International Journal of Sport, Exercise and Health Research 2021; 5(2): 50-54

Research Article

IJSEHR 2021; 5(2): 50-54

www.sportscienceresearch.com
Received: 14-06-2021
Accepted: 26-07-2021

Does exercise produce hypertrophy and an increase in the stiffness of hamstring tendons?

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Abstract

Background: Anterior Cruciate ligament (ACL) tears are the most common ligamentous injury in the knee in athletes. To return to active sporting activity, ACL reconstructions are often necessary. Hamstring tendon autografts are most commonly used in Anterior Cruciate Ligament reconstruction [3]. An important consideration during ACL reconstruction is the size of the hamstring graft. Graft sizes of less that 8mm are reported to be a significant risk factor for graft failure [4]. Therefore, one should maximize the size of the tendon graft to avoid complications of graft failure. We hypothesize that 12 weeks of resistance training can produce hamstring tendons (gracilis, semitendinosus) hypertrophy and increase their stiffness. **Methods:** We conducted an interventional cohort study where subjects underwent 12 weeks of hamstring resistance training. A standardised ultrasound technique was used to measure the cross sectional tendon area of the gracilis and semitendinosus tendons before and after the intervention. Tendon elastography was used to measure tendon modulus. The primary outcome measure was the tendons' cross-sectional area and secondary outcome measure was the tendon modulus. **Results:** 9 participants completed the study. The median increase in cross-sectional area for left Semitendinosus, right Semitendinosus, and left Gracilis was $0.02mm^2$ (IQR = 0.07) (p-value = 0.76), $0.01mm^2$(IQR =0.03) (p-value = 0.73) and $0.01mm^2$(IQR = 0.02) (p-value = 0.44) respectively. There was a mean decrease in cross-sectional area of the right gracilis of $0.01mm^2$. Utilising tendon elastography with the ultrasound, the tendon modulus was measured and had increase in tendon modulus in the left and right Semitendinosus and right gracilis (-4.58 (p=0.03), -3.32 (p=0.13) and -0.03 (p=0.66) respectively). The tendon modulus had a mean decrease in the left gracilis of 0.7 (p=1). **Conclusion:** 12 weeks of resistance training resulted in potentially clinically significant increase in semitendinosus cross-sectional area. These findings suggest that it is possible to increase the cross-sectional area of hamstring tendons through resistance training, thus increasing their mechanical strength for better ACL reconstruction outcomes. Larger patient numbers are required to determine if statistically significant tendon hypertrophy can be achieved.

Keywords: Anterior Cruciate Ligament, Reconstruction, Tendon hypertrophy, Preoperative training, Resistance training.

INTRODUCTION

The ACL is an important ligament in the knee that confers stability to the knee especially in pivoting sports. ACL tears are a common injury in athletes, and result in significant loss of competitive sporting time. The number of ACL reconstructions are on the rise, numbering from 86,000 in 1994 to 130,000 in 2006 in the United States [1]. ACL reconstructions most commonly utilize hamstring tendon autograft for reconstruction and are the preferred graft choice for majority of sports surgeons in the world [2]. In particular, hamstring grafts are commonly utilized due to its greater cross-sectional area and maintenance of the integrity of the extensor mechanism [3].

Of note, one of the most significant complications of ACL reconstruction surgery is graft rupture, which causes continued instability of the knee and necessitates revision surgery especially if the patient wishes to return to a high level of sport. Many factors contribute to the likelihood of graft failure, one of which is the cross-sectional area of the hamstring graft. Current literature points to a small graft size of less than or equal to 8mm have a 6.8 fold higher risk of graft failure compared to graft sizes of more than 8mm [4].

With the literature pointing to reduced graft failure if graft sizes are larger than 8mm, it has also been noted that the stiffness of the tendon graft also contributes to stability in the ACL reconstruction [5]. It is therefore logical to surmise that measures with the aims of maximizing the size and stiffness of the

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hamstring tendon grafts can potentially minimize graft failure risk. These measures could involve pre-operative rehabilitation to achieve these aims prior to the ACL reconstruction.

Previous studies demonstrated that mechanical loading increased the cross-sectional area of the Quadriceps, Patella [6], and Achilles tendon of patients [7]. In addition, as an adaptive mechanism, mechanical loading of connective tissue stimulates cell signalling pathways to induce crosslinking and stiffening of fibrillar collagen matrices [8]. This has been shown to have clinical increases in patella tendon stiffness [6].

However, to our knowledge, there is no literature studying pre-operative rehabilitation for the purposes of inducing hamstring tendon hypertrophy.

This study therefore aimed to investigate the effect of targeted 12 week resistance training regime on the cross-sectional area and tendon modulus of hamstring tendons.

