„CAROL DAVILA" UNIVERSITY OF MEDICINE AND PHARMACY
BUCHAREST
DOCTORAL SCHOOL
FIELD MEDICINE

MUSCULOSKELETAL ULTRASOUND ASPECTS IN PATIENTS WITH PSORIASIS AND PSORIASIC ARTHRITIS

ABSTRACT OF THE DOCTORAL THESIS

PhD supervisor:
PROF. CODREANU CĂTĂLIN, PH.D.

PhD student:
MARINESCU (cas AGACHE) MIHAELA

MUSCULOSKELETAL ULTRASOUND ASPECTS IN PATIENTS WITH PSORIASIS AND PSORIASIC ARTHRITIS

Psoriatic Arthritis (PsA) is a chronic inflammatory condition that generally occurs in patients with psoriasis. PsA affects multiple structures, including joints, but also extra-articular, and extra-musculoskeletal sites, often making diagnosis challenging. Unlike other autoimmune mediated diseases, PsA lacks specific biomarkers in routine medical practice, which increases the importance of musculoskeletal ultrasound (MSUS) in disease management.

MSUS, an accessible imaging technique, has begun to play an increasingly important role in managing PsA. It can provide details about the extent of inflammation and assess many disease domains: joints, entheses, skin, nails, and dactylitis. MSUS represents a valuable tool both for diagnosis and for treatment monitoring and prognosis evaluation. It also detects subclinical involvement and impacts therapeutic decisions in the context of recommendations to initiate treatment as early as possible.

The relevance of this doctoral thesis topic is highlighted by global research efforts. In rheumatoid arthritis (RA), MSUS has made major progress, backed by validation studies for the assessed parameters. Searching the PubMed© database using keywords like “rheumatoid arthritis,” “psoriatic arthritis,” and “ultrasonography” shows that on average in recent years, articles about RA are six times more frequent than those about PsA. However, the number of publications dedicated to PsA has also doubled over the past 10 years, highlighting it as a current topic with multiple research directions.

MSUS has become increasingly accessible in recent years due to improvements in the performance and accuracy of modern ultrasound devices, including small portable units that provide acceptable morphological details, especially for accessible peripheral structures, delivering information about disease activity. It is a non-invasive, non-radiating, and significantly more cost-effective investigation compared to magnetic resonance imaging (MRI). MSUS accurately detects synovitis, enthesitis, dactylitis, and tenosynovitis. Although it cannot show bone abnormalities, it does detect abnormal vascularization, which is an indicator of inflammation. Multiple joints can be assessed in the same session, both statically and dynamically. However, MSUS is operator-dependent due to artifacts and requires in-depth imaging training, but it benefits from increased reproducibility. The growing role of MSUS in

diagnosing (even in early stages) and monitoring PsA patients is recognized in the European Alliance of Associations for Rheumatology (EULAR) recommendations.

In PsA, the greatest focus has been on enthesitis, a key feature in the pathogenesis of spondyloarthritis. Enthesitis was included in both the Classification criteria for Psoriatic Arthritis (CASPAR) developed in 2006 and in the domains defined by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA). Starting in 2019, enthesitis has also been mentioned in the EULAR treatment recommendations for PsA alongside other periarticular structures (tenosynovitis, dactylitis), as well as on the EULAR research agenda.

Interest in studying enthesitis has grown significantly in recent years for several reasons. Increasing evidence highlights its central role in disease pathogenesis, advances in imaging technologies (MSUS, MRI), and the introduction of new therapies into clinical practice have all contributed to this trend.

