Ultrasound in connective tissue diseases

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ABSTRACT

Rheumatologists have been using ultrasound (US) for the evaluation of patients affected by rheumatic disease for a long time. Actually this approach is becoming more and more diffuse and US is used for multiple purposes: diagnosis, disease activity assessment, prognosis, and therapy monitoring. The real "new" step for the rheumatologist has been moving from the "usual" musculoskeletal US to other fields of US, such as the assessment of vascular involvement (both macro and micro), skin, lung and even nails. In this paper we review the published literature related to the use of musculoskeletal, skin and lung US in patients affected by connective tissue diseases.

Introduction

Ultrasound (US) has recently increased its importance in the evaluation of the patients affected by rheumatic disease for diagnosis, disease activity assessment, prognosis, therapy monitoring and guided injections (1-8). The real "new" step for the rheumatologist has been moving from the "usual" musculoskeletal US to other fields of US such as the assessment of vascular involvement (both macro and micro) (9-12), skin (13), lung and even nails (14-15). Obviously, US has been used to image multisystem involvement (heart, kidney and vessel) but those items usually remain the "property" of other specialties, even if some of them are now possible points of interest for rheumatologists performing US (16-18). To date, there are still very few studies reported in the literature on the applications of US in the assessment of joint and tendon involvement in the course of connective tissue diseases (CTD) with respect to what is available for rheumatoid arthritis (RA) or spondyloarthritis. In the present review we will provide an update of the available data regarding the clinical application of US in patients with CTD such as systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), systemic sclerosis (SSc), polymyositis (PM), dermatomyositis (DM), mixed connective tissue disease (MCTD) and undifferentiated connective tissue disease (UCTD), both for musculoskeletal involvement and, briefly, the new areas of interest explored by rheumatologist ultrasonographers (*i.e.* the evaluation of skin and lung in SSc).

Systemic lupus erythematosus

Inflammatory musculoskeletal involvement in SLE patients is rather common, ranging from 69% to 95% and, in 70% of them, it represents the first symptom (19-20). The range of joint manifestations is quite wide, with mild arthralgia, mild symmetric synovitis affecting small- and medium-sized joints (usually at the onset of the disease), reducible, non-erosive deformities (Jaccoud's arthropathy) or even erosive arthritis resembling rheumatoid arthritis (traditionally called "rhupus") (21).

To the best of our knowledge, very few papers have explored SLE joint involvement using US. In 2004, Iagnocco *et al.* first examined 26 SLE patients (52 wrists) and demonstrated a high prevalence of synovitis (22/52 radio-ulno-carpal joints). Synovial proliferation was evidenced in 10 joints, effusion in 13, power Doppler (PD) signal in 5, and bone erosions in only one patient. Tenosynovitis was visualised in 15/26 patients while 27% of the examined wrists showed no alterations. The Authors found that the SLE disease activity index (SLEDAI) score was significantly higher in the group without tendon involvement; no correlations were noted between the presence of joint synovitis and the signs of systemic activity, identified as ESR and C3 levels and SLEDAI score, and suggested that the low articular inflammation found at the wrists does not influence systemic disease activity (22). Two years later, an ultrasound pictorial

assay on hand and wrist arthritis in SLE was published, showing joint effusion or synovial proliferation in 16 out of 17 patients in the wrist, while 12 patients had inflammatory involvement at the metacarpo-phalangeal joints (MCP). In this study only the 2nd and 3rd MCP and proximal inter-phalangeal (PIP) joints were assessed, detecting bone erosions in 8 subjects. Tendon involvement was also investigated and finger flexor tenosynovitis (2nd, 3rd and 4th finger) was demonstrated in 11 patients (23).

In 2007 Saketkoo *et al*. (24) published a case report on the detection of bone erosion with US in a SLE patient, revisiting the deformities caused by Jaccoud's arthropathy and then stressing the role of US in a better definition of joint involvement in SLE patients.

