Doppler techniques

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ABSTRACT

Over the last decade, there has been a growing body of evidence on the validity of Doppler ultrasound for assessing inflammatory changes in target anatomic structures involved in rheumatic diseases such as joints, tendons, entheses and vessels. The enhanced sensitivity for detecting low-velocity flow in synovium vessels achieved by current Doppler techniques has lead to the incorporation of Doppler US in the assessment of joint and inflammatory enthesis lesions. This review offers an overview of the key aspects of current applications and limitations of Doppler ultrasound in inflammatory rheumatic diseases. The basic principles of Doppler modes, Doppler scanning method, and Doppler artefacts and pitfalls in rheumatology ultrasound are also described.

Doppler physics and modes

Doppler ultrasound (US) is based on the Doppler effect, which was described by the Austrian physicist Christian Doppler in 1842. This physical phenomenon consists of a change in the frequency of a sound wave (*i.e.* Doppler shift) resulting from motion of either the source or the receiver. In medical Doppler US, the Doppler effect allows us to detect movement of red blood cells in vessels. Thus, Doppler US provides information on blood flow, which is related to the vascularisation of the anatomic structures (1).

Spectral Doppler was the first mode available in Doppler US. In this Doppler mode, the spectrum of flow velocities is represented graphically on the Y-axis and time on the X-axis. Thus spectral mode allows us to measure different blood flow parameters, some of which (*e.g.* resistive index) can be useful in rheumatology US.

Later, colour flow imaging or colour Doppler (CD) mode was developed in Doppler US. CD technique is the combination of the Doppler effect and real time US imaging. In CD mode, the information from Doppler technique is integrated in the B-mode (*i.e.* grey-scale) image as a colour signal. Real-time flow information as a colour signal is superimposed on the B-mode (*i.e.* grey-scale) image. Colours indicate direction of flow. Red usually indicates flow towards the transducer (*i.e.* artery) and blue indicates flow away from the transducer (*i.e.* vein).

Power Doppler (PD) mode is the most recent Doppler mode, which has been available in US technique since the 90s (2-5). While CD displays mean Doppler shift, PD displays power of the Doppler shift in each cell, representing only signal intensity (*i.e.* amount of red blood cells flowing). Consequently, PD potentially increased the sensitivity to detect low velocity flow from small vessels such as those involved in inflammatory processes, which are the key areas in rheumatic diseases (2-5). In addition, PD is almost angle independent, displays poorer delineation of the flow profile and pursatility and is more vulnerable to motion artefacts than CD. In recent years, the sensitivity of CD mode for detecting flow at the microvascular level has greatly improved in many high-end US machines. Thus, currently the choice of PD *versus* CD should be taken for each particular US machine. Nevertheless, PD is still recommended for use in rheumatology in many mid-range and entry-level US machines.

Doppler settings

Optimal adjustment of CD or PD Doppler setting is essential to enhance the quality of Doppler US assessment. Doppler settings should be adjusted to obtain the highest sensitivity for detecting flow with or without minimal artefacts. These parameters depend on the US equipment and are different according to the depth of the studied anatomic area. We can create some presets with appropriate Doppler parameters for dif-

ferent anatomic area (*e.g.* deep, intermediate and superficial joints), which are very helpful and save time in daily practice. The principal Doppler settings that we need to know for rheumatology Doppler US, either CD or PD, are described below (6).

– Focusing

As on B-mode, the focal point should be placed at the level of the target area.

– Doppler frequency

In general, high Doppler frequencies should be used for superficial anatomic areas and low Doppler frequencies for deep anatomic areas. However, optimal frequencies for different depths depend on the US machines.

– Pulse repetition frequency (PRF)

A low PRF enhances the sensitivity of Doppler to detect low velocity flow from small vessels in inflammatory disorders. However, a too low PRF produces motion artefacts due to movement of the patients, probe or artery wall or patient's voice. These artefacts can make the interpretation of real flow in the US images very difficult. Therefore, optimal PRF should be the lowest value that maximises Doppler sensitivity with no or minimal motion artefacts. This value usually ranges from 500 to 900 Hz depending on the US equipment.