In recent years, there has also been a particular focus on using MSUS in PsA patients to assess the upper limbs. Using high-frequency probes, the following features can be evaluated both in gray scale (GS) and power Doppler (PD) modes:

- Synovitis
- Paratenonitis of the extensor tendons of the fingers, described in the literature with the acronym PTI (Peritenon extensor tendon inflammation), which has high specificity for PsA
- Thickening of the pulley system (A1) at the volar aspect of the metacarpophalangeal (MCP) joints, a distinct feature of PsA
- Thickening of the central slip of the extensor tendon at the level of the proximal interphalangeal (PIP) joint and its distal insertion at the distal interphalangeal (DIP) joint, often associated with synovitis, supporting the synovio-entheseal complex theory
- Flexor tenosynovitis
- Subcutaneous tissue edema

Enthesitis scoring systems developed for spondyloarthritis have been less extensively evaluated in PsA. The 2018 OMERACT (Outcome Measures in Rheumatology) definition of enthesitis attempted to standardize the assessment and bring consistency to clinical studies. A recent systematic review of the literature on ultrasound features validating an enthesitis score highlights that there is no consensus on the number and location of enthesis sites that should be

minimally assessed. To date, there are no ultrasound scores specifically validated for enthesitis in terms of diagnosis and treatment response monitoring, representing an important research gap.

Enthesis involvement, a defining feature of PsA, can also be found in patients with psoriasis alone. Identifying subclinical enthesitis in these patients is necessary to assess the risk of potential progression to PsA, facilitating the adoption of appropriate therapeutic strategies and establishing a monitoring period.

Clinical assessment of entheses poses a challenge in daily medical practice, as other conditions—mechanical or inflammatory—can present with similar clinical expressions. As a diagnostic method, MSUS complements the clinical examination, increasing diagnostic accuracy. The most important element to detect is active enthesitis, which requires the presence of a PD signal, a fundamental ultrasound feature of enthesitis. Ultrasound-detected enthesitis can also be observed in patients engaging in intense physical activity, those with obesity, or metabolic syndrome, but in most of these cases, only hypoechogenicity or thickening of the tendon insertion is observed, with PD signals being rarer.

Synovitis in PsA appears similar to that in RA, with synovial hypertrophy, intra-articular effusion, PD signal, or erosions. However, the literature highlights that cases tend to be more severe in RA. Studies on PsA indicate a higher association of synovitis with changes in adjacent structures (tendons/entheses). Moreover, synovitis with erosions at the DIP joints is characteristic of PsA, while in RA, erosions and synovitis are more commonly found at the radiocarpal joint.

For synovitis, EULAR and OMERACT have developed and standardized a composite score—GLOESS (Global EULAR OMERACT Synovitis Score)—which has demonstrated validity for the ultrasound detection and scoring of synovitis both in RA and PsA. Moreover, this score has shown sensitivity to change under treatment, proving useful for monitoring disease progression. Musculoskeletal ultrasound (MSUS) has proven to be a valuable tool in monitoring patients in clinical remission, with ultrasound-detected synovitis identified as an important predictor of disease relapse. MSUS can detect subclinical synovitis and power Doppler (PD) signals in both PsA patients and those with psoriasis, as well as in healthy volunteers.

Dactylitis is included in the CASPAR classification criteria for PsA and is considered a negative prognostic factor due to its association with radiographic progression. The use of

MSUS has enabled a deeper understanding of the pathogenesis of dactylitis by identifying structural changes such as: flexor tenosynovitis of the fingers, subcutaneous tissue edema, thickening of the pulley system with PD signal, paratenonitis of the finger extensors, synovitis (MCP, PIP, DIP joints), pericapsular bone formation, enthesitis of the flexor tendons of the fingers. For dactylitis, the DACTOS (DACTylitis glObal Sonographic) score has been published, providing a semi-quantitative assessment in GS and PD for: synovitis in small joints of the hands, flexor tenosynovitis, extensor tendon and subcutaneous tissue inflammation. This score has also demonstrated sensitivity to change under treatment.

Furthermore, studies have shown a higher degree of joint damage in dactylitic fingers compared to unaffected ones. Dactylitis is also associated with higher swollen joint counts, increased CRP levels, and the presence of enthesitis as evidenced by ultrasound.

Tendon sheath involvement can result in various ultrasound findings, including: exudative or proliferative tenosynovitis, loss of fibrillar echotexture, partial or complete tendon ruptures. For tendons without a synovial sheath, findings may include enlargement, hypoechoic echotexture, with or without intratendinous PD signal.

