Low-load blood flow restriction training induces similar morphological and mechanical Achilles tendon adaptations compared with high-load resistance training

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[1]*Department of Sport and Sport Science, University of Freiburg, Freiburg, Germany;* [2]*Department of Neurosciences and Movement Sciences, Université de Fribourg, Fribourg, Switzerland; and* [3]*Department of Physical Performance, Norwegian School of Sport Sciences, Oslo, Norway*

Centner C, Lauber B, Seynnes OR, Jerger S, Sohnius T, Gollhofer A, König D. Low-load blood flow restriction training induces similar morphological and mechanical Achilles tendon adaptations compared with high-load resistance training. *J Appl Physiol* 127: 1660–1667, 2019. First published November 14, 2019; doi:10.1152/japplphysiol.00602.2019.—Low-load blood flow restriction (LL-BFR) training has gained increasing interest in the scientific community by demonstrating that increases in muscle mass and strength are comparable to conventional high-load (HL) resistance training. Although adaptations on the muscular level are well documented, there is little evidence on how LL-BFR training affects human myotendinous properties. Therefore, the aim of the present study was to investigate morphological and mechanical Achilles tendon adaptations after 14 wk of strength training. Fifty-five male volunteers (27.9 ± 5.1 yr) were randomly allocated into the following three groups: LL-BFR [20–35% of one-repetition maximum (1RM)], HL (70–85% 1RM), or a nonexercising control (CON) group. The LL-BFR and HL groups completed a resistance training program for 14 wk, and tendon morphology, mechanical as well as material properties, and muscle cross-sectional area (CSA) and isometric strength were assessed before and after the intervention. Both HL (+40.7%) and LL-BFR (+36.1%) training induced significant increases in tendon stiffness ($P < 0.05$) as well as tendon CSA (HL: +4.6%, LL-BFR: +7.8%, $P < 0.001$). These changes were comparable between groups without significant changes in Young's modulus. Furthermore, gastrocnemius medialis muscle CSA and plantar flexor strength significantly increased in both training groups ($P < 0.05$), whereas the CON group did not show significant changes in any of the evaluated parameters. In conclusion, the adaptive change in Achilles tendon properties following low-load resistance training with partial vascular occlusion appears comparable to that evoked by high-load resistance training.

NEW & NOTEWORTHY Low-load blood flow restriction (LL-BFR) training has been shown to induce beneficial adaptations at the muscular level. However, studies examining the effects on human tendon properties are rare. The findings provide first evidence that LL-BFR can increase Achilles tendon mechanical and morphological properties to a similar extent as conventional high-load resistance training. This is of particular importance for individuals who may not tolerate heavy training loads but still aim for improvements in myotendinous function.

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blood flow restriction; muscle mass; muscular strength; tendon stiffness; Young's modulus

INTRODUCTION

Although muscles are responsible for the generation of force, the transmission of these forces to the skeletal system is accomplished by tendinous structures that connect the muscles with the bony structures (9). The interaction of the muscle-tendon unit complex with the skeletal system is therefore crucial for human locomotion and all other types of movements (11).

It is well known that both muscle and tendon tissues demonstrate a remarkable degree of plasticity with training (46). For promoting increases in muscle mass and strength, it has generally been recommended to apply training loads of 70–85% of each individual's one-repetition maximum (1RM) (4). Furthermore, it was demonstrated that mechanical stress and strain (~4%) induced by resistance training can enhance morphological and functional properties of tendons (5, 58). Evidence from a recent meta-analysis (11) indicates that also in this context training loads > 70% of the 1RM are superior in promoting optimal adaptive responses in mechanical (stiffness) and material (Young's modulus) tendon properties compared with low-load (LL) training. With regard to the magnitude of these adaptations, significant increases of ~20–40% (33, 36, 52) in tendon stiffness as well as changes in tendon hypertrophy of ~3–10% (13, 33, 52) were observed.

Interestingly, a compelling number of studies have revealed that the addition of partial vascular occlusion [i.e., blood flow restriction (BFR)] during LL resistance training (20–40% 1RM) induces substantial muscle growth (18, 25, 40, 47) and strength gains (37) comparable to adaptations seen with conventional high-load (HL) training (14, 39). However, it is largely unknown to what extent training with BFR facilitates changes in human tendon properties. Although one study was conducted to investigate the effects of LL-BFR training on patellar tendon properties (35), the interpretation of the results is difficult because of unstandardized load progressions between groups.

Accordingly, the main purpose of the present study was to investigate the effects of LL-BFR training (20–35% 1RM) on in vivo tendon properties and compare these effects with

conventional HL (70–85% 1RM) resistance training. On the basis of the findings of previous studies (5, 11), we hypothesized that the stress and strain (being ~1/3 of conventional HL resistance exercise) during LL-BFR would not be sufficient to elicit adaptations in mechanical, morphological, as well as material properties of the Achilles tendon. Given that LL-BFR training is frequently applied in clinical rehabilitation (28, 45), it is necessary to investigate tendon adaptive responses to this regimen since adaptations at the muscular level without concomitant changes of tendon properties might lead to increased risks of myotendinous injuries (44).

