascular regions were considered abnormal findings [loss of two consecutive loops of nail bed] [5].

Statistical Analysis: Statistical analyses had been performed using SPSS software for Windows, version 21.0. Dates are given as mean ± standard deviation and percent. We used Anova test [F-test] and Chi-square tests for comparison between groups. Values of $p < 0.05$ were considered statistically significant.

Figure [1]: Micro Viewer Capillaroscopy

RESULTS

A total of 100 patients enrolled in this study were divided into 3 groups, there was no significance among groups regarding age, gender, and disease duration [Table 1]. Regarding laboratory results, there was no significance among groups except for BUN which was higher in group I than groups II and III [p <0.001] [Table 2].

Considering HRCT of chest, the lung is a frequent target of autoimmune mediated injury in patients with RA included in this work; ground glass opacities in 53.3%, honey combing in 33.3%, pulmonary nodules in 20%, bronchiectasis and air trapping in 16.7%. While SSc-ILD patients reported higher incidence of ground glass opacities [76.7%], honeycombing [30%], reticular infiltration [30%], irregular pleural lines [30%], subpleural & septal lines [46.7%], interstitial thickening [20%] but no one had bronchiectasis or air trapping. We observed that Idiopathic ILD group had higher frequencies of honey combing changes [65%] and ground glass opacities [70%] [Table 3].

There was a significant difference [p-value =0.040] between the studied groups as regards FVC [%]. However, there was no significant difference between studied groups with regard FEV-1 [%], FEV-1/ FVC [%] and MMEF [Table 4].

According to nailfold capillaroscopic findings, all patients with normal capillaroscopic nailfold findings were in the idiopathic ILD only group. CTD-ILD group has a significant lower mean capillary density than idiopathic ILD [p= <0.05]. Also, RA-ILD, IPF, and SSC-ILD subgroups had more severe capillaroscopic abnormalities. The RA-ILD subgroup's capillary density was significantly lower than that of the idiopathic ILD only group. Furthermore, we found that [SSc –ILD] group had the lowest significant capillary number [ranged from 4-9/mm] & the highest significant capillary width [ranged from 29-76/µm] and the shortest significant capillary length [ranged from 75-256/µm] in comparison to the other groups. There was highly significant difference [p. < 0.001] among groups regarding giant capillaries, avascular areas, capillary hemorrhage, Capillary number, Capillary length and Capillary width. Also, there was significant difference among groups regarding Tortuous capillaries [p-value=0.006] and Capillary neo-formation [p-value=0.029] [Table 5].

Table [1]: Demographic data of the patients

		Group I [N=30] RA with ILD	Group II [N=30] SSc with ILD	Group III [N=40] Idiopathic ILD	P-Value
Age [Years]	Mean ± SD Range	51.05 ± 8.84 33-62	52.3 ± 4.5 30-63	52.33 ± 9.35 35-56	0.29 * NS
Gender [M/F]		21/9	20/10	28/12	0.42 NS
Disease duration [Months]	Mean ± SD Range	10.16 ± 5.14 4-24	9.3 ± 0.57 9-10	8.78 ± 4.62 4-22	0.68* NS

*Anova test [F-test] and Chi-square tests were used, P<0.05 NS: No statistically significant difference, P>0.05.

Table [2]: Distribution of laboratory results among groups

Variable		Group I [30]	Group II [30]	Group III [40]	ANOVA	
		RA with ILD	SSc with ILD	Idiopathic ILD	F	P
WBC [10^3/uL]	Range Mean ±SD	4.9 - 14.3 9.20 ± 2.89	4.9 - 14.5 8.39 ± 2.66	5 - 15.8 9.02 ± 3.0	1.373	0.251
Hb [gm/dl]	Range Mean ±SD	9.8 - 15.5 12.53 ± 1.29	8.4 - 14.4 11.64 ± 1.57	10.9 - 15.7 12.84 ± 1.23	2.089	0.091
PLT [10^3/Ul]	Range Mean ±SD	200 - 626 341.15 ± 102.99	218 - 506 346.65 ± 83.26	196 - 412 305.6 ± 61.82	2.432	0.055
AST[IU/L]	Range Mean ±SD	10 - 39 21.85 ± 6.34	9 - 31 18.35 ± 6.47	6 - 37 20.35 ± 7.56	0.929	0.452
ALT[IU/L]	Range Mean ±SD	8 - 47 19.30 ± 8.99	6 - 40 17.05 ± 8.42	11 - 38 21.60 ± 6.79	1.005	0.411
BUN [mg/dl]	Range Mean ±SD	12 - 40 22.0 ± 5.96	7 - 39 20.55 ± 7.29	9 - 27 18.95 ± 4.19	6.918	<0.001
ESR [mm/hr]	Range Mean ±SD	15 - 120 49.90 ± 32.17	10 - 95 44.40 ± 19.55	7 - 50 31.85 ± 12.35	2.035	0.098
CRP [mg/dl]	Range Mean ±SD	2.8 - 48 14.58 ± 12.65	2 - 48 12.15 ± 11.34	3.6 - 21 ± 4.49	0.804	0.527

