ORIGINAL PAPER

Nailfold capillaroscopy in the rheumatological current clinical practice in Italy: results of a national survey

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**List of participants in alphabetical order is reported in the attached file*

SUMMARY

This cross-sectional online study was designed by the study group on Capillaroscopy and Microcirculation in Rheumatic Diseases (CAP) of the Italian Society of Rheumatology (SIR) to provide an overview of the management of nailfold capillaroscopy in Italian rheumatology centers. Therefore, SIR distributed the survey to its members in July 2021, and each center's physician with the most expertise in capillaroscopy completed the questionnaire. The survey was completed by 102 centers, with at least one representative from each Italian region. Ninety-three centers perform capillaroscopy, and 52 (56) conduct more than 200 investigations annually. Seventy-eight (84%) of respondents have more than five years of experience with the technique, and 75 centers (80.6%) have received certification from specific national or international training courses. In 85 centers, a videocapillaroscope with 200x magnification is employed (91.4%). The average waiting period for the examination is 2.4 months, and less than 3 months in 64 of the locations (68.8%). The study demonstrates that capillaroscopy is an integral part of both the diagnostic phase of Raynaud's phenomenon and the monitoring of autoimmune connective tissue diseases (CTDs). However, the reporting methods and timing of patient follow-up are heterogeneous.

Key words: *Capillaroscopy, microcirculation, Raynaud's phenomenon, systemic sclerosis.*

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INTRODUCTION

Nailfold capillaroscopy is a validated and non-invasive imaging technique that plays a critical role in the differential diagnosis of primary and secondary Raynaud's phenomenon (RP), as highlighted in recent NICE (National Institute for Health and Care Excellence) recommendations (1). In addition, the use of this technique is essential in the diagnosis and follow-up of certain connective tissue diseases (CTDs) (2-4), and it is included in the 2013 classification criteria for systemic sclerosis (SSc) of the American College of Rheumatology (ACR)/European Alliance of Associations for Rheumatology (EULAR) (5), in LeRoy-Medsger criteria (6), and in those for the VEDOSS (very early diagnosis of SSc) (7).

Since the beginning of the 20th century, nailfold capillaroscopy has gradually become a part of clinical microcirculation research (8). In the 1970s, Maricq described the capillaroscopic abnormalities typical of SSc, which include giant capillaries and/or

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a reduction in capillary number, disorganization of the capillary network, neoangiogenesis, and alterations in blood flow (9). Then, Cutolo described the most prevalent scleroderma patterns currently in use, which he defined as 'early,' 'active,' and 'late' patterns. In addition to the qualitative description of capillaroscopy, which permits the distinction between normal and pathological patterns, semi-quantitative scoring methods have been developed (10, 11).

Digital videocapillaroscopy (NVC), a 'gold standard' device whose high sensitivity enables the acquisition of high-quality images at varying magnification and the storage and analysis of each frame separately, has been developed concurrently with the expanding use of this investigation (12, 13).

Notably, for many years, the EULAR study group on microcirculation in rheumatic diseases (MC RD) has focused on the standardization of capillaroscopy in clinical and research settings by producing seminal studies (13-15). A good example is the fast-track algorithm, which allows novices in the field of capillaroscopy to distinguish a scleroderma pattern from a non-scleroderma pattern quickly and accurately (14).

This effort was made to overcome the heterogeneity in reporting by the growing interest in nailfold capillaroscopy in rheumatology, as evidenced by the number of participants in national and international courses on this topic and the increasing number of related scientific publications (12-14).

In this context, in May of 2020, the steering committee of the Italian Society of Rheumatology (SIR) authorized the study group (SG) on capillaroscopy and microcirculation in rheumatic diseases (CAPSIR), which held its first virtual meeting in the same year.

Despite the growing interest in this imaging technique in clinical and research settings, data on its current application in Italy are not yet available. The SG CAPSIR devised the first study (CAPSIR_1) to determine its prevalence, how capillaroscopy is performed, and potential barriers to its use in Italian rheumatology clinics. In addition, we solicited the experts' opinions on potential unmet needs and future research agenda topics.

MATERIALS AND METHODS

The CAPSIR_1 project is an online transversal study proposed during the first SG CAPSIR meeting in November 2021. The SG steering committee approved the online questionnaire first, followed by the SIR steering committee. The survey consists primarily of closed multiple-choice questions and a few open-ended questions. SIR e-mailed the link (to Google Forms) to its more than 1200 members. From July 15 to August 31, 2021, the questionnaire was accessible to the capillaroscopy expert with the most experience at rheumatological centers.