In PsA, MSUS is also useful for detecting bursitis, most commonly affecting: the subacromial-subdeltoid bursa and bursae associated with the Achilles tendon and quadriceps tendon

Although not the first-line investigation, MSUS can be used in PsA to detect structural lesions such as erosions and new bone formation, enabling earlier diagnosis and reducing repeated exposure to radiographic investigations.

For skin evaluation, high-frequency probes over 18 MHz are required. In cutaneous psoriatic lesions, MSUS reveals heterogeneous thickening of the epidermis, with or without acoustic shadowing, and hypoechoic thickening of the dermis.

Regarding nail involvement, most studies assessing patients with psoriasis or PsA have used common parameters such as: nail bed thickness (NBT) and nail matrix thickness (NMT). Spectral PD signal is used to calculate the resistive index. The thickness of the extensor tendon entheses at the fingers, which is greater in PsA patients, has been correlated with nail morphology, especially the presence of onycholysis or hyperkeratosis. However, the presence of PD signal at the nail level has shown variability across studies, including variability among healthy individuals. Ultrasound-detected nail changes have also proven sensitive to change

under treatment. Limitations of nail studies include: lack of standardization (no defined number of fingers or nails to be assessed), sensitivity to change and reproducibility, particularly when using gel on nails.

The relationship between distal interphalangeal (DIP) joint involvement and nail disease has generated increased interest among dermatologists and rheumatologists, especially after histological evidence demonstrated that the extensor tendon fibers are closely connected to the periosteum of the distal phalanx as well as the nail bed and matrix. Consequently, the nail has been considered a link between the skin and joints. However, published studies show high variability in design, and interventional studies in this field remain limited.

One of the primary indications for MSUS is patients with psoriasis and joint pain. In PsA, a diagnostic delay of six months can lead to significant joint damage and functional impairment.

The transition from psoriasis to PsA typically occurs over time, on average about 10 years after the onset of skin disease. In the absence of serological markers and a universally accepted definition of early PsA, EULAR has defined three transitional stages: stage 1 – patients with high-risk cutaneous psoriasis, stage 2 – subclinical stage, stage 3 – clinical PsA phenotype.

The goal is to guide future studies toward early systemic treatment to prevent the development of PsA. High-risk PsA patients include those with extensive psoriasis, nail involvement, obesity, or a family history of psoriasis.The subclinical stage includes patients with psoriasis who experience arthralgia and imaging evidence of joint or entheseal inflammation, but no clinical synovitis. Clinical stage patients present with psoriasis and clinical synovitis.

MSUS has proven to be a valuable tool for differential diagnosis, helping distinguish PsA from other conditions such as fibromyalgia, rheumatoid arthritis, and hand osteoarthritis, which may present with overlapping clinical features. Moreover, ultrasound findings in PsA—such as enthesitis, synovitis, or nail involvement—are known to change under treatment, making these parameters increasingly used in clinical trials to demonstrate the efficacy of therapeutic products in specific disease domains.

Among the current controversies regarding MSUS in PsA, the following can be noted:

- lack of standardized ultrasound assessment methods: Although several scoring systems exist, no standardized method allows for comparison across studies to establish diagnostic criteria or treatment protocols.

- discrepancy between clinical and ultrasound findings: There is a need to identify a gold standard method to clarify these discrepancies and the significance of subclinical changes.
- reproducibility issues: Ultrasound results vary significantly depending on the observer, equipment, and operator expertise.
- clear definition of pathological findings, including threshold values and the role of PD examination
- specificity of ultrasound entheseal lesions for PsA
- detection of early PsA changes

Efforts are ongoing to achieve standardization (definition, weighting of inflammatory vs. structural lesions in scoring, equipment settings, probe positioning), validation and prediction, medical education, integration of ultrasound equipment into clinical practice, and the development of new technological devices.

Research directions confirm that musculoskeletal ultrasound (MSUS) is an imaging investigation with multiple perspectives in Psoriatic Arthritis (PsA), particularly in diagnosis, subclinical involvement detection, differential diagnosis, disease progression monitoring, and treatment assessment, proving useful for optimizing patient care.