F-test [Anova] was used, P<0.05: Statistically significant

Table [3]: High resolution computed tomography [HRCT] of chest groups

Chest HRCT	Group I [30]		Group II [30]		Group III [40]		X^2 test	
	RA with ILD		SSc with ILD		Idiopathic ILD			
	No.	%	No.	%	No.	%	X^2	P
Ground glass opacities	16	53.3	23	76.7	28	70	2.927	0.231
Honey combing	10	33.3	9	30	26	65	5.837	**0.05**
Reticular infiltration	9	30	9	30	16	40	0.600	0.741
Bronchiectasis	5	16.7	0	0	4	10	3.055	0.217
Interstitial thickening	10	33.3	6	20	12	30	1.15	0.56
Irregular pleural margin	12	40	9	30	16	40	0.574	0.75
Subpleural/septal lines	16	53.3	14	46.7	24	60	0.94	0.626
Air trapping	3	10	0	0	4	10	2.14	0.34
Pulmonary nodules	6	20	3	10	6	15	0.784	0.68
NSIP type	19	63.3	21	70	14	35	5.837	0.05
UIP type	10	33.3	10	33.3	26	65	5.837	**0.05**

X^2: Chi-square test, P<0.05: Statistically significant

Table [4]: Pulmonary function parameters among the studied groups of patients

Variable		Group I [30]	Group II [30]	Group III [40]	ANOVA	
		RA with ILD	SSc with ILD	Idiopathic ILD	F	P
FVC [%]	Range	49.3-112.8	75.09±14.4	34.2-103	3.407	**0.040**
	Mean ±SD	73.2±16.99	48.7-69.5	64.91±4.51		
FEV-1[%]	Range	43.9-108.2	73.74±12.7	35-103.5	1.661	0.199
	Mean ±SD	73.74±12.7	72.14±16.4	50.2-77.9		
FEV-1/ FVC [%]	Range	72-98.5	84.27±7.4	74.5-92.5	1.565	0.218
	Mean ±SD	84.27±7.4	74.5-92.5	84.46±5.2	1.565	0.199
MMEF	Range	23.4-96.4	63.6±21.97	23-130.9	1.906	0.158
	Mean ±SD	74.47±28.9	19.6-98.4	79.0±25.9		

F-test [Anova] was used, P<0.05: Statistically significant

Table [5]: Nailfold capillaroscopic findings among the studied groups

Variable		Group I [30] RA with ILD		Group II [30] SSc with ILD		Group III [40] Idiopathic ILD		Test F/x^2	Test P
		No.	%	No.	%	No.	%		
Giant capillaries		0	0	27	90	0	0	67.9	<0.001
Tortuous capillaries		16	53.3	5	16.7	16	40	14.4	0.006
Avascular areas		0	0	30	100	0	0	80.0	<0.001
Capillary neoformation		10	33.3	16	53.3	10	25	10.8	0.029
Capillary hemorrhage		11	36.7	28	93.3	13	32.2	38.7	<0.001
Capillary No./mm [9-12]	Range	9-12		4-9		10-14		65.8	<0.001
	Mean ±SD	10.85±1.0		6.65±1.27		11.85±1.4			
Capillary Length/µm [200-300]	Range	108-256		75-256		118-234		18.2	<0.001
	Mean ±SD	153.4±41		107.4±39.7		184.2±30.2			
Capillary width/µm [<20]	Range	11-44.6		29-76		22-43.3		18.08	<0.001
	Mean ±SD	25.8±10.5		47.29±15.3		26.42±4.5			

x^2: Chi-square test and f test [Anova] were used, P<0.05: Statistically significant