More recently, Ossandon *et al*. (25) published the results of a new study on joint involvement in a SLE patient demonstrating that knee effusion was present in almost half of the group of 26 unselected SLE patients, with a non-statistically different prevalence from that observed in a group of RA patients, while proliferation, erosions and PD signal were more frequent in the RA group.

In the same year, Demirkaya *et al*. (26) studied 30 juvenile SLE patients (comparing them to healthy subjects), and an increased involvement of the knee, ankle, wrist and elbow joint, as well as of flexor and extensor tendons of the hand was shown, with an interesting decreased tendon thicknesses in the 3rd finger of the juvenile SLE patient group. This last finding did not correlate with disease duration or SLEDAI scores but underscored the potentially disabling scenario of tendon pathologies in those patients.

An Italian multicentre study (27) was then published in 2009, involving 50 SLE patients and demonstrating a high prevalence of wrist synovitis (80%), which was an unexpected finding in a population of unselected SLE patients where 20/50 of them did not complain of wrist pain. In this study, the Authors examined not only the radiocarpal joint but also the intercarpal (that could have had increased the prevalence of synovitis). Wrist tenosynovitis was found in only 10% of the patients but different areas were examined with respect to Iagnocco's study (22). With regard to the hand, joint synovitis was found in 50% of the patients (2nd and 3rd MCP and PIP joints were scanned). Bone erosions were described in only one patient. In that paper, cartilage damage was also assessed, with 12% of structural changes in the cohort of patients (considered due to synovitis and not to osteoarthritis because of the lack of any alteration of the bone-condral profile and because of the mean age (39.6±12.3 yrs) of the population studied. Finally, tendon involvement was noted in 12% of patients with tenosynovitis of the wrist (only extensor ulnaris carpi was assessed) and in 22% of the hands (flexor tendons of the 2nd and 3rd finger). No statistically significant correlations between US joint or tendon involvement and disease activity parameter levels, systemic involvement or disease duration were found. The Authors concluded by remarking on the fact that their results probably reflect the existence of a mild joint (possibly more frequent at the wrists), as well as tendon inflammation which, most of the time, does not reach such a level of activity that can produce structural damage, as hypothesised by Ossandon *et al*. (25). Moreover, the absence of correlation between systemic disease activity parameters and US joint findings reinforces the importance of a patient assessment that also includes musculoskeletal US to better classify SLE patients, especially in those cases in which physical examination is not conclusive.

Possible final results have been provided by Gabba *et al*. (28) who studied 108 patients with SLE (all of them had experienced musculoskeletal involvement during their disease course but only 39 were active at the moment of the examination). They found joint involvement in 42/108 patients (38.8%) while tendons were inflamed in 22/108 (20.3%). A synovitis (effusion and/or synovial proliferation with or without PD signal) was found in 25% of the patients (12.9% and 15.7%, respectively for the wrist and the hand) and bone erosions were quite frequent (25.9%) in this population, mostly in the hand (24.1% *vs*. 4.6% in the wrist). Flexor tenosynovitis was shown in 32/108 patients (29.6%), extensor synovitis in 37/108 (34.2%) and both were found in 22/108 (20.3%) of the total group. PD positivity was found in 17% and 12% of joints and tendons, respectively. Older age at diagnosis was associated with the general presence of US changes; for joint synovitis an independent association was established for the higher SLEDAI score while, for tendon involvement, it was found with disease onset. The really interesting point of this paper is the fact that they divided the patients into three groups (non-deforming x-ray non-erosive arthropathy, Jaccoud's arthropathy and Rhupus syndrome) and the results showed that US abnormalities depends on the SLE arthropathy (as expected), showing tendon abnormalities more frequently in the first two subgroups, while a higher percentage of US joint changes (including synovial proliferation and bone erosions) were recorded in the last one, supporting the hypothesis that Rhupus is a true overlap syndrome between RA and SLE. Those differences were in accordance with the categorical MS-BILAG score and the Authors also hypothesised that Jaccoud's arthropathy could be a late manifestation of a long-standing x-ray non-erosive arthropathy.