– Doppler gain

A high Doppler gain increases the Doppler sensitivity but also the noise artefacts. Hence, Doppler gain should be increased until random noise appears. As stated by Rubin (2), because no flow should be visualised in the bone, colour gain should be set just below the level at which colour noise appeared underlying bone. Optimal Doppler gain is highly dependent on the machine.

– Wall filter

Low wall filters enhance the sensitivity of Doppler for detecting flow from small vessels.

– Doppler box

The colour box should be adjusted to the region of interest, which should include the studied anatomic structure (*e.g.* joints, entheses), the bony margins and a variable view of surrounding tissues. This box can be extended to the top of the image (*i.e.* patient's skin) to recognise reverberation artefacts produced by superficial vessels (6).

Table I. Principal artefacts in rheumatology Doppler US.

Artefacts	Technical basis	How to avoid or minimise
Motion or random flashes	Too low PRF produces detection of slight movements of the patients or the examiner, artery walls or patient's voice	Adjusting PRF to maximise Doppler sensitivity with no or minimal artefacts
Ramdon noise	Too high Doppler gain	Adjusting Doppler gain at or just below the level that generates no or minimal random noise
Mirror	Mirror colour images under highly reflecting surfaces such as bones	The real vessel and its mirror image under the bone surface are easily recognised
Blooming	Colour beyond the vessel wall due to high gain	This artifact is recognised by temporarily reducing the gain
Reverberation	Superficial vessels produce false color signals at deeper locations such as within synovial spaces	This artifact is recognised extending the colour box to the top of the image

US: ultrasound; PRF: pulse repetition frequency.

– Colour priority

This setting should be maximised over grey-scale priority when detecting blood flow is the primary objective of the US investigation.

Doppler scanning method

Doppler examination should be performed after morphological B-mode examination of the investigated anatomic structures. The valuable information about blood perfusion provided by Doppler US is always complementary to the morphological information provided by B-mode US.

– Training

A thorough knowledge of musculoskeletal US on B-mode is necessary before starting the training on Doppler modes. The morphological information of the anatomic structures provided by the B-mode images allows us to know the location of the vascularisation detected by Doppler mode and thus interpret the nature, normal (*i.e.* feeding vessels) or pathological, of blood perfusion.

– Patient and examiner positioning

The patient and the examiner must be comfortable to avoid motion artefacts. The patient should be quiet because voice can produce motion artefacts. The examined area must be relaxed; tension in muscle, tendons and joints produces motion artefacts. The scanning arm and hand of the examiner must rest in a comfortable way to avoid motion artefacts.

– Scanning of joints and entheses

Joints should be scanned in neutral position instead of in extended or flexed position; overextension or flexion of the joint can tighten the joint capsule resulting in compression of vessels and consequent reduction of detectable flow (7). Entheses should be scanned with the joint in neutral position, otherwise increase in the intratendinous tension can produce entheseal vessel collapse (8).

– Scanning pressure

Care should be taken not to apply too much pressure with the probe in superficial joints so as not to compress the vessels and overlook the colour signal. A thick layer of gel should be applied between the probe and the patient's skin which should be visible in the US image to ensure minimal scanning pressure.

– Knowledge of anatomy

Knowledge of the location of the feeding vessels of joints, tendon and entheses avoid misinterpretation of these normal vessels as pathologic vascularisation (Online Fig. 1).

Doppler artefacts

Correct use of Doppler US requires recognition of artefacts, which can lead to misinterpretation of relevant findings in rheumatic diseases (Online Figs. 5-8). Table I shows the principal artefacts in rheumatology Doppler US (6).