After providing informed consent to participate in the study, the representative of each rheumatology center was asked to indicate whether his or her center performed capillaroscopy. In the event of a negative response, the questions centered on the reasons, while in the event of a positive response, the questionnaire centered on:

1) the characteristics of the centers, the experience and training of the dedicated staff, and the willingness to participate in future research projects;
2) the method to perform capillaroscopy (equipment used and medical reports);
3) the booking procedures for the analysis and specific fast-track services; iv) the indications for capillaroscopy and the timing of follow-up of the different rheumatic diseases.

The collected data are presented with descriptive statistics that quantitatively characterize the outcomes using absolute numbers and percentages.

RESULTS

Characteristics of respondents and caseload

As shown in Figure 1, 102 centers, with at least one representative from each Italian region, completed the survey.

Nine (8.8%) of the 102 rheumatological centers do not perform capillaroscopy due to lack of specialized training personnel, the cost of equipment, or the availability of nearby centers to refer patients for the investigation. These respondents expressed

interest in integrating this tool into their offerings to patients.

The 93 centers that managed nailfold capillaroscopy in their facilities were included in the primary analysis. Forty-three (46.2%) are public hospitals, 34 (36.6%) are university hospitals, 7 (7.5%) are IRCSS (Institute for Hospitalization and Scientific Care), 5 (5.4%) are district outpatient services, and 4 (4.3%) are private clinics. Figure 2 depicts the annual number of capillaroscopies performed in centers that participated in the study. Seven (7.5%) centers perform fewer than 50 services per year, 15 (16.1%) between 50 and 100 examinations, 19 (20.4%) between 101 and 200, 26 (28%) between 201 and 400, and 26 (28%) more than 400 capillaroscopies per year.

The survey revealed that physicians always perform the examination. In 18 (19.4%) of the centers, capillaroscopy is performed by a single individual, while in the remaining 75 (80.6%) centers, the examination is performed by two or more individuals. The majority of respondents who practice capillaroscopy are rheumatologists (67, 72%) with more than five years of experience (78, 84%) who have obtained the certification of dedicated national or international training courses (75, 80.6%) and are interested in participating in national (88, 94.6%) and international (75, 80.6%) studies on the subject (Figure 3). Twelve (12.9%) centers are participating in the EULAR SG on capillaroscopy and microcirculation in rheumatic diseases. In rheumatology centers where trainees are present, 72.3% of them perform capillaroscopy as required by their training program.

There are 36 (38.7%) participants with scientific publications on capillaroscopy. Specifically, 26 (72.2%) have fewer than five publications on the subject, while 14 (38.8%) have more than five (Figure 3C).

Capillaroscopic technique and reporting results

The NVC with 200x magnification is used in 85 (91.4%) of the centers. In 32 centers (34.4%), there is more than one capillaroscopic instrument, and in 62 centers (66.7%) there is a dedicated room.

In 64 (68.8%) of the centers, the average waiting time for a capillaroscopy is less than 3 months. The majority of requests come from rheumatologists (41, 44%) and general practitioners (45, 48.4%). In 77 (82.8%) of the centers, the examination is also performed within the context of internal hospital consultation. In 40 (43%) of the

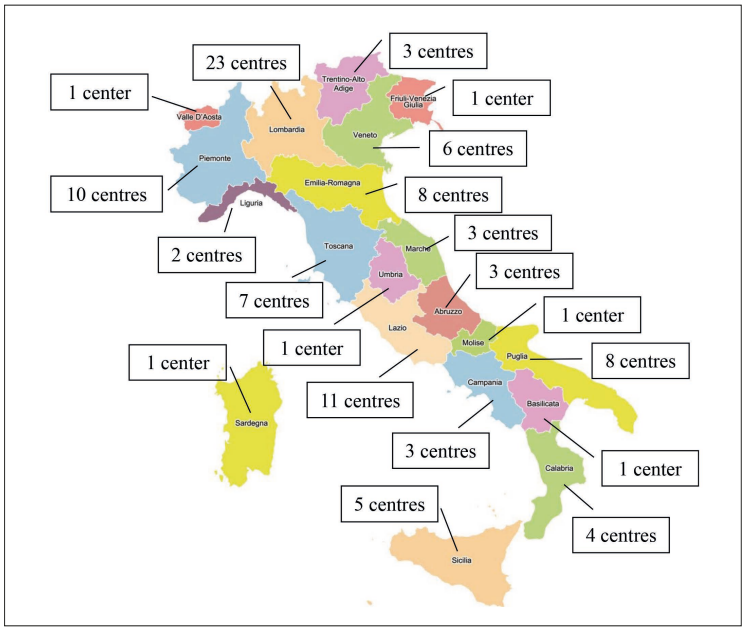

Figure 1 - Geographical distribution of the 102 centers that participated in the CAPSIR_1 study.