The research hypothesis of this thesis consists in analyzing the relationship between clinical evaluation and ultrasound findings regarding disease activity, by highlighting subclinical manifestations in patients with psoriasis or identifying changes in PsA patients, with a particular focus on entheses. Entheses, central to the pathogenesis, diagnosis, and management of spondyloarthritis, remain a current research focus in PsA.

This thesis comprises four studies, including both patients with psoriasis and patients with PsA with various disease activity levels. An inter-observer study on the elementary lesions of enthesitis, defined by OMERACT criteria, was also performed. In the final section, a proposed ultrasound score aiming to stratify active inflammatory enthesitis was introduced. Across all studies, entheseal evaluations included: hypoechogenicity, increased thickness, erosions, enthesophytes, calcifications, bursitis presence, and PD signal

The objective of the first study was to describe the prevalence of enthesitis at various sites in a group of patients with psoriasis with or without PsA and to identify specific enthesis sites or ultrasound changes that could differentiate the two conditions.

Adult patients with psoriasis and PsA were clinically examined at entheseal sites using the SPARCC score and underwent MSUS on nine bilateral entheses: supraspinatus tendon, common extensor tendon of the fingers, common flexor tendon of the fingers, triceps tendon, quadriceps tendon, proximal and distal patellar tendon, Achilles tendon, and plantar fascia. At each site, the following features were assessed: thickening, hypoechogenicity, calcifications, enthesophytes, erosions, and PD signal. The evaluated entheses allowed calculation of the following ultrasound scores: Glasgow Ultrasound Enthesitis Scoring System (GUESS), Madrid Sonographic Enthesitis Index (MASEI),Belgrade Ultrasound Enthesitis Score (BUSES).Enthesitis was also assessed for lower limb entheses based on the OMERACT definition.

Among the 28 patients with psoriasis and PsA included in the study, enthesitis—a hallmark of spondyloarthritis—was evaluated in detail both clinically and ultrasonographically. In PsA patients, 27.7% of the examined entheses were painful, with the most frequent sites being the common flexor tendon insertion on the medial epicondyle and the common extensor tendon insertion on the lateral epicondyle. In psoriasis patients, 24.0% of entheses were painful, with similar predominant sites. Clinical examination revealed no statistically significant differences between the psoriasis and PsA groups regarding painful entheses.

22.6% of entheses in PsA patients and 17.1% in psoriasis patients showed at least one ultrasound abnormality: hypoechogenicity, thickening, calcifications/enthesophytes, erosions, or PD signal. The most frequently affected sites in both groups were: quadriceps tendon insertion, common extensor tendon insertion on the lateral epicondyle, supraspinatus tendon insertion on the humerus and achilles tendon insertion on the calcaneus

Based on EULAR's transition stages from psoriasis to PsA, 75% of the patients with psoriasis in this study fit the subclinical stage, presenting with arthralgia. Risk factors included nail psoriasis (33.3%) and obesity (25%).

In this subgroup, 17.1% of entheses displayed at least one ultrasound change, and OMERACT-defined enthesitis was detected in 12.0% of the evaluated sites.

Overall, the most common ultrasound lesions in this cohort were hypoechogenicity and calcifications/enthesophytes. PD signal was rarely observed, mainly at the lateral epicondyle and the tibial insertion of the distal patellar tendon.

No significantly higher numbers of OMERACT-defined enthesitis were observed in obese or metabolic syndrome patients with PsA.

Ultrasound scores (BUSES, GUESS, MASEI) showed significantly higher median values in PsA patients compared to psoriasis-only patients.

The highest agreement between clinical and ultrasound findings was noted at: lateral epicondyle and superior patellar ligament

Thus, the first study supports existing literature by demonstrating the utility of ultrasound in detecting enthesitis in psoriasis and PsA patients and in identifying subclinical enthesitis, which may assist in early diagnosis and treatment of PsA.

The second study aimed to assess the ultrasound prevalence of synovitis and active enthesitis in a group of PsA patients achieving therapeutic targets (remission or low disease activity), evaluated using the DAPSA composite index and undergoing treatment with b/tsDMARDs. It also aimed to evaluate correlations between ultrasound findings and clinical enthesitis assessment, as well as to explore ultrasound parameters as predictors of relapse over six months.

