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Published in:
Rheumatology Advances in Practice

DOI:
[10.1093/rap/rkab056](https://doi.org/10.1093/rap/rkab056)

Publication date:
2021

Document Version
Publisher's PDF, also known as Version of record

[Link to publication in ResearchOnline](#)

Citation for published version (Harvard):
Patience, A, Steultjens, MP & Hendry, GJ 2021, 'Ultrasound features of achilles enthesitis in psoriatic arthritis: a systematic review', *Rheumatology Advances in Practice*, vol. 5, no. Supplement 2, pp. ii19-ii34.
<https://doi.org/10.1093/rap/rkab056>

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Systematic review

Ultrasound features of Achilles enthesitis in psoriatic arthritis: a systematic review

Aimie Patience¹, Martijn P. Steultjens¹ and Gordon J. Hendry¹

Abstract

Objectives The objectives were to evaluate the methodological and reporting quality of ultrasound (US) studies of Achilles enthesitis in people with psoriatic arthritis (PsA), to identify the definitions and scoring systems adopted and to estimate the prevalence of ultrasound features of Achilles enthesitis in this population.

Methods A systematic literature review was conducted using the AMED, CINAHL, MEDLINE, ProQuest and Web of Science databases. Eligible studies had to measure US features of Achilles enthesitis in people with PsA. Methodological quality was assessed using a modified Downs and Black Quality Index tool. US protocol reporting was assessed using a checklist informed by the European League Against Rheumatism (EULAR) recommendations for the reporting of US studies in rheumatic and musculoskeletal diseases.

Results Fifteen studies were included. One study was scored as high methodological quality, 9 as moderate and 5 as low. Significant heterogeneity was observed in the prevalence, descriptions, scoring of features and quality of US protocol reporting. Prevalence estimates (% of entheses) reported included hypoechogenicity [mean 5.9% (s.d. 0.9)], increased thickness [mean 22.1% (s.d. 12.2)], erosions [mean 3.3% (s.d. 2.5)], calcifications [mean 42.6% (s.d. 15.6)], enthesophytes [mean 41.3% (s.d. 15.6)] and Doppler signal [mean 11.8% (s.d. 10.1)].

Conclusions The review highlighted significant variations in prevalence figures that could potentially be explained by the range of definitions and scoring criteria available, but also due to the inconsistent reporting of US protocols. Uptake of the EULAR recommendations and using the latest definitions and validated scoring criteria would allow for a better understanding of the frequency and severity of individual features of pathology.

Key words: psoriatic arthritis, Achilles tendon, ultrasound, enthesitis, scoring, systematic review

Key messages

- There is significant variation in the reported prevalence of Achilles enthesitis ultrasound features in PsA.
- Studies should adopt up-to-date, validated definitions and scoring of ultrasound pathology at the Achilles tendon/entheses.
- Uptake of the new EULAR recommendations should address the inconsistency in ultrasound reporting highlighted.

Introduction

Enthesitis is a hallmark feature of psoriatic arthritis (PsA) and presents as inflammation at the site of soft tissue insertion to bone [1]. The most common site of enthesitis in PsA is the Achilles tendon insertion to the calcaneum [2, 3]. Enthesitis can significantly limit a person's ability to carry out essential activities of daily living and can impact health-related quality of life [4]. Achilles

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Submitted 15 April 2021; accepted 28 July 2021

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enthesitis is often difficult to treat and can persist despite the initiation or escalation of pharmacological management. The current recommended first-line therapies for enthesitis in PsA are non-steroidal anti-inflammatory drugs (NSAIDs) and physiotherapy. Persistent symptoms may require escalation to biologic therapies (TNF inhibitors, IL-12/IL-23i) and/or corticosteroid injection [5].

Ultrasound (US) is highly sensitive for assessing inflammation and can detect different features of enthesitis including tendon thickening, hypoechogenicity, erosions, enthesophytes and subclinical enthesitis in people with PsA [6, 7]. Access to US imaging varies so enthesitis diagnosis is often based on clinical assessment, typically measured using the Leeds Enthesitis Index [8]. Clinical assessment may be able to detect swelling that could be indicative of moderate to severe thickening of the Achilles tendon but can be difficult to distinguish from the presence of an enlarged retrocalcaneal bursa, hindfoot joint effusion or oedema [9]. Unlike US, clinical assessment cannot measure pathology and compare it to a normative value and is unlikely to be able to assess other pathological features of enthesitis (e.g. enthesophytes and erosion). Clinical assessment of Achilles enthesitis in people with PsA has shown poor correlation with US [10]. Furthermore, it is difficult to differentiate between the pain response of fibromyalgia (FM) and PsA-related enthesitis at enthesal sites [11].

US has shown good sensitivity and specificity for detecting Achilles enthesal pathology in PsA and there are a variety of US feature definitions and scoring systems available. The Glasgow Ultrasound Enthesitis Scoring System (GUESS) [12] provides definitions of enthesal abnormality in the lower limbs in patients with spondyloarthritis (SpA) (36 bilateral enthesal sites scored present/absent, total/36 points). The Achilles subscale of the GUESS criteria (8/36 bilateral enthesal sites) refers to Achilles tendon thickness ≥ 5.29 mm, retrocalcaneal bursitis, posterior pole of calcaneus erosion and posterior pole of calcaneus enthesophytes. The OMERACT US Task Force defines enthesopathy as ‘abnormally hypoechoic (loss of normal fibrillar architecture) and/or thickened tendon or ligament at its bony attachment (may occasionally contain hyperechoic foci consistent with calcification), seen in 2 perpendicular planes that may exhibit Doppler signal and/or bony changes including enthesophytes, erosions, or irregularity’ [13]. The Madrid Sonographic Enthesitis Index (MASEI) offers both binary and semi-quantitative scoring of Achilles enthesal features and has been shown to have face validity as a diagnostic tool for patients with SpA [14]. In an attempt to provide homogeneity in assessing and reporting US enthesitis, a Delphi study elicited agreement for the inclusion of hypoechogenicity, increased tendon thickness, enthesophytes, calcifications, erosions and Doppler signal ≥ 2 mm from the bony insertion as features of enthesitis [15]. The OMERACT Ultrasound Task Force subsequently evaluated the reliability of the definitions and scoring for enthesitis in SpA and agreed on an accepted definition that separates US features

into inflammatory (Doppler signal, hypoechogenicity, thickened enthesitis) and structural (calcifications/enthesophytes and erosions at the enthesitis) with each component scored as either present/absent [7].