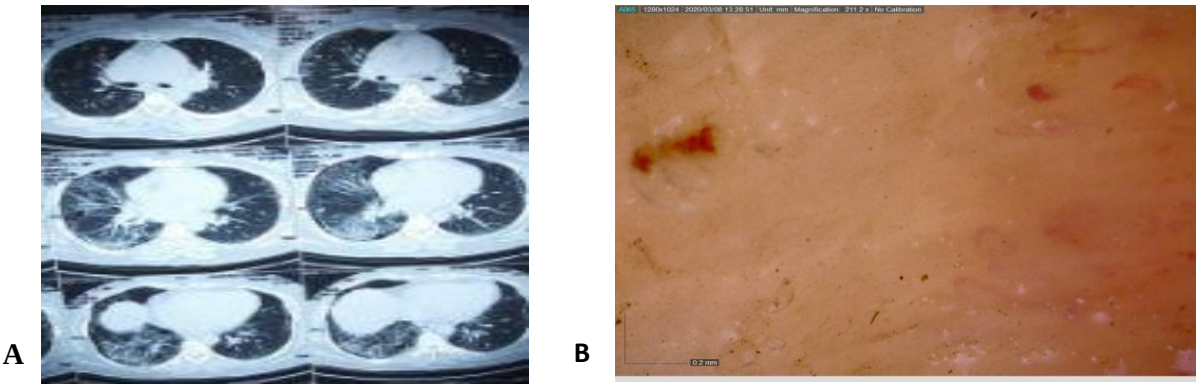

Figure [2]: Female patients 40 years old presented with Raynaud's phenomena, distal skin thinking of both hands up to MCP associated with dysphagia and chronic cough. There were dyspnea grade 2 gradual onset progressive coarse bilateral extensive crackles. Pulmonary function test demonstrates sever Restrictive pattern. A: HRCT of the chest shows ground glass changes basal peripheral reticulations subpleural sparing. B: NFC shows giant capillaries, hge and avascular areas

DISCUSSION

In this study, we evaluate patients with ILD by Nailfold capillaroscopy and studied the association of capillaroscopic alterations among patients with CTD associated ILD. We discussed the different patterns of pulmonary affection and demonstrated that the lung is a frequent target of autoimmune mediated injury in patients with RA included in this work; ground glass opacities in 53.3%, honey-combing in 33.3%, pulmonary nodules in 20%, bronchiectasis and air trapping in 16.7%. While SSc-ILD patients reported a higher incidence of ground glass opacities [76.7%], honey combing [30%], reticular infiltration [30%], irregular pleural lines [30%], subpleural & septal lines [46.7%], interstitial thickening [20%] but no one had bronchiectasis or air trapping. We observed that [Idiopathic ILD] group had higher frequencies of honeycombing changes in 65% and ground glass opacities in 70% of patients.

Our findings were near to those of **Yilmazer *et al.*** [6] who found that 42% of RA patients had irregularities in the pleural margins, 31% had septal/subpleural irregularities, 13% had ground glass density, 11.5% had honeycombing and 2.3% had a subpleural cyst. Pulmonary nodules were present in 16.4% of the patients, and bronchiectatic changes in 3%. Furthermore, these results were concurrent also with **Hafez *et al.*** [7] who reported that the most common findings among 30 SSc patients with IPF were ground-glass opacity detected in 83.3%, septal thickening 56.7%, honeycombing [43.3%], and bronchiectasis in 23.3% of patients.

CTD-ILD group has a significant lower mean capillary density than idiopathic ILD [p= <0.05]. Also, RA-ILD, IPF, and SSC-ILD subgroups had more severe capillaroscopic abnormality. The RA-ILD subgroup's capillary density was significantly lower than that of the idiopathic ILD only group.

Regarding Nailfold-capillaroscopy testing, especially the identification of RA-ILD patients, our results agreed with those of **Lin *et al.*** [8] in Taiwan; they found that the most frequent findings in RA patients with ILD were tortuosity, elongated capillaries and subpapillary venous plexus. Similar results were reported by **Karadogan *et al.*** [9] who showed that 100% of RA-ILD patients had tortuous capillaries [28.5%], capillary micro-hemorrhage [28.5%], capillary neoformation in total of 14 patients. Moreover, they found that none of RA patients with ILD had mega-capillaries or avascular regions or a specific scleroderma type.

Regarding the identification of SSc-ILD patients and Idiopathic ILD group; in agreement with our results, a study carried out by **Corrado *et al.*** [10] in Italy, they noticed that giant capillaries were present in 100% of SSc-ILD patients, but they were absent in the idiopathic ILD. They also revealed that capillary hemorrhages were common in SSc patients with pulmonary fibrosis, as they were present in 52% of cases although micro-hemorrhages were observed in limited areas in 20% of patients with idiopathic IPF.