Applications of Doppler ultrasound in rheumatology

Synovitis and tenosynovitis

Synovial inflammation consists of periarticular vasodilatation followed by synovial proliferation, which is accompanied by angiogenesis resulting in intra-articular blood vessel formation (9). Angiogenesis of the synovial and tenosynovial membrane is considered to be a primary pathogenic mechanism responsible for the joint and tendon aggressiveness in rheumatoid arthritis (RA) and other inflammatory arthritis (9,10). CD and PD US techniques detect pathologic flow within the synovial and tenosynovial hypertrophy, which is a sign of inflammatory activity (Figs. 1-3). This has led to Doppler US playing an increasingly important role in the evaluation and monitoring of patients with inflammatory arthritis in clinical practice and clinical trials (11). Interestingly, recent studies have reported the presence of subclinical synovitis with Doppler-detected activity in around 50% of RA patients in clinical remission treated with synthetic or biologic disease-modifying anti-rheumatic drugs (DMARDs) (12-24). However, the impact of Doppler-targeted therapy on RA outcomes in these patients has not been established yet.

In addition to inflammatory arthritis, synovial Doppler signal can be found in other conditions such as pigmented villonodular synovitis (Online Fig. 2), microcrystalline arthropathies or osteoarthritis.

Validity

There is an increasing number of studies on the concurrent validity of Doppler-detected synovial inflammation using histology (25-28) or contrast-enhanced magnetic resonance imaging as gold standard (29, 30). Other studies have shown close association between Doppler-detected synovitis and clinical or laboratory markers of inflammation in RA (31-35). Synovial Doppler signal has demonstrated predictive value in relation to structural damage progression in both clinically active (36-42) and inactive (14, 22, 24) RA patients treated with synthetic or biologic DMARDs. In addition, subclinical Doppler-detected synovitis has shown predictive value in relation to disease flare or relapse in RA patients in clinical remission (15, 18, 20, 24).

Reliability

Despite the high operator dependence of US, Doppler technique has shown good interobserver and intraobserver reliability in synovitis and tenosynovitis detection and scoring. This reliability was similar using quantitative or semiquantitative scoring systems (43-47).

Responsiveness

Many longitudinal studies have demonstrated a significant reduction of joint inflammation evaluated by Doppler US (*e.g.* PD or CD) in different joints and joint combinations of RA patients on different treatments, including intra-articular corticosteroid injections, systemic corticosteroid therapy, synthetic and biologic DMARDs (32, 36-38, 40, 44, 48-58). In these studies, changes in Doppler-detected synovitis were associated with clinical and laboratory response to therapy.

Diagnostic value

In a small number of studies, the presence of synovial Doppler signal has shown diagnostic value in relation to the development of chronic arthritis or RA in patients with early undifferentiated synovitis (59-62). However, more studies are needed to establish the diagnostic and therapeutic impact of Doppler findings in patients with arthralgia or very early arthritis.

Enthesitis

Entheses are the sites where tendons, ligaments, muscle, fascia or joint capsules attached to the bone (63). Inflammation of entheses or enthesitis is the principal pathological feature of spondyloarthritis (SpA) (64). Histological studies on enthesitis have described local inflammation, fibrosis, erosion, ossification and adjacent bursitis (64).

Abnormal blood flow in peripheral entheses detected with Doppler US has been described in active SpA patients, mainly in the lower limbs (65-69) (Fig. 4). Even more important, the presence of Doppler signal at the anatomic locations of the entheses (*i.e.* very close to or at the bone profile) has demonstrated high specificity for diagnosing SpA in patients with early axial or peripheral symptoms (65, 68, 69). In patients with psoriasis, the presence of entheseal Doppler signal seems to be associated with the development of psoriatic arthritis (70). Doppler-detected enthesitis has shown good reliability (71) and responsiveness (72) in SpA patients.