The study included 51 PsA patients meeting CASPAR criteria in remission (DAPSA < 4) or low disease activity (DAPSA < 14) were clinically and ultrasonographically assessed. Using data from the Romanian Registry of Rheumatic Diseases (RRBR), patients were monitored six months post-assessment to record any relapse (DAPSA > 14), which could lead to changes in b/tsDMARD therapy.

Evaluations included: bilateral clinical and ultrasound assessments (GS and PD) of the following entheses: common extensor tendon insertion at the lateral epicondyle, quadriceps tendon insertion on the patella, distal patellar tendon insertion on the tibia, achilles tendon insertion on the calcaneus. Clinically, pain upon standardized pressure was recorded. Ultrasound findings classified entheses as active if they met the OMERACT definition for enthesitis and had a PD score ≥ 1 (scoring scale: 0–3; 0 = absent, 1 = minimal, 2 = moderate, 3 = intense).

Joint assessments were performed on small joints of the hands and feet (RCC, MCP 1–5, MTP 1–5 bilaterally), with synovitis considered active if PD score was ≥ 1.

In the sample of 51 PsA patients who were in the therapeutic target as defined by DAPSA, at least one clinically painful enthesis was identified in 27.5% of patients, most commonly at the patellar tendon and common extensor tendon of the fingers. Additionally, a high frequency of ultrasound-detected active enthesitis and synovitis was observed in 19.6% and 17.6% of the evaluated patients, respectively. The most frequently affected tendons showing ultrasound-

confirmed active enthesitis at their insertion were the quadriceps tendon and the common extensor tendon of the fingers. When compared to the ultrasound gold standard, the performance of clinical tests for detecting enthesitis was inferior. The common extensor tendon insertion on the lateral epicondyle demonstrated the best correlation between clinical findings and ultrasound-confirmed active enthesitis. There was a higher frequency of clinical enthesitis, ultrasound-active enthesitis, and ultrasound-active synovitis in patients with low disease activity (LDA) compared to those in remission, but these differences were not statistically significant.

In patients who relapsed after six months, a statistically significant difference was observed in the following baseline parameters: pain VAS ($p < 0.001$), global VAS ($p = 0.010$), DAPSA score ($p = 0.005$), number of clinically painful entheses ($p = 0.002$), presence of active Achilles tendon enthesitis ($p < 0.005$).

These results highlight the usefulness of MSUS in detecting subclinical disease activity and monitoring treatment response in PsA. The ability of ultrasound to detect active enthesitis and synovitis, even in patients considered to be in remission, underscores its important role in the complex management of PsA.

Ultrasound-detected active synovitis and active enthesitis in PsA patients in remission could potentially serve as predictors of disease relapse and contribute to the development of a standardized approach or algorithm for using ultrasound in monitoring PsA progression. This goal aligns with findings from various studies advocating for the integration of MSUS into clinical practice to improve disease management and treatment optimization.

Twenty years after the first ultrasound description of enthesitis, the OMERACT group defined the core ultrasound features of enthesitis in 2014 by consensus, aiming to standardize clinical studies. OMERACT later validated this definition in 2018, considering as positive findings either hypoechogenicity or increased thickness of the enthesis within 2 mm from the bone, with or without PD signal, or the presence of enthesophytes, erosions, or calcifications.

The third study aimed to assess inter-observer agreement among rheumatologists routinely using MSUS, focusing on the diagnosis of Achilles enthesitis, evaluation of PD signal activity, and the presence of each ultrasound feature of enthesitis (hypoechogenicity, thickening, erosions, enthesophytes, calcifications) according to OMERACT criteria, specifically at the Achilles tendon insertion in a PsA patient cohort.

The Achilles tendon insertion was chosen due to its easy accessibility, making it a reference anatomical site for ultrasound assessment in all major enthesitis scoring systems. It is the most frequently involved tendon in PsA, where PD activity and erosions are highly discriminatory compared to healthy individuals (rarely present in non-PsA patients).

