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Effect of a 12-week Eccentric and Isometric Training in Achilles Tendinopathy on the Gastrocnemius Muscle: an Ultrasound Shear Wave Elastography Study

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LISTS OF ABBREVIATIONS

SWE: shear wave elastography
ROI: region of interest
EE: eccentric exercises
ISO: isometric exercises
AT: Achilles tendinopathy
MG: medial gastrocnemius
ML: lateral gastrocnemius

SUMMARY

Background. Eccentric exercises (EE) and isometric exercises (ISO) are standard treatment options for Achilles tendinopathy, but still their exact effect remains uncertain. Shear Wave Elastography (SWE) was used to examine the influence of these exercises on the elastic properties of Mm. gastrocnemii medialis and lateralis in a 12-week training program.

Methods. Prospective study with patients suffering from Achilles tendinopathy, which were randomised into 2 groups and conducted exercises for 12 weeks on the symptomatic limb: EE (n=15, 9 male, 55a ± 6.5) and EE+ISO (n=15, 10 male, 47a ± 16.1). Shear Wave Elastography of the gastrocnemius medialis (MG) and lateralis (ML) was made before exercises (T0), after 4 (T1) and 12 weeks (T2) using an established protocol.

Results. Muscles of asymptomatic and symptomatic legs did not differ at baseline neither for EE (p=0.139) nor for EE+ISO (p=0.778). SWE values of MG and ML of symptomatic limbs showed no significant alterations neither for EE and EE+ISO nor for the whole population (p=0.567-0.746) without any difference between EE vs. EE+ISO for the whole study period (T0: p=0.247, T1: p=0.990, T2: p=0.516). Contrary, MG and ML of the asymptomatic untrained limb showed increased SWE values over the course for the EE-group (p=0.041) and the whole population (p=0.003) with a significant difference of the symptomatic and asymptomatic limb at T2 for the EE group (p=0.01) and the whole population (p=0.03). MG and ML of asymptomatic limbs differed significantly between EE vs. EE+ISO at T2 (p=0.03), showing higher SWE values for EE.

Conclusions. Using Shear Wave Elastography there was no measurable effect neither for EE nor for EE+ISO on MG and ML of symptomatic limbs over a 12-week intervention period. Contrary, in the asymptomatic untrained limb elastic properties increased in the EE group which might be based on the cross-education effect.

KEY WORDS
Achilles tendinopathy; shear wave elastography; muscle; eccentric exercises; isometric exercises

INTRODUCTION

The current gold standard for the treatment of Achilles tendinopathy (AT) are eccentric exercises (EE)(1). Beneficial effects of EE might be structural improvement of the tendon integrity, changes of tendon length, neuromuscular or -chemical effects as well as intratendinous changes in fluid movement (2). Recently it has been advocated that isometric exercises (ISO) might be a further option (3), since performing EE can be very painful and therefore some patients quit exercises due to too much pain. Contrary, ISO should be conducted pain free and is based on the assumption that painless muscular activation has a central neuroplastic effect and resets aberrant neural motor pathways, which developed due to painful muscular load. Moreover, in active athletes reduced plantarflexor strength is considered as the primary modifiable risk factor for AT requiring a specific training for the muscle and not only the tendon (4). In patellar tendinopathy clinical studies showed good results with ISO, reducing pain intensity after four weeks without a mandatory reduction of load (5, 6). In comparison to ISO, EE have a higher level of gene expression, upregulation of muscle cell activity and anabolic pathways as well as a greater increase in muscle strength (7). However, the exact therapeutic effect of both EE and ISO is still unknown and previous investigations were more concentrated on the tendon itself e.g. examining the remodeling capacity, instead of including also the muscle as part of the whole muscle-tendon unit. Especially, elastic properties of the muscle tendon unit in vivo have not been sufficiently studied yet (2).