Vasculitis

Colour Doppler US of superficial arteries has been widely used to detect vasculitis (73-79). Hypoechoic thickening of the artery wall (*i.e.* circumferential halo detected in transverse and longitudinal plane) is the most specific sign for vessel inflammation (specificity >90%). In addition, turbulent flow and arterial stenosis or occlusion are more sensitive signs (sensitivity >75%) but less specific for arteritis (76). These colour Doppler findings have been described in the temporal, occipital, and facial arteries, as well as in extracranela arteries such as axillary, subclavian, common carotid arteries and other peripheral arteries in giant cell arteritis (GCA) (73-75, 78). Some experienced ultrasonographer have proposed that US Doppler performed with an appropriate machine can replace the temporal artery biopsy as complementary tools in the clinical diagnosis of the above disease. Alternatively, colour Doppler can be very helpful in guiding the biopsy of the most involved and the most accessible area of the temporal artery to enhance the diagnostic capability of these diagnostic tools in GCA. Colour Doppler US has shown responsiveness in GCA after few weeks of appropriate corticosteroid treatment (80).

Soft tissue diseases

The presence of abnormal blood flow detected with Doppler US has been described around or inside soft tissue lesions (*e.g.* tendinosis, tendon tear, bursitis) (81) (Online Fig. 3). More recently, Doppler US has been used to distinguish active tendinosis (*i.e.* increased Doppler-detected blood flow inside the tendon degenerative area) from

inactive tendinosis (*i.e.* no or minimal normal Doppler-detected blood flow inside the tendon degenerative area) (82). These active areas in tendinosis seem to correspond with proliferation of new vessels, which may be part of a healing process and/or an inflammatory process. This distinction can be useful to choose the most appropriate treatment for tendinosis.

Methods of quantification of inflammatory findings in rheumatology Doppler US

Pathologic blood flow can be detected with Doppler US in different synovial recesses accessible by US evaluation in peripheral joints. In inflammatory arthritis, colour or power Doppler signal within synovial hypertrophy is the main pathologic marker of inflammatory activity (25-30). Several systems for quantifying Doppler-detected synovitis in RA joints have been used in published studies (83). These systems have been qualitative (29), semiquantitative (12, 14, 15, 17, 20, 23-26, 31, 32, 34, 38, 41, 43, 50-55, 58) or quantitative (25, 30, 36, 44, 49, 84) and have included any number of scanned joints ranging from 78 joints to a reduced number of target RA joints such as wrist, hand, or toe joints (85). These variables have made comparison of study results difficult.

A binary scoring of synovitis according to the presence or absence of synovial Doppler signal at synovial sites can be feasible, easy and reliable but not sensitive to change. Most research groups have used a four-grade semiquantitative scoring system (*i.e.* 0, no Doppler signal; 1, isolated Doppler signal; 2, moderate Doppler signal; 3, severe Doppler signal) for synovial Doppler signal. This system is easily applicable in clinical practice and clinical trials, and is reliable and responsive to therapeutic interventions. In fact, the EULAR-OMERACT (European League Against Rheumatism-Outcome Measures in Rheumatology) group for musculoskeletal US has agreed on the use of four-grade semiquantitative scoring systems for both, B-mode-detected and Doppler-detected synovitis, which have demonstrated good multi-examiner intraobserver, interobserver and intera-

