Received: 17 February 2021 | Revised: 16 April 2021 | Accepted: 23 April 2021

DOI: 10.1111/sms.13979

ORIGINAL ARTICLE

WILEY

Prevention of strain-induced impairments of patellar tendon micromorphology in adolescent athletes

Falk Mersmann[1,2] | **Theresa Domroes**[1,2] | **Nikolaos Pentidis**[1,2] | **Meng-Shiuan Tsai**[1,2] | **Sebastian Bohm**[1,2] | **Arno Schroll**[1,2] | **Adamantios Arampatzis**[1,2]

[1]Department of Training and Movement Sciences, Humboldt-Universität zu Berlin, Berlin, Germany

[2]Berlin School of Movement Science, Humboldt-Universität zu Berlin, Berlin, Germany

Correspondence
Falk Mersmann, Department of Training and Movement Sciences, Humboldt-Universität zu Berlin, Philippstr. 13, Haus 11, 10115 Berlin, Germany.
Email: falk.mersmann@hu-berlin.de

Funding information
Federal Institute of Sport Science (BISp), Grant/Award Number: 070501/18-20; Foundation Stiftung Oskar-Helene-Heim, Germany; German Academic Exchange Service (D.A.A.D.)

High-level patellar tendon strain may cause impairments of the tendon's micromorphological integrity in growing athletes and increase the risk for tendinopathy. This study investigated if an evidence-based tendon exercise intervention prevents high-level patellar tendon strain, impairments of micromorphology and pain in adolescent basketball players (male, 13–15 years). At three time points over a season (M1-3), tendon mechanical properties were measured using ultrasound and dynamometry, proximal tendon micromorphology with a spatial frequency analysis and pain and disability using VISA-P scores. The control group (CON, $n = 19$) followed the usual strength training plan, including sprint and change-of-direction drills. In the intervention group (INT, $n = 14$), three sessions per week with functional exercises were integrated into the training, providing repetitive high-magnitude tendon loading for at least 3 s per repetition. The frequency of high-level strain (ie, ≥9%) continuously decreased in INT, while tending to increase in CON since tendon force increased in both ($p < 0.001$), yet tendon stiffness only in INT ($p = 0.004$). In CON, tendon strain was inversely associated with tendon peak spatial frequency at all time points ($p < 0.05$), indicating impairments of tendon micromorphological integrity with higher strain, but not at M2 and M3 in INT. Descriptively, the fraction of asymptomatic athletes at baseline was similar in both groups (~70%) and increased to 100% in M3 in INT, while remaining unchanged in CON. We suggest that functional high-load tendon exercises could reduce the prevalence of high-level patellar tendon strain and associated impairments of its micromorphology in adolescent athletes, providing new opportunities for tendinopathy prevention.

KEYWORDS
exercise, maturation, muscle-tendon imbalances, prevention, tendinopathy

1 | INTRODUCTION

Tendinopathy is a common issue among athletes, especially in sports disciplines that feature a high frequency of jumps and change-of-direction movements.[1] It has been proposed recently that plyometric loading may imply an exceptional risk for tendon overuse, as research suggests that it is a greater stimulus for muscle than tendon adaptation.[2] An imbalance of

muscle strength and tendon stiffness (ie, tendon force is too high with regard to the stiffness of the tendon) can increase tendon strain during maximum effort muscle contractions. This implies a reduction of the tendon safety factor, which describes the ratio of ultimate to operating strain, and may cause successive damage to the extracellular matrix of the tendon.[3,4] Though the etiology of tendinopathy is certainly multifactorial in nature, strain-induced tissue damage is considered an important factor for the risk of tendon overuse.

Adolescence is a critical phase for the development of the musculoskeletal system and tendons in particular. The prevalence of tendinopathy seems to increase during adolescence[5] and *in vivo* studies on the mechanical properties of the patellar tendon suggest that a high level of tendon strain due to muscle-tendon imbalances is a common issue in adolescent athletes,[6] especially when the dominant type of sport-related loading is plyometric.[7,8] Recently, we used a spatial frequency analysis of ultrasound images to quantify the packing density and orientation of collagen bundles of the proximal patellar tendon of adolescent basketball players.[9] With this non-invasive approach to estimate the micromorphological integrity of the tissue,[10] we were able to demonstrate that athletes who had higher levels of tendon strain during maximum isometric contractions showed impairments of the proximal tendon micromorphology,[9] similar to those reported for adult athletes with tendinopathy.[11] In fact, those adolescent athletes that had persistent tendon pain symptoms or became symptomatic within the next two months following our assessment had both higher values of tendon strain and a lower estimate of micromorphological integrity compared to asymptomatic athletes or those recovering from tendinopathy.[9] Therefore, specifically targeting the prevention of muscle-tendon imbalances and high-level tendon strain may reduce impairments of tendon micromorphology and provide new possibilities in the prevention of tendinopathy.

It is now clear that tendons adapt to mechanical loading during growth[6,12] and there is reason to believe that the time after the adolescent growth spurt might be a window of increased tendon plasticity[13,14] before the rate of tissue turnover strongly reduces in adulthood.[15] Systematic research suggests that an effective training stimulus for the tendon is characterized by a repeated application of ~4.5–6.5% tendon strain over about 3 s.[16-18] Especially the long strain duration may be a key factor that could explain why the adaptation of tendon stiffness to such loading protocols seems to be more pronounced in comparison with plyometric loading in adults[18,19] and in children.[12,20] As tendon adaptation seems to be independent of the type of muscle contraction used to load the tendon,[21] this type of stimulus can be applied in a variety of exercises. Therefore, the purpose of the present study was to apply an evidence-based functional high-load tendon exercise intervention in an adolescent group of basketball athletes, which is a risk group for tendinopathy,[1] and to investigate its effects on patellar tendon strain, micromorphology and pain over the course of a competitive season. In comparison with a control group, we hypothesized to observe a decrease of the frequency of high-level strain in the intervention group with positive consequences on both tendon micromorphology and the prevalence of tendon pain and pain-related disability.