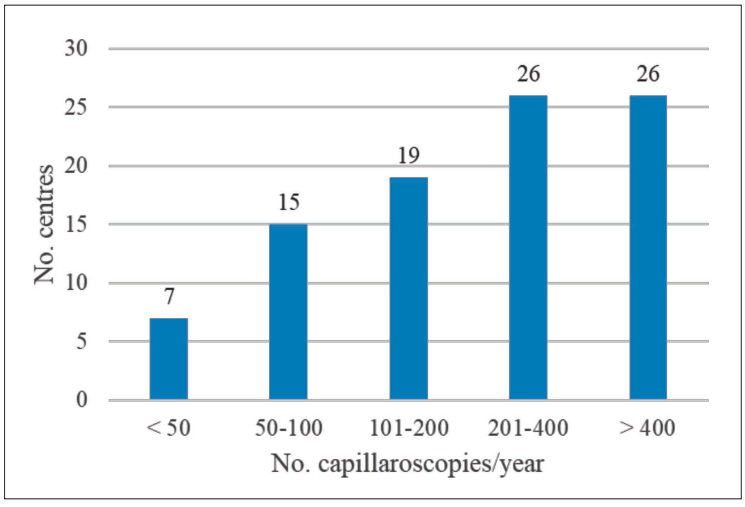

Figure 2 - Annual capillaroscopy procedures performed by the 93 Italian rheumatology centers that participated in CAPSIR_1.

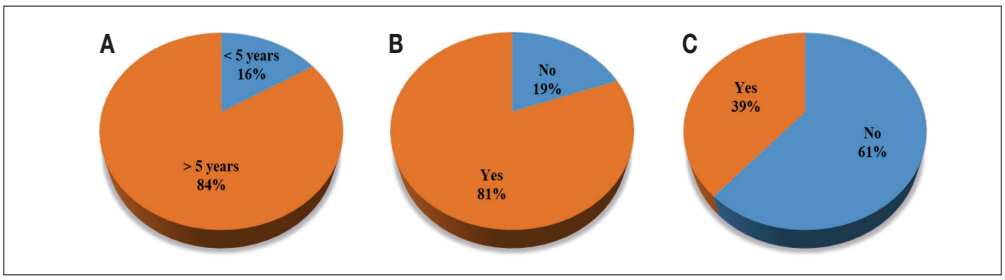

Figure 3 - Description of CAPSIR_1 participant in terms of years of capillaroscopy experience (A), method certification obtained through national or international courses (B), and related scientific publications (C).

centers, reservations can be made both at the facility and at the local level, whereas in 41 (44%) of the centers reservations can only be made at the headquarters.

The classification proposed by Cutolo has been utilized in 85 (91.4%) of medical reports to describe scleroderma patterns. As illustrated in Figure 4, the reporting methods are diverse. Sixty-nine (74.2%) of the centers produce medical reports with capillaroscopic images attached. In 50 (53.8%) of these centers, the images are annotated with free-form text, and in 19 centers (20.4%), with a pre-printed multiple-choice format. In 24 (25.8%) of the centers, the report lacks images, while the text is either free (in 16 centers,17.2) or pre-printed (in 8 centers, 8.6%).

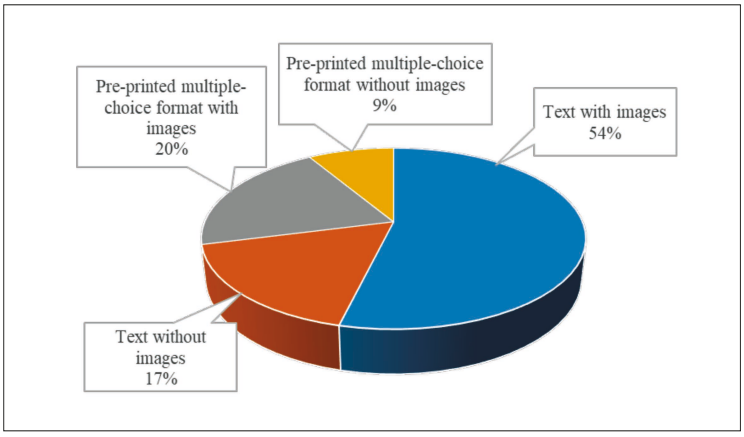

Figure 4 - Reporting techniques utilized by rheumatology centers participating in CAPSIR_1.

