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Achilles and patellar tendinopathy display opposite changes in elastic properties: A shear wave elastography study

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To compare tendon elastic and structural properties of healthy individuals with those with Achilles or patellar tendinopathy. Sixty-seven participants (22 Achilles tendinopathy, 17 patellar tendinopathy, and 28 healthy controls) were recruited between March 2015 and March 2016. Shear wave velocity (SWV), an index of tissue elastic modulus, and tendon thickness were measured bilaterally at mid-tendon and insertional regions of Achilles and patellar tendons by an examiner blinded to group. Analysis of covariance, adjusted for age, body mass index, and sex was used to compare differences in tendon thickness and SWV between the two tendinopathy groups (relative to controls) and regions. Tendon thickness was included as a covariate for analysis of SWV. Compared to controls, participants with Achilles tendinopathy had lower SWV at the distal insertion (Mean difference MD; 95% CI: −1.56; −2.49 to −0.62 m/s; $P < .001$) and greater thickness at the mid-tendon (MD 0.19; 0.05-0.33 cm; $P = .007$). Compared to controls, participants with patellar tendinopathy had higher SWV at both regions (MD 1.25; 0.40-2.10 m/s; $P = .005$) and greater thickness proximally (MD 0.17; 0.06-0.29 cm; $P = .003$). Compared to controls, participants with Achilles and patellar tendinopathy displayed lower Achilles tendon elastic modulus and higher patellar tendon elastic modulus, respectively. More research is needed to explore whether maturation, aging, or chronic load underlie these findings and whether current management programs for Achilles and patellar tendinopathy need to be tailored to the tendon.

KEYWORDS
Aixplorer, elasticity, jumper's knee, musculo-skeletal, pain, rehabilitation, stiffness, ultrasound

1 | INTRODUCTION

Painful disorders of the Achilles and patellar tendons are a major problem in competitive and recreational sports as well as the sedentary population. More than half (52%) of elite runners develop Achilles tendinopathy during their lifetime,[1] while the prevalence of current or previous patellar tendinopathy in volleyball or basketball athletes is similar (50%-55%).[2] Ultrasonography is widely used for diagnosis of tendinopathy; however, classical ultrasound findings show limited correlation with symptoms[3,4] and lack fundamental information on tissue mechanical properties.

Shear wave elastography is a relatively new ultrasound imaging technique that allows non-invasive estimation of soft-tissue viscoelastic properties in vivo by measurement of shear wave velocity (SWV) (in meters per second) generated by the ultrasound pulse.[5] Importantly, as the SWV may be determined from a relatively small region of tissue (as opposed to the whole structure), it can provide direct measurement of specific regions of interest within tendon,[6,7] which is important because discrete areas of pathology are reported in people with tendinopathy.[8]

Using this technique, lower elastic modulus was demonstrated in patients with Achilles tendinopathy,[9,10] whereas both higher[11] and lower[10] elastic modulus were reported in separate studies of patients with patellar tendinopathy. By estimating patellar tendon stiffness from the relationship between the force applied to the tendon and its associated proximal insertion displacement assessed through B-mode ultrasound, inconsistent findings are also reported (no change[12] or decreased[8] stiffness). However, this indirect method to assess tendon stiffness has two major drawbacks: (a) the tendon force is indirectly estimated (as the force is applied externally to a body segment, rather than directly on the tendon) and (b) only global properties of the whole tendon can be estimated. While similar histological appearance is documented in patellar and Achilles tendinopathy,[13] other factors, including age, body composition, and training might also modulate the elastic properties of tendon.[14] For example, athletes with patellar tendinopathy are significantly younger (mean age 23 ± 3 years), taller (mean height 185 ± 10 cm), and heavier (mean weight 77 ± 11 kg), although of similar body mass index (BMI) (mean BMI 23 ± 2 kg/m^2) than those without symptoms.[15] In comparison, participants with Achilles tendinopathy are older (mean age 53 ± 12 years) and have higher BMI (mean 35 ± 8 kg/m^2) than control participants.[16]

Methodological differences surrounding measurement of tendon properties may also contribute to the variability between studies.[17] Of relevance to the shear wave elastography technique for tendons, shear wavelengths can be greater than tendon thickness, leading to guided wave propogation.[18] Within this context, the relationship between group velocity of the shear wave estimated by commercialized ultrasound shear wave elastography techniques and tendon elastic modulus is affected by tendon thickness. Thus, information about both SWV and thickness must be sought to interpret changes in SWV as changes in elastic properties. In addition, some authors[9] have reported measurement artefacts during shear wave elastography acquisition, including signal void areas within an elastogram. While their presence has been suggested to be a potential marker of intratendinous damage,[9] comprehensive evaluation of its presence is lacking.