2 | METHODS

2.1 | Participants and experimental design

The present study investigated *in vivo* patellar tendon strain, micromorphology as well as the prevalence of tendon pain and disability in male adolescent elite basketball players at three measurement time points during a competitive season (M1: pre-season, M2 and M3: in-season; 10 weeks between time points) and the effect of a functional high-load tendon exercise intervention. The necessary sample size was calculated in a power analysis (G*Power, version 3.1.6; HHU). We estimated a large effect ($d = 1.2$) of the intervention on the fluctuations of tendon strain over a year (ie, indicator for the individual variability in maximum), considering the large differences we observed earlier between adolescent volleyball athletes and untrained peers ($d = 1.8$).[7] For a power of 0.8, a sample size of 12 participants per group was calculated. Taking into account a potential drop-out, we recruited 19 top-level basketball athletes in the age of 13 to 15 years from two first junior division teams and assigned them to the control group, which received only their regular sport-specific training. In the following season, 14 athletes from the same teams (ie, same age class) agreed to participate as intervention group, including two athletes that had already been part of the control group. The weekly training duration in both years was approximately eight hours (excluding competition) and included about 1 hour of exercises specifically for strength conditioning. However, the athletes did not participate in machine-based strength training. Exclusion criteria were neurological or musculoskeletal impairments relevant for the purpose of the study, except for patellar tendinopathy. The athletes filled out the validated German version of the VISA-P questionnaire to assess the prevalence of tendon pain and disability,[22] considering the symptoms of the past week. Symptomatic athletes were included if they confirmed that maximum strength testing was possible. One athlete diagnosed with Osgood-Schlatter disease was excluded from the analysis of pain, yet muscle and tendon data were included considering no evident reductions in training participation and the apparent lack of disease-related changes of tendon mechanical properties.[23] The participants and their legal guardians gave written informed consent to the experimental procedures, which were approved by the ethics committee of the Humboldt-Universität zu Berlin (vote from

16.02.2018) and carried out in accordance with the declaration of Helsinki. All measurements were performed on the dominant leg, which was defined as the leg used for kicking a ball. The biological maturity (*maturity offset*: estimated years from peak height velocity) of the athletes was predicted using age and sitting height in the recalibrated prediction equation for boys suggested by Moore and others.[24] Three athletes of the control and one of the intervention group did not participate in M3, leading to a total of 54 and 41 observations in the control and intervention group, respectively.

2.2 | Tendon exercise intervention

The exercise program for the intervention group was designed with respect to the stimulus characteristics of the most effective loading protocol in our earlier systematic research on human tendon adaptation *in vivo*.[16-18] We developed a collection of functional exercises aiming to provide high-intensity loading for the tendon (to induce sufficient strain) for at least 3 s per repetition, which could be learned and performed by adolescents and only involved equipment available in a regular gymnasium setting. The exercises were variations of lunges and squats as well as isometric contractions in a sling trainer system. The loading intensity was increased over the season based on the skills and capacities of the athletes (changing from double- to single-leg support and/or using additional weights). A detailed description of the exercises and the respective variations to increase the loading intensity is available as supplementary material to this article. The overall duration of the intervention was about 20 min and was integrated three times a week into the physical conditioning program of the athletes without affecting the total training time of the athletes. In the control group, the respective strength-oriented exercises for the lower extremities were mainly sprint and change-of-direction drills and did not involve a mechanical stimulus similar to the specific tendon loading exercises.

2.3 | Assessment of tendon micromorphology

Tendon micromorphology was assessed based on a spatial frequency analysis of ultrasound images of the proximal part of the patellar tendon (Figure 1). The participants were positioned supine with the knee flexed to 90°, which was measured based on reflective markers placed on the greater trochanter, the lateral femoral epicondyle, and lateral malleolus, recorded using a Vicon motion capture system with nine cameras (version 1.7.1; Vicon Motion Systems; 250 Hz). Two short sequences were captured with a 5-cm linear transducer of an ultrasound system (My Lab60; Esaote; LA523, 13 MHz, depth: 3.0 cm) placed over the patellar tendon parallel to its longitudinal axis below the most distal apex of the patella. In the analysis, a polygonal region of interest (ROI) was defined in a custom-written MATLAB interface (version R2016b; MathWorks), with the length corresponding to 40% of the tendon rest length of each participant (measured as described in the section *Measurement of Patellar Tendon Mechanical Properties*) and its height covering the full thickness of the tendon. The ROI spanned from the deep insertion to the central portion of the tendon. Within this ROI, as many kernels of 32 × 32 pixels as possible were analyzed as suggested by Bashford and colleagues,[10] by applying a 2D Fast Fourier transform (FFT) and a high-pass filter with a radial frequency response and half-power cutoff frequency of 1.23 mm^{-1}. The filtered kernels were zero-padded in both directions to a size of 128 × 128 pixels, and the average distance of the peak spatial frequency (PSF) from the spectral origin in the frequency spectrum of the two trials was used as a measure of the packing density and alignment of the collagen bundles.[10] Low values of PSF correspond to a less compacted and more isotropic speckle pattern in the ultrasound images, which is characteristic for tendinopathic tendons.[10] At the patellar tendon, PSF values of 1.4 to 1.8 mm^{-1} (interquartile range) have been reported for athletes with tendinopathy and values between 1.7 and 2.0 mm^{-1} for healthy controls.[11]

2.4 | Assessment of vastus lateralis muscle architecture

Changes in muscle strength may occur due to neural and/or muscular adaptation. Since alterations of muscle thickness and pennation angle can provide insight into radial muscle adaptation, vastus lateralis architecture was measured in a seated position at ∼60% thigh length and 60° knee flexion using a 10-cm linear ultrasound probe (LA923; 7.5 MHz, depth: 7.4 cm, focal point: 0.9 and 1.9, no image filter). The vastus lateralis was chosen as representative of the knee extensors due to its high muscle volume.[25] The analysis of the ultrasound images has been previously described in more detail.[26] In short, the upper and deeper aponeuroses were defined by setting reference points along the aponeuroses, which were then approximated by a linear least squares fitting. Subsequently, visible features of multiple fascicles were identified using a semi-automatic algorithm, and a reference fascicle was calculated based on the average inclination of the fascicle portions. The intersection points of the reference fascicle with the two aponeuroses were used to calculate muscle thickness and the pennation angle to the deeper aponeurosis.

2.5 | Assessment of quadriceps muscle strength

Muscle strength of the knee extensors was measured as the maximum knee extension moment during isometric maximum voluntary contractions (MVC) on a dynamometer (Biodex Medical System 3). The resultant knee joint moments were calculated using an established inverse dynamics approach,[27] and the contribution of the antagonistic muscles due to co-contraction was accounted for based on electromyographic (EMG) data.[28] The analog signals of the dynamometer and EMG data (Myon m320RX, Myon AG, Baar, CH) of the long head of the biceps femoris were captured at 1000 Hz and transmitted to the Vicon system via a 16-channel A-D converter.

After a standardized warm-up, the participants were fixed with a trunk angle of 85° (full hip extension = 0°) to the dynamometer seat using a non-elastic belt. Ten submaximal isometric contractions with increasing effort served as an additional warm-up, preconditioning of the tendon and familiarization. Subsequently, three maximum effort contractions were performed at resting knee joint angles of 65°, 70°, and 75° (full knee extension = 0°, values refer to the joint angle determined via the dynamometer), as the approximate optimum angle during contractions is commonly reached from these starting positions. A resting period of 3 min was granted between trials. Due to the non-rigidity of the human-dynamometer system,[27] the actual knee joint angles from the kinematic model corresponding to the MVCs were on average 50 ± 7°. To account for the effect of gravity, an additional passive knee extension trial at 5 °/s was recorded with the shank of the participants fixed to the dynamometer lever pad. Finally, two trials of isometric knee flexion contractions with a slightly lower and higher EMG activity as registered during the knee extensions were recorded to establish an activation-flexion moment relationship that was used to estimate the knee flexion moments generated during isometric contractions by the antagonists. [28]

