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Review

Ultrasound Measurement of Local Deformation in the Human Free Achilles Tendon Produced by Dynamic Muscle-Induced Loading: A Systematic Review

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Achilles tendinopathy is the most prevalent lower limb tendinopathy, yet it remains poorly understood, with mismatches between observed structure and reported function. Recent studies have hypothesised that Achilles tendon (AT) healthy function is associated with variable deformation across the tendon width during use, focusing on quantifying sub-tendon deformation. Here, the aim of this work was to synthesise recent advances exploring human free AT tissue-level deformation during use. Following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, PubMed, Embase, Scopus and Web of Science were systematically searched. Study quality and risk of bias were assessed. Thirteen articles were retained, yielding data on free AT deformation patterns. Seven were categorised as high-quality and six as medium-quality studies. Evidence consistently reports that healthy and young tendons deform non-uniformly, with the deeper layer displacing 18%–80% more than the superficial layer. Non-uniformity decreased by 12%–85% with increasing age and by 42%–91% in the presence of injury. There is limited evidence of large effect that AT deformation patterns during dynamic loading are non-uniform and may act as a biomarker of tendon health, risk of injury and rehabilitation impact. Better considered participant recruitment and improved measurement procedures would particularly improve study quality, to explore links between tendon structure, function, aging and disease in distinct populations.

Introduction

The Achilles tendon is the common tendon of the gastrocnemius and soleus muscles and inserts onto the calcaneus, therefore serving as a dynamic link to enable efficient locomotion. Despite being the largest lower limb tendon, it is the most vulnerable to tendinopathy with increasing year-on-year prevalence [1]. Its incidence is highest in running sports [2–4] but it affects people across the spectrum of low to high activity and, therefore, affects everyday life activity. Sixty percent of Achilles tendinopathy occurs in the mid-portion of the free tendon 2–6 cm above the calcaneal insertion [5] and is the focus of this review, with the 20% incidence of insertional tendinopathy being regarded as a different diagnosis [6].

Ultrasound B-mode or Doppler imaging has been widely used clinically to investigate structural tendon pathology such as ruptures, partial ruptures, intra-tendinous tears [7] thickening, disruption in the fibrillar pattern and tendon vascularisation [8–10]. However, there is a well-established mismatch between observed morphology and the degree of reported pain or function for all tendons [11]. *In vivo* measurement of tendon mechanical properties has therefore become an important focus of recent research into tendon health, using ultrasound to investigate biomechanical tendon behaviour, for example, tracking the myotendinous junction with B-mode imaging to calculate tendon extension during loading [12,13].

Recent findings, however, indicate that tendons deform non-uniformly during dynamic movement, with recent *ex vivo* studies determining that fascicular and sub-tendon sliding enables tendon stretch and recoil rather than fascicular extension in isolation, further indicating that regional variation of local tendon strain is a fundamental element of healthy function [14]. Importantly, there is increasing evidence that observed differences in the extent of sliding are associated with aging and pathology [15,16]. The development of *in vivo* imaging approaches has subsequently focussed on a variety of ways to quantify these local strains throughout the Achilles tendon during movement, to offer improved structural characterisation by quantifying this tissue property. Analysis techniques are typically based on speckle tracking [17–19]. As speckle pattern is generally stable and unique for any specific type of tissue, it is relatively simple to pattern-match speckle from frame to frame using a search algorithm and track its movement to calculate tissue displacement. Whilst the highly aligned structure of tendon creates some

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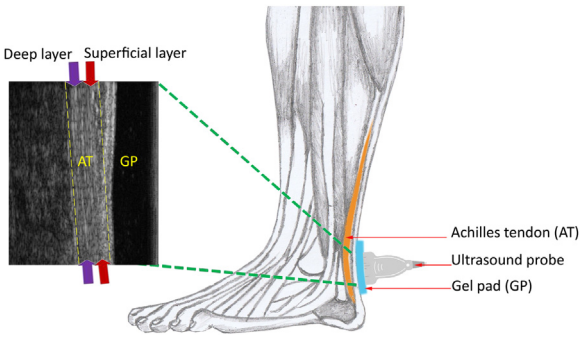

Figure 1. Schematic of a typical experimental setup used to acquire ultrasound data and measure tendon deformation. In the associated ultrasound frame, the deep (DL) and superficial (SL) layers of the Achilles tendon are highlighted with *red arrows*.

challenges in detecting clear speckle patterns, these approaches have been adopted to explore the non-uniformity of tendon displacement by dividing the tendon into two to three equal segments across the width and independently reporting their displacement in the long axes, to determine superficial and deep tendon displacement (Fig. 1). A review of studies exploring Achilles tendon strain distribution highlighted that most explore global tissue strains and recommended that improved regional-level understanding of Achilles tendon deformation is important [20]. These tissue-level deformations in health and disease, and the ultrasound methods used to measure them, are subsequently the focus of this review.

This knowledge has the potential to bridge the gap between ultrasound measurements of structure and patient-reported pain and dysfunction, therefore potentially improving tendinopathy management, which is currently sub-optimal. For example, an imaging biomarker that was either prognostic of or responsive to symptomatic change could guide treatment decision making and rehabilitation progression. We aimed to synthesise findings about mid-portion Achilles tendon and sub-tendon deformation during dynamic loading in different populations and under different conditions and assess whether these measures are consistently associated with aging, the presence of pathology or the loading parameter. The secondary aim was to help establish improved research practice by rigorously considering the quality and risk of bias of the various techniques and study designs that have been used to investigate tendon deformation patterns to inform future research design. Finally, we aimed to identify what is yet to be measured using an evidence gap map.

Methods

Our systematic review was guided by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [21] and registered in the PROSPERO (International Prospective Register of Systematic Reviews) database (CRD42020191478).

Search strategy

A search was conducted of PubMed, Embase, Scopus and Web of Science from inception to September 2020, and additional searches were made of citing and cited articles. The search strategy used a range of keywords in four categories which were combined: (i) ultrasound, (ii) Achilles tendon (iii), tendinopathy, and (iv) biomechanical properties. The keywords for the search strategy are outlined in the following, with use of an asterisk to denote truncation and ensure a database search for all forms of the word. Full search strategies are outlined in appendix Supplement 1 in the Supplementary Material (online only). ultrasound OR sonography OR ultrasonography OR "Speckle track*" OR "Strain imag*" OR "Shear wave elastography" OR "Sono elastography" OR "Ultrasound elastography" **AND** Achilles OR calcaneal OR "Tendo Achilles" OR "Triceps surae" OR "Calf muscle" **AND** tendinopathy OR tendinosis OR tendinitis OR injury OR rupture OR tend* **AND** "Tendon mechanics" OR strain OR force OR elasticity OR "Young* modulus" OR elongation OR displacement OR deformation OR lengthening OR "Cross sectional area" OR stiffness OR stress OR tension OR Load* OR Contract* OR stretch*

Identified titles and abstracts were downloaded into EndNote, version ×7 (Thomson Reuters, Philadelphia, PA, USA), and duplicates were deleted and imported into Rayyan for screening (QCRI, https://rayyan.qcri.org/) [22]. At the first stage of selection, titles and abstracts of the studies were screened against the inclusion and exclusion criteria by two independent reviewers (G.S., S.R.). After screening, the blinding was disabled, and any conflicts were resolved with senior authors available to mediate but not required.