Recently, Shear Wave Elastography (SWE) has been used to measure tissue elasticity as a real-time diagnostic imaging technique, which provides quantitative measurements of tissue elasticity (kPa). SWE generates an acoustic impulse which deflects the examined tissue. By this, a transversal dispersing shear wave is developed. A high frequent ultrasound is able to depict the spread of the shear wave and by this the quantitative tissue elasticity (kPa; m/s) is deduced (8). The usage of SWE measuring muscular elastic properties might add further aspects for a better understanding about the effects of ISO and EE in muscles.

Several studies examined the usage of SWE on muscular tissue and concluded, that it is an adequate modality to evaluate muscular properties offering reproducible results (9-11). Moreover, Dubois et al. (10) could find an inter-operator reproducibility of 0.87-0.91 as well as an intra-operator repeatability of 0.91-0.94 for general use in muscular tissue. These findings could be confirmed by Lacourpaille et al. (12) evaluating the gastrocnemius medialis muscle (intra-session reliability: 0.950; inter-day reliability: 0.922; inter-observer reliability: 0.728) and Taniguchi et al. (13) evaluating the resting human medial and lateral gastrocnemius demonstrating a high ICC (0.97-0.98) with a coefficient of variation and a standard error of measurement under 4% and 0,2 kPa, respectively. Using SWE, effects of static stretching on the calf muscles were noticeable in healthy individuals: static stretching of calf muscle reduced muscular stiffness with immediate and long-term effects after five weeks on both Mm. gastrocnemii (14-16). However, after only one session of stretching, the immediate reduction of muscular elastic properties is recurrent after 20 minutes (13).

Using SWE, the goal of this study was to evaluate long-term effects after 4 and 12 weeks on the calf muscle elasticity of participants conducting EE and ISO to treat AT, in order to provide a better understanding of the therapeutic effect of these exercise types on muscular tissue.

METHODS

Study design

In this prospective study individuals with symptomatic AT were randomly assigned by sealed numbered envelopes to either a group performing single EE or to a group performing combined EE and ISO. There was a decision against a group only conducting isolated ISO, assuming low compliance if EE as the standard treatment would have been withholded. The muscular elasticity of both calf muscles was evaluated by SWE examinations at three measurement points: start (T0), first follow-up after 4 weeks (T1) and second follow-up after 12 weeks (T2). The investigation was approved by the clinical ethics committee of the local medical faculty (EK 059/17) and all participants provided written informed consent. We conducted the research ethically according international standards following Padulo et al. (17). Inclusion criteria were AT with provoked pain by palpation, age >= 18 years, minimum symptom duration of 8 weeks and the physical ability to perform the physiotherapeutic exercises. Exclusion criteria were known neuromuscular diseases, over- or underweight (BMI>35; BMI<17), a previous Achilles tendon rupture or foot operation. All criteria were carefully evaluated by an experienced physician, who confirmed the diagnosis by clinical examination and ultrasound evaluating neovascularisation, tendon thickness, hypoechogenicity and fascicle irregularities.

Eccentric and Isometric exercises

At baseline, the accurate performance of EE and ISO were demonstrated and the participants received a handout with further explanations. Exercises were administered by orthopedic surgeons experienced with the conservative treatment of Achilles tendinopathy. At every single appointment exact performance of exercises was controlled. All exercises were performed as home-based exercises and the exact performance of the exercises was checked at every further appointment. The EE group performed exercises twice a day with three sets of 15 repetitions on a step. Participants started standing on the forefoot while lowering the heel with an extended knee slowly under the level of the step holding this position for two seconds (18). The EE+ISO group performed EE the same way as group 1. Additionally, they performed ISO once per day with five sets of 45 seconds each. There were in total three level of loads with progressive intensity depending on the pain sensation of the patients. At load level 1 patients were standing 45 seconds on the tip of toes of both legs, whereas at load level 2 they were standing with all their body weight just on the symptomatic leg. At level 3 individuals should add further load by pushing themselves down while standing under a door frame. The ISO protocol was self-designed aiming to be simple and easily applicable without using technical aid in order to increase compliance. Therefore, a metronome as described in studies by Rio et al. has not been used (5, 6). **Table I** as well as **figure 1** and **figure 2** give an overview about the different treatment regimes.