2.6 | Measurement of patellar tendon mechanical properties

The force-elongation relationship of the patellar tendon was determined by combining inverse dynamics and ultrasound imaging. The 10-cm ultrasound probe was fixed over the longitudinal axis of the patellar tendon with a modified knee brace. The tendon elongation was captured during five trials of isometric ramp contractions (ie, steadily increasing effort from rest to maximum in about 5 s). To calculate patellar tendon forces, the knee extension moments were divided by the tendon moment arm, which was determined for each participant based on magnetic resonance images (MRI) acquired within 1 week before M1.[9] For M2 and M3, the change in the individual moment arm was predicted by the changes in anthropometry.[7] As the patellar tendon moment arm changes with the knee joint angle, the moment arm, which was determined for a full knee extension, was then adjusted to the respective knee joint angles during the isometric contractions based on literature data that describes the change as function of joint angle.[29] The maximum tendon force (TF_{max}) refers to the force calculated for the highest MVC trial of each participant. The elongation of the tendon during the ramp contractions was determined by tracking the displacement of the deep insertion of the tendon at the patella and tibial tuberosity using a semi-automatic software (Tracker Video Analysis and Modeling Tool V. 5.06, Open Source Physics,). Tendon slackness at rest was accounted for by considering the actual rest length of the tendon, which was measured using a spline fit through the deep insertion marks and two additional points along the lower border of the slack tendon.[8] The force-elongation relationship of the five trials of each participant was averaged to achieve excellent reliability.[30] As tendon forces generated during ramp contractions are usually lower compared to an MVC, tendon stiffness was calculated as slope of a linear regression between 50% and 80% TF_{max}. Maximum tendon strain was then calculated by extrapolating the slope of the linear force-elongation relationship (assessed during the ramp contractions) to TF_{max}. The predicted maximum elongation was then normalized to the tendon rest length to obtain maximum tendon strain.

2.7 | Statistics

Though two athletes participated in the control and intervention group, the groups were treated as independent samples in the statistical analysis, which is a more conservative approach compared to the assumption of dependent samples. Baseline data (M1) of age were compared between groups with Student's *t* test for independent samples. All other parameters were analyzed with a linear mixed model for repeated measures and restricted maximum likelihood estimation using the *nlme* package in RStudio (version 1.2.1335, RStudio, Inc.). Linear mixed models are robust against violations of the normality assumption,[31] which was not given for the anthropometric data based on a Kolmogorov-Smirnov test with Lilliefors correction, and they have the strength of being able to handle missing data. One participant from the intervention group was not included in the analysis of tendon mechanical properties due to artifacts in the ultrasound recordings at all time points. In case of a significant interaction or main effect of time, *post-hoc* tests were applied using the *emmeans* package. The p-values were adjusted with the false discovery rate procedure of Benjamini-Hochberg; specifically, testing differences between groups at M1 and differences between M1 and the other time points analyzed

separately for both groups (ie, five comparisons). As indicator for muscle-tendon imbalances, we examined the frequency of athletes that reached maximum tendon strain levels of ≥9%, considering the potentially detrimental effect of high-level strain on the structural integrity of tendons.[4] The association of maximum tendon strain and proximal tendon PSF was analyzed using Pearson correlation coefficients (r) to examine the relationship of mechanical demand and micromorphology in both groups.[9] Further, we analyzed the frequencies of VISA-P scores in 10-point intervals and the frequencies of clinically relevant increases or decreases of the scores (± 13 points, that is, minimum clinically important difference).[22] The alpha level for all statistical tests was set to 0.05.

3 | RESULTS

There was no significant difference in chronological age between groups at baseline (control: 14.8 ± 0.5 years, intervention: 14.7 ± 0.7; $p = 0.86$). There was a main effect of time on the maturity offset, body height, and mass ($p < 0.001$); however, there was no significant effect of group ($p = 0.82$, 0.77, and 0.33, respectively; Table 1). There was a time-by-group interaction on maturity offset ($p < 0.001$); however, *post-hoc* analysis showed a significant increase of the estimated years to peak height velocity in both groups from baseline already to M2 ($p < 0.001$) and no baseline difference between groups ($p = 0.34$). No significant main effects of time and group or time-by-group interactions were found for maximum tendon strain ($p = 0.69$, 0.96 and 0.82, respectively) or proximal tendon PSF ($p = 0.50$, 0.16 and 0.59; Table 2). However, the frequency of athletes that had maximum tendon strain values over 9% showed a continuous decrease in the intervention group, while tending to increase in the controls (Figure 2). In the control group, tendon strain was inversely correlated with proximal tendon PSF at all time points (M1: $r = -0.644$, $p = 0.003$; M2: $r = -0.545$, $p = 0.016$, M3: $r = -0.663$, $p = 0.007$; Figure 3), indicating a lower