METHODS

Subjects

Based on the findings of a recent study investigating the chronic effects of resistance training on Achilles tendon stiffness (56), an a priori power analysis (G*Power 3.1.9.2) was conducted. The results indicated that a total of $n = 36$ participants were needed to identify the observed effect sizes as statistically significant ($f = 0.28$, power = 0.8, $\alpha = 0.05$). Considering a potential dropout rate of 20–25%, a total of 55 healthy men between the age of 18 and 40 yr were recruited. All subjects were untrained (according to the Freiburg Questionnaire of Physical Activity) and had a maximum of 1–2 h of physical activity per week. Participants diagnosed with acute or chronic injuries of the Achilles tendon, uncontrolled hypertension, or any other chronic disease were excluded from the trial. Moreover, smokers and subjects with a history of deep vein thrombosis or a body mass index exceeding 30 kg/m^2 were not included.

Approval of the study was obtained from the local ethics committee, and all procedures were in accordance with the latest revision of the Declaration of Helsinki. The trial was registered at the German Clinical Trials Register (DRKS00018884). Before commencing the trial, all subjects gave written informed consent.

Study Design

A between-group repeated-measures design was implemented to assess tendon properties, muscle cross-sectional area (CSA), and muscular strength in young men before and after 14 wk of either LL-BFR or HL.

One week before the intervention, subjects underwent a preliminary screening, which comprised a medical anamnesis and physical examination to confirm agreement with the abovementioned inclusion criteria. If subjects were eligible, they were randomly allocated (without identification to assessors) into one of the following experimental groups: HL resistance training (70–85% 1RM), LL (20–35% 1RM) resistance training with BFR (LL-BFR), and a control (CON) group without any training. A random number generator was used for allocation sequence generation. Subsequently, muscle CSA of the gastrocnemius medialis muscle was assessed. Additionally, Achilles tendon properties and unilateral maximal plantar flexion torque were determined. All testing was conducted at the Department of Sport and Sport Science at the University of Freiburg before and after the 14-wk intervention period. A total training duration of >12 wk has previously been suggested to efficiently induce tendon adaptive responses (11). All measurements and training procedures were supervised and completed at the Department of Sport and Sport Science of the University of Freiburg, and all outcome assessors were blinded to participants' group assignments.

Training Procedures

The training consisted of three weekly sessions for 14 wk. Training days were separated by at least 1-day rest between two consecutive sessions to ensure adequate recovery. Each training session was preceded by a 10-min standardized warm-up on a stationary cycle ergometer at ~50 W.

High-load training. The HL protocol consisted of three sets of 6–12 repetitions of dynamic standing (Multipress Genius Eco; FREI, Kirchzarten, Germany) and sitting (Body-Solid Seated Calf Raise Machine, GSCR349) calf raises with the load being progressively increased every 4 wk from 70% to 85% 1RM. On these occasions, dynamic 1RM testings were implemented to adjust the load for the current strength level of each individual. All exercises were performed in full range of motion (full plantar flexion to full dorsal extension) (34), with an interset rest period of 1 min. Three minutes of rest was provided between exercises.

Low-load blood flow restriction training. Participants in the LL-BFR group performed the same exercises as the HL group but with a training load of 20% 1RM being progressively increased by 5% every 4 wk until 35% 1RM in the last 2 wk was reached. Similar to the HL group, dynamic strength testings were implemented to reevaluate the current strength level and adequately adjust the load. For each exercise, four sets with 30 repetitions in the first set and 15 repetitions in the remaining three sets were completed. This protocol was chosen because this has been frequently applied in the BFR literature (38, 54). During each exercise, a 12-cm-wide pneumatic nylon tourniquet (Zimmer Biomet, Warsaw, IN) was proximally positioned with a snug fit on each thigh. Before each training, arterial occlusion pressure (AOP) was determined in a standing position for each participant. The cuff was gradually increased until the arterial pulse at the posterior tibial artery was no longer detected by Doppler ultrasound (Handydop; Kranzbühler, Solingen, Germany). This point was defined as 100% of arterial occlusion. For training routines, cuff pressure was set to 50% (38, 54) of each individual's AOP (A.T.S. 3000; Zimmer Biomet, Warsaw, IN) and kept inflated during the entire session including the 60-s interset rest periods. Between the two exercises, the cuff was deflated for 3 min.

To increase compliance with the training program, all participants were afforded a brief cooldown consisting of front and side planks as well as bridging exercises. All routines were supervised by specially trained sport scientists to ensure proper exercise technique.

One-Repetition Maximum Assessment

Dynamic 1RM testings for sitting and standing calf raises were conducted at the beginning and every 4 wk during the training intervention. Before commencing the assessment, participants completed a specific warm-up of two sets with 10 repetitions with a submaximal load. Subsequently, two additional warm-up sets allowing three to five repetitions were performed (8). For the actual 1RM test, the correct technique implied lifting the weight in a full range of motion reaching from maximum dorsal extension to maximum plantar flexion. Additionally, no movement was allowed in the knee joint, which was fully extended (but not locked) during all trials. After each successful lift the load was increased by 5–10% until the participants failed to lift the weight through the full range of motion with a proper technique (8, 48). Each trial was separated by a 4-min resting period to ensure recovery. All final 1RMs were achieved within five attempts.