A similar conclusion about the higher burden of disease in the rhupus group was reached in the same year by Tani *et al*. (29), who studied a cohort of 103 consecutive SLE patients in order to determine the prevalence of Rhupus syndrome, finding 10 patients who were classified as rhupus. All of the patients were evaluated with US and a 0.2 T MRI without using any contrast media agent, assessing musculoskeletal involvement at the level of the non-dominant hand and wrist. Wrist effusion, synovial hypertrophy and bone erosions were detected in 3, 6 and 2 rhupus patients, respectively, while in the hand the prevalences were 5, 6 and 3. The scoring system used for joint effusion, synovial hypertrophy and erosions (0–3 score) showed a significantly higher average score in rhupus with respect to SLE patients (both in wrist and

hand, apart from erosions in the wrist) and not different with respect to the RA control group. Tendon involvement was observed in 5 (50%) patients with rhupus, significantly more than SLE patients and not different with respect to the disease control group (RA patients). Interestingly, using MRI, the cumulative erosive burden in rhupus patients was significantly higher than in the SLE patients and similar to the RA group.

US has also been used to assess therapy efficacy in patients with SLE (30, 31). Kaya *et al*. assessed knee cartilage thickness in SLE patients (32) using US. The Authors did not find any significant difference between the SLE and control (healthy subjects, HS) group. However, differences reached a statistical significance when only SLE patients under corticosteroid therapy were considered, showing an increased thickness with respect to HS. The Authors attributed this finding to a favourable effect of corticosteroid on chondrogenesis, as previously reported (33, 34).

In the same year, the same group studied the muscle architecture in patients with SLE (35) demonstrating significant greater values of vastus lateralis muscle thickness and pennation angle in patients with SLE with respect to HS; to explain this, the Author proposed that the greater pennation angle, associated to a non-modified length of the fascicle, depended on the increased thickness, possibly due to oedema. The same results were also found when only patients on corticosteroid treatment were compared with the control group. At the same time, the knee muscle strength of SLE patients was lower compared to the HS.

An interesting application of US coupled with colour and power Doppler has been reported in 22 patients affected by SLE, which showed haemodynamic changes in blood flow to the proximal femur even in the absence of osteonecrosis. The Authors suggest colour Doppler evaluation of femoral head perfusion as a predictive test for haemodynamic deterioration (36).

Systemic sclerosis

US can be applied to SSc patients to assess multiple aspects of the disease such as joint and tendon involvement, the presence of subcutaneous calcification, the skin features and, quite recently, also the lung involvement. The first study investigating the role of US in the evaluation of SSc joints was published in 2000 by Grassi *et al*. (37), demonstrating that the most frequent findings are soft tissue calcifications at the distal phalanx of the hand as well as narrowing of the distance between phalangeal apex and skin surface. The superior ability of US with respect to conventional x-ray in showing digital calcification, particularly over the palmar aspect of the finger, was later confirmed in a review by Boutry *et al*. (38).

Several years after Grassi's contribution, a new paper on US joint assessment was published in 2009 by Cuomo *et al*. (39), who studied 45 SSc patients comparing them both to HS and RA and fibromyalgia patients. Joint effusion was frequent (22/45; 49%); synovial proliferation was present in 19/45 (42%) patients and in 5 of them erosion were seen. Interestingly, no differences were found with respect to the RA group in the prevalence of synovial effusion and osteophytes (58%), while synovial proliferation, PD signal, erosions and joint space narrowing, were more frequent in the RA group. US-detected synovitis was found to be positively related only to the CRP levels. Periarticular calcinosis was found in 12/45 (27%) patients.

Another study published in the same year by Generini *et al*. (40) reported that US assessment of the hand and wrist joints showed bone erosions of MCP and PIP in 8/15 patients (synovitis was detected in 3 of those patients), and tenosynovitis was found in 5 cases.