The purpose of our study was to determine whether tendon SWV (an index of elastic modulus) and thickness of healthy individuals differ from those with Achilles or patellar tendinopathy. We proposed that regional differences in SWV and thickness would be present in those with tendinopathy compared to controls. As other factors may also modulate the elastic properties of connective tissues, we also investigated the relationship between SWV and age, sex, and BMI. Last, we aimed to quantify elastography signal void in tendinopathic and healthy tendon.

2 | MATERIALS AND METHODS

Participants with or without tendinopathy were consecutively recruited by social media and local advertisement between March 2015 and March 2016. Inquiries were directed to an online screening questionnaire, and eligible participants were invited to attend physical screening by a musculo-skeletal physiotherapist not involved in testing. The inclusion criteria for patients with tendinopathy were self-reported tendon pain over the Achilles or patellar tendon of at least 20 on a 0-100 numerical rating scale (NRS), and of duration 12 weeks or more. Physical examination confirmed tendon pain on palpation and loading (by calf raise or decline squat). The number of single-leg calf raises or decline squats performed before pain onset was recorded. Exclusion criteria were corticosteroid injection (in previous 6 months), local surgery, or other specific pathology (eg, fracture, diabetes, inflammatory, systemic or neurological disease, malignancy, and radiculopathy). All participants were excluded if they had experienced back or other leg symptoms requiring treatment or limiting work/sport in the previous 6 months. This study was approved by the University of Queensland Medical Research Ethics Committee, and all participants provided written informed consent.

Participants with tendinopathy completed either the Achilles[19] or Patellar[20] versions of the Victorian Institute of Sport Assessment (VISA), to provide validated information about pain and disability for their (most) symptomatic leg. Total scores range from 0 to 100, 100 representing an asymptomatic, fully performing individual. In addition to basic demographic information (age, sex, height, and weight), all participants completed the Active Australia Questionnaire, to measure physical activity during the preceding week.[21] Total activity time (minutes) was calculated by adding the time spent in walking and moderate activity and twice the time spent in vigorous activity.

2.1 | Elastography acquisition

Upon arrival, participants rested in lying for five minutes prior to examination using the supersonic shear imaging technique (Aixplorer version 8.2; Supersonic Imagine, Aix-en-Provence, France) with 50 mm linear transducer (15-4 MHz). A single operator (BKC) performed all scans to eliminate interobserver variability.[22] Interday reliability was examined by testing both legs in six healthy participants on two occasions separated by 48 hours. Intraclass correlation coefficients (ICC) ranged from 0.71 to 0.80 for measurement of SWV and 0.78-0.97 for thickness measurements (Table 1).

Examination was performed blind to the physical examination and group by scanning bilateral patellar and Achilles

TABLE 1 Interday reliability (48-h interval) for measurement of tendon thickness and shear wave velocity in six healthy individuals

Tendon region	Session 1 mean (SD)	Session 2 mean (SD)	ICC (95% CI)
	Thickness (cm)		
Mid-Achilles	0.54 (0.22)	0.57 (0.22)	0.97 (0.92, 0.99)
Insertional Achilles	0.40 (0.08)	0.41 (0.06)	0.78 (0.47, 0.92)
Mid-patellar	0.34 (0.05)	0.34 (0.06)	0.84 (0.59, 0.94)
Proximal patellar	0.53 (0.07)	0.53 (0.07)	0.82 (0.56, 0.94)
	Shear wave velocity (m/s)		
Mid-Achilles	10.4 (1.1)	10.8 (0.8)	0.71 (0.24, 0.91)
Insertional Achilles	9.8 (1.6)	10.0 (1.2)	0.69 (0.11, 0.92)
Mid-patellar	6.1 (0.8)	6.0 (0.7)	0.71 (0.22, 0.91)
Proximal patellar	6.4 (1.2)	6.4 (1.2)	0.80 (0.42, 0.94)