Participants were adult PsA patients meeting CASPAR criteria, selected from the outpatient clinic of the "Dr. Ion Stoia" Rheumatic Disease Clinical Center. Patients underwent clinical and MSUS examinations of the Achilles tendon, evaluating the presence or absence of the following enthesitis features: hypoechogenicity, thickening, calcifications, enthesophytes, bone erosions and PD signal at the enthesis.

Additionally, the extra-entheseal PD signal and the presence of retrocalcaneal bursitis, with or without PD signal, were assessed. Two ultrasound machines were used: GE LOGIQ E10 (GS and PD) with a 4–20 MHz linear probe and MyLab Twice ESAOTE (GS and PD) with a 7–18 MHz linear probe. Patients were consecutively evaluated by four examiners on both machines, and findings were scored simultaneously. Images of the Achilles tendon insertion were collected for all patients and later reviewed.

Both the live inter-observer study and the recorded image review showed high agreement on the following OMERACT features: enthesophytes ($\kappa > 0.6$), erosions ($\kappa > 0.5$) and enthesis thickness ($\kappa > 0.5$).However, low agreement was noted for hypoechogenicity (κ between 0.1 and 0.4), confirming its subjective and operator-dependent nature.

The lower agreement on PD signal detection ($\kappa = 0.35/0.45$) in the live inter-observer study highlights the need for educational interventions on PD signal detection and interpretation in MSUS.

The PD signal is a key feature in evaluating active enthesitis, especially in PsA and SpA. Its accuracy depends on both the quality of the ultrasound machine (requiring high-end equipment) and the examiner's expertise and experience.

In 2018, OMERACT published a consensus on the core ultrasound lesions defining enthesitis in spondyloarthritis. However, the group did not specify particular anatomical sites or define "active enthesitis", especially inflammatory enthesitis, which was an essential step toward standardizing future studies in this field. Ultrasound-detected enthesitis abnormalities, such as PD signal, are associated with joint damage and may serve as biomarkers of disease

severity. The forth study aimed to identify specific ultrasound diagnostic criteria to detect active, inflammatory enthesitis in PsA patients.

The methodology was the same like in the third study, using Achilles tendon insertion images focused on the enthesis, with PD signal distance measurements from the cortical bone, according to EULAR imaging guidelines, and displaying all potential pathological enthesitis features. 75 images were analyzed by 10 rheumatologists, each with at least 5 years of MSUS expertise.

The Achilles tendon was again selected for its superficial location, making it easy to assess. However, confounding factors such as age and body mass index—both associated with an increased risk of tendinosis and calcifications—were noted as potential limitations.

Each image was evaluated for: enthesis thickening, hypoechogenicity, enthesophytes, calcifications, bone erosions, PD signal at the enthesis. Bursitis presence and vascularization were also assessed. At the end, the evaluators were asked to classify each of 20 enthesis images as indicating “inflammatory enthesitis”, with three possible responses: “yes”/ “no”/ “possibly”.

Following the database analysis, hypoechogenicity was again identified as the least reproducible ultrasound feature among evaluators, consistent with the findings from the previous study. PD signal was detected in 9.8% of evaluations without confirmed enthesitis.
It was observed that 84.4% of enthesitis cases labeled as definitely inflammatory displayed at least four ultrasound features from the enthesitis definition.

Hypoechogenicity, increased thickness, erosions, bursitis, and the presence of PD signal—whether in the enthesis, in erosions, or in the bursa—were all associated with active inflammatory enthesitis. Erosions and PD signal in erosions showed statistically significant differences between "probable" and "definite" enthesitis. Only in "definite" enthesitis were PD signals of grade 2 or 3 identified in erosions or simultaneously in the enthesis and erosions.
For bursal PD signal, grade 3 was exclusively found in "definite" enthesitis.

Considering the findings, for a patient diagnosed by GS ultrasound with enthesitis (i.e., showing either thickening or hypoechogenicity), the following scoring system is proposed, which is based on the OMERACT definitions:

- 2 points for PD signal > 1 at the enthesis
- 1 point for PD signal grade 1 at the enthesis
- 1 point for presence of at least one erosion

- 1 point for PD signal in the erosion
- 1 point for PD signal > 2 in bursitis

An inflammatory enthesitis is defined by a total score of at least 2.