One year later Chitale *et al*. (41) studied 17 patients affected by SSc and presenting arthralgia, using both US and MRI (the latter only in few cases). Tenosynovitis was the more common finding in the series, seen in 8/17 (47%) of the patients at the baseline US examination (while 6/13 at the 6-month follow-up), while synovitis was detected only in one patient (6%) at baseline and in 3/13 (23%) at follow-up. These results suggested that inflammatory joint disease and tendinopathy were persistent in many patients. No erosions were identified in the US examination, and no significant relationships were found between any demographic data and inflammation on US and MRI.

More recently, Elhai *et al*. (42) studying wrists and hands of 52 SSc and 24 RA patients, found at least one joint with synovitis in 46% of the SSc subjects and PD signal was seen in the 57% of them with no significant difference with respect to the control group; however, in the RA group there was a significantly higher PD grade (on a scale 0–3). Tenosynovitis was more rare, with a prevalence of 27% and 25% in the two groups, respectively. The interesting data was the presence of a hyperechoic tendon sheath thickening (a pattern considered as sclerosing) in the SSc group: this pattern was not found in the RA patients. As expected, soft tissue calcifications were found only in SSc subjects. US examination resulted to be more sensitive with respect to clinical examination. Patients with a CRP value >10 mg/l were more likely to have synovitis/tenosynovitis and PD positivity. Interestingly, SSc patients with a disease duration ≤3 years had significantly more clinical synovitis than patients with longer disease, even if the prevalence of US synovitis was not different. Tenosynovitis was more likely seen in patients with tendon friction rubs (TFR), a higher distal palmar crease and in those with higher numbers of painful and swollen joints. The pattern of sclerosing tenosynovitis was associated with TFR. Tenosynovitis was associated with a higher modified Rodnan skin score (mRss), presence of anti-Scl-70 antibodies and active or severe disease.

The last paper focusing on synovitis was recently published by Iagnocco *et al*. (43), who found joint effusion in 7% and 54% hands and wrists of 46 SSc patients, respectively; while synovial hypertrophy was assessed in 3% and 46% of hand and wrist joints, with a prevalence of PD positivity of 1.7% and 43% respectively (with both findings significantly higher than in HS). These results showed that the disease is more aggressive than expected by using only clinical examination. Only

6% of the tendons studied presented synovitis (with PD signal in 29%), but it was present in 43.5% of the SSc patients. No significant US differences were noted between limited and diffuse SSc patients and no correlations were found between the presence of TFR and tenosynovitis, or between US findings and mRss, disease duration and CRP positivity.

Also focusing on tendons, and trying to give an answer to the existence of TFR, Cuomo *et al*. (44) scanned 55 SSc patients and 30 HS on the MCP areas (extensor and flexor tendons), wrist (extensor and flexor tendons), knee (patellar) and ankles (anterior, posterior, lateral and medial tendon compartiment), and also calculated the thickness of retinacula. They found tenosynovitis/tendinitis in 21 patients. Interestingly, the retinacula had an hyperechoic appearance compared to the adjacent tendons in the SSc group, but hypoechoic in the HS. After comparing the data from the two groups, a significant difference in the thickness of the retinacula was found on both the wrist extensor and ankle anterior compartment between diffuse SSc with TFR and HS, or limited SSc or diffuse SSc without TFR.

Another paper focusing on TFR was recently produced by Stoenoiu *et al*. (45) who gave a different interpretation of the TFR. They found tenosynovitis more frequently in the ankle with TFR than in those without, but the difference was not statistically significant (perhaps also because of the low number of patients with these findings); synovitis was present in about 50% of the patients. They did not find any relationship between the presence of TFR and the thickness of the retinacula. However, the striking news was the discovery of a MRI evident juxtatendinous subcutaneous soft tissue infiltrate in the patients with TFR at the ankle (and only in one without TFR) and the Author proposed to replace the term TFR in tissue friction rubs.

Another interesting approach to disability assessment in SSc patients was published by Tagliafico *et al*. (46) who examined the hands of 28 patients, focusing on the thickness of the A1 pulley, using HS as controls. The pulley thickness, measured on transverse planes as previously reported (47), resulted to be greater in the SSc group than in the HS. It also strongly correlated with the Hand Mobility in Scleroderma Test (HAMIS) score and, moderately, with disease duration. Intra- and inter-observer agreement was good (and better than the agreement for the HAMIS). A reduction in the thickness of the pulley was noted in both groups from the A1 pulley of the first digit to the fifth digit, possibly due to the anatomical feature of the pulley itself.