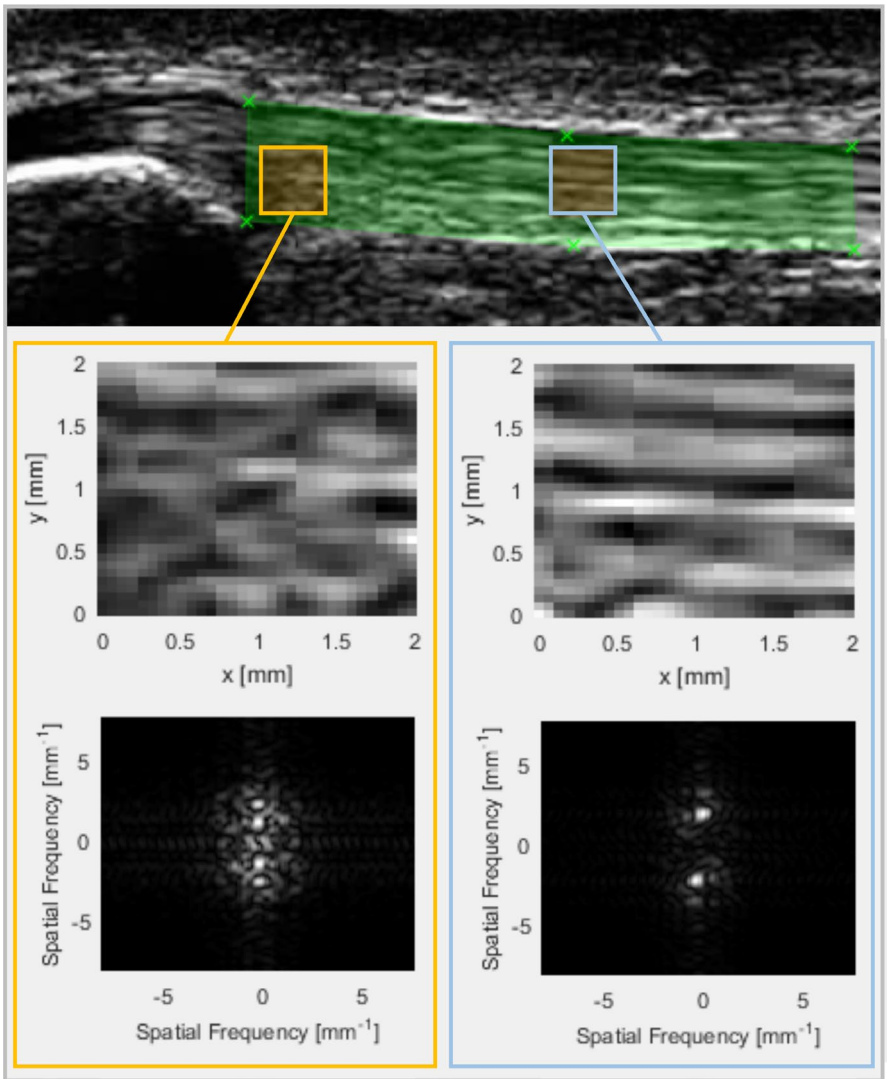

FIGURE 1 Patellar tendon micromorphology was assessed by applying a spatial frequency analysis on ultrasound images obtained from the proximal patellar tendon. All possible 32 × 32 pixel kernels within a polygonal region of interest with a length of 40% of the tendon rest length (green) were filtered and 2D Fast Fourier transformed. The yellow and blue squares represent two kernels with a low and high degree of fascicle packing and alignment and, thus, peak spatial frequency (1.4 and 2.2 mm^{-1}, respectively). The panels below the enlarged kernels show the respective frequency spectrum. The average peak spatial frequency value of all kernels was used in the statistical analysis

TABLE 1 Anthropometric data, average VISA-P scores and number of symptomatic athletes of the control and intervention group for each measurement time point (M1-3) over a competitive season

	Control			Intervention		
	M1 $n = 19$	M2 $n = 19$	M3 $n = 16$	M1 $n = 14$	M2 $n = 14$	M3 $n = 13$
Maturity offset (y)[*,†]	0.91 ± 0.64 (0.91)	1.42 ± 0.65[‡] (1.42)	1.54 ± 0.69[‡] (1.61)	1.15 ± 0.74 (1.15)	1.33 ± 0.78[‡] (1.33)	1.52 ± 0.78[‡] (1.58)
Height (cm)[*]	183 ± 9 (183)	185 ± 10[‡] (185)	186 ± 10[‡] (186)	183 ± 9 (183)	183 ± 9 (183)	184 ± 9[‡] (184)
Mass (kg)[*]	70.4 ± 10.4 (70.4)	71.7 ± 10.3 (71.7)	73.2 ± 12.2[‡] (73.2)	67.2 ± 10.8 (67.2)	67.5 ± 10.3 (67.5)	68.7 ± 9.9[‡] (69.4)
VISA-P score	92.4 ± 13.1	91.4 ± 11.5	96.1 ± 6.9	94.4 ± 10.1	97.7 ± 5.1	99.7 ± 1.1
No. of sympt. athletes	5	7	4	4	2	0

Note: The numbers are average ± SD of the given experimental data. The values in brackets show the group average predicted by the linear mixed model. Maturity offset refers to the estimated years to peak height velocity. Symptomatic was defined as VISA-P score ≤90.

[*]Significant main effect of time;

[†]Significant time-by-group interaction;

[‡]Significantly different to M1 (*post-hoc* test); $p < 0.05$.

TABLE 2 Maximum tendon strain, rest length, and proximal tendon peak spatial frequency (PSF) of the adolescent basketball athletes in the control and intervention group for each measurement time point (M1-3) over a competitive season

	Control			Intervention		
	M1 $n = 19$	M2 $n = 19$	M3 $n = 16$	M1 $n = 14$	M2 $n = 14$	M3 $n = 13$
Max. tendon strain (%)	8.1 ± 1.5 (8.1)	8.0 ± 1.2 (8.0)	8.5 ± 1.8 (8.4)	8.1 ± 2 (8.1)	8.2 ± 1.3 (8.2)	8.1 ± 2.1 (8.1)
Rest length (mm)	52.4 ± 6.2 (52.9)	53.1 ± 6.1 (53.4)	54.4 ± 6.6 (53.7)	51.5 ± 5 (51.5)	51.4 ± 4 9 (51.4)	52.8 ± 4.5 (51.6)
PSF (mm^{-1})	1.77 ± 0.23 (1.77)	1.77 ± 0.18 (1.77)	1.79 ± 0.29 (1.79)	1.78 ± 0.15 (1.79)	1.87 ± 0.16 (1.87)	1.83 ± 0.11 (1.83)

Note: The numbers are average ± SD of the given experimental data. The values in brackets show the group average predicted by the linear mixed model.

micromorphological integrity in tendons that are subjected to high levels of strain. This association was also present in the intervention group at baseline ($r = -0.59$, $p = 0.034$), yet not at M2 ($r = 0.17$, $p = 0.579$) or M3, ($r = -0.323$, $p = 0.333$), suggesting no reduction of proximal tendon PSF with an increase of strain after ten and 20 weeks of the intervention (Figure 3).

Figure 4 shows the frequencies of the VISA-P scores in 10-point intervals as well as the rates of clinically significant worsening or improvement. The frequency of scores of 100–91 points (ie, asymptomatic) was similar in both groups at M1 (~70%). In the intervention group, the scores steadily increased to 100% at M3, indicating a continuous decrease of patellar tendon pain. In the control group, the values decreased at M2 and reached only baseline level at M3 (Figure 4). Further, there was a higher rate of clinically significant improvements and a lower rate of worsening of tendon pain in the intervention compared to the control group (Figure 4).

Tendon force increased significantly in both groups (time: $p < 0.001$, group: $p = 0.12$, interaction: $p = 0.73$), with a significant change compared to M1 already at M2 ($p = 0.046$) in the control and at M3 in the intervention group ($p = 0.03$; Figure 5). Baseline differences were not significant ($p = 0.14$). Similarly, there was an effect of time ($p = 0.004$) without a significant effect of group ($p = 0.22$) or time-by-group interaction ($p = 0.40$) on tendon stiffness (Figure 5). However, *post-hoc* analysis showed that the increase of stiffness was only significant in the intervention group (M1 to M3; $p = 0.004$). Moreover, there was a significant correlation between maximum tendon strain at M1 and the relative increase in stiffness from M1 to M3 in the intervention group ($r = 0.762$; $p = 0.006$), indicating a higher increase of stiffness in athletes that initially had high levels of strain. This correlation was not significant in the control group ($r = 0.507$; $p = 0.054$).

There was a significant main effect of time on absolute ($p < 0.001$) but not body mass-normalized knee extension

moments during the MVCs ($p = 0.052$), with no significant main effect of group ($p = 0.70$ and 0.62) or interaction ($p = 0.64$ and 0.54; Table 3). The *post-hoc* analysis showed a significant increase of the absolute strength values from M1 to M2 ($p = 0.047$) and M3 ($p = 0.007$) in the control and to M3 in the intervention group ($p = 0.007$), with no significant baseline differences ($p = 0.54$). A significant main effect of time was also observed on vastus lateralis muscle thickness ($p = 0.03$; group: $p = 0.68$; interaction: $p = 0.71$), yet all *post-hoc* comparisons were non-significant (Table 3). No main effects of time ($p = 0.99$) and group ($p = 0.19$) or interaction ($p = 0.35$) were found on the pennation angle (Table 3).

