Best Practice & Research Clinical Rheumatology 30 (2016) 670–687

Contents lists available at ScienceDirect

Best Practice & Research Clinical Rheumatology

journal homepage: www.elsevierhealth.com/berh

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Imaging of connective tissue diseases: Beyond visceral organ imaging?

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Keywords:
Systemic sclerosis
Sjögren syndrome
Raynaud phenomenon
Ultrasonography
Nailfold capillaroscopy
Connective tissue diseases
Microcirculation
Salivary glands
Modified Rodnan skin score (mRSS)

A B S T R A C T

Connective tissues diseases (CTDs) can also be diagnosed early by "external" and safe imaging methods beyond the visceral organ analysis. This study aims to explore various imaging techniques used in diagnosing CTDs. Skin impairment in systemic sclerosis (SSc) may be recognized and studied by the modified Rodnan skin score (mRSS), which has some drawbacks, whereas high-frequency ultrasound (US) seems advantageous for the early identification of skin involvement. Salivary gland involvement in Sjögren syndrome (SS) can be assessed using standard tests such as unstimulated salivary flow test, salivary gland scintigraphy or contrast sialography. However, US of the major salivary glands, as an alternative, seems a reliable method with good sensitivity and specificity for the diagnosis of SS. Both the qualitative and quantitative nailfold capillaroscopic (NVC) assessments in SSc patients affected by the Raynaud's phenomenon (RP) may assist in making a differential diagnosis between primary and secondary RP. Microcirculatory imaging by NVC, along with the laser Doppler analysis, seems useful in the prediction of complications and prognosis in CTDs (i.e. SSc) and in monitoring therapeutic trials.

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http://dx.doi.org/10.1016/j.berh.2016.10.002
1521-6942/

A. Utility of musculoskeletal imaging in connective tissue diseases

The autoimmune connective tissue diseases (CTDs) may have both genetic and environmental causes (influencing their epigenetic control) and are characterized as a group, by the presence of overactivity of the immune system that results in the production of autoantibodies.

The classic CTDs include:

Systemic lupus erythematosus (SLE), which can afflict every organ system.

Rheumatoid arthritis (RA), which is a systemic disorder wherein immune cells mainly attack and inflame the synovial tissue around joints, but can also affect the heart, lungs and eyes.

Systemic sclerosis (SSc), characterized by the involvement of microcirculation impairment followed by progressive fibrosis in the skin but also internal organs.

Sjögren's syndrome (SS), which is a chronic, slowly progressing disease that mainly manifests in the inability to secrete saliva and tears. It can occur alone or with RA, SSc or SLE.

Mixed CTD (MCTD), which is a disorder wherein features of various CTDs such as SLE, SSc, dermatomyositis (DM), polymyositis (PM); anti-synthetase syndrome and, occasionally, SS syndrome can coexist and overlap.

This review aims to analyse recently emerged various imaging techniques in the diagnosis of CTDs. These techniques evaluate the involvement of superficial organs in the manifestation of CTDs such as skin, dermal microvessels and glands, over and above the “visceral” organ involvement.

We explore the utility of musculoskeletal imaging in CTDs, then analyse whether imaging of skin and salivary glands in connective tissue diseases is sufficiently addressed to be implemented in clinical practice, followed by the qualitative and quantitative assessments of the diagnostic and prognostic value of microcirculation imaging in CTDs.

The recent availability of non-invasive and safe imaging tools such as ultrasonography and video-capillaroscopy has permitted to also evaluate the “superficial” manifestation of the CTDs, such as skin, dermal microvessels, and gland involvement, beyond the “visceral” organ involvement.

In fact, CTDs such as SSc and SS are characterized from the beginning by a limited visceral involvement, and on the contrary, they express early “external” clinical signals that need to be evaluated and possibly quantified.

Therefore, today, the differential diagnosis during the early manifestation of CTDs (like the presence of Raynaud phenomenon (RP), or lymphonodal gland enlargement or increasing skin thickness and/or joint temperature) is an easier task because of the image analysis with the tools mentioned above, and in the “pocket” of an increasing number of rheumatologists. Among the most challenging CTDs that can be evaluated by the “external” imaging analysis, SSc and SS will be analysed in particular.

B. Is imaging of skin and salivary glands in connective tissues diseases sufficiently addressed to be implemented in clinical practice?

B1. Skin involvement in systemic sclerosis

One of the most promising and applicable CTDs for the skin imaging analysis is SSc. It is an autoimmune CTD characterized by a diffuse microangiopathy, autoimmunity and fibrosis of the skin and various internal organs. It is divided into systemic disease and localized scleroderma. In SSc, various lesions occur in the internal organs, whereas in localized scleroderma, the internal organs are not involved.

Cutaneous changes in the texture and appearance of the skin are the markers for disease classification and activity [1–3]. The skin damage observed is related to an excessive dermal deposition of collagenous and non-collagenous extracellular matrix components because of an altered production and remodelling of tissue fibroblasts and myofibroblasts [4–8].

Skin impairment in SSc follows a course of oedema, sclerosis and atrophy. The oedematous phase is expressed by painless pitting oedema of the hands and fingers, which may also affect the feet and legs as well as the forearms. This situation usually evolves quite quickly into fibrosis, with a decrease in skin elasticity. This second phase, which may persist for many years, is characterized by hard, shiny, taut