Data Acquisition with SWE

A standardized SWE protocol of the left and right Mm. gastrocnemii has been used for each measurement point. Examinations were conducted with an ultrasound system (Aixplorer™, Supersonic Imagine, Aix-en-Provence, France) with a high-resolution linear 18 MHz transducer, (SuperLinear™ SL 18-4, Supersonic Imagine, Aix-en-Provence, France) in longitudinal planes.

Muscle stiffness of the medial gastrocnemius (MG) and lateral gastrocnemius (LG) muscle of both legs was measured using previously published standardized protocols (10, 12, 14, 19): measurements were done separately in the MG and ML at 1/3 of the lower leg length from the popliteal crease to the lateral malleolus, where almost the maximal cross-sectional area in the lower leg is observed (20). To reduce passive torque of the calf muscle and thus

Table I. Overview about eccentric and isometric exercises.

	Eccentric exercises	Isometric exercises
frequency per day	2	1
sets with repetitions	3 x 15	5 x 1
pain	might be painful	should be conducted painfree
technique and adaptive load levels	standing in plantarflexion on the forefoot on a step and lowering down the heel with an extended knee slowly under the level (midportion)/ at the level (insertion) of the step. To avoid concentric muscle contraction participants need to lift the heel into the starting position with the help of the other leg.	adjustment depending on pain **level 1**: standing 45 sec. on tip of toes of both legs **level 2**: standing 45 sec. on tip of toes of the symptomatic leg **level 3**: standing 45 sec. on tip of toes of the symptomatic leg with pushing down while standing under a door frame