Capillaroscopy utilization in clinical practice

The differential diagnosis of RP is the primary reason for referral to capillaroscopy in 83 (89.2%) of the centers, while 37 centers (39.8%) report having a dedicated path to this type of patient and to conduct sensitization courses, as well as produce educational materials about it.

As shown in Table I, the survey uncovered disparities in the timing of capillaroscopy use for monitoring patients with RP, CTD, and SSc. In patients with SSc, 45 (48.4%) of the centers also study peripheral blood flow, and 64 (68.8%) of the participants undergo nailfold videocapillaroscopy to evaluate the effect of therapies on the microcirculation.

Table I - Capillaroscopic follow-up times for different clinical subsets in rheumatological centers that participated in CAPSIR_1.

	Capillaroscopic follow-up Mean (range) months	No. centers that perform 2nd capillaroscopy within 12 months of baseline	No. centers that perform 2nd capillaroscopy after 12 months of baseline	No. centers that do not perform capillaroscopic follow-up
RP ANA -	14.45 (6-36)	3 (3.2%)	87 (93.6%)	3 (3.2%)
RP ANA +	8.7 (5-20)	61 (65.6%)	32 (34.4%)	0
SSc	10 (1-24)	35 (37.7%)	55 (59.1%)	3 (3.2%)
CTDs (other than SSc)	13.3 (3-60)	27 (29%)	61 (65.6%)	5 (5.4%)

RP, Raynaud's phenomenon; CTD, connective tissue disease; SSc, systemic sclerosis; ANA, antinuclear antibodies.

DISCUSSION AND CONCLUSIONS

This is the first study to investigate the current management of nailfold capillaroscopy in Italian rheumatology centers. Participation in the study was significant in terms of geographic distribution, with at least one representative per region, and the number of participants. Thus, the survey was able to accurately evaluate various health services (public and private hospitals, IRCCS); in addition participants have consolidated experience on this topic, as evidenced by the number of years of experience in capillaroscopy, their training, and the large number of investigations performed annually (58 percent of Italian rheumatology centers among SIR members perform more than 200 exams/year).

A key finding is that this technique is available in the majority of Italian centers (75, 80.6%) where multiple physicians can perform the exam. This is different from findings of a recent study in the United Kingdom, where only 41% of respondents were able to perform the exam in their center (16). The NVC with 200x magnification is the most frequently utilized instrument (85 centers, 91.4%). This information also differs from clinical settings in UK, where dermatoscopy and USB microscopy are frequently employed (16).

With the national health service, the average waiting time for a capillaroscopy was 2.4 months, and less than 3 months in 64 (68.8%) of the centers, with hospital and district booking options.

The standardization of reporting results in clinical practice remains a crucial issue, as the methods used vary from free text with capillaroscopic images to a pre-printed multiple-choice model without images. This aspect, also known in the context of research, was studied by the EULAR SG, which just published an international consensus on the subject (15).

Patients are referred for capillaroscopy primarily to determine the differential diagnosis of RP, despite the fact that only in a minority of centers (37.8 to 39.8%) there is a specific fast track for patients with this clinical symptom and printed information about it is available.

The study demonstrates that the capillaroscopic examination is an integral part of both the diagnostic and monitoring phases of CTD care. This method is utilized with variable timing depending on the center.

Due to the fact that only SIR members participated in this study, information from other specialists or non-SIR members who performed the examination in clinical practice could not be retrieved.

This is the first study to provide an up-to-date overview of contemporary capillaroscopic practice in Italy. Key strengths include a sample that is broadly representative of each Italian region, with 102 participants from university and district hospitals. There were discrepancies in the reporting and timing of exam administration.

In this regard, the preparation of a possible unified report has begun, based on recent suggestions and preliminary approaches, and addressing the need for further prospective scientific research on the critical issues identified in this study (2, 12-15). To increase the utility of our efforts, we will propose and discuss national projects with the EULAR SG on capillaroscopy and microcirculation in rheu- matic diseases.

Authorship

The authors directly contributed to the planning, execution, analysis, or report of this scientific article and approved its final version.

Conflicts of interest

The authors do not have any conflict of interest.

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