ICC, Intraclass correlation coefficient.

tendons in a randomized order for all participants. For Achilles measurements, participants lay in prone with their leg extended and ankle resting over the edge of the plinth. The participant's resting ankle angle was measured using a handheld goniometer. For patellar tendon measurement, participants lay in supine, supported in 30° knee flexion and neutral hip rotation. Based on previous report of the slack angle of the Achilles tendon (43.7 ± 3.2° plantarflexion)[23] and unpublished observations of the patellar tendon, both positions were assumed to have some passive tension on the respective tendons. Participants were told to remain completely relaxed during testing.

The ultrasound transducer head was aligned in the longitudinal plane with collagen fibers, applying minimal pressure.[24] Tendon thickness was measured from longitudinal B-mode images using the inbuilt Aixplorer distance function. For the Achilles tendon, the maximum perpendicular distance between anterior and posterior tendon boundaries was measured over the free tendon (2-4 cm proximal to the Achilles insertion) and immediately proximal to the calcaneal attachment. For the patellar tendon, the maximum perpendicular distance immediately distal to the apex of the patellar and at the midpoint between patellar and tibial attachments was measured. Using the shear wave elastography mode (penetration; persistence low; smoothing 5), the transducer was held for ~10 seconds duration, and two or three measurements were repeated in each location. For the Achilles tendon, separate images were collected for measurement of mid-tendon and insertional regions, while both patellar regions could be visualized without moving the transducer.

2.2 | Data extraction

Elastography clips (10 seconds duration, sampling rate of 1.5-1.8 Hz) were converted into PNG images (~20-26 images), then processed offline using customized Matlab scripts (R2016a; The Mathworks, Natick, MA, USA) by a research assistant who was blinded to group. Regions of interest (ROIs) were manually traced on the adjacent B-mode image keeping within the peritendinous boundary. For the Achilles tendon, ROIs were measured at the free tendon (ROI length ~3 cm) and immediately proximal to the calcaneal attachment (ROI length ~1 cm). For the patellar tendon, ROIs were measured mid-way between proximal and distal attachments (ROI length ~2 cm) and 0.5 cm from the apex of the patella (ROI length ~0.5 cm). The mean SWV (m/s) was averaged over the ROIs of consecutive images. The Matlab script ensured that regions with signal void were not confused with a low value. The amount of signal void within each ROI, defined as the percentage of all pixels without elastography color, was also calculated. Examples of Achilles and patellar elastograms (highlighting signal void) are provided in Figures 1 and 2, respectively.

2.3 | Statistical analysis

For Achilles tendinopathy (AT) and patellar tendinopathy (PT) groups, only the symptomatic or most symptomatic tendon (in bilateral cases) was included in analysis. For healthy control (HC) participants, we randomly matched both Achilles and patellar tendons to ensure an equivalent proportion of left/right legs to the analyzed sample, as recommended by previous studies.[25] This approach was deemed appropriate given the predominantly left-sided manifestation of AT in this study (77%) and others (73%),[26] and evidence of asymmetry of Achilles tendon elastic modulus between legs.[25] Repeated measures ANCOVAs were used to compare tendon SWV and thickness between groups (AT vs HC or PT vs HC) and regions (mid-tendon vs insertion). Where significant group-by-region interaction was observed, generalized linear models (GLM) were used to estimate mean differences (MD) and 95% confidence intervals (CI) between groups for each tendon region. Age, BMI, and sex were included as covariates in all models.