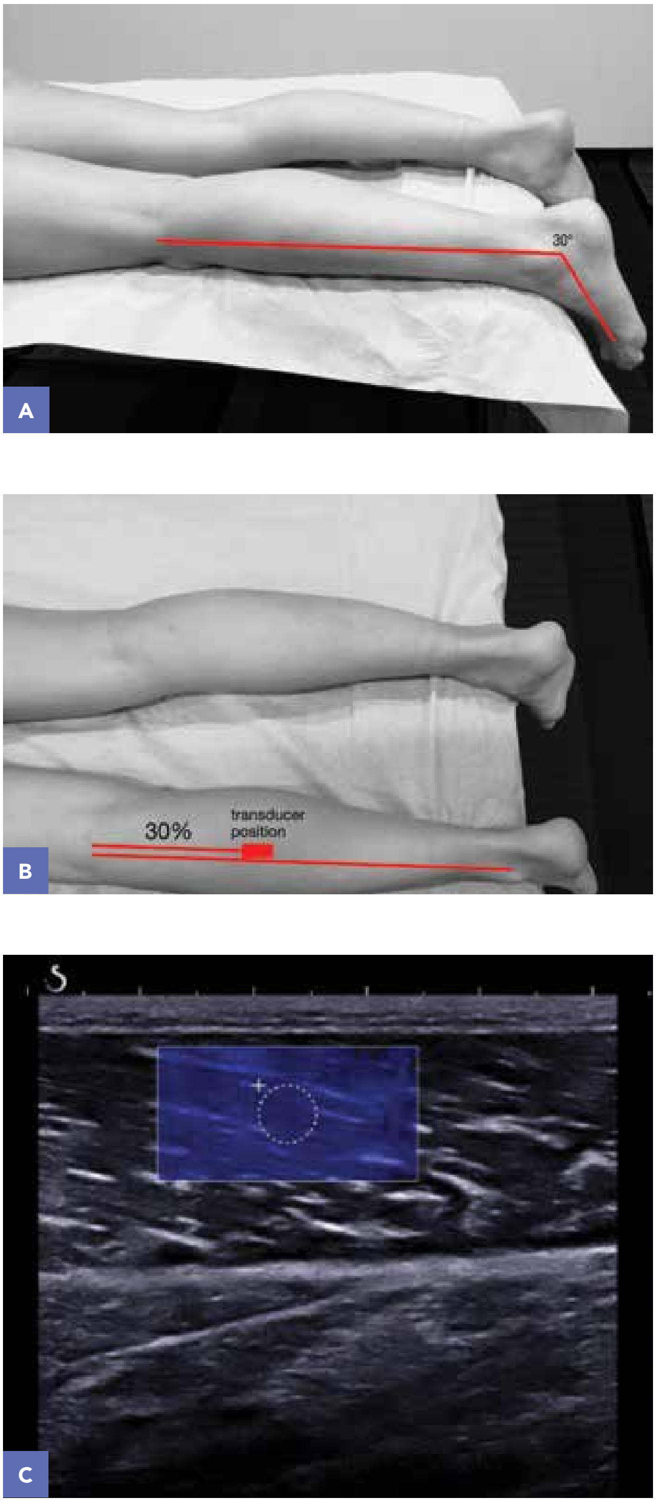

Figure 3. Example of SWE elastography for ML. Measurement was made in 30° plantar flexion and at 1/3 of the lower leg length from the popliteal crease to the lateral malleolus in the longitudinal plane.

muscular preload the ankle was positioned in 30% plantarflexion without active contractions. For data acquisition the probe was strictly hold in a parallel plane to the muscle fibers controlled by the B-Mode image to avoid measurement errors due to anisotropy (**figure 1**) (9, 11, 12). Maximum Young's modulus was measured in longitudinal plane of MG and LG in both legs (**figure 3**).

The acquired SWE-information was evaluated quantitatively in Kilopascal (kPa), up to a maximum tissue rigidity of 300 kPa (10m/s). The standard size of SWE-measurement window was 2 cm^2 with a Region of Interest of 5-mm for MG and LG in the most rigid part of the measurement window. Primary outcome measures were the mean SWE values in the MG and LG.

Statistical analysis

For all analyses, SPSS 22.0 was used to assess statistical significance, which was defined as $p<0.05$. Normal distribution was evaluated with a Kolmogorov-Smirnov-Test and Chi^2-Test. One-way ANOVA with repeated measures (Greenhouse-Geisser) were made to examine significant changes over time for the SWE values. Post hoc tests used the Bonferoni correction. Paired and unpaired T-Test examined significant differences of SWE-values within the group and between groups.

RESULTS

Table II gives an overview of the demographic data of each group. According to the demographic data, there is no statistically significant difference between the two groups. In the first 4 weeks all patients were performing EE twice and ISO once per day, while afterwards compliance decreased in both groups equally and exercises were in average only performed once per day as patients stated in the follow-up.

Table III depicts, that at baseline (T0) there were no significant differences between muscular SWE-values of right and left as well as symptomatic and asymptomatic limbs according EE vs. EE+ISO or MG vs. ML (p=0.087-0.943). Furthermore, muscles of asymptomatic and symptomatic limbs did not differ at baseline neither for EE (p=0.139) nor for EE+ISO (p=0.778) (**table IV**).

Table IV points out, that during the whole follow-up period the different treatment regimes did not influence SWE values of MG/ML of legs with symptomatic tendons neither for the two different study groups nor for the whole population (p=0.567-0.746). Contrary, there was a significant effect in untrained MG/ML of asymptomatic limbs of the EE-group (F(2,38)=3.472, p=0.041) and the pooled analysis of MG/ML in both groups (F(2,66)=6.524, p=0.003), showing increased SWE values over the course. This further resulted in significant differences between MG/ML of trained symptomatic and untrained asymptomatic limbs at T2 for the EE group (p=0.01) and both groups together (p=0.03).

Furthermore, there was no notable difference of SWE values between EE vs. EE+ISO for symptomatic legs for the different measurement points within the intervention period (T0: p=0.247, T1: p=0.990, T2: p=0.516). This also counted partially for asymptomatic legs for T0 and T1 (T0: p=0.05, T1: p=0.07), but at T2 there was a significant difference between EE vs. EE+ISO (T2: p=0.03), showing higher SWE values in the EE group.

DISCUSSION

This prospective study compares the influence of a 12-week training program of EE vs. EE+ISO on elastic properties of the MG and ML evaluated with SWE in patients suffering from Achilles tendinopathy. Analysis revealed no significant change in SWE values of muscles with symptomatic tendons over the whole study period. However, SWE examination yield increased elastic properties of untrained muscles of asymptomatic legs in EE.