4 | DISCUSSION

The present study investigated the effects of a functional high-load tendon exercise intervention on patellar tendon mechanical properties, micromorphology and the prevalence of pain and disability in adolescent elite basketball athletes, which is a high-risk group for tendinopathy.[1] At the descriptive level, we observed the expected reduction of the frequency of high-level tendon strain in the athletes of the intervention group and there were favorable effects on the prevalence of tendon pain and disability compared to a control group that followed their usual training schedule. Moreover, there was a significant inverse association of tendon strain with proximal tendon PSF, suggesting impairments of tendon micromorphology at higher levels of strain in both groups at baseline. This association was, however, resolved in the intervention group after ten (M2) and 20 weeks (M3), respectively, indicating that tendon-specific loading could have the potential to protect the structural integrity of the tendon from high levels of strain.

Imbalances of muscle strength and tendon stiffness can increase tendon strain and thus the mechanical demand for tendons, especially in athletes that are subjected to a high volume of plyometric loading.[2] Tendon strain of over 9% can be considered a transition range into high levels of strain that may initiate matrix damage.[4] The strain-induced deterioration of the mechanical integrity of the extracellular matrix, disruption of mechanotransduction to embedded tenocytes, and disturbance of tissue homeostasis are considered potential key factors in the etiology of tendinopathy.[32,33] The descriptive analysis of the frequency of athletes that had maximum tendon strain values over 9% in the present study suggests that about 20 min of specific tendon exercises, providing high-intensity loading for at least 3 s per loading cycle, applied three times per week over a 20-week period in a competitive season, could reduce the prevalence of high-level patellar tendon strain in adolescent athletes. There was a continuous trend towards a decrease of the frequencies of high-level strain in the intervention group, while tending to increase in the controls. The apparent prevention of muscle-tendon imbalances and high-level tendon strain was probably based on changes in tendon stiffness, which increased significantly in the intervention (18%) but not in the control

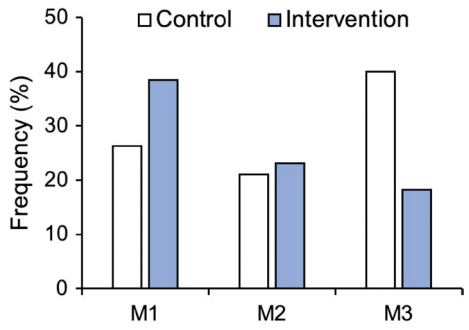

FIGURE 2 Frequency of adolescent athletes demonstrating high-level maximum patellar tendon strain in the control (white) and intervention group (blue) in the three measurement sessions (M1-3) over the competitive season. *High level* refers to tendon strain exceeding 9%

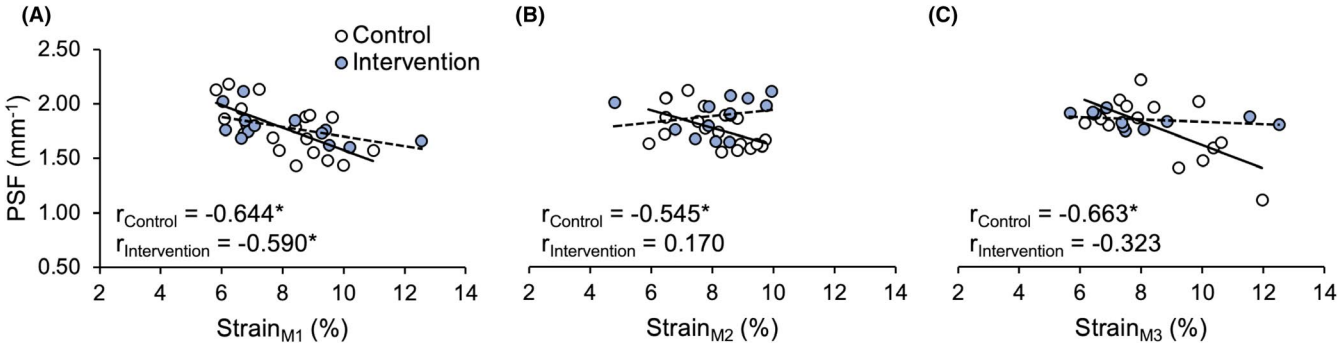

FIGURE 3 Correlation of maximum patellar tendon strain and proximal peak spatial frequency (PSF) at M1 (A), M2 (B), and M3 (C) in adolescent basketball athletes of the control (white) and intervention group (blue), respectively. The lines represent the associations for the control (solid) and intervention group (dashed). *r* Pearson correlation coefficient; * significant association; $p < 0.05$

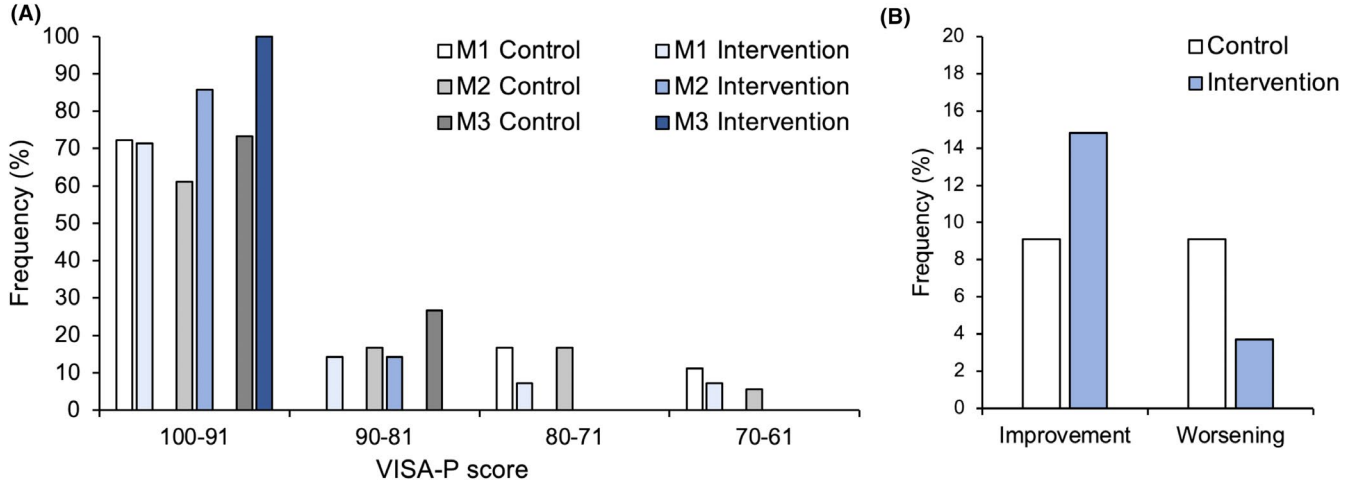

FIGURE 4 (A) Frequency of athletes reporting respective VISA-P scores in 10-point intervals at the three measurement time points (M1-3) over the season in the control ($n = 18$; white/gray) and intervention group ($n = 14$; blue). (B) Frequency of clinically significant improvement or worsening (ie, ±13 points of the VISA-P score) considering all observations (ie, sum of respective athletes over the three measurements per group) in the control ($n = 51$) and intervention group ($n = 41$), respectively