Heterogeneous definitions of US-detected pathologies and scoring systems may affect the validity and generalizability of results of US studies of enthesitis in PsA. Thus it is important that studies adopt contemporary standardized definitions, employ validated scoring systems and systematically describe US scanning protocols. The EULAR recommendations for the reporting of US studies in rheumatic and musculoskeletal diseases (RMDs) [16] are the first to provide a checklist to aid the reporting of US imaging in rheumatology research. The checklist covers domains such as the blinding of sonographers, scanning acquisition and scoring, equipment (e.g. US machine and transducer brand and model) and equipment settings (conventional B-mode and Doppler). Until these recommendations are widely implemented, it is likely that study heterogeneity may limit the generalizability and clinical utility of findings. Evaluation of the current literature with regards to the quality of the evidence and reporting of US features of enthesitis in PsA will provide a key point of reference whereby reports of US pathology can be interpreted in the context of study heterogeneity, which may help to inform development of an optimum systematic approach to enthesitis management with US in the future.

Accordingly, the primary aims of this systematic review were to evaluate the methodological and reporting quality of US studies of enthesitis at the Achilles tendon in people with PsA, to identify the definitions and scoring systems adopted and to estimate the prevalence of US features of enthesitis in this population.

Methods

Review protocol

The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) 2020 guideline were followed throughout the review process (Supplementary Table S1, available at *Rheumatology Advances in Practice* online) [17].

Search strategy

Five electronic databases were searched [AMED, CINAHL and MEDLINE (via EBSCO host); ProQuest (Health and Medical Collection and Nursing and Allied Health Database) and Web of Science core collection] from conception of the study to 10 March 2021 and the ‘auto-alert’ function delivered weekly updates of any subsequent publications until April 2021. Peer-reviewed studies that included a reference to at least one of the following were sought for inclusion: hypoechogenicity, increased thickness of the tendon, erosions, bursitis, calcifications, enthesophytes and Doppler signal detected on US at the Achilles tendon in patients with PsA. Key words and combinations specific to each

TABLE 1 Search strategy

	Articles, n
AMED (EBSCO host)	
S1 'psoriatic arthritis' OR PsA OR 'psoriatic arthropath*' OR spondyloarth*	152
S2 'achilles tend*' OR 'tendo achilles' OR 'achilles paraten*' OR 'calcaneal tendon' OR 'tendo calcaneus' OR 'achilles enthes*' OR 'achilles insertion' OR 'achilles burs*' OR 'retrocalcaneal burs*' OR PDUS OR 'colour doppler' OR 'colour doppler' or elastograph*	1290
S3 ultrasound OR scan OR sonograph* OR ultrasonograph* OR US OR MSUS OR 'power doppler' OR PDUS OR 'colour doppler' OR 'colour doppler' or elastograph*	6424
S4 S1 AND S2 AND S3	3
CINAHL (EBSCO host)	
S1 'psoriatic arthritis' OR PsA OR 'psoriatic arthropath*' OR spondyloarth*	9396
S2 'achilles tend*' OR 'tendo achilles' OR 'achilles paraten*' OR 'calcaneal tendon' OR 'tendo calcaneus' OR 'achilles enthes*' OR 'achilles insertion' OR 'achilles burs*' OR 'retrocalcaneal burs*' OR PDUS OR 'colour doppler' OR 'colour doppler' or elastograph*	4409
S3 ultrasound OR scan OR sonograph* OR ultrasonograph* OR US OR MSUS OR 'power doppler' OR PDUS OR 'colour doppler' OR 'colour doppler' or elastograph*	284 805
S4 S1 AND S2 AND S3	22
MEDLINE (EBSCO host)	
S1 'psoriatic arthritis' OR PsA OR 'psoriatic arthropath*' OR spondyloarth*	41 296
S2 'achilles tend*' OR 'tendo achilles' OR 'achilles paraten*' OR 'calcaneal tendon' OR 'tendo calcaneus' OR 'achilles enthes*' OR 'achilles insertion' OR 'achilles burs*' OR 'retrocalcaneal burs*' OR PDUS OR 'colour doppler' OR 'colour doppler' or elastograph*	9143
S3 ultrasound OR scan OR sonograph* OR ultrasonograph* OR US OR MSUS OR 'power doppler' OR PDUS OR 'colour doppler' OR 'colour doppler' or elastograph*	1 033 146
S4 S1 AND S2 AND S3	67
ProQuest (Health and Medical Collection and Nursing and Allied Health Database)	
S1 'psoriatic arthritis' OR PsA OR 'psoriatic arthropath*' OR spondyloarth*	16 493
S2 'achilles tend*' OR 'tendo achilles' OR 'achilles paraten*' OR 'calcaneal tendon' OR 'tendo calcaneus' OR 'achilles enthes*' OR 'achilles insertion' OR 'achilles burs*' OR 'retrocalcaneal burs*' OR PDUS OR 'colour doppler' OR 'colour doppler' or elastograph*	2726
S3 ultrasound OR scan OR sonograph* OR ultrasonograph* OR US OR MSUS OR 'power doppler' OR PDUS OR 'colour doppler' OR 'colour doppler' or elastograph*	702 600
S4 S1 AND S2 AND S3	61
Web of Science (Core Collection)	
S1 TOPIC=('psoriatic arthritis' OR PsA OR 'psoriatic arthropath*' OR spondyloarth*)	40 194
S2 TOPIC=('achilles tend*' OR 'tendo achilles' OR 'achilles paraten*' OR 'calcaneal tendon' OR 'tendo calcaneus' OR 'achilles enthes*' OR 'achilles insertion' OR 'achilles burs*' OR 'retrocalcaneal burs*')	8034
S3 TOPIC=(ultrasound OR scan OR sonograph* OR ultrasonograph* OR US OR MSUS OR 'power doppler' OR PDUS OR 'colour doppler' OR 'colour doppler' OR elastograph*)	1 901 299
S4 S1 AND S2 AND S3	79
Total number of articles	232
Total number without duplicates	146

database were used relating to PsA, Achilles tendon enthesitis/pathology and US scoring (Table 1). The search strategy, including a search of reference lists for further eligible texts, was conducted by one reviewer (A.P.).