The present study is the first which compares the influence of EE on MG and ML using SWE in a 12 weeks program.

Table II. Demographic data.

		EE: (n=15)		**EE+ISO: (n=15)**	
right insertion	left insertion	6	5	2	2
right midportion	left midportion	7	4	9	11
male	female	9	6	10	5
age (years)		55 (44-62; SD 6.5)		47 (21-73; SD 16.1)	
sport (hours/week)		2,8 (0-6; SD 1.9)		4 (0-9; 3.48)	
weight (kg)		76.4 (54-115; SD 14.7)		75.7 (57-93; SD 12.10)	
height (cm)		174 (164-193; SD 9,6)		177 (160-190; SD 9.16)	
Body Mass Index (kg/m^2)		25 (19-34; SD 3.5)		25 (20-28; SD 2.27)	

Table III. Initial (T0) muscular SWE- values (kPa) comparing intraindividual differences between MG vs. ML and EE vs. EE+ISO finding no significant differences for the left and right or asymptomtic and symptomatic limb.

				EE	EE + ISO	T-Test p-value
T0	right	MG	mean kPa	13.2 (SD 7.4) n=15	13.1 (SD 5.7) n=15	0.943
		LG	mean kPa	10.3 (SD 5.0) n=15	11.1 (SD 4.8) n=15	0.613
			T-Test p-value	0.152	0.216	
	left	MG	mean kPa	12.6 (SD 4.8) n=15	11.7 (SD 4.8) n=15	0.532
		LG	mean kPa	11.6 (SD 4.1) n=15	13.0 (SD 5.3) n=15	0.352
			T-Test p-value	0.477	0.396	
	asymptomatic	MG	mean kPa	14.0 (SD 3.8) n=10	12.0 (SD 4.5) n=7	0.331
		ML	mean kPa	13.7 (SD 4.7) n=10	10.3 (SD 1.3) n=7	0.087
			T-Test p-value	0.867	p=0.307	
	symptomatic	MG	mean kPa	12.9 (SD 5.7) n=20	10.3 (SD 4.2) n=23	0.084
		ML	mean kPa	10.9 (SD 3.5) n=20	11.2 (SD 5.4) n=23	0.092
			T-Test p-value	0.090	p=0.333	

Table IV. Effect of a 12week training with EE or EE+ISO on SWE- values (kPa) of the MG and ML. There was a significant alteration (*) in MG/ML of limbs with asymptomatic tendons over the course.

		MG/ML sym. limbs (n=40)	**MG/ML asym. limbs (n=20)**	**T-Test p-value**	**MG/ML all limbs (n= 60)**
EE	T0	11.9 (SD 4.8)	13.8 (SD 4.1)	0.139	12.6 (SD 4.6)
	T1	11.2 (SD 4.1)	11.6 (SD 4.7)	0.708	11.4 (SD 4.3)
	T2	12.0 (SD 3.7)	15.4 (SD 6.1)	0.010*	13.1 (SD 4.9)
Anova		F (2,78) = 0.572, p=0.567	F(2,38)=3.472, p =0.041*		F (2,118) =3.057, p= 0.051
		MG/ML sym. limbs (n=46)	MG/ML asym. limbs (n=14)		MG/ML all limbs (n=60)
EE+ISO	T0	10.8 (SD 4.8)	11.1 (SD 3.3)	0.778	10.8 (SD 4.5)
	T1	11.2 (SD 4.3)	8.6 (SD 4.3)	0.059	10.6 (SD 4.4)
	T2	11.3 (SD 4.9)	11.4 (SD 3.0)	0.985	11.3 (SD 4.5)
Anova		F (2,90)=0.294, p=0,746	F= (1,18)=3.809, p=0.055		F (2,118)=0,607, p= 0.546
		MG/ML sym. limbs (n=86)	MG/ML asym. limbs (n=34)		MG/ML all limbs (n=120)
all	T0	11.3 (SD 4.8)	13.0 (SD 4.1)	0.131	11.8 (SD 4.6)
	T1	11.2 (SD 4.2)	11.0 (SD 4.4)	0.376	11.0 (SD 4.3)
	T2	11.6 (SD 4.4)	14.2 (SD 5.3)	0.030*	12.3 (SD 4.8)
Anova		F(2,170)=0.319, p=0.727	F(2,238)=3.101, p=0.047		F(2,66)=6.524, p=0.003*