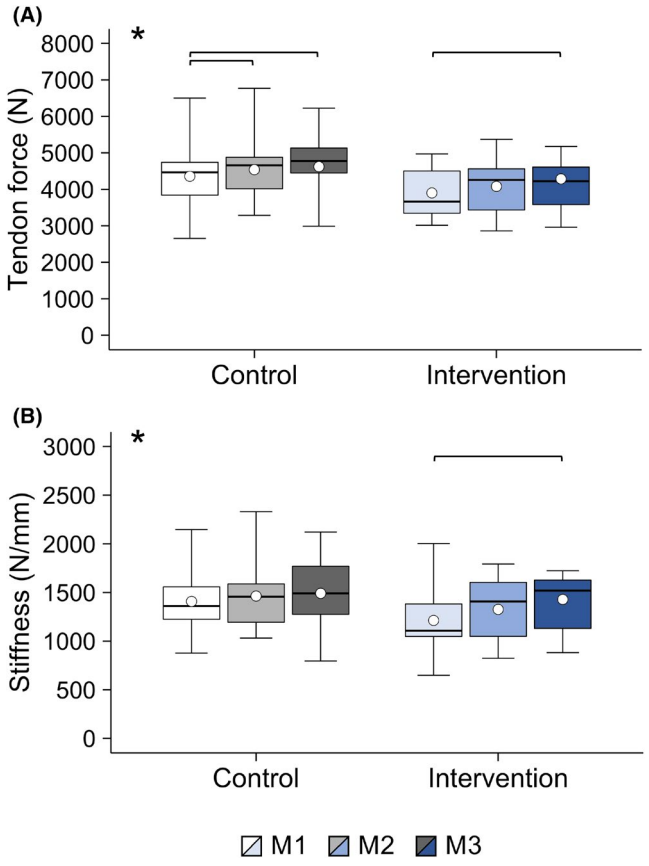

FIGURE 5 (A) Maximum patellar tendon force and (B) tendon stiffness of the adolescent basketball athletes in the control (white/gray) and intervention group (blue) at the three measurement time points (M1-M3) over the season. The given experimental data are shown in box plots, while the average values predicted by the linear mixed model are shown in white circles. * Significant main effect of time; brackets indicate significant *post-hoc* comparisons; $p < 0.05$

group (6%), though both groups experienced a significant increase of tendon force. It should be noted that the time-by-group interaction on tendon stiffness was not significant. However, this was likely due to the marked heterogeneity of the changes in the control group (M1-3: 64 ± 318 N/mm) as the increase of tendon stiffness in the intervention was clearly greater and more consistent (221 ± 159 N/mm). Though not fully conclusive, the findings support the view that the sport-specific and predominantly plyometric loading is not an effective stimulus for increasing tendon stiffness.[2] Studies directly comparing the effects of plyometric training to loading regimen that cause lower strain rates and longer strain durations consistently show lower adaptive responses of the tendon following the plyometric loading protocols.[18,19,34] Increasing the duration of high-intensity loading cycles by means of specific exercises, however, seems more adequate to promote the resilience of tendons. In this study, especially athletes that had high levels of strain at baseline experienced a marked increase of tendon stiffness due to the intervention. There was a strong correlation of maximum tendon strain at baseline and the relative increase in stiffness in the intervention but not the control group. As it is beyond the scope of this study, future work may verify if particularly those athletes with high-level tendon strain and reduced safety factor for tendon overuse benefit from exercise interventions with optimized tendon loading.

It has been shown *in vitro* that the repetitive application of high-level strain deteriorates the structural integrity of tendinous tissue.[3,4] One way to estimate the latter *in vivo* is by means of a spatial frequency analysis of ultrasound images of tendons.[10,11] Recently, we already found evidence that there is an inverse association of *in vivo* patellar tendon

TABLE 3 Knee extension moments during the maximum voluntary contractions (MVC), MVC normalized to body mass, vastus lateralis (VL) thickness and pennation angle of the adolescent basketball athletes in the control and intervention group for each measurement time point (M1-3) over a competitive season

	Control			Intervention		
	M1 $n = 19$	M2 $n = 19$	M3 $n = 16$	M1 $n = 14$	M2 $n = 14$	M3 $n = 13$
MVC (Nm)*	249 ± 41 (253)	260 ± 40‡ (264)	268 ± 41‡ (270)	245 ± 50 (243)	259 ± 56 (256)	267 ± 57‡ (269)
MVC_{norm} (Nm/kg)	3.62 ± 0.5 (3.62)	3.71 ± 0.48 (3.71)	3.77 ± 0.54 (3.73)	3.62 ± 0.49 (3.62)	3.79 ± 0.51 (3.79)	3.87 ± 0.68 (3.90)
VL thickness (mm)*	20.9 ± 3.5 (20.9)	21.2 ± 3.1 (21.2)	21.3 ± 3.6 (21.5)	21.1 ± 2.8 (21.1)	21.5 ± 3.4 (21.5)	22.6 ± 2.5 (22.3)
VL pennation angle (°)	10.2 ± 1.6 (10.2)	10.1 ± 1.6 (10.1)	10.0 ± 1.6 (9.9)	10.5 ± 1.3 (10.5)	10.7 ± 1.1 (10.7)	10.9 ± 1.1 (10.9)

Note: The numbers are average ± SD of the given experimental data. The values in brackets show the group average predicted by the linear mixed model.

*Significant main effect of time;

‡Significantly different to M1 (*post-hoc* test); $p < 0.05$.

strain and the PSF at the proximal tendon,[9] which is also the most common site of pain and histological abnormalities in tendinopathy. This association was confirmed in the control group of the present study at all time points and in the intervention group at baseline, yet no significant decrease in the micromorphological integrity with increasing strain was observed in the intervention group at M2 and M3. This might suggest that the tendon exercise stimulus attenuated strain-induced deteriorations of the micromorphological integrity of the tissue.

The physiological mechanisms behind both the trend towards a reduction of high-level tendon strain and the attenuation of strain-induced impairments of the proximal tendon micromorphology are yet unclear. The maintenance and regeneration of tendons following loading as well as adaptive changes of their mechanical properties are likely based on distinct mechanisms of mechanotransduction and the associated metabolic responses to the type of loading applied.[35,36] The long duration of load application in the selected exercises has been shown to be favorable for tendon adaptation.[16,18] It may be speculated that an increase of strain duration during loading leads to a more homogeneous strain distribution within the extracellular matrix due to the viscoelastic properties of the tissue.[37] A uniform stimulation of the embedded tenocytes could be beneficial for a balanced matrix turnover and maintenance of the structural integrity of the tissue. Given a sufficient stimulation of anabolic signaling, this may also lead to an increase in tendon stiffness.