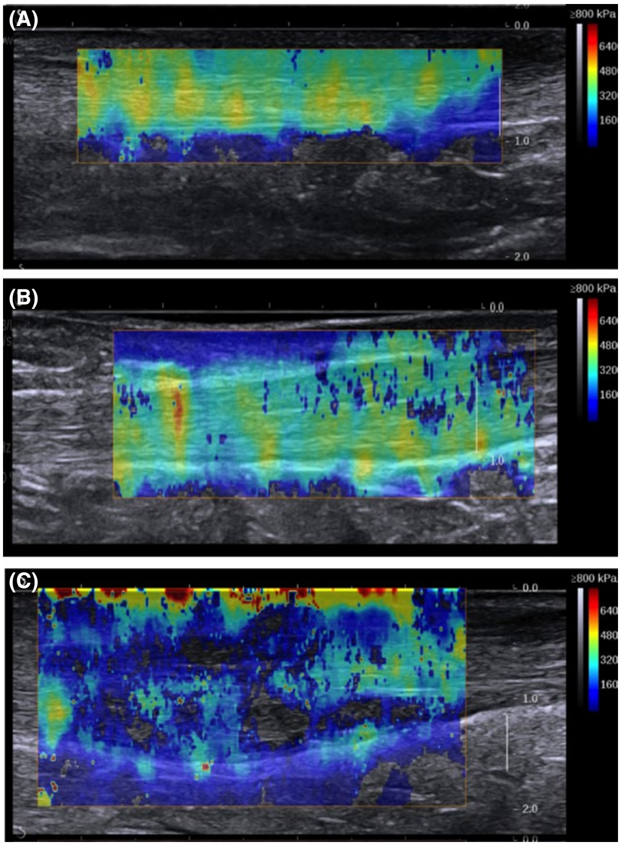

FIGURE 1 Example shear wave elastograms of the Achilles tendon from healthy control (A) and Achilles tendinopathy participants (B and C). Signal void highlighted (asterisk) in C

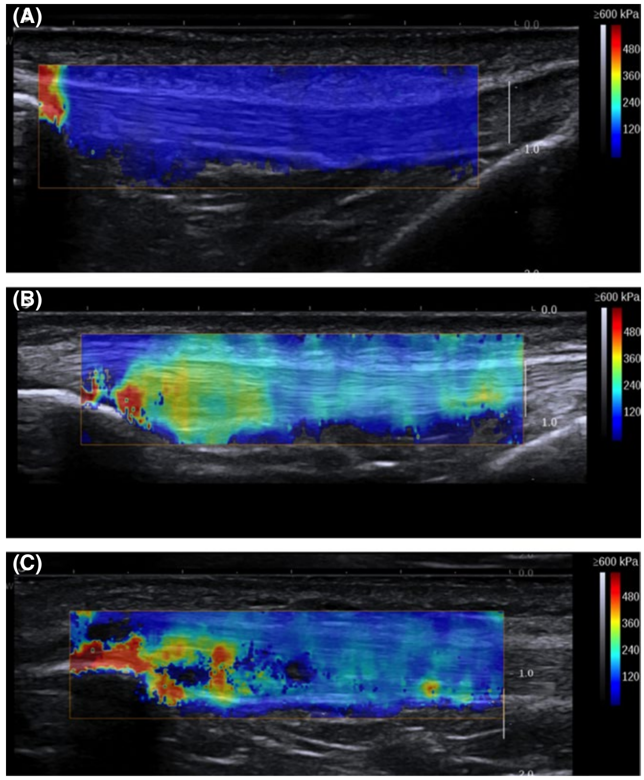

FIGURE 2 Shear wave elastograms of the patellar tendon from healthy control (A) and Achilles tendinopathy participants (B and C). Signal void highlighted (asterisk) in C

In addition, we included tendon thickness as a covariate in analyses of SWV, based on evidence that tendon thickness may affect SWV.[18,27] We dichotomized signal void as present if it affected more than 5% of pixels within the ROI, and differences between groups were compared using Pearson Chi-square statistic.

Receiver operating characteristic (ROC) analysis was performed to determine the threshold, specificity, and sensitivity to differentiate HC from AT or PT, using the Youden's index to identify the cut-point.[28] Finally, Pearson correlations were computed to identify relationships between SWV and demographic or injury factors (the latter for tendinopathy groups only). Statistical analysis was performed using SPSS (22.0 IBM Corp Armonk, New York, United States). Significance was set at $P < .05$.

3 | RESULTS

3.1 | Participants

Sixty-seven adults (22 with AT, 17 with PT, and 28 HC who were free of tendon pain) were recruited. Demographic and injury information are summarized in Table 2, and reasons for participant exclusion are listed in Fig. S1. Participants with AT were significantly older than those with PT ($P < .001$) and had higher BMI than HC ($P < .001$). Total activity time was not statistically different between the three groups ($P = .343$). Similar symptom duration ($P = .943$) and pain/disability levels ($P = .781$) were found for AT and PT groups. The resting ankle angle adopted during Achilles tendon testing was not different between groups (mean plantarflexion angle 24.3 ± 5.0°).