In previous publications elastic properties of the calf muscles and tendons were examined with B-Mode ultrasound in combination with a dynamometer to deduce elastic modulus in kPA and were mainly based on asymptomatic individuals (21-23). In this setup the authors deduced an elastic modulus by measuring changes in tendon/muscle length in relation to an external force generated by the dynamometer. The results are inconsistent: Mahieu et al. (22) reported a reduction of the resistive torque of the plantar flexors due to 6 weeks of EE, which is mainly caused by alterations of the muscle rather than of the tendon. Morissey et al. (23) and Geremia et al. (21) put the main focus on the Achilles tendon and were not studying effects on the calf muscles. However, Morissey et al. (23) demonstrated, that tendon stiffness decreases under EE after 6 weeks, while Geremia et al. reported an increase of the tendon stiffness after 4 weeks (21). Interestingly, the above mentioned studies were based on a healthy population without any previous history of Achilles tendinopathy, which might be a reason for the different findings compared to the present study besides using SWE instead of a dynamometer (21-23).

Nevertheless, there are also previous studies using SWE to examine physiotherapeutic effects, but they mainly investigated the effects of static stretching of the plantarflexors, so comparison to previous findings is limited (14-16). These studies demonstrated a reduced immediate and long-term muscular stiffness after static stretching (14-16). The reduction of muscular stiffness by static stretching might be explained by the passive lengthening of muscular tissue especially the sarcomere and thus reduced stiffness (14). As in the last phase of EE the tendon and muscular tissue is also stretched, one could hypothesize that muscular stiffness would also decrease during the 3 months training of the present study. This would confirm Akagi et al. results, who reported a decrease of muscular stiffness after 5 weeks of static stretching (14). Nevertheless, this study could not prove this hypothesis. However, Leung et al. demonstrated in their study, that EE (10sets of 15 repetitions) lead to an immediate increase of nearly 75% of the initial SWE-values (MG: pre.16.9 kPa vs. post 28.4 kPa; ML: 16.0kPA vs 25.3 kPa) (24). Considering the inconsistent findings in the literature, there are other several possible reasons to address: different training protocols with immediate vs. long-term measurements, measurements conducted in dominant vs. non dominant, left vs. right, asymptomatic vs. symptomatic limb as well as interventions on symptomatic vs. asymptomatic patients with possible different load levels at baseline (24) (25).

To our knowledge, training effects on muscles of the untrained limb have not been studied in the current liter-