Inclusion and exclusion criteria

All titles were screened and the subsequent abstracts and full-text papers were reviewed (Supplementary Fig. S1, available at *Rheumatology Advances in Practice* online). Selected studies had to describe original research findings, be published in the English language in a peer-reviewed journal, assess adults ≥18 years of age and describe US features of the Achilles tendon and/or the Achilles entheses in a PsA population. Pharmacological studies were included if they provided sufficient information at baseline. Studies did not have to include a

healthy control group for comparison and no limit was set on the date of publication. Studies that indicate only the presence/absence of Achilles enthesitis were excluded. Review articles, case studies/reports, abstracts, research papers involving non-human subjects and non-English articles were excluded.

Assessment of methodological quality

Methodological quality was independently assessed by two reviewers (A.P. and G.H.) and a modified version of the Quality Index (QI) tool by Downs and Black was used to assess the quality of studies (Table 2) [18]. The 15 items that were included allowed for identification of methodological pitfalls including sampling methods, use of valid and reliable outcome measures and appropriate adjusting for confounding variables in the statistical analysis. A modified version of Q10 was

TABLE 2 Modified Downs and Black Quality Index checklist

1	Is the hypothesis/aim/objective of the study clearly described?
2	Are the main outcomes to be measured clearly described in the Introduction or Methods section? If the main outcomes are first mentioned in the Results section, the question should be answered no. All primary outcomes should be described for yes.
3	Are the characteristics of the patients included in the study clearly described? In cohort studies and trials, inclusion and/or exclusion criteria should be given. In case-control studies, a case definition and the source for controls should be given. Single case studies must state the source of the patient.
5	Are the distributions of principal confounders in each group of subjects to be compared clearly described? A list of principal confounders is provided. YES = age, severity.
6	Are the main findings of the study clearly described? Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions.
7	Does the study provide estimates of the random variability in the data for the main outcomes? In non-normally distributed data the IQR of results should be reported. In normally distributed data the s.e., s.d. or CI should be reported.
10	Have 95% CIs and/or actual <i>P</i> -values been reported for the main outcomes, except where the <i>P</i> -value is <0.001?
11	Were the subjects asked to participate in the study representative of the entire population from which they were recruited? The study must identify the source population for patients and describe how the patients were selected.
12	Were those subjects who were prepared to participate representative of the entire population from which they were recruited? The proportion of those asked who agreed should be stated.
16	If any of the results of the study were based on 'data dredging', was this made clear? Any analyses that had not been planned at the outset of the study should be clearly indicated. Retrospective = no, prospective = yes.
18	Were the statistical tests used to assess the main outcomes appropriate? The statistical techniques used must be appropriate to the data. If no tests were done, but would have been appropriate to do = no.
20	Were the main outcome measures used accurate (valid and reliable)? Where outcome measures are clearly yes/no/UTD described, which refer to other work or that demonstrates the outcome measures are accurate = yes. All primary outcomes valid and reliable for yes.
21	Were the patients in the cases and controls (case-control studies) recruited from the same population? The question should be answered UTD for cohort and case-control studies where there is no information concerning the source of patients.
22	Were study subjects in the cases and controls (case-control studies) recruited over the same period of time? For a study that does not specify the time period over which patients were recruited, the question should be answered as UTD.
25	Was there adequate adjustment for confounding in the analyses from which the main findings were drawn? In non-randomized studies, if the effect of the main confounders was not investigated or no adjustment was made in the final analyses the question should be answered as no. If no significant difference between groups shown then yes.

incorporated from MacLehose *et al.* [19]. A binary scoring of 1 for 'yes' or 0 for 'unable to determine/no' was applied to each item and studies were rated overall as high (>85%), moderate (≥60%) or low (<60%) based on a previous study that utilized a similarly modified Downs and Black QI criteria for assessing the risk of bias [20].

Assessment of the US reporting protocol

During the development of this review the 2021 EULAR recommendations for the reporting of US studies in RMDs [16] were published. Although the EULAR recommendations were not intended for scoring published work, we believed it was important to incorporate aspects of the new consensus-based checklist (specifically around scoring and measurement reporting) into the review design in the absence of any validated scoring criteria.

Data extraction

A standardized data extraction form was used to obtain information on the study design, participant characteristics, description of the US machine and settings, imaging techniques and the frequency and descriptions of Achilles tendon/entheses US characteristics. The use of scoring or measurement tools and validation status were reported.

Descriptive analyses

Descriptive statistics, including means, s.d.s, medians, ranges and interquartile ranges (IQRs) were used to summarize prevalence estimates of US features.

Results

The database search identified 232 records to be screened. Following the removal of duplicates and the