Selection criteria

The review included experimental studies, including validation ($n < 5$), case–control and prospective studies that investigate deformation in the free Achilles tendon using ultrasound. There was no restriction on language. Participants aged >18 y of either or both sexes were included. Studies including healthy participants or patients with mid-portion Achilles tendinopathy were included in this review. There was no upper age limit. Studies had to measure free Achilles tendon deformation, but those where there was only a global measurement of tendon deformation (tracking anatomical landmarks) were excluded. Studies were excluded if they included participants with other foot pathologies, systemic inflammatory conditions or neurological, endocrine and metabolic disorders. Studies that did not report ultrasound imaging localised to the free Achilles tendon were excluded. Unpublished, non-peer-reviewed, intervention studies, studies that did not involve humans, *in vitro* studies, phantom studies, opinion articles, case series, letters to the editor, non-English articles, abstracts and case reports were excluded.

Outcome

The outcomes of interest were ultrasound-based measures of deformation, displacement and strain within the free Achilles tendon at the tissue level (see Table 1 for operational definitions of these terminologies).

Methodological quality assessment

The methodological study quality was assessed using a scale initially developed by Law and MacDermid [23] and modified by Galna et al. [24]. The tool consists of 14 questions that address issues of internal validity, external validity and reporting, to enable methods to be replicated. Each question was scored as 0 or 1 indicating low and high quality, respectively. All included studies were independently assessed by two reviewers (G.S. and S.R.) for methodological quality. Disagreements between reviewers were discussed and were resolved by asking a third reviewer (D.M.). The level of agreement between the two reviewers was

Table 1
Definitions of key terms used in the review

Term	Operational definition
Tendon displacement	Magnitude of the change in position of tendon as a whole or part in a particular direction
Tendon deformation/non-uniform deformation	Changes in size or shape of the tendon. Non-uniform deformation is reported as a relative change in displacement between different portions of the tendon region (*e.g.*, deep vs. superficial).
Tendon strain	Amount of deformation experienced by the tendon normalised to its original size and shape

measured using the Cohen unweighted κ (J) statistic (SPSS Statistics, version 20.0.0, IBM, Armonk, NY, USA). The total average domain score for each article was calculated (total score/14). This was categorised as low (≤0.40), medium (0.41–0.74) or excellent (≥0.75) [25]. The lowest-quality studies were subsequently excluded from this review to avoid any associated bias in our conclusion.

Risk-of-bias assessment

The risk of bias was evaluated by two reviewers using Quality Assessment of Diagnostic Accuracy Studies, version 2 (QUADAS-2) [26], treating the included studies as ones of diagnostic accuracy [27]. The tool includes four domains: patient selection, index test, reference standard and flow and timing. Applicability is assessed across the first three domains through the signalling questions. Risk of bias is assessed across all four domains. Disagreements between reviewers were resolved by discussion and consensus. Firstly, we defined the review question in terms of patients, index test, reference standard and target condition. In reviews, the index test is evaluated as the test accuracy of the intervention. Therefore, here the scope of the question is "What is the capability of measuring the local deformation in the human free Achilles tendon?" To explore the index test domain, a reference standard is typically compared against the index test, with the assumption that the reference standard has 100% accuracy. However, with no threshold for defining a reference standard and diverse deformation behaviour among the population, we individually assessed the methodology of each study to check their confidence in terms of internal validity. Studies self-reporting a validity check were judged valid. Assessment of inter-operator consistency was also looked for, to estimate technique precision and consistency. Where reported, confidence in measurement reliability was increased. If we did not find information on validation in the study, we wrote to the authors to query completion of validity assessment (a tailored QUADAS-2 can be found in appendix Supplement 2 [online only]).

Data extraction and analysis

Data were extracted for participant characteristics (age, sex, weight, height, body mass index [BMI], tendon health state) and the details of both the loading protocol and ultrasound imaging techniques. The reported outcomes related to tendon mechanical properties (displacement, deformation and strain) were extracted by two primary independent reviewers (G.S. and S.R.) in a standard template (Appendix Supplements 3 and 4, online only) and Table 2.

Table 2
Ultrasound-based techniques implemented to investigate the behaviour of the free Achilles tendon during the different loading tasks

Study	Type of US data	USPO-f (MHz)	Technique
Slane and Thelen 2014 [31]	RF	10	Block matching 2-D normalised cross-correlation
Slane and Thelen 2015 [38]	RF	10	
Franz et al. 2015 [36]	RF	10	
Franz and Thelen 2015 [37]	RF	10	
Fröberg et al. 2017 [32]	B-mode	14	
Bogaerts et al. 2017 [35]	B-mode	21	
Stenroth et al. 2019 [34]	RF	10	
Clark and Franz 2018 [33]	RF	10	
Beyer et al. 2018 [15]	B-mode	10	
Clark and Franz 2020 [16]	RF	10	
Couppé et al. 2020 [39]	B-mode	6.5	
Khair et al. 2021 [40]	B-mode	10	
Khair et al. 2022 [41]	B-mode	10	

RF, radiofrequency; US, ultrasound; USPO-f, ultrasound probe operational frequency.

Strength of evidence and meta-analysis

Evidence levels were determined according to the Van Tulder criteria, with strong evidence indicated by consistent findings among multiple high-quality studies; moderate evidence indicated by one high-quality study or consistent findings among multiple low-quality studies; and limited evidence indicating one low-quality study; or conflicting evidence where studies did not agree being resolved by meta-analysis where possible [28].

Where there was judged to be methodological homogeneity, data concerning exercise, measurement approach and outcome were pooled for meta-analysis using the Cochrane Review Manager Software (version 5.3, Nordic Cochrane Centre, Cochrane Collaboration, Copenhagen, Denmark, 2014). Standardised mean differences (SMD; Hedges' adjusted g) with 95% confidence intervals (CIs) were calculated for the difference between the displacement in the deep layer and superficial layer of the tendon, and for comparisons of non-uniform deformation between healthy and injured participants. Statistical heterogeneity was considered if the observed true effects in variance rather than sampling error (I^2) were greater than 25% [29]. Because of the small samples and number of studies, we anticipated that deformation results may vary across studies and therefore used a random effects meta-analysis model [30]. The effect sizes of Achilles tendon deformation data were estimated using Cohen's d within samples and Hedges' g between groups: ≥0.8 indicated large, 0.5–0.8 moderate and 0.2–0.5 small effect sizes.