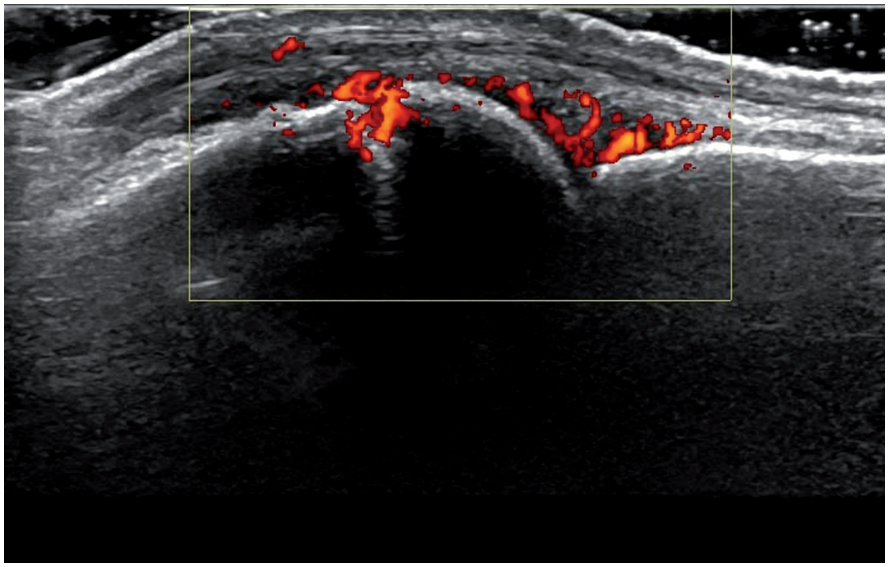

Fig. 1. Longitudinal ultrasound image of the dorsal aspect of a metacarpophalangeal joint that shows severe power Doppler signal within the synovial hypertrophy.

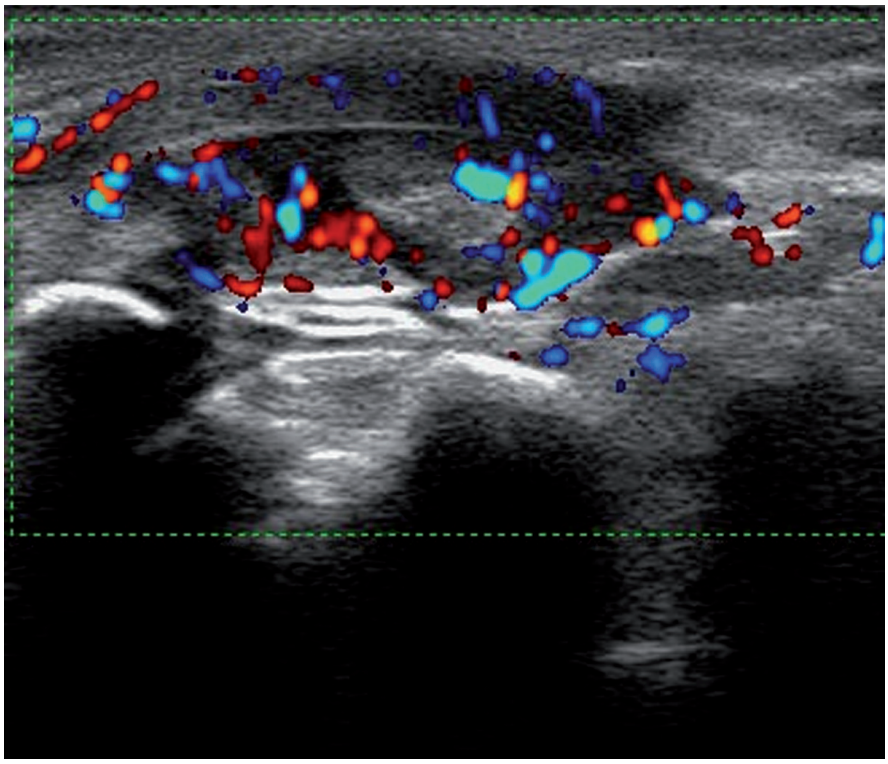

Fig. 2. Transverse ultrasound image of the tibialis posterior tendon that shows tenosynovitis on B-mode and power Doppler mode (diffuse Doppler signal within the distended synovial sheath).

chine reliability in RA patients (86-88). Quantitative assessment of synovial Doppler signal has the advantages of being more objectives than semiquantitative assessment. In addition, quantitative systems use continuous variables which can be more sensitive to change than semiquantitative variables. Quantitative Doppler scoring systems include computer-assisted measurement of colour pixels in a specific area of interest (Online Fig. 4) (25, 30, 36, 44, 49, 84) and spectral Doppler analysis with measurement of the resistive index (30, 44, 49, 84). Low values of RI indicate an inflammation process. Both Doppler parameters have been shown highly reliable and responsive to thera-