In addition to the protective effects on tendon micromorphology, there were promising results considering the prevalence of tendon pain and pain-related disability in the adolescent athletes at the descriptive level. In both groups, approximately 70% of the players could be considered asymptomatic at baseline. While there was no positive development (considering the number of asymptomatic athletes) in the control group, an increasing number of athletes became pain-free over time in the intervention group and all athletes scored higher than 96 points in the final VISA-P assessment at M3. Though there is no simple relationship between tendon structure and pain,[32] it may be argued that the reduction of high-level tendon strain and attenuation of strain-induced impairments of micromorphology outlined above could also reduce the expression of nociceptive substances. Structural abnormalities are also present in asymptomatic tendons, but the risk for the development of symptoms is about four times higher in tendons that show indications of an impairment of tendon structure.[38] Considering the rather small sample size and descriptive nature of the data analysis in this study, the effects on pain prevalence may need confirmation in an epidemiological study. However, very recently we applied a similar high-load exercise intervention to a group of adolescent handball players and observed a comparable reduction in tendon pain prevalence.[39] In that study, one third of the athletes in the control group reported at least once a clinically significant aggravation of symptoms, while all of the athletes in the intervention group remained or became pain-free during the season. Taken together, the data are promising indications that high-load tendon exercise interventions may have a relevant contribution to the prevention and treatment of tendon pain in young athletes. As no changes or between-group differences with regard to tendon stiffness were observed in the earlier trial—maybe in part due to the lower training frequency compared to the present study (ie, two vs. three times per week)—the findings underline that beneficial effects on the prevalence of tendon pain and pain-related disability can be achieved in athletes also without a reduction of habitual tendon strain.

There was a significant effect of time on both knee extensor muscle strength and vastus lateralis thickness, yet the pennation angle remained unchanged. As the changes in vastus lateralis thickness between M1 and M3 were smaller (ie, 3–6%) than the increase in strength (7–11%) and did not reach

statistical significance in the post-hoc comparisons, one may assume that neural adaptation had a major contribution to the observed strength gains. Both strength and muscle thickness increased in both groups to a similar extent. This was not surprising, considering that both groups had the same overall volume of training. Still, this finding is important as it suggests that tendon exercise routines for the prevention of strain-induced tissue impairments and pain can be integrated into adolescent elite athlete training programs without compromising the development of muscle strength and size.

There are some limitations to this study that warrant discussion. First, due to the time-consuming procedures involved with the assessment of tendon mechanical properties and muscle architecture in vivo, the sample size in this study is rather small. For this reason, nominal scaled data as the frequency of high-level tendon strain and the prevalence of pain and pain-related disability were analyzed at the descriptive level and the results need to be interpreted carefully. Due to Osgood-Schlatter disease in one and ultrasound artifacts in another case, two participants were excluded in some analyses but not others. We took this approach to increase the statistical power and a general exclusion of the two participants did not change the direction of the outcomes. Further, there was a group-by-time interaction on the estimated maturity and the average values suggest a greater increase of maturity in the control group, which may have biased the results. However, as maturation is associated with an increase of both muscle strength and tendon stiffness,[6,7] a potential bias would rather lead to an under- than overestimation of the intervention effects. Finally, the actual loading both during the common training and the exercises introduced in the intervention group was not experimentally controlled. This is an inherent limitation of a study that aims to translate knowledge from fundamental science (in terms of effective loading for tendons) into the practical field and thus uncertainties remain about the actual tendon strain during the functional exercises used in this study. Future studies may provide information on the strain behavior of the patellar tendon during these exercises and evaluate approaches to individualize load prescription .[40]

5 | PERSPECTIVES

Integrating specific high-load exercises that provide an evidence-based stimulus for tendon adaptation into the training routine of adolescent athletes seems to be an effective means to attenuate strain-induced impairments of tendon micromorphology and could further reduce the frequency of high-level tendon strain as well as the prevalence of tendon pain and pain-related disability. While the underlying mechanisms at the cellular level may be addressed in future research, direct recommendations can be drawn for the practical field. Five sets of four repetitions of high-intensity exercises (aiming to induce sufficient tendon strain of about 4.5% to 6.5%) applied over at least 3 s per cycle take about 15 to 20 min and can be incorporated three times a week in elite training schedules. Especially in sports associated with a high volume of plyometric loading due to jumps and change-of-direction movements, high-load tendon exercise programs may be firmly established into future physical development models for youth athletes.

ACKNOWLEDGEMENTS

This work was financially supported by the Federal Institute of Sport Science (BISp), Germany (AZ 070501/18-20). The MRI data acquisition was kindly funded by the Foundation Stiftung Oskar-Helene-Heim, Germany. NP was a scholarship holder of the German Academic Exchange Service (D.A.A.D.). M-ST held an Elsa-Neumann scholarship.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ORCID

Falk Mersmann https://orcid.org/0000-0001-7180-7109
Theresa Domroes https://orcid.org/0000-0001-9941-6716
Sebastian Bohm https://orcid.org/0000-0002-5720-3672
Adamantios Arampatzis https://orcid.org/0000-0002-4985-0335

REFERENCES

1. Lian OB, Engebretsen L, Bahr R. Prevalence of jumper's knee among elite athletes from different sports: a cross-sectional study. *Am J Sports Med*. 2005;33(4):561-567.
2. Mersmann F, Bohm S, Arampatzis A. Imbalances in the development of muscle and tendon as risk factor for tendinopathies in youth athletes: a review of current evidence and concepts of prevention. *Front Physiol*. 2017;8:987.
3. Wren TAL, Lindsey DP, Beaupré GS, Carter DR. Effects of creep and cyclic loading on the mechanical properties and failure of human Achilles tendons. *Ann Biomed Eng*. 2003;31(6):710-717.
4. Wang T, Lin Z, Day RE, et al. Programmable mechanical stimulation influences tendon homeostasis in a bioreactor system. *Biotechnol Bioeng*. 2013;110(5):1495-1507.
5. Simpson M, Rio E, Cook J. At what age do children and adolescents develop lower limb tendon pathology or tendinopathy? A systematic review and meta-analysis. *Sports Med*. 2016;46(4):545-557.
6. Charcharis G, Mersmann F, Bohm S, Arampatzis A. Morphological and mechanical properties of the quadriceps femoris muscle-tendon unit from adolescence to adulthood: effects of age and athletic training. *Front Physiol*. 2019;10:1082.
7. Mersmann F, Bohm S, Schroll A, Marzilger R, Arampatzis A. Athletic training affects the uniformity of muscle and tendon adaptation during adolescence. *J Appl Physiol*. 2016;121:893-899.
8. Mersmann F, Charcharis G, Bohm S, Arampatzis A. Muscle and tendon adaptation in adolescence: elite volleyball athletes compared to untrained boys and girls. *Front Physiol*. 2017;8:613.
9. Mersmann F, Pentidis N, Tsai MS, Schroll A, Arampatzis A. Patellar tendon strain associates to tendon structural abnormalities in adolescent athletes. *Front Physiol*. 2019;10:963.