Another aspect that has been studied using US is the occurrence of carpal tunnel syndrome (CTS) in asymptomatic SSc patients (48). Sixty-four patients were compared with 30 HS and the median nerve was measured (cross-sectional area – MNA, transverse – MNT, and anteroposterior – MNAP) at the proximal inlet of the carpal tunnel using a transverse scan. The flattening ratio (MNFR) was also calculated. Using the already published cut-offs (MNA >9mm^2 – Duncan and >12 mm^2 – Naranjo; MNFR >3.3 mm^2), a statistically significant difference was found between the two groups for MNA, MNT and MNFR. No correlations between SSc clinical features and the median nerve were found so the Author concluded that CTS can be present in any phase of disease. In the study by Tagliafico *et al*. (49), the cross sectional area (CSA) of the nerves of SSc patients had results similar to the control group at the four measurement sites. Moreover, as for Bandinelli *et al*., at the carpal tunnel level, the CSA of the median and ulnar nerves in SSc patients did not correlate with clinical symptoms, disease duration and nerve conduction studies.

The use of US to assess the skin was first published in 1979 by Alexander and Miller who measured skin thickness by a 15 MHz US (50). However, given the development of very high frequency probes (20 MHz or more), which are mandatory to clearly distinguish epidermidis, dermis and subcutaneous fat, has allowed not only the determination of thickness but also a qualitative assessment of the skin. Thus, in recent times, several papers have reported the sonographic skin findings in diffuse or localised scleroderma (51-55). However, those studies present a relevant lack of homogeneity (*i.e*. very different frequency of the probes used, ranging from 10 to 32 MHz; inconsistencies relating to the skin depth examined).

In 2003, a longitudinal study (56) (using a 20 MHz ultrasound probe) in 16 patients (8 with diffuse and 8 with limited SSc) showed thickening and decreased echogenicity of the dermis in sclerotic skin in the early phases of the diseases. The degree of thickening tended to diminish with time and, at 4 years of disease duration, thickness was significantly decreased in the forearm and chest and echogenicity increased in the hands. The Authors concluded that US seemed to be a good non-invasive tool to monitor disease progression. Similar results have recently been confirmed, showing the correlation with the mRss (57, 58). The US "use" of mRss was already explored with the proposal of a 17-point dermal US scoring method (using a 22 MHz US probe) based on the measurement of dermal thickness at the same sites of the mRss, providing a possible useful measure of outcome in the future (59). However, a systematic review exploring the role of US in skin involvement in SSc patients has recently been released (60).

In SSc patients with short disease duration, it has been shown that US is able to detect the oedematous phase that may precede palpable skin involvement (it could be useful in the identification of very early patients with a diffuse skin involvement) (61). Recently quantitative US has shown a decrease in the skin thickness after photochemotherapy in SSc (62). More recently, sonoelastography, a new technique that couples US and ultrasonic elastography (UE) has also been applied to skin; it is an imaging technique that allows a non-invasive visualisation of the elastic properties of tissues under examination, providing a coloured map superimposed on the grey-scale US imaging, measuring tissue deformation as a response to an external force, assuming that the deformation is lower in rigid tissues, compared with the elas-

tic, soft tissues. This method is based on comparing the radiofrequency of ultrasonic waves obtained before and after an easily made compression with a conventional transducer, using a free hand technique (63, 64).