Evidence gap map

The extracted data were used to build an evidence gap map where we tabulated the data for measurements during varied tasks in specific populations (young, old, injured, uninjured). Each cell was annotated to depict the direction of the relationship, effect size and level of evidence. The gap map design is thus able to demonstrate where there is a need for future higher-quality research studies and should help to avoid undue repetition where there is ample existing high-quality research.

Results

Yield

The electronic database literature search was conducted on 12 December 2022. We identified 4499 potentially relevant publications, and after removing duplicates, 2441 remained. After screening title and abstract, we assessed 41 publications in full text and retained 13 (Fig. 2).

Methodological quality assessment

The quality of the reviewed articles is summarised in the Table 3. A strong level of agreement (Cohen's κ) was found between item scores from the two reviewers (κ = 0.91, SE = 0.05; SPSS Statistics, version 27.0.0). Overall, descriptions of the recruitment and sampling procedures (0.38), reliability of the methodology (0.42), controlled covariates (0.36), and inclusion and exclusion criteria (0.58) were the most poorly scored criteria. One study was excluded from the review based on the quality assessment score. There were eight high-quality reports, nine medium-quality reports and one low-quality report.

Risk of bias

The risk of bias regarding patient selection was low in four studies [31–34], whereas nine studies had a high risk of bias for patient selection [35–41].

The high risk of bias was due mainly to selection bias related to participant enrolment, typically as recruitment focused on individuals working at the authors' research institutions. The risk of bias related to the index test was low in all studies, with nine studies using the same

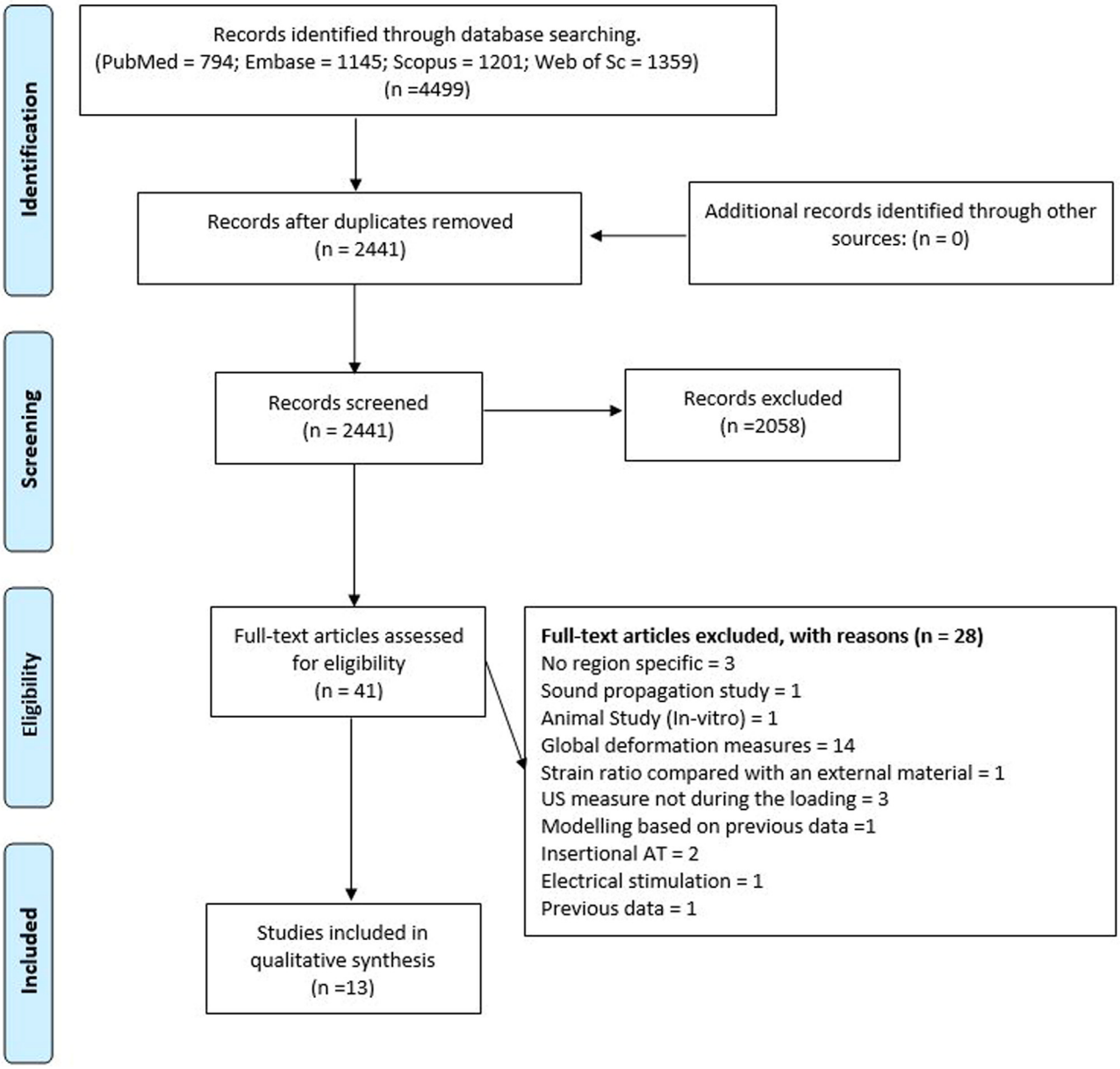

Figure 2. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2009 flow diagram of study selection process. AT, Achilles tendon; US, ultrasound.

index test as initially reported by Slane and Thelen [19]. Risk of bias related to the reference standard was also low in all studies; three studies reported their own validation method [31,32,38] eight studies relied on previously validated methods [16,33–37,40,41]. Risk of bias related to flow and timing was low in all studies (Fig. 3a). The applicability from signalling questions showed low risk of bias in all the studies (Fig. 3b).

