

recognition). Maricq et al. described last century, with the widefield technique (magnification X12–14) the scleroderma pattern. This pathognomonic combination contains the following: a striking widening of all three segments of the capillary loop (arterial, venous and intermediate), loss of capillaries, disorganization of the nailfold capillary bed. Many branched “bushy” capillaries may also be observed. In 2000, Cutolo et al. qualitatively assessed the nailfolds of an SSc cohort with patients fulfilling the American College of Rheumatology (ACR) criteria for SSc with the nailfold videocapillaroscopic (NVC) technique (magnification X200). According to the different proportions of the hallmark parameters of the scleroderma pattern (giants, capillary loss, hemorrhages and (neo)angiogenesis Cutolo et al. defined three patterns “early”, “active” and “late”.

The central role of capillaroscopy in distinction between a primary and secondary RP due to SSc is reflected by the fact that capillaroscopy is one of the new ACR/EULAR criteria for classifying a patient as having SSc.

Besides playing a paramount role in distinguishing a primary from secondary RP, capillaroscopy has an additional role. It can inform the rheumatologist dealing with a patient population with merely the RP and no other signs of a CTD, who will futurely develop SSc. This role is reflected by capillaroscopy playing a central role in the LeRoy and VEDOSS criteria for (very) early diagnosis of SSc.

What about capillaroscopic morphology in connective tissue diseases other than SSc?

No large scale prospective cohorts exist describing capillaroscopic morphology in connective tissue diseases other than SSc. Moreover, several morphological definitions exist across literature of different schools. The EULAR Study Group on microcirculation in Rheumatic diseases was set up in 2014 to tackle, in between others these working points.

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SP0099 WHY CAPILLAROSCOPY CAN PREDICT DISEASE SEVERITY AND PROGNOSIS

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Nailfold capillaroscopy (NVC) is today considered to be safe biomarker in order to make an early diagnosis of selected Connective Tissue Diseases (CTDs) in presence of Raynaud’s phenomenon, and to measure progressive microvascular and tissues damage including response to long term treatment. Systemic sclerosis is the only CTD to date in which prognostic indices have been described to predict clinical complications. Predictions have been made based on baseline capillaroscopic images and based on sequential capillaroscopic follow-up.

Baseline qualitative-assessed scleroderma patterns have been described to be linked with future organ involvement in any of the nine organ systems affected by SSc according to the disease severity scale of Medsger (general, peripheral vascular, skin, joint, muscle, gastrointestinal tract, lung, heart and kidney) (1). Additionally, baseline capillaroscopic evaluations have been linked to future development of digital trophic lesions in SSc. A simple scoring system has been used recently in the largest pan-European study evaluating the role of capillaroscopy in predicting digital ulcers in SSc (2). More specifically, in this study, simply the number of capillaries per linear mm had been evaluated. Besides counting the number of capillaries/capillary alterations, dimensions can also be measured. The latter has also been used in prediction of patients with RP whether, because of SSc, there will be a possibility for them to develop a secondary RP. Similarly, it has recently been attested that if the average capillary diameter (average of the largest apical, efferent and afferent limb in 16 fields, more specifically 2 fields per finger, fingers 2–5 from each hand) is less than 30 μm in a group of patients with RP but without scleroderma characteristic findings on nailfold videocapillaroscopy (NVC), the patient has a low chance of developing SSc, while if $>30 \mu\text{m}$, then the patient has 50% chance to develop SSc (3). Concerning the ability of capillaroscopy to measure response to treatment, there are yet no prospective randomized, double-blind, placebo-controlled trials, evaluating the ability of capillaroscopy to monitor response to therapy concerning RP-related outcome measures. It is noteworthy and promising that in small studies showing response of immunosuppressive/vasomodulating treatment on disease severity, outcome measures are available (4–6).

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SP0100 HOW TO SELECT THE MOST APPROPRIATE CAPILLAROSCOPIC DEVICE: PROS AND CONS

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One of the most important indications for performing capillaroscopy is to differentiate between primary and secondary Raynaud’s syndrome. Different kinds of microscopes are at hand and generally vary in terms of picture quality or price. Before purchasing a microscope and capillaroscopy software, several considerations about the required standards of examination should be made; some of which are summarized as follows:

- The region of interest (ROI). Normal capillaries have a mean diameter of about 8 μm . For an accurate assessment a magnification of 100–200x is recommended, for an overview the magnification of 50x is sufficient.
- Measurement. Beside qualitative measures like changes in vessel architecture, there should be the possibility of quantifying the number of capillaries/mm or vessel diameters.
- Documentation. All parts of the examination have to be stored and assigned to patient and case.
- Practical aspects and handling of the device.
- Different kinds of microscopes are on the market of which three will be discussed in detail. Briefly summarized:
- Stereo microscopes.

Advantages: Very good image quality, zooming in and out without problems, relatively easy to use.