3.2 | Achilles tendinopathy

Compared to HC, participants with AT had greater thickness at the mid-Achilles (MD 95% CI: 0.19; 0.05-0.33 cm; $P = .007$), but not at the Achilles insertion ($P = .80$) (group-by-region interaction, $P = .035$, Figure 3A). Compared to HC, participants with AT had lower SWV at the Achilles insertion (MD −1.56; −2.49 to −0.62 m/s; $P < .001$), but not mid-tendon region ($P = .456$) (group-by-region interaction, $P < .001$, Figure 3C). Signal void of more than 5% of the ROI was present in four HC (8.9%) and 10 AT (45.5%) cases (Pearson Chi-square $P = .001$).

Using ROC analysis, mid-Achilles thickness above 0.64 cm, SWV below 9.7 m/s and signal void above 1.5% of the ROI were identified as cut-points to differentiate HC and AT (Table 3). Lower Achilles SWV was associated with higher age ($r = -.49$, $P < .001$), greater BMI ($r = -.53$, $P < .001$), greater pain and disability as measured by VISA-A

TABLE 2 Demographic and injury characteristics for Healthy control, Patellar tendinopathy, and Achilles tendinopathy cohorts

	Healthy control	Patellar tendinopathy	Achilles tendinopathy
n	28	17	22
Demographic information			
Age (y)	38.3 (16.7)	29.4 (6.6)	47.5 (11.4)*
BMI (kg/m^2)	22.8 (2.7)	25.4 (3.3)	28.1 (5.3)*
Female sex n (%)	17 (61%)	4 (24%)*	9 (41%)
Total activity time (min)	582.2 (451.9)	797.9 (481.3)	642.4 (491.3)
Injury information			
Injury duration (y)		3.8 (3.4)	3.7 (6.9)
VISA-A or VISA-P (0-100)		57.1 (14.4)	58.6 (16.5)
Worst pain (NRS, 0-10)		5.2 (2.3)	6.0 (2.1)
Average pain (NRS, 0-10)		3.4 (2.1)	4.2 (1.9)
Resting pain (NRS, 0-10)		1.2 (2.4)	1.4 (1.5)
Calf raises (repetitions to pain onset)		NA	9.7 (8.6)
Decline squats (repetitions to pain onset)		2.1 (1.7)	NA
Symptom distribution n (%)			
Bilateral tendinopathy		9 (53%)	14 (64%)
Proximal: distal symptoms		15 (88%): 2 (12%)	NA
Mid-tendon: insertional symptoms		NA	19 (87%): 9 (41%)

NRS, numerical rating scale; Data represent mean (SD) unless otherwise specified.
*Significant ($P < .05$) differences compared to healthy controls.

($r = .49$, $P = .046$), and fewer single-leg calf raises before pain onset ($r = .646$, $P = .001$).

3.3 | Patellar tendinopathy

Compared to HC, participants with PT had greater thickness at the proximal patellar (MD 0.17; 0.06-0.29 cm; $P = .003$), but not mid-patellar ($P = .31$) region (group-by-region interaction, $P = .01$, Figure 3B). Compared to HC, participants with PT had higher SWV of the patellar tendon at both regions (MD 1.25; 0.40-2.10 m/s; $P = .005$, Figure 3D). Signal void of more than 5% of the ROI was present in 0 HC and 3 PT (17%) cases (Pearson Chi-square $P = .021$).

Using ROC analysis, proximal patellar thickness above 0.62 cm, SWV above 6.9 m/s, and signal void above 0.7% of the ROI were identified cut-points to differentiate HC and PT (Table 3). Lower proximal patellar SWV was correlated with age ($r = -.368$, $P = .013$) only.