10. Bashford GR, Tomsen N, Arya S, Burnfield JM, Kulig K. Tendinopathy discrimination by use of spatial frequency parameters in ultrasound b-mode images. *IEEE Trans Med Imaging*. 2008;27(5):608-615.
11. Kulig K, Landel R, Chang YJ, et al. Patellar tendon morphology in volleyball athletes with and without patellar tendinopathy. *Scand J Med Sci Spor*. 2013;23(2):e81-e88.
12. Waugh CM, Korff T, Fath F, Blazevich AJ. Effects of resistance training on tendon mechanical properties and rapid force production in prepubertal children. *J Appl Physiol*. 2014;117(3):257-266.
13. Mersmann F, Laube G, Bohm S, Arampatzis A. Muscle and tendon morphology in early-adolescent athletes and untrained peers. *Front Physiol*. 2020;11:1029.
14. Mersmann F, Bohm S, Schroll A, Boeth H, Duda GN, Arampatzis A. Muscle and tendon adaptation in adolescent athletes: a longitudinal study. *Scand J Med Sci Spor*. 2017;27(1):75-82.
15. Zhang C, Couppé C, Scheijen JLJM, et al. Regional collagen turnover and composition of the human patellar tendon. *J Appl Physiol*. 2020;128(4):884-891.
16. Arampatzis A, Peper A, Bierbaum S, Albracht K. Plasticity of human Achilles tendon mechanical and morphological properties in response to cyclic strain. *J Biomech*. 2010;43(16):3073-3079.
17. Arampatzis A, Karamanidis K, Albracht K. Adaptational responses of the human Achilles tendon by modulation of the applied cyclic strain magnitude. *J Exp Biol*. 2007;210(Pt 15):2743-2753.
18. Bohm S, Mersmann F, Tettke M, Kraft M, Arampatzis A. Human Achilles tendon plasticity in response to cyclic strain: effect of rate and duration. *J Exp Biol*. 2014;217(22):4010-4017.
19. Burgess KE, Connick MJ, Graham-Smith P, Pearson SJ. Plyometric vs. isometric training influences on tendon properties and muscle output. *J Strength Cond Res*. 2007;21(3):986-995.
20. Pentidis N, Mersmann F, Bohm S, Giannakou E, Aggelousis N, Arampatzis A. Triceps surae muscle-tendon unit properties in pre-adolescent children: a comparison of artistic gymnastic athletes and non-athletes. *Front Physiol*. 2019;10:615-.
21. Bohm S, Mersmann F, Arampatzis A. Human tendon adaptation in response to mechanical loading: a systematic review and meta-analysis of exercise intervention studies on healthy adults. *Sports Med Open*. 2015;1:7.
22. Lohrer H, Nauck T. Cross-cultural adaptation and validation of the VISA-P questionnaire for German-speaking patients with patellar tendinopathy. *J Orthop Sport Phys*. 2011.41(3):180–190.
23. Enomoto S, Tsushima A, Oda T, Kaga M. The passive mechanical properties of muscles and tendons in children affected by Osgood-Schlatter disease. *J Pediatr Orthop*. 2020;40(4):e243-e247.
24. Moore SA, McKay HA, Macdonald H, et al. Enhancing a somatic maturity prediction model. *Med Sci Sport Exer*. 2015;47(8):1755-1764.
25. Mersmann F, Bohm S, Schroll A, Boeth H, Duda G, Arampatzis A. Muscle shape consistency and muscle volume prediction of thigh muscles. *Scand J Med Sci Spor*. 2015;25(2):e208-e213.
26. Marzilger R, Legerlotz K, Panteli C, Bohm S, Arampatzis A. Reliability of a semi-automated algorithm for the vastus lateralis muscle architecture measurement based on ultrasound images. *Eur J Appl Physiol*. 2018;118(2):291-301.
27. Arampatzis A, Karamanidis K, De Monte G, Stafilidis S, Morey-Klapsing G, Bruggemann G. Differences between measured and resultant joint moments during voluntary and artificially elicited isometric knee extension contractions. *Clin Biomech*. 2004;19(3):277-283.
28. Mademli L, Arampatzis A, Morey-Klapsing G, Bruggemann G. Effect of ankle joint position and electrode placement on the estimation of the antagonistic moment during maximal plantarflexion. *J Electromyogr Kinesiol*. 2004;14(5):591-597.
29. Herzog W, Read LJ. Lines of action and moment arms of the major force-carrying structures crossing the human knee joint. *J Anat*. 1993;182(Pt 2):213-230.
30. Schulze F, Mersmann F, Bohm S, Arampatzis A. A wide number of trials is required to achieve acceptable reliability for measurement patellar tendon elongation in vivo. *Gait Posture*. 2012;35(2):334-338.
31. Jacqmin-Gadda H, Sibillot S, Proust C. Robustness of the linear mixed model to misspecified error distribution. *Comput Stat Data Anal*. 2007;51(10):5142-5154.
32. Cook JL, Rio E, Purdam CR, Docking SI. Revisiting the continuum model of tendon pathology: what is its merit in clinical practice and research? *Br J Sports Med*. 2016;50(19):1187-1191.
33. Magnusson SP, Langberg H, Kjaer M. The pathogenesis of tendinopathy: balancing the response to loading. *Nat Rev Rheumatol*. 2010;6(5):262-268.
34. Kubo K, Morimoto M, Komuro T, et al. Effects of plyometric and weight training on muscle-tendon complex and jump performance. *Med Sci Sport Exer*. 2007;39(10):1801-1810.
35. Magnusson SP, Heinemeier KM, Kjaer M. Collagen Homeostasis and Metabolism. *Adv Exp Med Biol*. 2016;920(4-5):11-25.
36. Dyment NA, Galloway JL. Regenerative biology of tendon: mechanisms for renewal and repair. *Curr Mol Biol Rep*. 2015;1(3):124-131.
37. Baar K. Stress relaxation and targeted nutrition to treat patellar tendinopathy. *Int J Sport Nutr Exerc Metab*. 2019:29(4):453-457.
38. McAuliffe S, McCreesh K, Culloty F, Purtill H, O'Sullivan K. Can ultrasound imaging predict the development of Achilles and patellar tendinopathy? A systematic review and meta-analysis. *Br J Sports Med*. 2016;50(24):1516-1523.
39. Mersmann F, Laube G, Marzilger R, Bohm S, Schroll A, Arampatzis A. A functional high-load exercise intervention for the patellar tendon reduces tendon pain prevalence during a competitive season in adolescent handball players. *Front Physiol*. 2021;12.626225
40. Arampatzis A, Mersmann F, Bohm S. Individualized muscle-tendon assessment and training. *Front Physiol*. 2020;11:723.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Mersmann F, Domroes T, Pentidis N, et al. Prevention of strain-induced impairments of patellar tendon micromorphology in adolescent athletes. *Scand J Med Sci Sports*. 2021;31:1708–1718. https://doi.org/10.1111/sms.13979