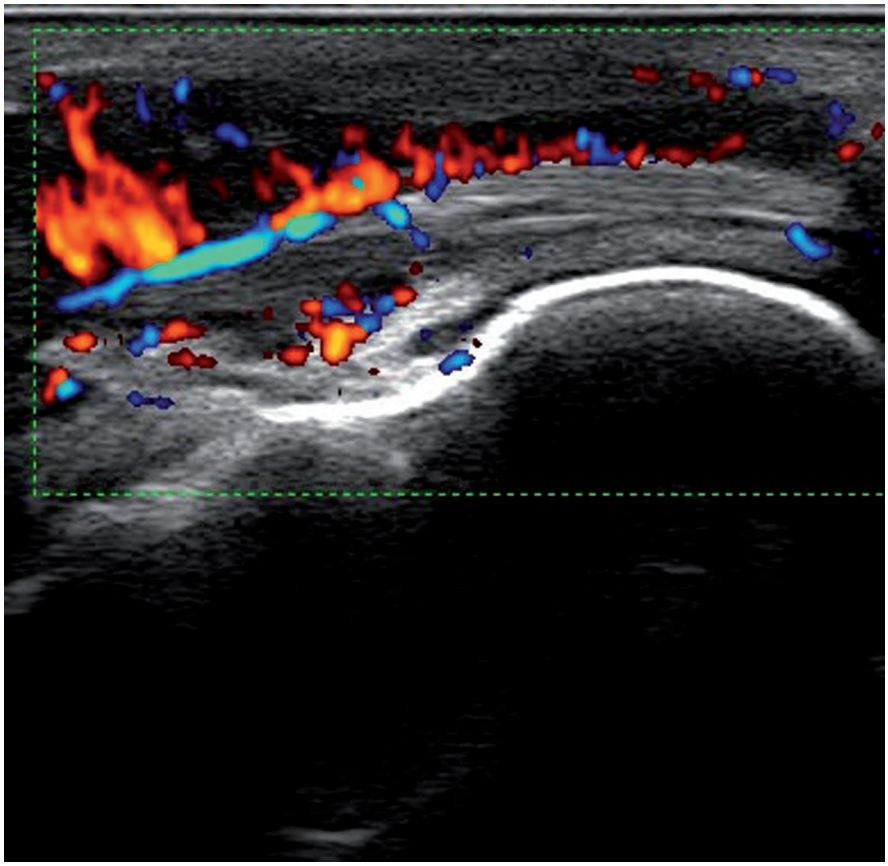

Fig. 3. Longitudinal ultrasound image of the tibialis posterior tendon that shows tenosynovitis on B-mode and power Doppler mode (diffuse Doppler signal within the distended synovial sheath).