Maximum Voluntary Torque

Unilateral isometric maximum voluntary contraction (MVC) torque at 90° plantar flexion was measured with an isokinetic dynamometer (ISOMED 2000; Ferstl, Germany). Subjects were placed in supine position with restricted shoulders and hips. During the entire procedure knee and hips were fully extended. The highest MVC was used for data analysis.

Muscle Cross-Sectional Area

Panoramic ultrasound (US) images (Aplio 400; Toshiba, Tokyo, Japan) were taken with a 9-MHz transducer (6-mm width) by an experienced sonographer. Recent studies have repeatedly confirmed

panoramic US imaging to be a valid and reliable tool for monitoring changes in muscle mass (3, 51). For assessing muscle CSA of the right gastrocnemius medialis muscle, transversal images were acquired with participants lying in a ventral position with their legs hanging down from the table, being fully extended. To ensure a standardized 90° ankle position, a custom-build orthosis was placed at the ankle during the time of the measurements. After a resting period of 20 min in this exact position, which was implemented to account for fluid shifts (10), measurements were conducted at 30% of tibia length (from popliteal crease to lateral malleolus) (15, 31), with participants being instructed to relax their muscles as much as possible. During the entire assessment, a sufficient amount of transmission gel was applied in order to obviate pressure of the probe on the skin (51). To ensure that there was no compression of the muscle, each acquired image was manually checked for an identifiable layer of transmission gel between the transducer and the skin.

Three images were obtained and subsequently transferred to a personal computer. Digitizing analysis software (ImageJ 1.51; NIH, Bethesda, MD) was used to manually trace the images and calculate muscle CSA. To get a stable mean, each image was evaluated three times and the mean of all three images was used for calculations. This technique has recently been identified as highly reliable with a coefficient of variation (CV) of 2.4–4.1% (51).

Achilles Tendon Properties

Tendon cross-sectional area. Achilles tendon CSA was determined by acquiring time series of several transversal US images (8 MHz, ArtUs EXT-1H; Telemed, Vilnius, Lithuania) at 25% of Achilles tendon length measured from tuberositas calcanei to the most distal aspect of the gastrocnemius muscle (7). Images were transferred to a personal computer and analyzed with ImageJ (1.51; NIH), and the average of three images was used for further calculations. To assess CV of repeated measurements, the same assessment was repeated after a 72-h time period in a group of 10 subjects. The respective CV was 4.8% and thus in an acceptable range (58).

Tendon mechanical and material properties. To assess tendon stiffness, elongation of the Achilles tendon was determined during ramped isometric contractions by B-mode US scans at 100 Hz at the gastrocnemius medialis myotendinous junction. Additionally, plantar flexion torque recordings (1,000 Hz) and two-dimensional (2D) kinematic data (100 Hz) were simultaneously sampled. A hypoechoic marker was placed at the myotendinous junction and kept in line with a marker at the US transducer to correct for potential probe movements. To optimize US image quality during the ramped isometric protocol, a gel pad was positioned between the skin and the transducer. Changes in ankle angle were tracked with 2D motion analysis cameras (Simi Motion, Munich, Germany) with three LED markers placed at the tibia, malleolus medialis, and first metatarsal bone of the right leg.

After familiarization with the procedure and preconditioning of the tendon with five trials at 80% of MVC (41), participants were instructed to steadily exert torque to their individual maximum with a standardized loading rate of 50 Nm/s. This loading rate was chosen because it resulted in a ramped isometric plantar-flexion contraction lasting between 3 and 5 s for all subjects (7, 56). During this process, visual online feedback of the torque signal was provided. Achilles tendon force was calculated by dividing plantar flexion torque by the tendon moment arm with a subsequent correction for ankle joint rotation by kinematic data.

Tendon moment arm was calculated by measuring the perpendicular distance from the inferior tip of both medial (*L1*) and lateral (*L2*) malleolus (center of rotation) to the posterior part of the Achilles tendon (32, 50). For this purpose pictures were taken from the medial and lateral sagittal planes (Sony Cyber-shot DSC-RX100 Digital Camera). In accordance with previous studies, the mean of these two measurements ($L_{1,2}$) was used for further calculations (32, 50). Subsequently, the intersection of *L1* and *L2* was indicated with a needle and the perpendicular distance (M) from the needle to the tendon's line of action was measured (32). Tendon moment arm was then determined by subtracting M from $L_{1,2}$ (for detailed descriptions see Refs. 32 and 50). All analyses were conducted with ImageJ (1.51; NIH).