Disadvantages: device is not mobile, in patients with finger contractures examinations are difficult to perform, relatively high costs.

• Videocapillaroscopes:

Advantages: Very good image quality, easy to use, “gold standard” for capillaroscopy.

Disadvantages: No overview, zooming in and out not applicable (change of lenses required), relatively high costs.

• USB microscopes:

Advantages: low costs, zooming in and out without problems, easy to use.

Disadvantages: limited picture quality, documentation laborious.

Selecting a capillaroscopic device depends on the conditions of use (“quick look” vs. “academic evaluation and follow up”), which should be clarified before buying a device. The price range is significant and usually differs between 100€ for USB microscopes and up to 10,000€ for stereo and videocapillaroscopes

Literature:

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THURSDAY, 15 JUNE 2017

Ultrasound, clinical, diagnostic and therapeutic skills I & II

SP0101 DIAGNOSTIC AND THERAPEUTIC ULTRASOUND-GUIDED PROCEDURES

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The lecture will provide an overview of sonography-guided musculoskeletal interventions which can be grouped broadly as diagnostic and therapeutic procedures. Primarily diagnostic procedures include arthrocentesis, biopsy from various musculoskeletal tissues (synovial, bone, muscle etc.), aspiration of fluid from cystic lesions, tendon sheaths and bursae. The therapeutic group features joint and soft tissue injections, needling of periarticular calcification, including barbotage. Both indirect and direct-guidance techniques will be detailed and published literature on accuracy, outcome and safety of sonographic-guided interventions will be reviewed.

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SP0102 HOW TO PERFORM A QUICK AND EFFICIENT PHYSICAL EXAMINATION

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The GALS (Gait, Arms, Legs, Spine) screen is a quick and reasonably sensitive way to detect common musculoskeletal (MSK) abnormalities as part of a general medical assessment (1). However, for a person with MSK complaints a detailed assessment is required to determine the diagnosis and the impact of the condition on that person. The key starting point is the history. This needs to be holistic and individualised as the enquiry proceeds since the impact of any condition is

person specific and influenced by many factors (e.g. psychosocial factors, illness perceptions, sleep, comorbidity etc.). A thorough history alone usually suggests the single most likely cause for the patient's problem(s). The history should then guide the subsequent physical examination – an efficient targeted “rapier” approach is recommended in which the practitioner selects the appropriate skills from a range of competencies according to specific elements in the history. This contrasts with a more lengthy hypothesis-free “general screen” in which the same set of uniform procedures is undertaken in each patient.

This presentation will cover key principles and considerations of assessment and illustrate how the history guides the subsequent “rapier” examination (2). Examples include:

(1) in the *history*: determination of pain localisation and features that associate with radiated pain; important pain and stiffness characteristics that differentiate mechanical usage-related pain, inflammatory pain, acute crystal synovitis pain, destructive bone pain and neurogenic pain; non-specific symptoms of inflammation (2) in the *examination*: usual order of inspection at rest, inspection during movement, then palpation at rest and during movement of symptomatic regions; contrasting clinical findings that quickly differentiate joint and peri-articular problems; initial selection of the movement(s) that is affected first and most severely by arthropathy - the tight pack position(s); detection of “stress pain” (pain worse in tight-pack positions but reduced/absent in loose-pack positions - the most sensitive sign of inflammation); examination for effusion, soft-tissue and firm swelling; use of resisted active movements and stress tests for peri-articular lesions; a targeted screen for asymptomatic disease prompted by main diagnosis. EULAR learning resources available at http://www.eular.org/edu_training_dvd.cfm include: (1) The “GALS” screen and (2) Principles of the musculoskeletal history and examination.

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SP0103 HOW TO ASSESS US COMPETENCY SKILLS

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To optimize and standardize musculoskeletal ultrasonography education for rheumatologists, there is a need for competency assessments addressing the required training and practical and theoretical skills. Because of the increasing use of MSUS in rheumatology, there has been a focus over the past years on training.

A minimum training requirements are described by The European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) where a 3 levels competency assessment (COMPASS) has been developed for rheumatologists, including an in-detail description of what theoretical and practical competencies to be acquired at each level with a related log book (1). The rheumatology-COMPASS levels are closely related to the levels of the EULAR MSUS courses, thereby ensuring that the content is supported by already provided courses such as the EULAR and EULAR-endorsed MSUS courses to facilitate the implementation of the rheumatology-COMPASS. In COMPASS level 1 the course contents resemble the EULAR MSUS basic and intermediate courses, level 2 resembles the EULAR MSUS advanced course whereas level 3 requires attendance in a “teach-the-teachers course” or experience as a teacher in at least 2 international MSUS courses. Level 3 also includes an academic level requiring research activity and acceptance of level 1 and 2 sonographers for training.