TABLE 3 Studies included in the review

Reference	Study setting	Study population	US feature of Achilles pathology	Frequency	Description of US features	Scoring of US features	Validated/non-validated
Ahmed <i>et al.</i> [3]	Unknown Main author: Kuwait	65 PsA (35 active, 30 'inactive' controls) (CASPAR criteria)	Active PsA (/70 AT entheses): Thickened Enthesophyte Bone erosion Bursitis	10/70 (34.5%) 13/70 (14.9%) 2/70 (2.3%) 2/70 (2.3%)	No definitions provided	Achilles tendon >5.29 mm thickened (we assume from Balint <i>et al.</i> [12]), but no source identified	Not applicable
Bandinelli <i>et al.</i> [30]	Florence, Italy ePsA Clinic of the Division of Rheumatology of the University of Florence	92 PsA (CASPAR criteria) with onset of rheumatologic inflammatory symptoms >1 year, with and without psoriasis. 40 healthy controls	Early PsA: (/92 R entheses and 92 I entheses) Thickness Enthesophytes Bursitis Erosions PD	R 38%, L 29.3% R 52.1%, L 55.4% R 5.4%, L 7.6% R 2%, L 1% R 14.1%, L 18.5%	GUESS criteria [12]: Thickness: measured at the point of the maximal thickness proximal to the bone insertion. Achilles >5.29 mm Enthesophytes: as an ossification of entheses with irregularity of cortical bone insertion Erosions: a cortical break with a step down defect of bone contour (visible in the longitudinal and transverse axis) Bursitis: a well-circumscribed, localized anechoic or hypoechoic area at the site of an anatomical bursa, compressible by the transducer, with short axis >2 mm	GUESS [12] criteria to score/assess thickness, enthesophytes, bursitis, bony erosions. PD signal: binary (present/absent) and semi-quantitative (D'Agostino <i>et al.</i> [21]) Total PD calculated by adding PD scores of each tendon (16 entheses)	GUESS = validated D'Agostino PD scoring
EIMallah <i>et al.</i> [31]	Egypt Ain Shams University Hospitals	31 axial or peripheral SpA according to the Assessment of SpondyloArthritis International Society (ASAS) classification criteria. 12 PsA, 12 AS, 7 ReA	PsA (R/12, L/12): Erosions Calcification Hypoechogenicity Thickening PD	R 0 (0%), L 0 (0%) R 3 (25%), L 3 (25%) R 1 (8.3%), L 0 (0%) R 1 (8.3%), L 0 (0%) R 0 (0%), L 0 (0%)	No in-text definition provided but referred to Terslev <i>et al.</i> [15] in Methods and OMERACT 2018 [7] in Introduction	B-mode and PD binary present/absent. Enthesitis classified into 5 stages according to D'Agostino <i>et al.</i> [22]: vascularization at the cortical junction without abnormal findings in B mode 2a. vascularization associated with swelling and/or decreased echogenicity at the cortical junction in B mode 3a. same as stage 2a, plus erosions of cortical bone and/or calcification of enthesis, and optional surrounding bursitis.	D'Agostino (2003) not validated

(continued)

TABLE 3 Continued

Reference	Study setting	Study population	US feature of Achilles pathology	Frequency	Description of US features	Scoring of US features	Validated/non-validated
Falsetti <i>et al.</i> [32]	Italy Institute of Rheumatology of the University of Siena	56 erosive OA, 209 nodal OA, 158 RA, 125 PsA and 50 controls. PsA (Moll and Wright criteria)	PsA (/125 subjects): Achilles tendon enthesitis Deep retrocalcaneal bursitis Posterior calcaneal erosions	10/125 (8%) 8/125 (6%) 6/125 (5%)	Reference to 4 papers for definitions [23–26]: Enthesitis: heterogeneous hypoechogenicity and thickening of enthesis, possibly associated with enthesophytosis, erosions, and peritendinous oedema Bursae: anechoic bursal space widening (interpreted as effusion), homogeneous echoic or irregularly echoic widening Erosions: an interruption of the cortical bone profile	2b. abnormal findings in B mode as in stage 2a, but without vascularization 3b. abnormal findings in B mode as in stage 3a, but without vascularization Inflammatory US features graded semi-quantitatively: grade 1 (mild, grade 2 (moderate) and grade 3 (considerable)	Not validated
Farouk <i>et al.</i> [33]	Egypt Rheumatology, Dermatology Departments and Rheumatology outpatient clinic, Ain Shams University Hospital	30 psoriasis, 30 PsA as controls (CASPAR criteria)	PsA (/30 subjects): Enthesial ‘abnormalities’	14/30 (46.7%)	Early US features of enthesitis: loss of normal fibrillar echogenicity, hypoechoic swelling of tendon insertion, effusion, increase of blood flow (PD) and retrocalcaneal bursitis [27, 28]	No scoring/grading of pathology	Not applicable
Fiorenza <i>et al.</i> [34]	Italy Rheumatology Department of the University Hospital of Messina	23 FM, 39 FM and PsA, 39 PsA (CASPAR criteria)	PsA only + PsA and FM (/156 AT entheses): Thickening Bursitis Erosions Enthesophytes PD signal	63 (40.3%) 13 (8.3%) 6 (3.8%) 86 (55.1%) 46 (29.4%)	Enthesial pathology defined by OMERACT (2018) [7] definitions: Enthesal thickness was measured at the point of maximal thickness 2 mm proximal to the bony insertion >5.29 mm Bursitis: well-circumscribed, localised anechoic or hypoechoic area at the site of an anatomical bursa that could be compressed by the transducer Erosions: cortical interruptions with a step-down contour defect	Scored using GUESS criteria [12] PD evaluated ≤2mm from tendon insertion to bone	GUESS = validated

(continued)

TABLE 3 Continued

Reference	Study setting	Study population	US feature of Achilles pathology	Frequency	Description of US features	Scoring of US features	Validated/non-validated
Freeston <i>et al.</i> [35]	Unknown Main author: UK	42 new-onset PsA (CASPAR criteria), 10 healthy controls	Early PsA Retrocalcaneal bursa effusion grade (296 entheses): 0 1 2 3 Erosive changes Bone spurs	189 (75%) 42 (16.7%) 18 (7.1%) 3 (1.2%) <4% 41	Enthesophytes: step-up bony prominence at the end of a normal bone profile Mention of EULAR-OMERACT Ultrasound Group but no in-text reference provided Divided into 'active inflammation' and 'structural change' PD signal found within the tendon 2 mm proximal to the bony insertion (not in the body of the tendon or bursa) Erosions had to be identified in two planes and near tendon insertion	B-mode and PD scored semi-quantitatively based on Brown <i>et al.</i> in RA [29] Greyscale (GS) = composite score of thickening and hypoechogenicity. Highest score = GS score Bursae scored 0–3 for bursal effusion Structural change binary present/absent score GS > 1 and/or a PD score > 0 = US enthesal abnormality	Not validated
Galluzzo <i>et al.</i> [36]	Italy Rheumatology Unit of the University of Pisa	31 PsA (Moll and Wright criteria), 9 healthy controls	Foci of retrocalcaneal bursitis Enthesopathic foci at Achilles tendon	10/31 6/31 (11 entheses)	Enthesitis: thickening of tendon insertion, focal intra-tendinous changes, calcium deposits at insertion and perosteal changes Bursitis: enlarged retrocalcaneal bursa which is oval-shaped, hypoechoic swelling Tendon measured 1 cm and 2 cm from insertion	No scoring/grading of pathology	Not applicable
Litinsky <i>et al.</i> [42]	Israel Departments of Rheumatology of the Tel Aviv Sourasky Medical Center (Tel Aviv, Israel) and the Rambam Medical Center (Haifa, Israel)	43 PsA (CASPAR criteria). Group 1 = 19 PsA beginning MTX, group 2 = 23 PsA starting ADA	Group 1 Mean AT thickness at baseline (s.d.) Group 2 Mean AT thickness at baseline (s.d.)	R 0.39 (0.10) L 0.36 (0.08) R 0.34 (0.10) L 0.37 (0.08)		No scoring/grading of pathology	Not applicable
Marchesoni <i>et al.</i> [37]	Italy UOC Day Hospital of	30 fibromyalgia, 30 PsA (CASPAR criteria)	Enthesopathy /60 AT entheses) Inflammatory lesions /60 AT	38 (63.3%) 35 (58.3%)	Enthesopathy defined by OMERACT (2007) definitions [7] detailed previously	0–4 semi-quantitative scoring system (0 = absent; 1 = mild;	Not validated