All acquired position and displacement data were filtered with a second-order low-pass Butterworth filter with a cutoff frequency of 15 Hz. Subsequently, Achilles tendon elongation was analyzed off-line with semiautomatic tracker software (Tracker, V 4.95) by tracking the closest visible fascicle insertion at the myotendinous junction of the gastrocnemius (56). Tendon stiffness was then calculated as the slope of the force-elongation curve between 50% and 80% MVC. This procedure has previously been used in the scientific literature (56). Young's modulus was calculated as the slope of the stress-strain curve between 50% and 80% MVC.

Lifestyle Parameters

To control nutritional behavior as a potential confounding variable, participants were advised to maintain their nutritional regimen during the study. Additionally, macronutrient status was tracked with Nutriguide 4.6 software (Nutri Science, Hausach, Germany). Subjects were instructed to record their food intake as precisely as possible during 3 days of the week (2 weekdays and 1 weekend day) before and after the intervention.

Furthermore, the level of self-reported physical activity was evaluated with the Freiburg Questionnaire of Physical Activity at the beginning and the end of the intervention period (26).

Statistics

Normal distribution and homogeneity of variances were checked for all variables. To detect changes over time and respective differences between the groups, a repeated-measures ANOVA (rmANOVA) with factors time (pre, post) × group (LL-BFR, HL, CON) was performed to test for interaction effects. Furthermore, within-group differences were evaluated with a paired Student's t test. In the case of significant interaction effects from the rmANOVA, Bonferroni-corrected Student's t tests were calculated to test for within- and between group differences. In addition, we performed an intention-to-treat (ITT) analysis for all $n = 55$ participants by using a multiple imputation approach (22). Outliers in main outcome criteria were excluded from the analysis if their values exceeded the mean ± 3 standard deviations (SDs).

All statistical analyses were done with SPSS 24.0 (IBM, Armonk, NY). Data are presented as means ± SD if not otherwise indicated. The level of significance was set to $P < 0.05$ for all tests.

RESULTS

A total of 38 participants (HL: $n = 14$, LL-BFR: $n = 11$; CON: $n = 13$) successfully completed the study, with $n = 6$ dropouts in the HL group, $n = 9$ dropouts in the LL-BFR group, and $n = 2$ dropouts in the CON group. None of the dropouts was related to side effects of the training (see Fig. 1).

Baseline characteristics of the participants are presented in Table 1. At the pretest, there was no significant difference between the groups either in anthropometric variables or in any of the main outcome variables ($P > 0.05$).

Achilles Tendon CSA

The results of the rmANOVA showed significant time ($F_{1,35} = 16.06$, $P < 0.01$, $\eta_p^2 = 0.315$) and interaction ($F_{2,35} = 4.42$, $P < 0.05$, $\eta_p^2 = 0.202$) effects, with greater changes in CSA in the HL and LL-BFR groups compared with CON. Achilles tendon CSA at 25% of tendon length increased from

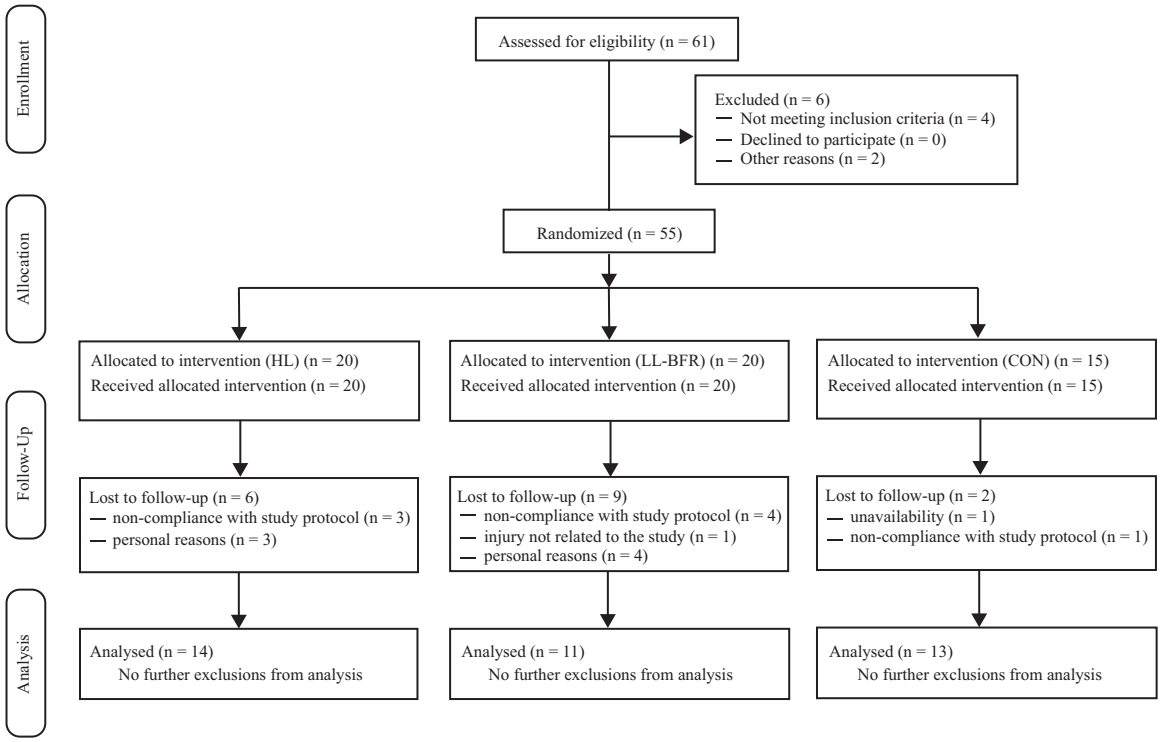

Fig. 1. Flowchart of subject recruitment. CON, control; HL, high load; LL-BFR, low load with blood flow restriction.