The EULAR MSUS courses have been organized since 1998 and the interest in these courses has been increasing. In 2007, the first 3 level EULAR MSUS course was conducted with great success and the 3 level courses (basic, intermediate and advanced) have been running ever since in relation to the EULAR congress, focusing mainly on the relevant content on the individual levels and the distribution between practical and theoretical skills.

EULAR has developed the following competence levels; level 1 and 2. The EULAR level 1 competency includes the performance of EULAR Online MSUS course and attendance to basic, intermediate and advanced MSUS courses, where attending the intermediate and advanced courses require a certain number of US examinations (however, if already reached COMPASS level 1, 2 or 3, there is no need of images for the EULAR courses), and the advanced course requires in addition to pass a practical examination. The EULAR level 2 competency is organized to ensure a minimum level of US knowledge for teachers in MSUS courses (2). This level includes the EULAR Teach the Teachers course as well as passing a theoretical and practical examination. Since there is a growing number of EULAR endorsed MSUS courses, it is of highly importance that the teachers in these courses have equal qualifications thereby providing comparable training and competencies beneficial for the clinical use of US. Information about the competence requirements is found at the EULAR website (<http://www.EULAR.org>).

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THURSDAY, 15 JUNE 2017

Macrophage M2 polarization: implications in fibrotizing diseases

SP0104 REPROGRAMMING OF MYELOID CELLS IN CANCER: MECHANISMS AND SIGNIFICANCE

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Chronic inflammation mediates tumor development by promoting a constant influx of inflammatory cells capable of modulating genes involved in cancerogenesis and creating micro and macroenvironments that support cancer growth. A major side effects of cancer inflammation is the pathological expansion and recruitment of myeloid cells endowed with immunosuppressive activity, to control the unresolved inflammation. Tumors reprogram myeloid cell differentiation and functions through various mechanisms, including altered metabolism, cancer-related inflammation and alteration of the hematopoietic output. These events govern the expansion of myeloid suppressor populations, mainly myeloid-derived suppressor cells (MDSCs) and tumor associated macrophages (TAMs). MDSCs and TAMs orchestrate tumor immunosuppression in concert with regulatory T cells, inhibitory cytokines and immune check points receptors, and act to subvert anti-tumor immunity, hence causing that eventually support immune evasion establishing a bottleneck for cancer immunotherapy. I will discuss inflammatory circuits and epigenetic events sustaining the expansion and the tumor-promoting reprogramming of myeloid cells in cancer bearers.

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SP0105 MACROPHAGES, METABOLISM AND INFLAMMATION

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Macrophages are a heterogeneity population implicated in several diseases and correlated with distinct tissue outcomes after injury. M2 macrophages have been associated with tissue repair whereas M1 macrophages participate in early phase of tissue damage. Recent works have also suggested that upon activation, macrophages can use distinguished nutrients as source of energy and these metabolic pathways lead to their activation and differentiation. Nutrient sensors are intimae associated with innate receptors and therefore connected with inflammatory response. Uric acid is a damage-associated molecular pattern (DAMP), released from ischemic tissues and dying cells which, when crystalized, is able to activate the NLRP3 inflammasome through frustrated phagocytosis. Soluble uric acid (sUA) is found in high concentrations in the serum of great apes, and even higher levels in some diseases, before the appearance of crystals. sUA can be released in a hypoxic environment and triggers NLRP3 through the production of mitochondrial ROS, with increased maximum and reserve oxygen consumption ratio (OCR) and higher VDAC protein levels. This process is followed by ASC speck formation, caspase-1 activation and IL-1 β release. These findings may have profound implications for inflammatory-related diseases. Support: FAPESP and CNPq.

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FRIDAY, 16 JUNE 2017

Mucosal B cells: gatekeepers of immune function

SP0106 THE LUNG AS A DRIVER OF RA-ASSOCIATED AUTOIMMUNITY

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Rheumatoid arthritis (RA) is a chronic inflammatory disease resulting from the complex interaction between genes and environment. In a large majority of patients this interaction leads to formation of disease-specific anti-citrullinated proteins antibodies (ACPA). Systemic autoimmunity may be triggered at mucosal sites (such as the lungs) long before the first signs of inflammation are starting in the joints. According to this model, smoking (and others environmental triggers) induces subclinical inflammation in the lungs, leading to increased local citrullination and formation of ACPA in genetically susceptible individuals. Lung changes on high-resolution computer tomography are present in both early-untreated ACPA positive RA and ACPA positive individuals at risk for but not yet having disease. Further, signs of subclinical inflammation and immune activation with germinal centers formation and ACPA enrichment is present in early untreated RA. Shared citrullinated targets have been described in the lungs and joints of patients with RA and more recent data unravels novel mechanisms showing how this extra-articular triggered autoimmunity progresses to joint-specific inflammation. Beside an initiating role, the lung might also be a secondary target for antibodies, especially in longstanding seropositive RA.

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