Meta-analysis

Three different meta-analyses were possible among five studies because of similarities in study characteristics. The remaining six studies could not be included in the meta-analysis, as the heterogeneity of the measurement methods meant pooling of the data across studies was not possible. The SMD for the tendon displacement in the deep layer was 0.60 (confidence interval [CI]: 0.11, 1.10), indicating larger displacement in the deep layer compared with the superficial layer of the free Achilles tendon among the healthy group. Heterogeneity was low, I^2 at 0% (Fig. 4). The SMD for tendon displacement in injured Achilles tendons was −1.21 (CI: −1.90, −0.52), indicating a reduction in the non-uniform deformation pattern of the free Achilles tendon among the injured group compared with healthy participants during standing single-leg heel-rise exercises in the extended knee position (Fig. 5). Deformation patterns were found to be more uniform among the injured compared with the healthy group during seated flexed-knee heel-rise exercise, with the weighted average effect size −1.98 (CI: −2.86, −1.11). In both conditions heterogeneity is low at 17% (Fig. 5). Similarly, the SMD for tendon displacement in injured Achilles tendons was −0.96 (CI: −1.60, −0.32), indicating a reduction in the non-uniform deformation pattern of the free Achilles tendon among the injured group compared with healthy Achilles tendon during submaximal voluntary contraction in the seated, extended-knee position (Fig. 6).

Sub-tendon displacement in the free Achilles tendon and evidence gap map

All studies explicitly reported sub-tendon displacement and were collated by means of the evidence gap map (Fig. 7).

Table 3
Methodological quality assessment of included studies

Question	Scoring Criteria	Froberg et. al. 2017	Bogaerts et. al. 2017	Clark et. al. 2018	Clark et. al. 2020	Franz et. al. 2015	Franz and Thelen 2015	Slane et. al. 2014	Slane et. al. 2015	Beyer et. al. 2018	Stenroth et. al. 2018	Couppe et.al. 2019	Khair et al 2021	Khair et al. 2022	Average
Research aims or questions stated clearly	1-Yes; 0.5-yes, lacking detail; 0-No														1.00
Participants detailed	Number														
	Age														
	Sex														
	Population														
	Average Sub-total	1.00	1.00	1.00	1.00	0.75	0.75	1.00	0.75	1.00	1.00	1.00	1.00	1.00	0.94
Recruitment and sampling methods described	1-Yes; 0.5-yes, lacking detail; 0-No														
Inclusion and exclusion criteria described	1-Yes; 0.5-yes, lacking detail; 0-No														
Controlled co-covariates	Age														
	Sex														
	Tendon pre-conditioning or warm-up														
	Average Sub-total	0.00	0.33	0.67	0.67	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.36
Key outcome variable clearly described	1-Yes; 0.5-only some defined; 0.5-yes, lacking detail; 0-No														
Adequate methodology able to repeat study	Participant sampling														
	Equipment														
	Procedure														
	Data processing														
	Statistical analysis														
	Average Sub-total	1.00	1.00	0.70	0.80	0.80	0.80	0.80	0.80	1.00	0.80	0.90	0.90	0.90	0.86
Methodology able to answer research question	Participant sampling														
	Equipment														
	Procedure														
	Data processing														
	Statistical analysis														
	Average Sub-total	1.00	0.80	1.00	0.80	1.00	1.00	0.80	0.70	1.00	0.90	0.80	0.80	0.80	0.88
Reliability of the methodology stated	1-Yes; 0.5-yes, lacking detail; 0-No														0.42
Internal validity of the methodology stated	1 - Yes; 0 - No														0.54
Research questions answered adequately in the discussion	1 - Yes; 0- No														1.00
Key findings supported by the results	1 - Yes; 0 - No														1.00
Key findings interpreted in a logical manner which is supported by reference	1 - Yes; 0 - No														1.00
Clinical implications stated	1-Yes; 0.5-yes, lacking detail; 0-No														0.69
	Average Score (Total score/14)														

Assessment tool adopted from Galna et al. [24]. Key: Review is confident question answered fully = score 1 = green traffic light; where there is a lack of detail = score 0.5 = amber traffic light; and no detail found = score 0 = black traffic light. An average score across all 14 questions is determined and is indicated at the bottom of the table using boxed traffic lights: high-quality study (≥0.75) = *green*, moderate-quality study (0.41–0.74) = *amber* and low-quality study (≤0.40) = *red*.

Findings in healthy population

The non-uniformity of Achilles tendon deformation was assessed in each instance, with increased differential in the displacement of the deep layer relative to the superficial layer, defined simply as increased deep layer displacement. When considering healthy individuals, there was limited evidence of large effect that the deep layer displaced more when increasing the walking speed [36], and limited evidence of large effect that the deep layer displaced more when reducing the knee angle during eccentric loading [31]. There was also limited evidence of small effect that the deep layer displaced more when reducing the knee angle [34], and moderate evidence of large effect that the deep layer displaced more when increasing the dorsiflexion angle, during the maximum voluntary isometric contraction (MVIC) [33]. Finally, there was strong evidence of moderate effect that the deep layer displaced more during a MVIC [33–35].

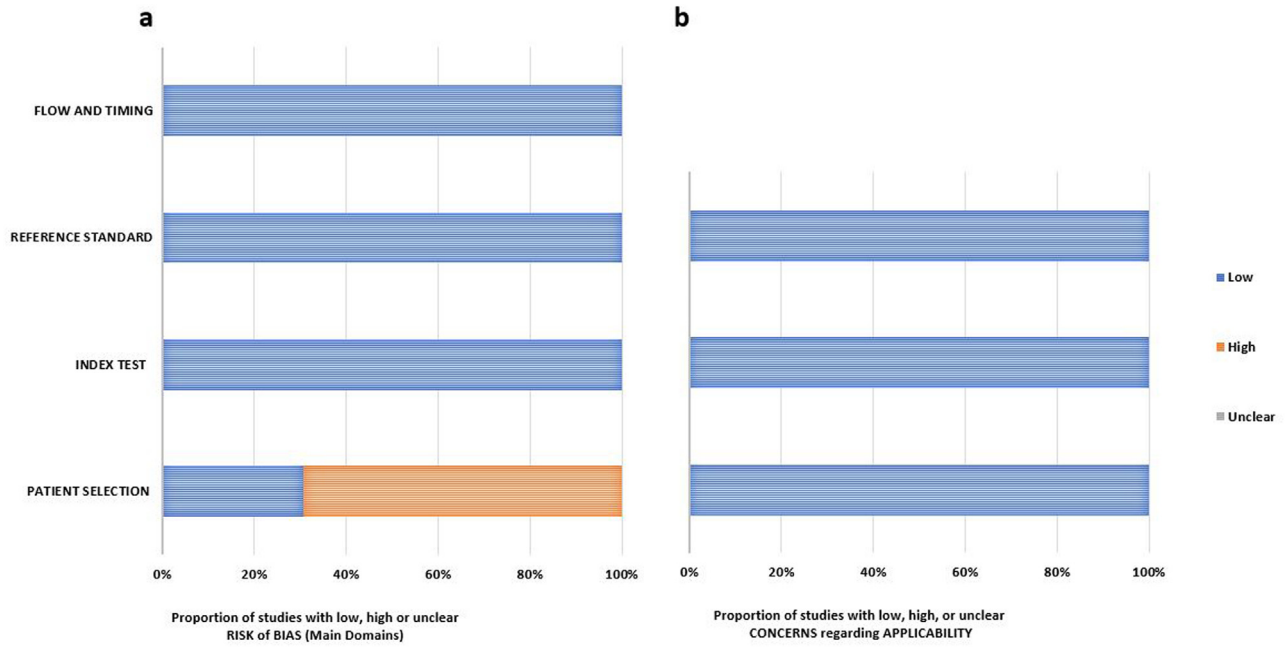

Figure 3. Risk of bias and applicability concerns graphs based on Quality Assessment of Diagnostic Accuracy Studies, version 2 (QUADAS-2). Authors' judgments about each domain for risk of bias (a) and applicability concerns (b) are both presented as percentages across the 11 studies. Studies with a high risk of bias and applicability concerns are highlighted in *orange*, those that are unclear in *grey* and those with low risk in *blue*.