70.3 ± 17.7 mm^2 to 73.5 ± 17.2 mm^2 (+4.6%) in the HL group ($P < 0.01$) and from 68.2 ± 11.4 mm^2 to 73.5 ± 14.4 mm^2 (+7.8%) in the LL-BFR group ($P < 0.05$). Tendon CSA of the CON group did not change ($P = 0.962$; 68.8 ± 14.7 mm^2 to 68.9 ± 15.5 mm^2; Fig. 2). After calculation of an ITT analysis, similar results were found, with a significantly higher increase in tendon CSA in both training groups compared with CON (time × group interaction: $P < 0.05$, $\eta_p^2 = 0.157$).

Achilles Tendon Properties

Evaluation of changes in tendon stiffness revealed significant time ($F_{1,33} = 19.32$, $P < 0.01$, $\eta_p^2 = 0.369$) and interaction ($F_{2,33} = 3.52$, $P < 0.05$, $\eta_p^2 = 0.176$) effects. After the 14-wk training program, both HL and LL-BFR groups increased their Achilles tendon stiffness from 401.5 ± 102.6 N/mm to 564.8 ± 157.6 N/mm (+40.7%) ($P < 0.05$) and from 388.7 ± 76.9 N/mm to 529.2 ± 142.8 N/mm (+36.1%) ($P < 0.05$), respectively (Fig. 3). No significant changes were observed in the CON group (pre: 442.6 ± 96.3 N/mm; post: 458.6 ± 86.5 N/mm). The ITT analysis demonstrated a significant main effect of time ($P < 0.01$, $\eta_p^2 = 0.339$) and a significant time × group interaction ($P < 0.01$, $\eta_p^2 = 0.213$). In contrast to the mechanical properties, material properties (assessed with the Young's modulus) remained unchanged, with no significant time effect ($F_{1,32} = 0.874$, $P = 0.357$, $\eta_p^2 = 0.027$) or interaction effect ($F_{2,32} = 1.46$, $P = 0.248$, $\eta_p^2 = 0.083$). After 14 wk, Young's modulus changed from 1,539.5 ± 491.6 MPa to 1,847.6 ± 481.4 MPa and from 1,638.5 ± 696.9 MPa to 1,495.1 ± 425.2 MPa in the HL and LL-BFR groups, respectively.

Table 1. *Descriptive and anthropometric characteristics*

Variable	HL (n = 14)	LL-BFR (n = 11)	CON (n = 13)
Age, yr	26.1 ± 4.2	27.1 ± 4.7	30.5 ± 5.7
Height, cm	179.7 ± 9.2	180.1 ± 8.3	178.4 ± 5.6
Weight, kg	76.4 ± 15.4	85.0 ± 9.3	77.9 ± 10.7
BMI, kg/m^2	23.5 ± 3.5	26.3 ± 3.5	24.5 ± 3.1

Values are means ± SD for n subjects. BMI, body mass index; CON, control group; HL, high-load group; LL-BFR, low-load blood flow restriction group.

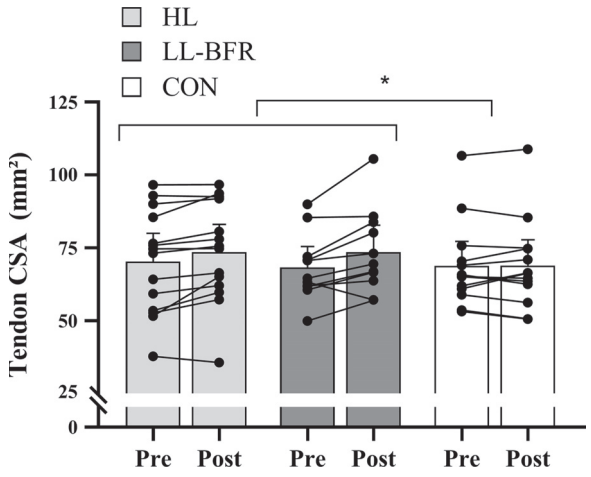

Fig. 2. Pre- and posttraining values of Achilles tendon cross-sectional area (CSA) in the high-load (HL), low-load blood flow restriction (LL-BFR), and nonexercising control (CON) groups. Data are means ± 95% confidence interval. Black dots represent individual data points. *Significantly different ($P < 0.05$) by repeated-measures ANOVA (time × group interaction).