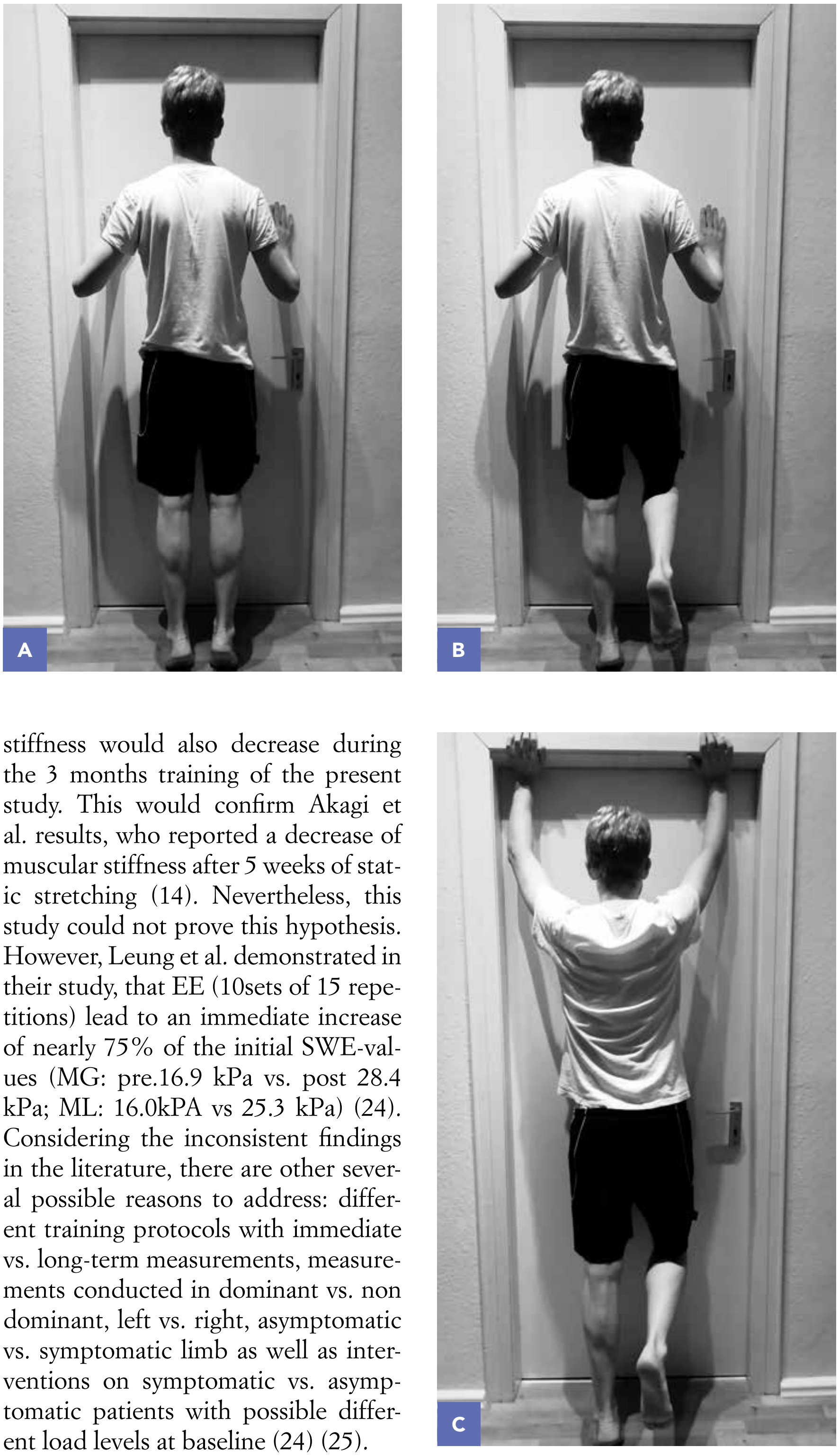

Figure 1. Exact performance of EE and ISO. Further explanation is given in **table I**.

ature using SWE or a dynamometer for evaluation. Interestingly, the EE group showed a significant increase of their elastic properties compared to baseline and also had significant higher absolute SWE values at T2 in comparison to the EE+ISO group. This might be based on the cross-education effect, which describes increased muscle strength and muscular activation patterns of the contralateral untrained muscles in a unilateral training program (26). In clinical practice this effect can be used for rehabilitation to minimize atrophy of the immobilized limb, by training the unaffected contralateral side (27). Recent studies evaluating the cross-education effect have already demonstrated, that EE have a higher muscle damage protective effect and that they have a higher ability to modulate the corticospinal excitability and the cross-transfer of strength in comparison to concentric exercises (28) (27). Assuming the cross-education effect being responsible for the significant SWE value increase in asymptomatic limbs of the EE group, the influence of ISO remains unclear, since the EE+ISO group did not show any alteration during the intervention period. However, it would be interesting to study in a next step if additive exercises of the asymptomatic limb improve outcome in unilateral Achilles tendinopathy.