(continued)

TABLE 3 Continued

Reference	Study setting	Study population	US feature of Achilles pathology	Frequency	Description of US features	Scoring of US features	Validated/non-validated
	Medical College	psoriasis and 20 healthy controls	Enthesophytes Bursitis Erosions PD	68 (56.67%) 9 (7.5%) 9 (7.5%) 18 (15.0%)		flow (grade 0); only one spot detected (mild or grade 1); 2 spots (moderate or grade 2); >3 spots (severe or grade 3) as per D'Agostino et al. [21]. Total PD score for each tendon calculated	D'Agostino, 2003 = not validated

screening of titles and abstracts, 20 papers were deemed eligible for full-text screening (Supplementary Fig. S1, available at *Rheumatology Advances in Practice* online). Five papers did not meet the eligibility criteria and were removed, thus 15 papers were included (Table 3) [3, 10, 30–42]. The date of publication ranged from 2000 [36] to 2020 [31, 34], with studies from Italy [30, 32, 34, 36–38], Egypt [31, 33], the UK [35, 40], Kuwait [3], Israel [42], Norway [10], China [41] and The Netherlands [43].

A total of 832 participants with PsA (1664 Achilles entheses) were assessed using US. The diagnosis of PsA was mostly based on the 2006 Classification for Psoriatic Arthritis (CASPAR) criteria [44], two studies [32, 36] published prior to 2006 used the Moll and Wright criteria [45] and two studies did not explicitly state the diagnostic criteria [31, 39]. The sample sizes of PsA patients were relatively small, ranging from 12 [31] to 141 [10]. Of the studies that reported a healthy control group ($n=7$), 183 healthy control participants were included (99 females, 84 males; mean age 42.3 years) [30, 32, 35, 36, 39–41]. Two studies identified PsA patients as a ‘control’ group (one as ‘inactive’ PsA and one comparing psoriasis to PsA) [3, 33]. The majority of studies focussed exclusively on PsA [3, 10, 30, 35, 36, 38–40, 42]; however, other comparator groups included patients with psoriasis [33, 41], FM [34, 37], SpA [31] and other types of arthritis [32].

Quality assessment

One study was rated as high quality [10], nine as moderate quality [3, 32, 34, 35, 37, 39–42] and five as low quality [30,31, 33, 36, 38] (Fig. 1). Very few studies provided sufficient information on their sampling methods, specifically the proportion of those asked who agreed to take part (Q12), the time period over which participants (and controls) were recruited (Q22) or the actual probability values for main outcome measures (Q10). The quality index scores ranged from 7/15 (47%) to 13/15 (87%) with a median score of 9 (IQR 2.5).

US protocol reporting

Further details of US protocol reporting can be found in Table 4 and Supplementary Table S2, available at *Rheumatology Advances in Practice* online. Measurements were performed by rheumatologists [10, 30, 34, 37, 41, 42], sonographers [35, 39] and radiologists [3, 38] and 10 studies reported blinding to the results of the clinical examination or other imaging results [30, 32–39, 41]. Levels of US proficiency described included ‘expert’ [3, 36], ‘experienced’ [10, 30, 32, 37, 38, 41] or ‘trained’ [34, 35, 39]. Patient positioning was detailed in seven studies as patients lying prone with their feet hanging off the examination table at 90° flexion [3, 10, 30, 34, 35, 39, 41]. Scanning in both longitudinal and transverse planes was reported in 8/15 studies [3, 10, 32, 33, 35, 36, 38, 39]. All studies reported details of both the brand and model of US machine and

Fig. 1 Quality assessment

Study author	Modified Downs and Black Qi tool questions															Score	
	1	2	3	5	6	7	10	11	12	16	18	20	21	22	25		
Michelsen et al	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	UTD	UTD	Y	13 (87%)
Fiorenza et al	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	UTD	N	12 (80%)
Wervers et al	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y	Y	Y	N	N	12 (80%)
Marchesoni et al	Y	Y	Y	Y	Y	Y	Y	Y	Y	UTD	Y	Y	Y	UTD	UTD	N	11 (73%)
Ahmed et al	Y	Y	Y	Y	Y	Y	Y	N	UTD	N	Y	Y	Y	Y	N	UTD	10 (67%)
Litinsky et al	Y	Y	Y	N	Y	Y	Y	N	Y	N	Y	Y	Y	Y	UTD	N	10 (67%)
Xie et al	Y	Y	Y	Y	Y	Y	Y	N	UTD	UTD	Y	Y	Y	Y	UTD	N	10 (67%)
Falsetti et al	Y	Y	Y	N	Y	Y	N	N	Y	N	Y	Y	Y	Y	UTD	UTD	9 (60%)
Freeston et al	Y	Y	Y	Y	Y	Y	N	N	UTD	Y	Y	Y	Y	UTD	UTD	N	9 (60%)
Woodburn et al	Y	Y	Y	Y	Y	Y	Y	N	UTD	N	Y	Y	Y	N	UTD	N	9 (60%)
Bandinelli et al	Y	Y	N	N	Y	Y	N	Y	N	Y	Y	Y	Y	UTD	UTD	N	8 (53%)
Farouk et al	N	Y	Y	Y	N	Y	N	UTD	N	Y	Y	Y	Y	Y	UTD	N	8 (53%)
ElMallah et al	Y	Y	Y	N	Y	N	N	N	N	Y	Y	Y	Y	UTD	UTD	N	7 (47%)
Galluzzo et al	N	N	N	UTD	Y	N	N	Y	N	Y	Y	Y	Y	UTD	UTD	UTD	7 (47%)
Perrotta et al	Y	Y	Y	N	Y	N	N	UTD	UTD	Y	Y	Y	Y	UTD	UTD	UTD	7 (47%)