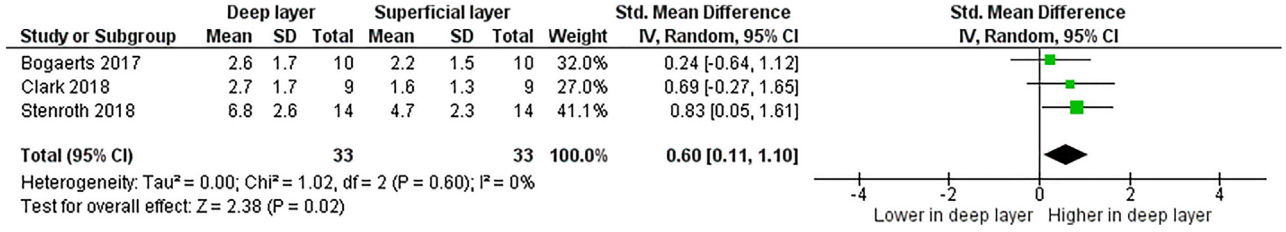

Figure 4. Forest plot describing the relationship between displacement in the deep and superficial layers of the Achilles tendon in healthy participants during maximum voluntary isometric contraction. CI, confidence interval; df, degrees of freedom; IV, initialization vector; SD, standard deviation.

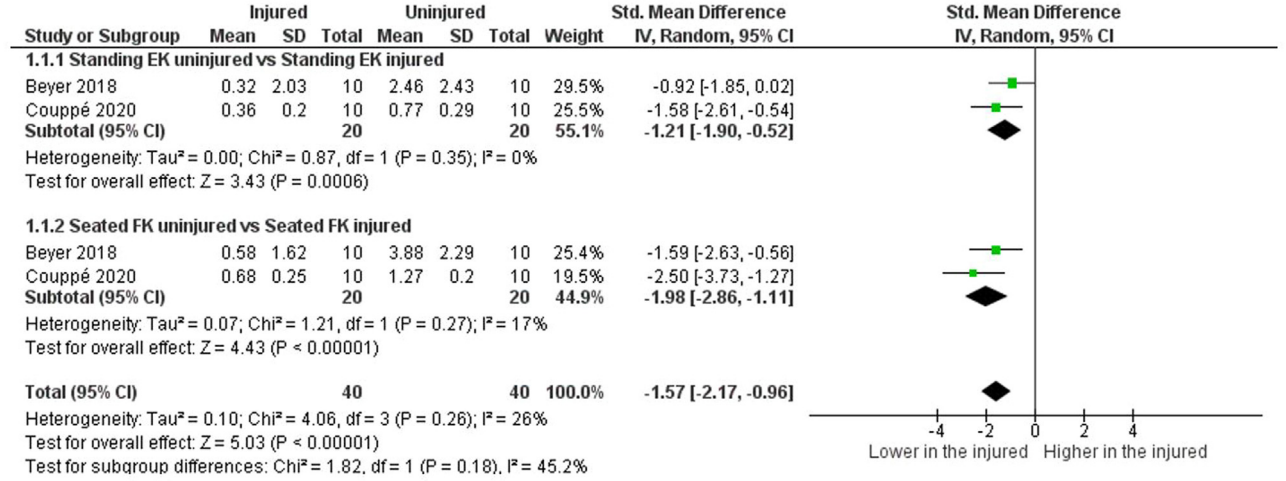

Figure 5. Forest plot describing how non-uniform deformation varies between injured and healthy during single-leg-standing, extended-knee heel raises (1.1.1) and seated flexed-knee heel raises (1.1.2). The data reveal the mean difference in displacement between the deep layer and superficial layer (mm). CI, confidence interval; df, degrees of freedom; EK, extended knee; FK, flexed knee; IV, initialization vector; SD, standard deviation.

Findings in older population

There was limited evidence of large effect that the deep layer displaced less in older people compared with younger people, especially in healthy people during eccentric loading [38]. There was limited evidence of large effect that deep layers displaced less in older people compared with young people during maximum voluntary contractions of the triceps surae while increasing ankle angle

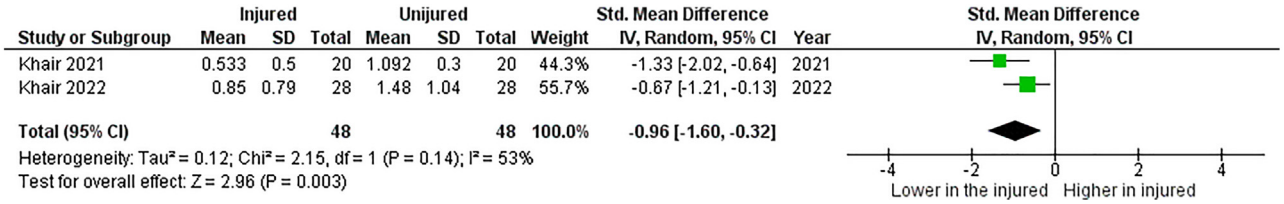

Figure 6. Forest plot, showing how non-uniform deformation varies between injured and uninjured: during seated extended knee submaximal voluntary contraction. CI, confidence interval; df, degrees of freedom; EK, extended knee; FK, flexed knee; IV, initialization vector; SD, standard deviation.