The results of this study have to been seen in light of the following limitations. Due to the study setup only static ultrasound alterations of the calf muscles could have been examined. However, the muscle is a dynamic contractile tissue being a link in the neuromuscular axis and the muscle tendon unit, so that further neuromuscular or tendinous parameters using electromyography or dynamometer might have an additional explanatory power. Therefore, we would recommend to use further modalities when studying the effects of the muscle training programs and to extent SWE application also on the tendon itself, as SWE showed promising results in tendon monitoring previously (29). Additionally, there was no evaluation of immediate effects of the training program at T0, T1 and T2 which might have shown adaptations directly after load in the long-term course. Moreover, the present study does neither include the clinical course of Achilles tendinopathy nor the effect of dominant vs. non-dominant limb. Furthermore, there was only an evaluation of MG and ML, but not the M. soleus being a further muscle of the triceps surae.

In conclusion, this study yields, that elastic properties of MG and ML of the symptomatic limb in patients suffering from Achilles tendinopathy do not show significant alterations in a 12-week training program neither in EE nor EE+ISO evaluated by SWE. Contrary, in the asymptomatic untrained limb EE lead to increased SWE values, which might be based on the cross-education effect.

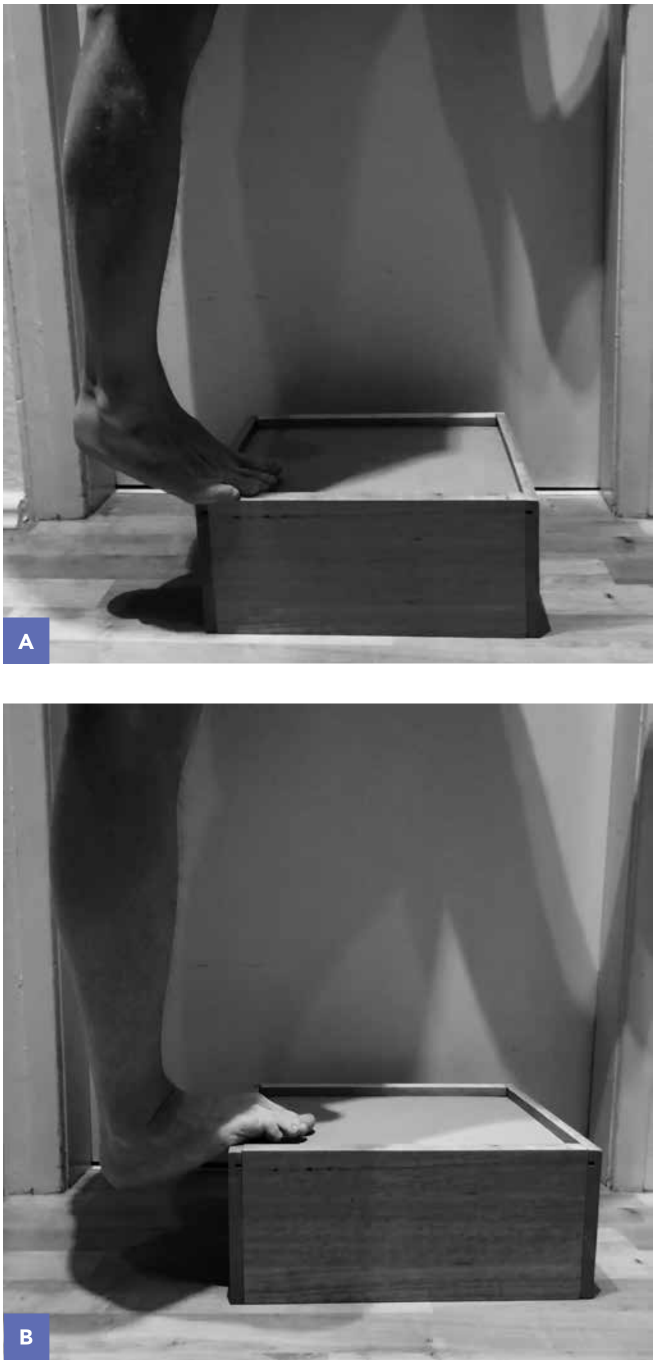

Figure 2 . Exact performance of EE. Further explanation is given in **table I**.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interets.

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