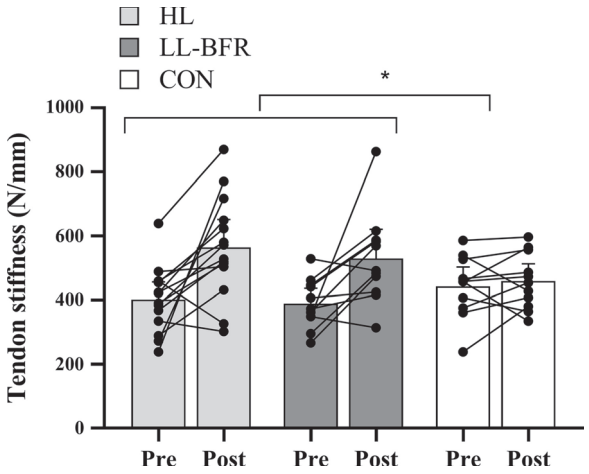

Fig. 3. Pre- and posttraining values of Achilles tendon stiffness in the high-load (HL), low-load blood flow restriction (LL-BFR), and nonexercising control (CON) groups. Data are means ± 95% confidence interval. Black dots represent individual data points. *Significantly different ($P < 0.05$) by repeated-measures ANOVA (time × group interaction).

Muscle CSA

The rmANOVA revealed significant time ($F_{1,34} = 30.55$, $P < 0.01$, $\eta_p^2 = 0.473$) and time × group ($F_{2,34} = 7.19$, $P < 0.01$, $\eta_p^2 = 0.297$) effects, with the HL ($P < 0.01$) and LL-BFR ($P < 0.05$) groups showing a significantly higher increase in muscle CSA compared with CON. Gastrocnemius medialis CSA increased from 14.3 ± 4.5 cm^2 to 15.4 ± 4.5 cm^2 (+7.7%) and from 16.5 ± 3.2 cm^2 to 18.0 ± 4.5 cm^2 (+9.1%) in the HL and LL-BFR groups, respectively (Fig. 4). The muscle CSA of the CON group did not change significantly (from 14.2 ± 1.6 cm^2 to 14.3 ± 1.6 cm^2). The ITT analysis revealed similar results, with a significant main effect of time ($P < 0.01$, $\eta_p^2 = 0.235$) and time × group interaction ($P < 0.05$, $\eta_p^2 = 0.163$).

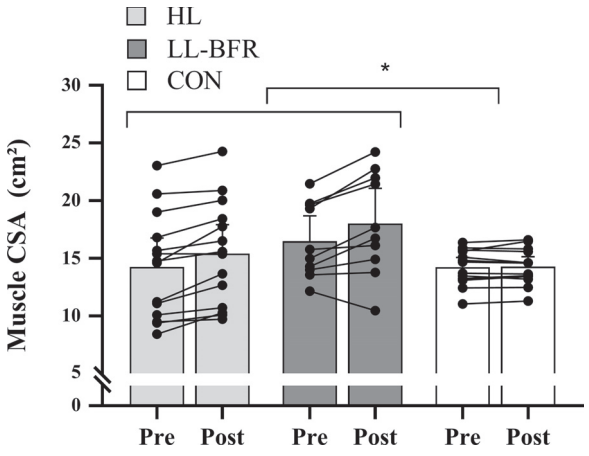

Fig. 4. Pre- and posttraining values of gastrocnemius medialis muscle cross-sectional area (CSA) in the high-load (HL), low-load blood flow restriction (LL-BFR), and nonexercising control (CON) groups. Data are means ± 95% confidence interval. Black dots represent individual data points. *Significantly different ($P < 0.05$) by repeated-measures ANOVA (time × group interaction).

Maximal Voluntary Torque

The rmANOVA showed a significant main effect of time ($F_{1,33} = 20.64$, $P < 0.01$, $\eta_p^2 = 0.385$) as well as a time × group interaction ($F_{2,33} = 7.39$, $P < 0.01$, $\eta_p^2 = 0.309$). After 14 wk of resistance training, both training groups significantly increased their maximal isometric voluntary contraction torque [HL: from 189.0 ± 83.1 Nm to 214.6 ± 86.1 Nm ($P < 0.05$); LL-BFR: from 226.7 ± 47.6 Nm to 248.9 ± 48.5 Nm ($P < 0.05$)] whereas maximal voluntary torque remained unchanged in the CON group (pre: 208.5 ± 35.4 Nm, post: 205.5 ± 38.9 Nm, $P = 0.52$; Fig. 5). Relative changes were +13.5% and +9.8% for the HL and LL-BFR groups, with −1.4% in the CON group. After calculation of an ITT analysis, a significant main effect of time ($P < 0.01$, $\eta_p^2 = 0.196$) and a significant time × group interaction ($P < 0.01$, $\eta_p^2 = 0.170$) were found.

Lifestyle Parameters

At baseline, the groups did not show significant differences in the level of physical activity or nutritional status ($P > 0.05$). After the intervention, no significant interaction effect was identified for either physical activity ($P = 0.330$, $\eta_p^2 = 0.06$) or protein ($P = 0.262$, $\eta_p^2 = 0.074$), fat ($P = 0.426$, $\eta_p^2 = 0.048$), or carbohydrate ($P = 0.801$, $\eta_p^2 = 0.013$) intake.