This thesis presents a proposed ultrasound score combining PD signal and structural damage (erosions), which demonstrated good overall performance, with a sensitivity of 67% and a specificity of 100%.

Using the same set of 75 ultrasound images from the Achilles tendon insertions of 10 PsA patients, an inter-observer study was conducted between the author and an internationally recognized expert in MSUS, Professor Dr. Emilio Filippucci, one of the authors of the OMERACT enthesitis definition and a prominent researcher in this field.

The study assessed agreement on the diagnosis of enthesitis and active enthesitis according to OMERACT.

Statistical analysis revealed: good agreement for enthesitis diagnosis ($\kappa = 0.529$), substantial agreement for active enthesitis diagnosis ($\kappa = 0.733$), without statistically significant differences.

This thesis highlights personal contributions in advancing the role of MSUS as a complementary tool to clinical assessment, offering additional insights into subclinical inflammatory activity in patients otherwise considered to have reached therapeutic targets.
Relying solely on clinical assessment may overlook ongoing subclinical inflammation, potentially leading to disease progression if left untreated.

The novelty of this study consists in using MSUS to detect active enthesitis and synovitis in PsA patients classified as being in therapeutic target (DAPSA < 14). A notable percentage of patients showed ultrasound evidence of active disease, with 19.6% presenting active enthesitis and 17.6% active synovitis. Ultrasound proved useful for preventing unnecessary treatment de-escalation in patients at risk of relapse.

This thesis presents the first published study focused on ultrasound monitoring of entheses in PsA patients in therapeutic target under b/tsDMARD treatment.

In the third study, inter-observer agreement data were presented for enthesitis components in PsA patients, a topic seldom addressed in the literature. Kappa values were calculated using Light's method for each enthesitis component, showing the level of agreement between observers in using standardized definitions—crucial for validating ultrasound as a diagnostic

tool. Most PsA enthesitis studies focus on prevalence and clinical correlations, not on observer agreement.

The forth study aimed to define diagnostic criteria for inflammatory enthesitis using advanced ultrasound techniques, contributing a valuable diagnostic and monitoring tool in PsA. A new ultrasound score was proposed, combining PD signal and erosions, which could be validated against a gold standard (e.g., MRI) or compared to a control group without inflammatory conditions. Developing and validating a PsA-specific score for inflammatory enthesitis diagnosis remains a key challenge.

It is essential to define the clinical relevance of ultrasound-detected inflammation. Inflammatory enthesitis implies more than active enthesitis; it refers to clinically relevant inflammation requiring therapeutic intervention and treatment adjustment based on its presence or absence.

Each study successfully met its scientific objectives, using high-performance ultrasound equipment, yielding results consistent with the specialized literature. Limitations include: small sample size, lack of a control group. However, the study's strengths include: evaluation of both cutaneous psoriasis patients and PsA patients with varying disease activity, comprehensive assessment of multiple entheses

The final two studies involved experienced MSUS specialists, including: an internationally recognized evaluator, two rheumatologists with EULAR "Teach the Teacher" certification

This thesis aligns with EULAR's research priorities, focusing on: correlation between clinical and ultrasound changes, reproducibility of ultrasound evaluation (inter-observer variability), clear definition of pathological changes and detection of subclinical alterations

Future research directions include collaboration with dermatology clinics to expand the patient database, with 24-month follow-up to monitor transition to PsA and risk factor identification for early diagnosis and organizing interdisciplinary meetings to tailor treatment based on individual patient profiles. We also propose to validate an inflammatory enthesitis score in a control group of patients with risk factors (e.g., obesity, metabolic syndrome) but without inflammatory rheumatic diseases

All articles published based on the research conducted in this thesis have received citations in specialized literature.

In the author’s opinion, this doctoral thesis makes an important contribution to advancing knowledge on the diagnostic value of ultrasound examination in PsA patients.