Score: Y (yes)=1, N (no) and UTD (unable to determine)=0. Total score = 15. Green: high quality (>85%); yellow: moderate quality (≥60%); red: low quality (<60%).

the type of transducer (multifrequency linear array). Frequency settings in B-mode (greyscale) US were discussed in three studies [37, 38, 40] and colour and/or power Doppler (PD) settings (e.g. pulse repetition frequency) in nine studies [10, 30, 34, 35, 37–41]. Additional scanning procedures included adjusting the room temperature for PD scanning [30, 41] and asking patients to stop NSAIDs prior to examination [33, 34].

Prevalence and scoring of Achilles tendon/entheses US features

When describing the prevalence of Achilles tendon/enthesal pathology, 9/15 (60%) studies referred to the absolute frequency and/or percentage of Achilles entheses (n = 1080 entheses) involved [3, 10, 30, 31, 34, 35, 37, 39, 41] and 6/19 (40%) studies only referred to the absolute frequency and/or percentage of participants (n = 292) affected [32, 33, 36, 38, 40, 42]. Of the studies that reported the frequency and percentage of participants affected, four of six [32, 36, 38, 42] stated that the Achilles entheses were scanned bilaterally and we deduced, based on the scoring system they adopted, that the other two studies [33, 40] also scanned bilaterally. Given the heterogeneity in reporting (entheses affected vs participants affected), we have reported both separately (Table 5).

US features according to the OMERACT 2018 consensus-based definition of enthesitis [7] include the following:

- Hypoechoogenicity was detected in 18/306 Achilles entheses [mean 5.9% (s.d. 0.9)] in two of nine studies [10, 31] and in 7/31 participants (33.3%) in one of six studies [38].
- Increased thickness was detected in 228/936 Achilles tendons [mean 22.1% (s.d. 12.2), median 17, range 4.2–40.4, IQR 20.6] in seven of nine studies [3, 10, 30, 31, 34, 39, 41] and in 15/63 participants [mean 26.2% (s.d. 7.2)] in two of six studies [38, 40].
- Erosions at the site of the Achilles tendon insertion at the posterior calcaneum were detected in 30/936 entheses [mean 3.3% (s.d. 2.5), median 2.9, range 0–

7.5, IQR 4.6] in seven of nine studies [3, 10, 30, 31, 34, 39, 41] and in 14/188 participants [mean 11.1% (s.d. 5.9), range 4.8–19] in three of six studies [32, 38, 40].

- Calcifications were detected in 191/406 entheses [mean 42.6% (s.d. 15.6), range 25–63] in three of nine studies [10, 31, 39] and in 13/21 (61.9%) participants in one of six studies [38].
- Enthesophytes were detected in 343/812 entheses [mean 41.3% (s.d. 15.6), median 53.8, range 18.6–56.7, IQR 32.9] in five of nine studies [3, 10, 30, 34, 41] and in 36/63 participants [mean 58.4% (s.d. 3.6)] in two of six studies [38, 40].
- Doppler signal at the site of insertion was detected in 109/929 entheses [mean 11.8% (s.d. 10.1), median 12, range 0–29.5, IQR 18.8] in six of nine studies [10, 30, 31, 34, 39, 41] and in 4/63 participants [mean 8.4% (s.d. 5.9)] in two of six studies [38, 40].

There was significant variation in the methods of scoring US features of enthesitis. Four studies used the GUESS criteria [30, 34, 40, 41], 1 the MASEI [39] and 3 described non-validated semi-quantitative scoring [10, 35, 37] including Brown *et al.* [29], which was used in RA for scoring B-mode and Doppler signal [35]. Doppler signal was scored both as binary (present/absent) [30, 31, 41] and semi-quantitatively as per the five stages described by D’Agostino *et al.* 2003 [31, 38] and three stages outlined by D’Agostino *et al.* 2009 [30, 41].

US features in healthy controls

Five of the seven studies that assessed a healthy control population reported the absolute frequency and/or percentage of Achilles entheses (N = 190 entheses) [30, 35, 39, 41] and two of seven reported the absolute frequency and/or percentage of participants (N = 88 participants) [32, 36, 40]. Hypoechoogenicity was not assessed in healthy control participants. Increased thickness was detected in 2/170 entheses [mean 1.7% (s.d. 2.4), range 0–2.5] in three studies [30, 39, 41] and in 0% of participants in one study [40]. Erosions were detected in 2/170 entheses [mean 1.3% (s.d. 1.9), range 0–4] in three studies [30, 39, 41] and in 0% of participants in two studies