DISCUSSION

To the best of our knowledge, this is the first study that evaluated the effects of LL-BFR training on functional and structural Achilles tendon properties. The overall findings revealed that, despite a much smaller training load, LL-BFR caused adaptions in Achilles tendon CSA and mechanical properties as well as in muscle mass and strength comparable to HL.

Tendon Properties

The results of our study showed that 14 wk of progressive LL-BFR and HL training serves as a potent stimulus for causing tendon hypertrophy compared with a nonexercising control group. Typically, morphological changes at the tendon

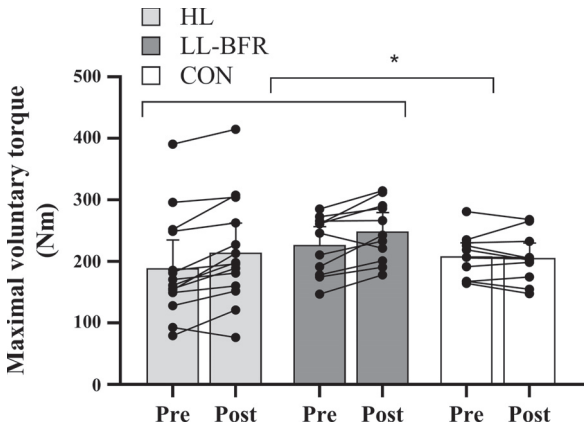

Fig. 5. Pre- and posttraining values of maximal voluntary contraction torque in the high-load (HL), low-load blood flow restriction (LL-BFR), and nonexercising control (CON) groups. Data are means ± 95% confidence interval. Black dots represent individual data points. *Significantly different ($P < 0.05$) by repeated-measures ANOVA (time × group interaction).

level have been reported to occur as a result of long-term or habitual loading (58). However, several studies show that structural adaptations can also be detected as early as 9–12 wk after heavy-load resistance training (5, 33, 52). The observed increases in Achilles tendon CSA in the present study in the HL group (+4.6%) greatly mirrored results from earlier investigations reporting changes in tendon CSA between ~4% and 7% following several weeks of exercise training (5, 33, 52). Interestingly, not only the HL but also the LL-BFR group displayed a significant increase in Achilles tendon CSA (+7.8%) with training loads well below those that have been used previously (33, 52). To date, only a single previous study has investigated the effects of BFR training on human tendon properties (35). The study of Kubo and colleagues (35) revealed that LL-BFR (20% 1RM) and HL (80% 1RM) training for the knee extensors failed to elicit substantial patellar tendon hypertrophy after 12 wk of resistance training. Potential reasons for this inconsistency might lie within the methodological approach. In their study, Kubo et al. (35) used an average of three tendon CSA values (25%, 50%, and 75% of tendon length) to assess tendon hypertrophy even though it was shown that exercise-induced changes in tendon CSA primarily occur at the proximal and distal sites of the tendon, with only minor or no changes in the midsection (33, 52). Averaging the values of the different assessment regions might therefore underestimate the actual increase in tendon size. Although our results indicate that LL-BFR and HL training are equally effective in facilitating tendon hypertrophy, our study design does not allow us to answer the question of the extent to which the hypoxic condition itself contributed to the increased tendon CSA. Although a previous animal experiment in horses showed that 2 wk of walking with BFR did not induce significant changes in tendon thickness compared with walking without BFR (1), there is evidence that indicates that a hypoxic milieu (as induced with BFR) stimulates the proliferation of tendon stem cells (30), potentially enhancing tendon repair (2). Furthermore, one study demonstrated that the addition of BFR to exercise increases the secretion of basic fibroblast growth factor (53), which is known to enhance fibroblast proliferation (29, 42) and thus might lead to increased collagen synthesis rates (59).

Besides the morphological changes, the results of the present study show that Achilles tendon stiffness was substantially improved after HL (+40.7%) and LL-BFR (+36.1%) training, with no changes in the CON group (+3.6%). This magnitude of increased Achilles tendon stiffness is comparable to what has previously been reported after 14 wk of resistance training with a load of 90% MVC (13). At first sight, the increased stiffness following LL-BFR training with loads of only 20–35% 1RM seems surprising given that a previous meta-analysis indicates that training loads of >70% MVC are needed to induce adaptations in tendon stiffness (11). Although previous research groups suggest that strain (~4%) is essential for adequate adaptations (5, 6), we suggest that strain and stress are not the only factors influencing mechanical tendon adaptations and that the number of loading cycles (52) and/or concurrent tissue hypoxia might mediate this response. In contrast to Kubo et al. (35), we did find an increase in tendon stiffness not only in the HL group but also in the LL-BFR group. Apart from the fact that Kubo et al. (35) investigated patellar tendon adaptations and we looked at the Achilles tendon, differences in the overall loading of the tendon might also explain the different results. Whereas Kubo and coworkers (35) only adjusted the load for the HL group, we also progressively increased the load in the LL-BFR in the present study.