4 | DISCUSSION

Using the non-invasive ultrasound-based technique of shear wave elastography, we observed lower insertional Achilles tendon elastic modulus and higher patellar tendon elastic modulus in participants with tendinopathy relative to healthy controls. Lower elastic modulus in Achilles tendinopathy is consistent with two recent studies using shear wave elastography,[9,10] and other force-deformation methods.[29] However, evidence for changes in patellar tendon mechanical properties in tendinopathy varies between methods[8,30] and studies.[10,11] Using shear wave elastography, Zhang (2014) found significantly greater elastic modulus and thickness for the proximal patellar tendon in 13 athletes with unilateral PT, compared to both the unaffected tendon and healthy control participants.[11] In contrast, Dirrichs et al[10] reported lower SWV in symptomatic compared to asymptomatic tendons in 38 participants with patellar tendinopathy. However, Dirrichs et al[10] reported using a much smaller ROI (standardized size of 1 mm) placed in the stiffest area of tendon.

Although causal relationships cannot be inferred from this cross-sectional study, it is possible that different pathobiological processes associated with maturation and aging may be at play in patellar and Achilles tendinopathy, respectively. Animal work demonstrates that maturation and aging have different influences on the physical, chemical, and mechanical properties of tendon.[31] In their experimental study in rats, Vogel et al[31] observed a sharp rise in elasticity during maturation and a smaller but significant decrease during aging. These changes in mechanical parameters were closely related

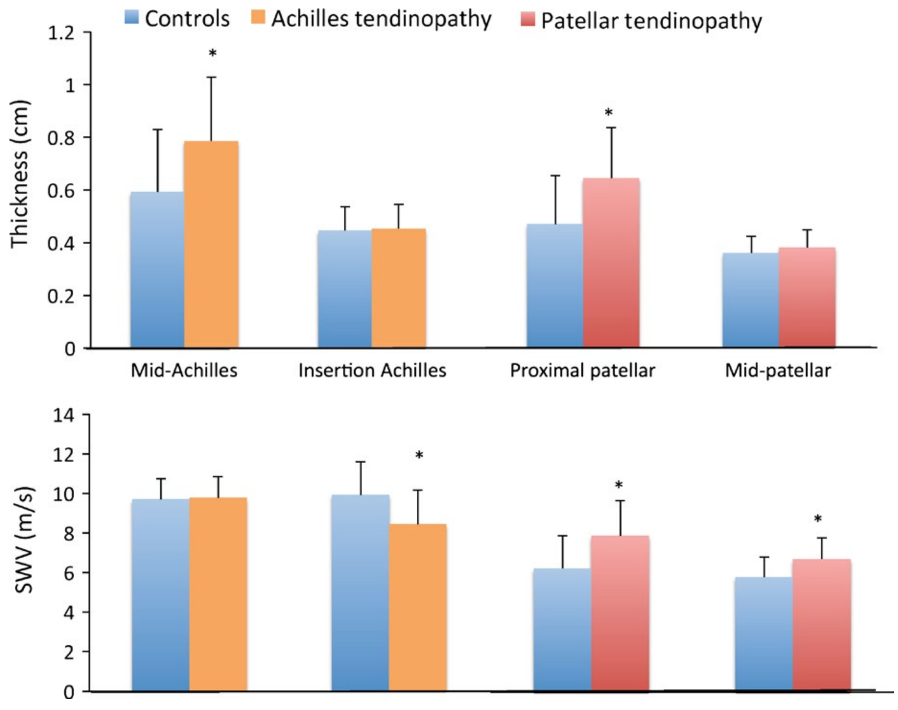

FIGURE 3 Thickness and Shear wave velocity (SWV) of the Achilles tendon (A and C) and patellar tendons (B and D) for healthy control (blue), Achilles tendinopathy (red), and patellar tendinopathy (orange). Values represent mean(SD). *Significant ($P < .05$) differences between tendinopathy and healthy control groups (determined by generalized linear model adjusted for age, body mass index, sex, and thickness (for SWV measures)

TABLE 3 Results of receiver operating characteristic analysis

	Mean threshold	Specificity	Sensitivity
	Thickness		
Mid-Achilles	≥0.64 cm	89.3%	72.7%
Insertional Achilles	≥0.44 cm	67.9%	59.1%
Proximal patellar	≥0.62 cm	100.0%	58.8%
Mid-patellar	≥0.33 cm	50.0%	82.4%
	Shear wave velocity		
Mid-Achilles	≤6.80 m/s	68.2%	75.0%
Insertional Achilles	≤9.68 m/s	81.0%	78.6%
Proximal patellar	≥6.90 m/s	82.1%	76.5%
Mid-patellar	≥7.03 m/s	92.9%	35.3%
	Signal void		
Mid-Achilles	≥1.5%	82.1%	59.1%
Insertional Achilles	≥5.1%	96.4%	38.1%
Proximal patellar	≥0.7%	96.4%	41.2%
Mid-patellar	≥0.5%	82.1%	41.2%