TABLE 4 US protocol reporting

Study author	Q6 Blinding		Q9 Scanning procedures				Q10 Scoring system			Q11 Validity/reliability		Q15 Equipment		Q16 US modalities and settings	
	a	b	a	b	c	d	a	b	c	a	b	a	b	a	b
Ahmed et al. [3]	N	Y (90° flexion)	Y (L/T)	N	N	Y (L/T)	N	N	Binary and semi-quantitative	N	Y	Y	N	N	N
Bandinelli et al. [30]	Y	Y (90° flexion)	N	Semi-quantitative	Lower limb	N	Semi-quantitative	Lower limb	Binary and semi-quantitative	Y	Y	Y	N	Y	Y
EIMallah et al. [31]	N	N	N	Binary	Multiple site ^a	N	Binary	Multiple site ^a	Binary and semi-quantitative	Y	Y	Y	N	N	N
Falsezzi et al. [32]	Y	N	Y (L/T)	Semi-quantitative	Achilles	N	Semi-quantitative	Achilles	No Doppler	N	Y	Y	N	N	N
Farouk et al. [33]	Y	N	Y (L/T)	N	N	N	N	N	N	N	Y	Y	N	N	N
Fiorenza et al. [34]	Y	Y (90° flexion)	N	Semi-quantitative	Lower limb	N	Semi-quantitative	Lower limb	Binary	Y	Y	Y	N	Y	Y
Freeston et al. [35]	Y	Y (90° flexion)	Y (L/T)	Semi-quantitative	Multiple site	N	Semi-quantitative	Multiple site	Semi-quantitative	N	Y	Y	N	Y	Y
Galluzzo et al. [36]	Y	N	Y (L/T)	N	N	N	N	N	N	N	Y	Y	N	N	N
Litinsky et al. [42]	N	N	N	N	N	N	N	N	N	N	Y	Y	N	N	N
Marchesoni et al. [37]	Y	N	N	Binary and semi-quantitative	Multiple site	N	Binary and semi-quantitative	Multiple site	Semi-quantitative	N	Y	Y	Y	Y	Y
Michelsen et al. [10]	N	Y (prone)	Y (L/T)	Semi-quantitative	Achilles	N	Semi-quantitative	Achilles	Semi-quantitative	N	Y	Y	N	N	Y
Perrotta et al. [38]	Y	N	Y (L/T)	Binary	Multiple site	N	Binary	Multiple site	Binary	N	Y	Y	Y	Y	Y
Wervers et al. [39]	Y	Y (90° flexion)	Y (L/T)	Semi-quantitative	Multiple site	N	Semi-quantitative	Multiple site	Semi-quantitative	Y	Y	Y	N	Y	Y
Woodburn et al. [40]	N	N	N	Semi-quantitative	Lower limb	N	Semi-quantitative	Lower limb	Binary	Y	Y	Y	Y	Y	Y
Xie et al. [41]	Y	Y (90° flexion)	N	Semi-quantitative	Lower limb	N	Semi-quantitative	Lower limb	Binary and semi-quantitative	Y	Y	Y	N	N	Y

Full descriptions of the questions can be found below. Questions are adapted from the EULAR recommendations (2021). Y: yes; N: no; L/T: scanned in longitudinal and transverse planes. ^aMultiple sites refers to scoring of enthesal sites in both the upper and lower limbs. Modified questions from the EULAR recommendations for the reporting of ultrasound studies in RMDs: Q6. Reporting the blinding of sonographers. Q9. Scanning acquisition: a) patient positioning (e.g. supine, prone), b) anatomical region positioning (e.g. flexion, neutral), d) transducer positioning (e.g. longitudinal, transverse). Q10. Ultrasound scoring system: a) B-mode/greyscale type (e.g. quantitative, semi-quantitative, binary), b) level (e.g. patient level, joint/anatomical region level) c) Doppler type (e.g. quantitative, semi-quantitative, binary). Q11. Ultrasound scoring system: a) references or results of previous validity and reliability studies. Q15. Equipment: a) brand and model of the ultrasound device, b) type and model of the transducer. Q16. Equipment—ultrasound modalities and settings: a) greyscale/B-mode, b) Doppler.

TABLE 5 Quantiles and point prevalence of US features of Achilles enthesitis in people with PsA

Ultrasound feature	Studies (/15), n	Point-prevalence of US feature, n/N (%)	Quantiles			Mean	s.d.	IQR
			25%	Median	75%			
Studies reporting no. of entheses (entheses assessed = 1080)	9 [3, 10, 30, 31, 34, 35, 37, 39, 41]							
Hypoechoogenicity	2 [10, 31]	18/306 (5.9)		5.1		5.1	0.9	
Increased thickness	7 [3, 10, 30, 31, 34, 39, 41]	228/936 (24.4)	13.1	17.0	33.7	22.1	12.2	20.6
Erosion(s)	7 [3, 10, 30, 31, 34, 39, 41]	30/936 (3.2)	1.4	2.9	6	3.3	2.5	4.6
Calcification(s)	3 [10, 31, 39]	191/406 (47.0)		39.7		42.6	15.6	
Enthesophytes	5 [3, 10, 30, 34, 41]	343/812 (42.2)	22.9	53.8	55.9	41.3	15.6	32.9
Doppler signal	6 [10, 30, 31, 34, 39, 41]	106/929 (11.4)	1	12	16.3	11.8	10.1	18.8
Studies reporting no. of subjects (no. of participants assessed = 292)	6 [32, 33, 36, 38, 40, 42]							
Hypoechoogenicity	1 [38]	7/31 (33.3)						
Increased thickness	2 [38, 40]	15/63 (23.8)		26.2		26.2	7.2	
Erosion(s)	3 [32, 38, 40]	14/188 (7.4)		9.5		11.1	5.9	
Calcification(s)	1 [38]	13/21 (61.9)						
Enthesophytes	2 [38, 40]	36/63 (57.1)		58.4		58.4	3.6	
Doppler signal	2 [38, 40]	4/63 (6.3)		8.4		8.4	5.9	

The data in this table detail summary statistics using percentages of entheses/participants in each study.

[32, 40]. Calcifications were detected in 4/50 entheses (8%) in one study [39]. Enthesophytes were reported in 3/120 entheses (mean 2.5%) in two studies [30, 41] and in 9/29 participants (31%) in one study [40]. Finally, PD signal at the Achilles enthesitis was reported in 1/170 entheses [mean 0.7% (s.d. 0.9), range 0–2] in three studies [30, 39, 41] and in 0% of participants in one study [40].

Discussion

The aims of this systematic review were to describe the definitions and scoring of US features of Achilles enthesitis in PsA, including assessment of the overall quality of studies and evaluation of the quality of the reporting of US protocols. Due to the heterogeneity observed in the definitions, scoring methods and quality of studies, a narrative and descriptive approach to the analysis and synthesis of the results was adopted. All of the 15 studies referred to at least one US feature at the Achilles tendon/entheses, but the lack of generalizability arising from the variation in definition and scoring could suggest the frequency and percentage of entheses/participants affected should be interpreted with caution. The quality of reporting of US protocols and procedures was not consistent across the studies and thus contributes further to the lack of generalizability of results.