When focusing on material tendon properties, Young's modulus of the Achilles tendon did not significantly change between the groups. Even though this lack of statistical significance is not in accordance with earlier studies (5, 13, 52), it is consistent with findings from Kongsgaard et al. (33), who reported that 12 wk of neither low-load nor high-load resistance training significantly affected patellar tendon modulus in young men. The contrast of the results to other studies might be related to differences in methodology and age. Comparably to Kongsgaard et al. (33), Couppé and coworkers (21) confirmed that in young men changes in tendon stiffness are largely explained by alterations in tendon size rather than material properties. This notion, however, needs to be further investigated. Another important point in this regard is that current in vivo techniques frequently may lack sensitivity to detect changes in tendon properties (24, 58).

Muscle Properties

The findings of the present study show that the addition of BFR to LL resistance training increases muscle CSA comparable to what is seen after conventional HL resistance training, in line with previous investigations (35, 43, 54). Kubo and coworkers (35), for example, found that muscle mass increased by ~7% in both HL and LL-BFR groups after a 12-wk resistance training period in young men. The slightly higher degree of muscle hypertrophy in the present study (HL: ~8%; LL-BFR: ~9%) might be attributed to the length of the intervention, which was 2 wk longer than that in the study of Kubo et al. (35).

At first sight, our results do not appear to corroborate previously published meta-analyses indicating that HL resistance training induces greater strength gains compared with LL-BFR resistance training (14, 39). However, the relative strength increases in the HL group (~14%) in the present study showed descriptively larger changes compared with the LL-BFR group (~10%). When examining potential reasons for these slightly inferior muscle strength adaptations following LL-BFR, evidence from a recent study suggests that parameters of neural drive seem to differ between the two training regimens (19). Cook and colleagues (19) infer that this might be related to a greater degree of motor unit recruitment and/or firing rates with HL. However, the interpretation of electromyography (EMG) regarding both factors is difficult since various variables including motor unit synchronization, fatigue, and motor unit cycling contribute to changes in EMG amplitude (23, 55, 57). Another frequently used method to investigate neural drive is the twitch interpolation technique (27). Studies comparing long-term HL and LL-BFR training state that the muscle activation level (assessed with superimposed electrical stimuli) significantly increased after 12 wk of heavy-load training (+3%), with no changes in LL-BFR (35). Similar findings were reported by Colomer-Poveda et al. (16), who demonstrated that 4 wk of LL training with and without BFR did not lead to changes in neural drive or motoneuronal excitability measured with V-wave and H-reflex stimulation. These results, however, contrast with recent findings from Cook and colleagues (20), who did not identify significant

changes in muscle activation following 6 weeks of HL and LL-BFR training. Besides physiological determinants, test specificity has been speculated to play a crucial role in this context (17). The phenomenon of specificity postulates that the closer the test mimics the trained movement, the better is the transfer from the training to this test (49). Consequently, it might be assumed that the HL training regimen is technically closer to the maximal voluntary torque testing compared with the LL resistance training with BFR.

Limitations

The present study design did not allow us to answer the question to what extent the BFR stimulus alone might be responsible for the muscular and tendinous adaptations because we did not include a group that trained with loads similar to the LL-BFR group but without vascular occlusion. Additionally, tendon stiffness was calculated at maximal individual torque level. Since the linear portion of the force-elongation curve is not always reached in vivo, this approach is sometimes biased by the maximal torque reached by the subjects. In this case, however, we observed up to 300% interindividual differences in torque (see Fig. 5), which would have resulted in the analysis of the toe region of the strongest subjects if we used a method based on a common force level. The bias induced by this approach would have been larger than with the method based on individual maximal torque, which at least guarantees that we consider the region closest to the linear portion of the curve. Furthermore, the US-based assessment of tendon CSA has been reported to lack sensitivity and high accuracy (12), indicating that further research is needed to evaluate these changes with more precise techniques such as MRI. With regard to the study population, it needs to be mentioned that our findings were obtained from young men and must therefore not necessarily be valid for female subjects or individuals of different ages. Additionally, further research is warranted before any clinical recommendations can be made.

Conclusions

The present study demonstrated that low-load (20–35% 1RM) blood flow restriction training can induce muscular and tendinous adaptations that are similar to high-load (70–85% 1RM) resistance training. These results are of high relevance for both sports and rehabilitation settings when the lifting of high training loads is contraindicated. Future studies, however, are required to further investigate potential adaptive mechanisms and strengthen the evidence for LL-BFR training in various populations including clinical patients.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

C.C., B.L., O.R.S., S.J., T.S., A.G., and D.K. conceived and designed research; C.C., S.J., and T.S. performed experiments; C.C., B.L., S.J., and T.S. analyzed data; C.C., B.L., O.R.S., S.J., T.S., A.G., and D.K. interpreted results of experiments; C.C. prepared figures; C.C. and B.L. drafted manuscript; C.C., B.L., O.R.S., S.J., T.S., A.G., and D.K. edited and revised manuscript; C.C., B.L., O.R.S., S.J., T.S., A.G., and D.K. approved final version of manuscript.

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