Few studies have demonstrated the ability of this new approach to discriminate between SSc and HS when examining the dermis. In fact, UE showed a homogeneous blue area, corresponding to the dermis visualised in a B-mode ultrasonographic image in SSc patients, while a predominance of a green pattern with sporadic areas of pale blue was observed in HS. The imaging pattern observed in the SSc group represents the reduction of strain in the dermis due to loss of elasticity. The Authors also tried to asses finger skin but the results were not encouraging because of the variable pattern obtained, probably due to the fact that the dermis was too thin and the bone hyperreflection maximal (65). Subsequently, Di Geso *et al*. (66) investigated the role and reliability of UE in the measurement of the dermal thickness at finger level (2^{nd} finger of the dominant hand on the dorsal aspect of proximal and middle phalanx) and an excellent correlation was obtained between the measurements of the dermal thickness using grey-scale and adopting UE (rho=0.99). The ICC values for the intra-observer agreement were 0.904 and 0.979, and 0.726 and 0.881 for the inter-observer agreement, using only grey-scale and also elastosonography, respectively. So, UE could improve the reliability of US dermal thickness measurements in fingers, identifying the interface dermis/hypodermis. The differences between these results with respect to Iagnocco *et al*. (65) could be related to the different machines and software used.

The application of US in the evaluation of lung fibrosis in SSc patients is still under investigation but the papers already published demonstrated the consistency between the results of US assessment and the lung high resolution computed tomography (HRCT) findings, regardless of the frequency of the probe or the scanning protocol (67-73). Given those results, US has been proposed as a possible alternative to HRCT in the screening and follow-up of such patients and a few attempts have been made to simplify the scanning protocol (74, 75).

Finally, colour Doppler US has been used to visualise and quantify changes in nailbed vascularity in response to vasodilatory treatment in connective tissue disease patients (mainly affected by SSc) (76, 77), and also to explore Raynaud's phenomenon or acrocyanosis (78).

Sjögren's syndrome

Joint involvement is not rare in SS (79) and US can be useful in its evaluation and also to investigate changes in salivary gland architecture. Iagnocco *et al*. studied knee involvement in patients with primary and secondary SS (associated with rheumatoid arthritis or CTD). They demonstrated mild synovitis in primary SS (pSS), while joint effusion was more frequently present in secondary SS with rheumatoid arthritis (80).

In 2009, Riente *et al*. (81) studied forty-eight patients with pSS performing bilateral US examination of the 1^{st}–5^{th} metacarpophalangeal (MCP), 2^{nd}–5^{th} proximal interphalangeal (PIP) joints and of flexor tendons. They observed clear evidence of inflammatory arthritis in 18.7% patients; bone erosions at MCP and/or PIP joint were visualised in 12.5% patients; in 10 (20.8%) patients a flexor tenosynovitis was shown. The latter findings, even if more frequent than in HS, did not reach a statistically significant difference. The presence of bone erosions in pSS patients is almost unexpected, so the study gave a different perspective to the disease, which possible leads to articular damage.

Another study focused on joints was produced the following year by Iagnocco *et al*. (82) involving thirty-two pSS patients. US demonstrated wrist synovitis in 12 (37.5%) out of 32 patients. Interestingly, US examination of the hand did not show any significant changes (synovitis was detected in only 0.3% hand joints) and no bone erosions were found. A statistically significant correlation was found between the SS Disease Damage Index (SSDDI) score and the degree of sonographic signs of synovial proliferation in the wrist. Patients with synovitis were those with a higher median age, higher median SSDDI and rheumatoid factor positive.

Recently, Amezcua-Guerra *et al*. (83) studied 17 patients with pSS, 18 with secondary Sjögren's syndrome (sSS), and 17 HS underwent US examinations of the elbow, wrist, hand, knee and ankle. In patients with pSS, synovitis was found with a high prevalence (76% for MCP, wrists and also knees) while the intra-articular PD signal was occasionally detected in wrists (12%), elbows (6%), and knees (6%). Erosions were evident in the wrists of three (18%) patients with pSS. Apparently, the demonstration of bone erosions in the 2nd MCP joints showed 28.8% sensitivity and 100% specificity for diagnosing sSS.

Very recently, Jousse-Joulin *et al*. (84) studied whether tendon pain in pSS is related to involvement of the tendons and entheses. Clinical examination, B-mode and PD-mode examination of 16 patients with active pSS and 9 HS were performed. Although 56% of the patients had clinical tender points, none had structural or blood-flow abnormalities evidenced by US, suggesting the absence of inflammation of the tendons and entheses in this disease.