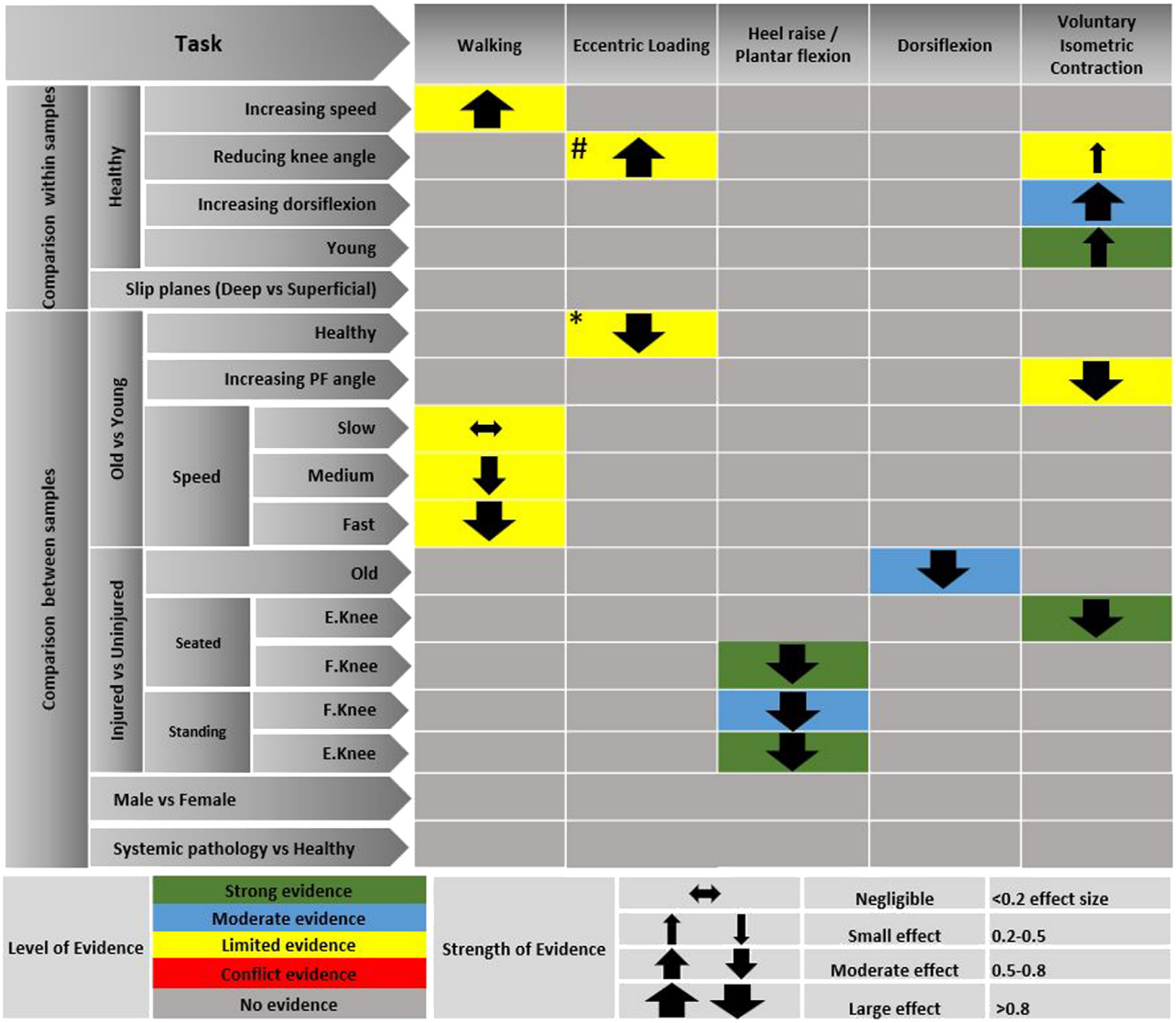

Figure 7. An evidence gap map of human free Achilles tendon deformation patterns measured using ultrasound. Arrow direction (upward = increase) represents the direction of deep tendon displacement compared with the superficial layer. Example interpretations: (between group) *During eccentric loading, there is limited evidence of large effect that the difference in deeper tendon displacement compared with superficial is less than that in younger participants. (within group) #During eccentric loading, there is limited evidence of large effect that reducing knee angle causes more deep tendon displacement compared to superficial. Degree of displacement of the deep Achilles tendon compared with the superficial layer.

from neutral position to 30° plantar flexion [16]. There was limited evidence of no effect that deep layers displaced less in older compared with younger people during walking at a slow speed, but there was limited evidence of moderate effect that deep layers displaced less in older compared with younger people during walking at a medium speed and limited evidence of large effect that deep layers displaced less in older compared with younger people during fast-speed walking [37].

Findings in injured population

There was a moderate evidence of large effect that deep layers displaced less in injured compared with uninjured people, especially in older people during dorsiflexion [32]. A comparison of injured and uninjured individuals also highlighted strong evidence of large effect that deep layers displaced less in injured people during the flexed-knee seated heel raise [15,39], moderate evidence of large

effect that deep layers displaced less in injured compared during the flexed knee standing heel raise [15], and strong evidence of large effect that deep layers displaced less in injured people during the extended knee standing heel raise [15,39]. Similarly, a comparison of injured and uninjured Achilles tendons highlighted strong evidence of large effect of more uniformity in injured Achilles tendon during the extended-knee seated submaximal voluntary contraction [15,16,35–39].

Absence of evidence

The synthesis of our evidence gap map clearly indicates that the exploration of regional tissue level deformation behaviour has steadily advanced, providing clear evidence of increased displacement in the deep layer during many types of normal Achilles tendon activity, implying that sliding between internal structures of the Achilles tendon must occur. However, exploration of the presence of, or location of, slip planes specifically has not been considered among any of the included studies in this review. There has been no work in any domain to compare male versus female for any of the studied loading protocols or exercises (Fig. 5). Further, fast movements or exercises that create and transfer a large force have not been studied and would be relevant to the clinical presentation.

Many studies focused on participants with healthy Achilles tendons, with only three research studies investigating *in vivo* Achilles tendon deformation in the presence of Achilles tendinopathy. Inflammatory diseases such as diabetes, hypercholesterolemia and alkaptonuria all affect tendon, but no studies exploring their impact on local mechanics were found, creating another important gap. No significant conflicting evidence was reported.

Tendinopathy

Three studies investigated participants with varying tendon injuries [15,32,39], comparing sub-tendon displacement in the injured limb with that in the contralateral healthy limb [15,32]. Couppé et al. [39] investigated the tendinopathic Achilles tendon during seated flexed-knee and standing extended-knee heel raises, reporting that the deep layer was displaced the most in all conditions, but with far less differential between regions in the tendinopathic tendon than the contralateral control (tendinopathic side: 0.52 ± 0.16 mm vs. asymptomatic contralateral side: 1.02 ± 0.18 mm). Fröberg et al. [32] and Beyer et al. [15] both looked at surgically repaired Achilles tendons. Fröberg et al. [32] revealed large differences in sub-tendon displacement between the deep layer and superficial layer in healthy tendons (3.3 ± 1.1, mean difference ± standard deviation [SD]) but noted little difference in the injured group relative to the control group (0.3 ± 0.2) during an active dorsiflexion. Similarly, Beyer et al. [15] compared non-uniformity during exercises standing with the knee flexed, standing with the knee extended and seated with the knee flexed, reporting that the displacement of the deep layer relative to the superficial layer was consistently smaller in the surgically repaired tendons.