Thresholds for tendon thickness (in cm), shear wave velocity (in m/s), and signal void (as a percentage of total ROI) to differentiate healthy and tendinopathic tendon have been calculated using the Youden's index. Specificity and sensitivity were generated at these cut-points.

to cross-linking of collagen. Significant increases in tendon elasticity with maturation[32] may explain why adolescent athletes have three times greater odds of patellar than Achilles tendinopathy.[33] In our study, older age was associated with lower Achilles tendon elastic properties, which is in agreement with previous investigations using shear wave elastography,[7,24] and other methods.[34] Differences in chronic load may alternatively contribute to our findings. Cassel et al[33] reported that athletes with patellar tendinopathy were taller and heavier and performed higher training volumes than athletes without patellar tendinopathy, attributes which may induce adaptation by increased tendon elastic modulus. It is tempting to speculate that a greater propensity for Achilles tendinopathy of the non-dominant leg or left in our study and others[26] may be due to its lower elastic modulus. Interestingly, biomechanical studies demonstrate that the effects of stress deprivation on connective tissue are more prolonged at the insertion than mid-tissue region,[35] potentially explaining the significant reduction in mechanical properties at the Achilles insertion. Of clinical importance, Achilles tendon elastic modulus was significantly correlated with self-reported pain and disability over the preceding week and with a rudimentary measure of the loading capacity of the Achilles tendon.

The strengths of this study include the blinded design and concurrent investigation of two different lower limb tendinopathies. We acknowledge that interpretation of differences in SWV as differences in elastic modulus is not straightforward, as larger tendon thickness can lead to a higher SWV due to the effects of guided wave propagation, independent of any change in actual tissue elasticity.[18,36] In the present study, no between-group difference in thickness was observed for the mid-patellar tendon and the Achilles tendon insertion, increasing our confidence in our interpretations that elastic properties were altered. However, it is possible the technique failed to detect a less stiff (but thicker) mid-Achilles tendon. This study extends upon previous ones by quantifying signal void within the measured ROI. Signal void over the Achilles insertion and proximal patellar tendon was highly specific (96%) to cases with tendinopathy. Although currently speculative, its presence may be due to intratendinous swelling or tears,[9] greater attenuation of shear waves as a result of altered viscosity,[27] or severe matrix disruption and increased anisotropy.[37] Further studies are needed to determine the impact of attenuation on SWV in the considered region and relate signal void to changes in matrix proteoglycan concentration due to tendinopathy.

Limitations of the current study include the moderate reliability estimates, small sample size, and heterogenous tendinopathy population, which included participants with symptoms at either mid-tendon or insertional regions. We chose to recruit both male and female control participants with a range of ages, rather than individually match participants on the basis of age or sex. Although not without limitation, statistical adjustment by including age, sex, and BMI as covariates in all models was performed in an attempt to explore which factors modulate changes in tendon elastic properties. Other potential confounding factors such as sporting history and muscle strength were not measured.

In summary, in the positions tested here, Achilles tendon SWV <9.7 m/s and patellar tendon SWV >6.9 m/s showed high specificity (81% and 82%, respectively) and sensitivity (79% and 77%) for detecting Achilles and patellar tendinopathy, respectively, suggesting this method may have important clinical utility for early detection of patients at risk of tendon pathology.

5 | PERSPECTIVE

Achilles and patellar tendinopathy share similar histopathology, but affect different age groups. The present study suggests that the two lower limb tendinopathies display different elastic properties when compared to tendons from healthy individuals. More research is needed to explore whether maturation, aging, or chronic load underlie these findings and whether current management programs for Achilles and patellar tendinopathy need to be tailored to the tendon.

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CONFLICT OF INTEREST

No conflict of interest, financial or otherwise, is declared by the authors.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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