All of those studies seem to confirm that pSS joint involvement is not rare, is possibly polyarticular, bilateral, and symmetrical, more frequently involving the MCP joints, wrists, and knees and, finally, with the possible presence of bone erosions.

Several studies based on the US findings in the parotid and submandibular glands in primary SS have been published, providing good results about comparison with other imaging tools, such as sialography, scintigraphy and MRI, and also about the reproducibility of an US scoring system. Given these data, US emerges as a very useful method for the diagnosis and follow-up of salivary gland involvement in SS patients. This concept is reflected by the recent proposal to add salivary gland US to the American European Classification Criteria Criteria (AECG) of pSS (it has been demonstrated that it

increases sensitivity without reducing specificity). Finally, US has been successfully used as an objective non-invasive tool for evaluating the response to the therapy (rituximab) effects in patients with pSS (85).

Polymyositis and dermatomyositis

Very few studies have been reported on the role of musculoskeletal US in PM and DM. However, using a 7-9 MHz linear transducer array it is possible to evaluate muscle changes in myositis. With normal muscle bulk, fascicles appear anechoic or hypoechoic relative to septae. An isoechoic appearance is considered extremely abnormal, reflecting diminished fascical size and closer space between fibrous septae. Reimers *et al*. (86) reported muscle atrophy and increased echogenicity in the upper and lower limbs both in childhood and adult PM and DM. Higher echogenicity and more pronounced atrophy were usually present in chronic myositis, lower echogenicity and muscle oedema in acute myositis. In another study involving 37 patients with DM or PM, the grey-scale evaluation of the muscle was correlated with PD. Disease of longer duration was significantly associated with more abnormal features on grey-scale examination, whilst PD signal was increased in disease of shorter duration (87). Recently, using contrast-enhanced US, muscle perfusion was studied in 35 patients suspected of having PM and DM. In all patients, blood flow, volume and flow velocity were measured and compared to the results of MRI and muscle biopsy. Eleven out of 35 patients had histologically confirmed DM or PM and significantly higher perfusion parameters. The Authors concluded that contrast-enhanced US could be an additional parameter for the diagnosis of inflammatory myopathy (88). Power Doppler has also been shown to be effective in visualising the change before and after treatment in a patient with inflammatory myopathy (89). US can also be useful to aid needle positioning during muscle biopsy (90, 91), however, MRI is still considered more sensitive than US in the detection of muscle oedema. Calcification can easily be detected because of high echointensity and acoustic shadowing on US images (90).

UE has been also used in the assessment of inflammatory myopathies (92). A group of 24 patients with musculoskeletal pathology was examined and a proportional concordance between the average values of the colour parameters and serum creatine kinase and serum lactic dehydrogenase was found, suggesting that UE could be an important tool in the management of patients with myositis.

Another interesting application of US was its use in differentiating between patients with sporadic inclusion body myositis (s-IBM) and those with s-IBM-mimicking diseases by muscle forearm assessment (93). The Authors compared the echo intensity (EI) of the flexor digitorum profundus (FDP) muscle and the flexor carpi ulnaris (FCU) muscles in a small group of patients with s-IBM, PM/DM and amyotrophic lateral sclerosis (ALS). Because of the identification of EI abnormalities in 100% of patients with s-IBM, 33% of those with PM/DM, and 33% of those with ALS and the observation of an "FDP-FCU echogenicity contrast", a US pattern involving a higher EI in the FDP than in the FCU, in all patients with s-IBM but in none of those with PM/DM or ALS, they concluded that "FDP-FCU echogenicity contrast" could be a sensitive diagnostic indicator of s-IBM.

Undifferentiated and mixed connective tissue disease

A study on 14 UCTD patients suggested that PD US has better accuracy than nailfold capillaroscopy in differentiating primary from secondary Raynaud's phenomenon and in assessing microvascular abnormalities (94).

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