Ageing

There were three studies that reported effects of ageing on tendon local displacements. Slane and Thelen compared young (24.1 ± 1.4 y) and middle-aged (49.0 ± 3.1 y) individuals during eccentric loading, finding a significant reduction in non-uniform deformation behaviour in the middle-aged group. Another study carried out by Franz and Thelen in 2015 [37], compared young (23.9 ± 1.8 y) and old (69.9 ± 1.6 y) individuals walking at three different speeds (0.75, 1.00 and 1.25 m/s). Results generally indicated that the deep tendon layer displaced more than the superficial layer in young participants; however, no differences in non-uniform deformation behaviour were evident at the slowest speed between younger and older participants. Another study carried out by Clark and Franz [16], comparing young and old participants at different plantar flexion angles (neutral 0°, 10°, 20°, 30°) during ramp maximum voluntary contractions, reported a similar loss of non-uniformity with ageing. The young peak soleus sub-tendon displacement averaged 51% more than the peak gastrocnemius sub-tendon tissue displacement, whereas in the older group there was only a 31% differential.

Knee angle

Two studies compared sub-tendon displacement at two different knee positions (extended knee and flexed knee). Slane and Thelen [31] explored young (24 ± 1 y) healthy people during eccentric loading, finding that the deeper layer of the tendon displaced more than the superficial layer in both extended- and flexed-knee conditions, with the highest displacement differential reported in the extended-knee position. By contrast, another study exploring tendon displacement during maximum voluntary contraction in young healthy participants conflictingly found that knee angle made no difference in reported non-uniformity in displacement [34].

Discussion

This is the first systematic review of the local deformation behaviour of the free Achilles tendon. Our synthesis supports the idea that healthy and young tendons deform non-uniformly, with the deeper layer displacing more than the superficial layer during dynamic loading. Further, data support that the superficial to deep displacement differential decreases among older and injured people.

Our gap map illustrates the pattern of deformation for a variety of loading conditions and populations and illustrates consistent deformation patterns in the healthy young group regardless of loading type, speed, knee angle and ankle angle. It also reveals that slow movements are typically preferred as the loading method when acquiring ultrasound data. Unlike *in vitro* or *ex vivo* experiments, it is particularly challenging to isolate the tendon during the *in vivo* tendon experiments; therefore, a dynamometer [35] or similar custom-made equipment [38] is typically adopted to isolate the lower limb, with most studies selecting isometric contraction as the loading method. For these reasons, there is arguably limited applicability to the type of fast, stretch-shortening contractions that lead to tendon injury, or its exacerbation, although the strength and consistency of the findings are notable, with the similarity between aging and injured tendon suggesting common mechanisms.

The triceps surae muscle complex includes two heads, one attaching above and the other below the knee, so it is widely presumed that changing the knee angle could play an important role in Achilles tendon deformation. In theory, a flexed knee should make the gastrocnemius less mechanically efficient and require the soleus to compensate by increased activation. Therefore, it could be expected that the deep portion of the tendon would deform more than the superficial layer when contracting the triceps surae muscle in knee flexion. However, the synthesis revealed conflicting findings, albeit with a variety of methods [15,34,38,39]. We calculated the effect size using the reported mean displacement value of deep layers and superficial layers, and reducing the knee angle is found to have only a small effect during a MVIC [34] but large effects during eccentric loading [38]. Overall, the effect was significant only with eccentric loading, but the deformation pattern is similar regardless of loading type and knee angle.

It can be argued that the conflicting association between muscle activation and differential strains within the Achilles tendon may be associated with the complex twisted pattern of the Achilles tendon. The heads of triceps surae muscle have differing muscle volumes and are clearly loaded differently between exercises, such that different magnitudes of

force at each sub-tendon may contribute to non-uniform deformation [42]. However, the twist in the Achilles tendon means that the posterior tendon layer is formed by fascicles from the medial gastrocnemius muscle head, whilst the anterior layers originate from the lateral gastrocnemius and soleus muscles [43,44]. It should be noted that these bundles are not parallel to each other but are heterogeneously twisted, especially in the free tendon area [44], and the twist is highly variable between individuals. Of further impact to the non-uniformity of Achilles tendon deformation, the mechanical property of each bundle of tendon fascicles arising from the separate muscle heads may also differ because of the different compositions of the associated muscle fibre.

Gastrocnemius is composed of 50% type 1 and 50% type 2 muscle fibres, with the soleus composed of 88% type 1 muscle fibres [45]. Indeed, a recent study comparing the *in vitro* mechanical behaviour of each sub-tendon reported that the soleus-associated portion of the Achilles tendon was more extensible than the sub-tendons associated with the gastrocnemius tendons [46].

An exploration of the impact of loading rate on tendon deformation pattern is of interest, owing to the strain-rate dependent behaviour of viscoelastic materials. Tendon has previously been reported to exhibit stiffer behaviour when loaded at faster rates *in vitro*, owing to less available time for viscous sliding between molecules. An exploration of the relationships between tendon loading rate and non-uniform deformation patterns may thus provide further insight into the shearing mechanisms enabling non-uniform behaviour. Walking speed is a key functional biomarker for a range of health-related outcomes in older people and enables a comparison of the impact of loading rate on tendon non-uniform behaviour. The gap map synthesis indicates that increasing walking speed has a large effect, in that the deep tendon layer displaces more in healthy young people with increasing speed [36]. These findings indicate that the viscoelastic effects of loading speed in isolation are not driving the non-uniformity of tendon displacement. However, it should be noted that the study only investigated gait at three different walking speeds (0.75, 1 and 1.25 m/s), and used a randomised order without reporting recovery time between tests, making it difficult to fully establish the association between viscoelastic behaviour and deformation pattern with different gait speeds. Further studies are needed to investigate local deformation behaviour of the free Achilles tendon during fast movements such as running, during which the Achilles tendon experiences loads of approximately eight times body weight [47]. Investigating progressive loading and the associated deformation patterns may help inform clinical rehabilitation of injury and possibly prevention. Further, the evidence gap map indicates that there is still a need for higher-quality studies to provide strong evidence in all the key domains, as many studies are at the development stage, with more applied studies needed in clinical settings and with athletic or clinical subgroups. For example, various endocrine or metabolic factors have been proposed as risk factors for tendinopathy [48] so investigating subgroups with systemic disease is indicated.