Furthermore, interestingly we found that [SSc –ILD] group had the lowest capillary number [ranged from 4-9/mm] & the highest capillary width [ranged from 29-76/μm] and the shortest capillary length [ranged from 75-256/μm] in comparison to the other groups. The results of **Corrado *et al.*** [10] showed that the mean capillary density ranged from [3–6/mm] in SSc-ILD patients and it ranged from [4–10/mm] in Idiopathic ILD patients; as expected, it was significantly lower in SSc-ILD patients compared to the idiopathic IPF. Also, **Castellví *et al.*** [11] conducted a study in Spain; they reported that loss of capillary density was associated SSc with ILD [$p < 0.01$]. The study of **Corrado *et al.*** [10] showed that the mean loop width ranged from [54–169/μm] in SSc-ILD group while, in Idiopathic ILD, it ranged from [26–60/μm]. However, they showed no significant difference between SSc-ILD and idiopathic ILD groups as regard the mean capillary length. Moreover, **Karadogan *et al.*** [9] found that mean capillary density, in RA-ILD group was significantly lower than that of the idiopathic ILD & RA without ILD.

Conclusions: We can conclude that nailfold-capillaroscopic abnormalities are more common in SSc-ILD patients than both RA-ILD and idiopathic ILD groups. So, it should be considered in ILD patients.

Conflict of interest: None to be declared.

REFERENCES

1. Wong AW, Ryerson CJ, Guler SA. Progression of fibrosing interstitial lung disease. Respir Res. 2020 Jan 29;21[1]:32. doi: 10.1186/s12931-020-1296-3.
2. Jeganathan N, Sathananthan M. Connective Tissue Disease-Related Interstitial Lung Disease: Prevalence, Patterns, Predictors, Prognosis, and Treatment. Lung. 2020 Oct;198[5]:735-759. doi: 10.1007/s00408-020-00383-w.
3. Chanprapaph K, Fakprapai W, Limtong P, Suchonwanit P. Nailfold Capillaroscopy With USB Digital Microscopy in Connective Tissue Diseases: A Comparative Study of 245 Patients and Healthy Controls. Front Med [Lausanne]. 2021 Aug 6;8:683900. doi: 10.3389/fmed.2021.683900.
4. Zhao T, Lin FA, Chen HP. Pattern of Nailfold Capillaroscopy in Patients With Systemic Lupus Erythematosus. Arch Rheumatol. 2020 Apr 20;35[4]:568-574. doi: 10.46497/ArchRheumatol.2020.7763.
5. Maricq HR. Widefield capillary microscopy. Technique and rating scale for abnormalities seen in scleroderma and related disorders. Arthritis Rheumatol. 1981 Sep;24[9]:1159-65. doi: 10.1002/art.1780240907
6. Yilmazer B, Gümüştaş S, Coşan F, İnan N, Ensaroğlu F, Erbağ G, Yıldız F, Çefle A. High-resolution computed tomography and rheumatoid arthritis: semi-quantitative evaluation of lung damage and its correlation with clinical and functional abnormalities. Radiol Med. 2016 Mar;121[3]:181-9. doi: 10.1007/s11547-015-0590-5.
7. Hafez EA, Hamza SH, Morad CS, Abd Alkader AA. Pulmonary manifestations in Egyptian patients with systemic sclerosis. Egypt Rheumatol. 2018 Jan 1;40[1]:39-44. doi: 10.1016/j.ejr.2017.06.004.
8. Lin KM, Cheng TT, Chen CJ. Clinical applications of nailfold capillaroscopy in different rheumatic diseases. J Intern Med Taiwan. 2009 Jun 1;20[3]:238-47.
9. Çakmakçı Karadoğan D, Balkarlı A, Önal Ö, Altınışık G, Çobankara V. The role of nailfold capillaroscopy in interstitial lung diseases - can it differentiate idiopathic cases from collagen tissue disease associated interstitial lung diseases? Tuberk Toraks. 2015;63[1]:22-30. doi: 10.5578/tt.8673.
10. Corrado A, Carpagnano GE, Gaudio A, Foschino-Barbaro MP, Cantatore FP. Nailfold capillaroscopic findings in systemic sclerosis related lung fibrosis and in idiopathic lung fibrosis. Joint Bone Spine. 2010 Dec;77[6]:570-4. doi: 10.1016/j.jbspin.2010.02.019.
11. Castellví I, Simeón-Aznar CP, Sarmiento M, Fortuna A, Mayos M, Geli C, *et al*. Association between nailfold capillaroscopy findings and pulmonary function tests in patients with systemic sclerosis. J Rheumatol. 2015 Feb;42[2]:222-7. doi: 10.3899/jrheum.140276.

International Journal of Medical Arts

https://ijma.journals.ekb.eg/
Print ISSN: 2636-4174
Online ISSN: 2682-3780