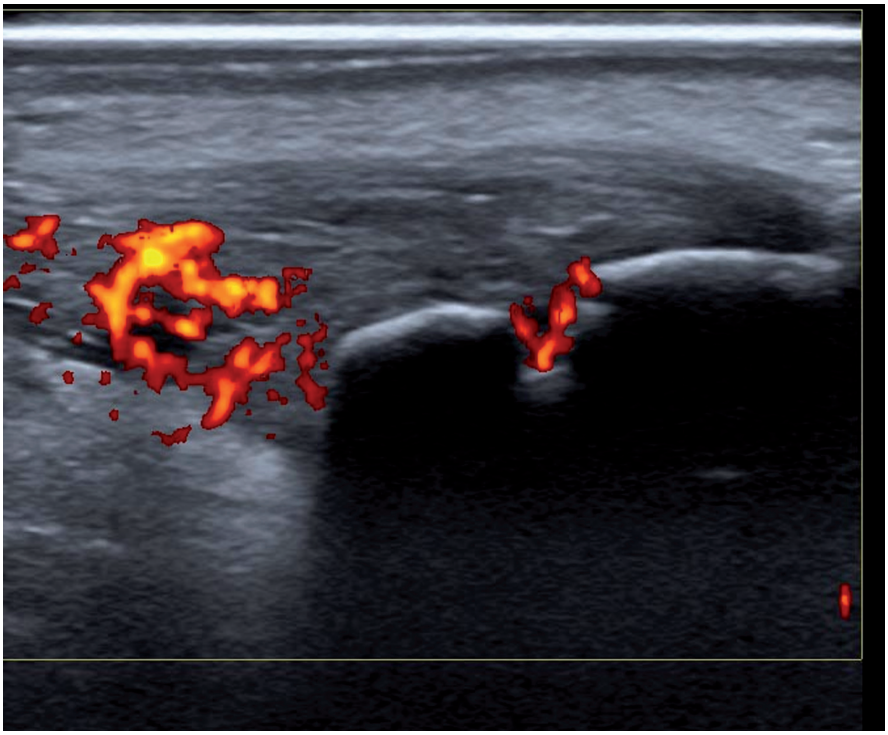

Fig. 4. Longitudinal ultrasound image of the Achilles tendon in a patient with spondyloarthritis. B-mode enthesopathy and power Doppler signal within a calcaneal bone erosion, the retrocalcaneal bursa area and the tendon substance are detected.

py (44-46, 84). However, they are time consuming and not feasible in clinical practice. Thus, they are probably more suitable for US research. In clinical practice, spectral Doppler can be useful to distinguish real flow versus artefacts in some occasional doubtful cases.

Recently, the EULAR-OMERACT group for musculoskeletal US has developed a scoring system for tenosynovitis in RA (47). A four-grade semiquantitative scoring system (*i.e.* grade 0, no Doppler signal; grade 1, focal Doppler signal; grade 2, multifocal Doppler signal; grade 3, diffuse Doppler signal) was agreed upon for scoring pathologic peritendinous (*i.e.* intra-sheath) Doppler signal in RA tenosynovitis (47). Intratendinous Doppler signal was not included in the elementary lesions of tenosynovitis because it could correspond to intratendinous tenosynovial angiogenesis, vasodilatation of intratendinous feeding vessels or hypervascularisation in areas of tendon repair. Nevertheless, the presence of intratendinous signal in addition to peritendinous signal was considered in the tenosynovitis scoring system (*i.e.* intratendinous signal increases the grades 1 and 2 by one point).

Regarding the global scoring of Doppler-detected synovitis (*i.e.* patient level), most published studies have included a limited number of target rheumatoid joints and few studies have included tenosynovitis as synovial sites assessed by Doppler US (85). The global score for Doppler synovitis was usually obtained from the sum of the Doppler score of each studied joint. Some studies have proposed reduced-joint Doppler US assessments (23, 54, 55, 62, 89). These studies have demonstrated appropriate metric properties of reduced-joint scoring systems for monitoring therapeutic response (54, 55, 89, 90), evaluating subclinical synovitis in RA patients in clinical remission (23), and diagnosing RA (62).

At the patient level, wrist-hand and ankle-foot tendons should be selected for scoring tenosynovitis because of their frequent involvement in inflammatory arthritis and their superficial location which is optimal for Doppler sensitivity (47, 91).

Some studies have included the presence of entheseal Doppler signal in the US assessment of SpA enthesopathy (65-69). However, there is no agreement on a scoring system for Doppler enthesitis in SpA patients.

Limitations of Doppler ultrasound in rheumatology

A number of technical limitations of Doppler US should be mentioned. The lower sensitivity of CD and PD to detect flow from small vessels in deep anatomic areas as compared with superficial areas limits the assessment of inflammatory activity in deep joints, tendons or entheses. In addition, adjusting the settings for optimal balance between high Doppler sensitivity and minimal artefacts is not easy in all US machines. Furthermore, the difficulty in standardising Doppler parameters among different US equipments limits both comparison between Doppler studies and the development of multicentre Doppler studies performed with different machines.

Conclusions

Doppler ultrasound is a valid imaging modality in assessment and monitoring of inflammatory arthritis with proven predictive value in relation to disease outcomes and has a promising diagnostic value. Doppler ultrasound of superficial vessels can also be used as a diagnostic tool in vasculitis. However, some technical issues such as the low sensitivity of Doppler in deep joints, the inability to standardise Doppler settings among different ultrasound machines, and the difficulty in adjusting maximal sensitivity and minimal artefacts limit the possibility that Doppler ultrasound can be fully incorporated into rheumatology practice and clinical trials.

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