Notably, our gap map shows no studies comparing deformation behaviour of the human free Achilles tendon between men and women. It would be useful to study the deformation behaviour between the sexes in all domains as men have been reported to be considerably more vulnerable to tendon injury than women [49,50]. This evidence may be confounded by difficulties in comparing sports and physical activity participation between groups; however, it is logical that hormonal differences may lead to ongoing or cyclical alterations in mechanical properties.

This review also aimed to understand deformation behaviour of human free Achilles tendon among older people during dynamic loading, predicated on the evidence that older people are more prone to tendon injury [51]. Disruption of collagen fibres, reduction in elastin content and reduction in the diameter of collagen fibrils have all been reported with ageing in tendon [52], changes that may explain the reduced ability of tendon to cope with high loads. Although only three studies investigating the effect of ageing on deformation patterns of the free Achilles tendon were included in this review, we found limited evidence of large effect that the difference in deeper tendon displacement compared with superficial is reduced with ageing, except at slow walking speeds (0.75 m/s) where it was a negligible effect [37]. This may be due to less muscular distinction between gastrocnemius and soleus during slow walking [53,54].

Additionally, we bring *in vitro* evidence to support the tissue-level changes specifically affecting non-uniform strain distribution in loaded tendon. Interfascicular and inter-fascicular bundle sliding has been found to decrease with age [55,56]. This has been linked to a reduction in, and disorganisation of, elastin and lubricin within the interfascicular matrix niche with ageing [57,58]. A loss of the proteins enabling fascicle sliding and recoil and subsequent stiffening of the inter-fascicular matrix niche may potentially explain why we see more uniform deformation patterns.

In addition to ageing, we are also interested in the deformation behaviour of human free Achilles tendon among the injured population. Although there are well-defined intrinsic and extrinsic factors in the literature purported to be causes of tendon injury, the aetiology is not clear and understanding injury mechanisms is difficult. It may be that the deformation behaviour of human free Achilles tendon could both predict injury and be a biomarker for rehabilitation stages after injury, therefore addressing the structure–function mismatch commonly reported for imaging modalities. We found consistent evidence that the non-uniformity of tendon displacement decreased with injury, mimicking the changes observed in aging tendons. It may be that aging and injury have some similarity in tendon deformation.

A number of ultrasound tissue characteristics studies and also *in vitro* studies have reported that collagen bundles get disrupted as a result of injury [59,60], so the ability for sliding between sub-tendon structures may become more difficult. In addition to this, formation of scar tissue in the injured tendon [15,32] or swelling and increased pressure associated with oedema and neovascularisation could further restrict sliding capacity. As healthy tendons exhibit a hierarchical order with a highly anisotropic structure organised to transfer large amounts of force through its long axis [61], all these may explain why we see reduced displacement differential between deep and superficial layers in injured populations.

Limitations

Most studies depend on previous validation, but it would be preferable to validate methods in each group to ensure reliability and validity. Similarly, the different techniques being explored and tested among healthy cohorts limit our ability to comment on the applicability of techniques among populations with tendinopathy or who are of different age ranges.

There was a deficit in assessing methodological quality assessment as there is no specific tool for quality assessment of the kind of development studies we reviewed. We did use a quality assessment tool similar to that used in other systematic reviews of motion analysis, which would ideally have undergone further validation. Similarly, we adapted the QUADAS-2 for the risk of bias assessment without changing domain and signalling questions. There were a number of domains that were not addressed adequately by any study. Specifically, many studies did not report sample size calculations or the sampling strategy. It is understandable that it can be difficult to recruit participants based on sample size calculations for these types of developmental study. The risk of bias assessment revealed a low likelihood of bias except for participant or patient selection. We believe it would be ideal to establish quality assessment and risk of bias tools for studies that have no fixed index test or reference standard.

Each study method included some limitations, suggesting that developing comprehensive study protocols that are shared and replicated across groups would enable inclusion of more studies in meta-analyses and, therefore, better synthesis of robust findings. Moreover, there is also need for longitudinal studies for all domains, as this would enable

one to establish sequences of deformation behaviour change with age or response to treatment among people with tendinopathy. This review underlines the need for high-quality studies to understand the deformation behaviour between different populations and different loading protocols.

Future directions

Consistent findings in this review indicate the possibility of using deformation patterns as a biomarker of tendon health. The possibility that early injury onset is associated with altered loading patterns is worth considering in further research. More immediately, tissue deformation may enable us to stage injury based on within-subject deformation pattern changes over time and under different loading conditions. For example, unexpected deformation patterns, or no change in deformation, may suggest that different approaches are required to treat a patient and care can therefore be further personalised.

Whilst these *in vivo* studies support the picture of non-uniform deformation in the tendon, it is important to note that they were not able to define tendon layers (superficial, medial and deep) to identify sub-tendons or explore with any consistency the location of possible slip planes between studies. In most cases, superficial, medical or deep regions in the tendon were manually defined, on the basis of assuming the anatomical volume of each sub-tendon is the same size, and the rotation of the tendon is consistent. Inter-individual variation emphasises the need for detecting sub-tendon boundaries in a more robust way. Further exploration in the field would benefit from more consistency and clarity in the definition of tendon regions and sub-tendons, and method development to differentiate distinct sub-tendons and enable detection of slippery boundaries in the human free Achilles tendon is crucial to enable functional biomechanical imaging that can bridge the structure–function gap in each clinical patient or research participant.

Conclusion

This review highlights a growing body of work exploring human Achilles tendon deformation behaviour across the three sub-tendons. Modelling and *in vitro* data are also contributing towards a growing picture that non-uniform deformation arises from slippery boundaries between the sub-tendons [62], mediated by the interconnecting interfascicular matrix (IFM).

Findings indicate the potential to bridge the structure–function gap in exploring tendon health, ageing and disease, through measures of non-uniform deformation of free Achilles tendon. Specifically, a reduction in non-uniform deformation is clearly associated with injury and ageing, and changes in the behaviour of this high-strain region of the free tendon represent a plausible reason for the high prevalence of mid-portion tendinopathy in sports. The gap map and evidence quality assessment reveal that more high-quality research is needed to understand sub-tendon deformation and free-tendon strain in both healthy and injured groups, particularly during fast movements. Sex differences also need to be established. It is also evident that sub-tendon boundary detection methods need to be established to enable more accurate quantification and detailed investigation of hypotheses linking non-uniform tendon deformation and tendon health. This synthesis of an exciting body of work gives promise that functional biomechanical imaging with sufficient resolution to detect early signs of tendon damage and guide rehabilitation progression is emerging.

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Conflict of interest

The authors declare no competing interests.

Data availability statement

The data that support the findings of this study are available from the corresponding author on reasonable request.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ultrasmedbio.2023.03.014.

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