US technology has advanced considerably since the early 2000s and this may account for some of the variability noted between the studies, as image acquisition and interpretation has greatly improved. Despite the technological advancement of US, our review has highlighted the potential pitfalls of US definitions of

Achilles enthesitis in PsA. For example, tendon thickening as a result of a biomechanical tendinopathy will appear the same on US as tendon thickening due to an inflammatory enthesitis, yet will be histologically different. Whether Achilles enthesitis in PsA is a biomechanical stress-induced inflammation of the enthesal tissues or an inflammatory-induced tendinopathy is still unknown [1, 46].

The majority of the studies were scored as low [30, 31, 33, 36, 38] or moderate quality [3, 32, 34, 35, 37, 39–42], with only one paper scoring high [10] based on the modified version of the Downs and Black QI criteria. Most studies were marked down based on their description of sampling methods. Additionally, very few studies adjusted for potential confounders in the analysis of results, which is now partly addressed in the EULAR recommendations under the reporting of ‘contextual factors’ (e.g. exercise, alcohol, caffeine and smoking) [16].

The identification of contextual factors was not widely reported in the studies included. Two studies [30, 41] reported adjusting the room temperature to 20°C for the assessment of Doppler US with reference to D’Agostino *et al.* [22], however, there is no substantial evidence to suggest there is any effect. One study asked patients to refrain from taking NSAIDs 3 weeks prior to examination [33] and another 24 hours prior to examination [34]. There is evidence to suggest that NSAID use could mask both B-mode features and PD signal and ultimately result in a better US score [47].

Scoring of US features varied between the studies with four using the GUESS scoring criteria, one using the MASEI and the rest either scoring features as

present/absent, using non-validated semi-quantitative scoring (score 0–3) or not scoring US features at all. Doppler US was scored separately in three studies, either from 0–3 or 0–5, and they all referred to D'Agostino *et al.* [21, 22]. Similarly, the definitions of US features were not consistent throughout the studies (Table 3), with the GUESS, MASEI and variations of the OMERACT US Task Force recommendations being used irrespective of the date of publication. Although there are similarities between the definitions, the results are not entirely comparable. With the ever-evolving technological advances of point-of-care US and the increase in accessibility and uptake by clinicians (with varying levels of US training and experience), it is even more imperative to have clear definitions and a widely accepted validated scoring criteria that is appropriate for both clinical practice and research.

We observed substantial variation in the prevalence figures for features of enthesitis at the Achilles tendon, but due to heterogeneity, it is unclear whether the variation can be explained by protocol variations or sample characteristics such as disease duration/severity. Only 5/15 studies specifically recruited newly diagnosed (<2 years) PsA patients, and reported prevalence figures were similar between these studies and those with a longer disease duration. Prevalence estimates should be interpreted with caution, as included studies mostly adopted non-probability sampling largely involving consecutive recruiting of outpatients and so may be vulnerable to bias.

The potential implications for standardizing the use of validated definitions and scoring systems for assessing the Achilles tendon in PsA and clear US protocol reporting are significant. First, it will allow us to better understand the prevalence of US features of pathology and levels of severity of symptoms associated with Achilles enthesal and tendon disease. This information could then be used to aid the stratification of treatment, particularly non-medical management, based on the severity and/or type of pathology present. The grouping of US features into structural and inflammatory components in the most recent OMERACT guidance [8] could be used as a starting point to tailor treatment accordingly. The current provision and efficacy of non-medical management of Achilles enthesitis in PsA has not been researched, and based on this lack of evidence, care provision will likely vary considerably. Another clinical consideration for management is the overlap of a PsA disease-driven enthesitis at the Achilles and biomechanically driven Achilles tendinopathy. Although Achilles tendinopathy in healthy people is typically found at the mid-portion of the tendon, it can also be detected at the insertion [48]. The US criteria for staging Achilles tendinopathy in healthy populations (based on the continuum model of tendon pathology) has a number of similarities with the US definition of enthesitis in PsA (e.g. altered echotexture, thickening and the presence of vascularity)

[49]. It is also worth noting that US features of Achilles enthesitis can also be detected in healthy individuals, particularly the presence of enthesophytes and tendon thickening [50].

This systematic review has some limitations that merit attention. The EULAR 2021 recommendations were not intended for use as a scoring checklist for published research but were used as guidance in the absence of a suitable alternative. A number of papers were excluded based on their reporting of the simple presence/absence of Achilles enthesitis only, as we specifically wanted to identify the description, scoring and prevalence of these US features. As such, the number of papers included in this study was small ($n = 15$) relative to the body of literature that has assessed for simple presence/absence of Achilles enthesitis in PsA.

Recommendations for future research include the development of a validated checklist or scoring system to assess the quality of US studies in rheumatology. There may be future potential for evaluating the effectiveness of tailoring medical and non-medical management approaches based on the presence and/or severity of certain US features at the Achilles tendon/entheses in PsA to improve symptoms. There is a paucity of evidence for the non-medical management of Achilles enthesitis and enthesopathy in PsA and at present the management is similar regardless of whether structural and/or inflammatory features are present [5]. There may be scope for the phenotyping of PsA-driven enthesitis based on clinical characteristics and US-detected pathologies.

Recommendations for authors of future studies reporting Achilles tendon/entheses features in PsA include using the most up-to-date, reliable definitions and scoring for US features (currently Balint *et al.* [7]), report both the number of entheses and the number of participants affected to allow for synthesis of results and use the 2021 EULAR recommendations [16] as a guide for reporting US protocols and procedures.

Funding: This article was published as part of the *Rheumatology Advances in Practice Trainee Publishing Programme*, supported by a grant from Biogen.

Disclosure statement: The authors have declared no conflicts of interest.

Data availability statement

Data are available upon reasonable request to the corresponding author. All data relevant to the study are included in the article.

Supplementary data

Supplementary data are available at *Rheumatology Advances in Practice* online.

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