MATERIALS AND METHODS

Study design

From January to July 2019, a prospective cohort study was conducted in a tertiary hospital. Inclusion criteria for this study comprised healthy participants aged 21 to 40 years of age, and who agreed to commit to three times a week of self-training and follow-up in the study. Exclusion criteria comprised participants who have had a prior hamstring injury, prior anterior cruciate ligament reconstruction with hamstring harvest, who are physically challenged and are unable to fulfil physical training standards required of the trial, and patients who have connective tissue diseases. Patients who have diabetes mellitus, who were already attending a training program three times a week, or who were involved in any other clinical study were also deemed ineligible to be involved in this study.

Physical training programme

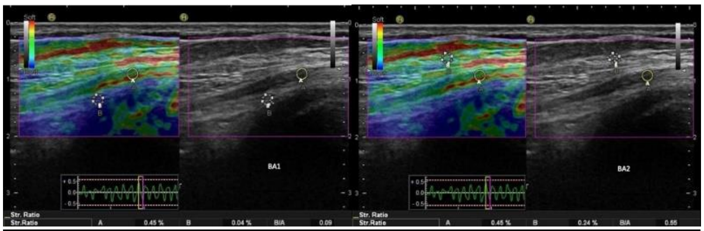
All participants attended a standardized, targeted physical training program. This consisted of hamstring resistance training for 12 consecutive weeks, conducted 3 times a week on non-consecutive days (total of 36 training sessions). Attendance was taken at every session and done in the institutional gym to ensure compliance. The exercise consisted of: 5 minute warm-up, followed by 5 sets of 8 repetitions with a weights machine. Each repetition is conducted at 80% of the participants maximum repetition weight. 2 minutes rest was given in between sets. The technique was as follows: Single-leg hamstring exercises were performed with a hamstring weights machine with the pad placed just above the ankle, with the knee flexed past 90 degrees on each repetition. The resistance exercise was tailored by the physiotherapist to work on the semi-tendinosus and gracialis muscles by internally rotating the foot to preferentially work the gracialis and semitendinosus.

In order to optimize tendon hypertrophy, the weight of maximum repetition was individualized according to the respective patient's profile and re-assessed by the study physiotherapist on the first, tenth, twentieth and thirtieth session. This ensured that the weight was consistently at 80% of the max repetition weight, allowing maximum gains. A standardised exercise technique was taught to each participant and checked for technique and form during each assessment by the physiotherapist.

Outcomes

The primary outcome measure was the cross-sectional area of the tendon. The tendon cross-sectional area and tendon modulus was measured via ultrasound by a blinded senior consultant sports physician. A standardised technique was use for measurement of the hamstring tendons. The ultrasound probe was placed at the level of the posterior border of the tibia with the knee is flexed at 90 degrees, and with the ultrasound probe directed 90 degrees to the skin. This gave the most consistent image of the hamstring tendons and provided a standardised measure of the tendon cross-sectional area.

The secondary outcome was tendon modulus. Ultrasound elastography is used to approximate the stiffness of tissue, known as the Young's modulus. Ultrasound elastography utilises the difference in density of the hamstring tendon compared to the surrounding soft tissue as a surrogate of the stiffness of the tendon. This required a constant comparator and was therefore calculated in comparison to the surrounding connective tissue with respect to the tendon. For each muscle pre- and post-intervention, two stiffness coefficients, "BA1" and "BA2", were measured with "A" representing the hamstring tendon and "B" representing the connective tissue used as a comparator. Stiffness coefficient "BA1" was used for comparison with the deep connective tissue and stiffness coefficient "BA2" was used for comparison with the superficial connective tissue. A negative value indicates an increase in stiffness, while a positive value indicates a decrease in stiffness. 2 stiffness coefficients are calculated in order to determine that the change in stiffness of the tendon post-intervention is consistent.



BA1: Comparison to deep tissues, BA2: Comparison to superficial tissues

Figure 1: Ultrasound elastography images

3. STATISTICAL ANALYSIS

Descriptive data within each demographic factor was expressed as frequencies (n), percentages (%) and median scores (Inter-Quartile Range).

Normality of the residual error was tested using visual examination of the histogram of the continuous variables. The histograms for the variables did not suggest a normal distribution and alongside the small sample size of 9, the Mann Whitney U-test was used. Microsoft Excel was utilized. A significance level of 0.05 was set for all statistical tests.

RESULTS

Demographics

A total of 17 participants were recruited and 9 participants completed the study. Participants were healthy volunteers from the hospital, and consisted of doctors and physiotherapists. As exercise was mandated to be in the institutional gym, 5 of the 8 dropouts could not adhere to the 80% requirement of exercise and were therefore excluded from the study. 2 participants voluntarily withdrew due to time constraints and 1 participant unknowingly performed different sets from the prescribed exercise and was thus excluded. The baseline characteristics are shown in Table 1. The median age of participants was 27 years old. There are similar numbers of male and female participants. None of the participants were smokers, and the median BMI was within the optimal range.

55.6% (n=5) of participants were female. The median height of participants was 1.66 metres (Interquartile Range, IQR = 0.07), median weight was 58kg (IQR = 11.0) and a median BMI was 21.0 (IQR = 4.31).

Table 1: Baseline characteristics

Number of Participants		9
Gender	Male:	4 (44.4%)
	Female:	5 (55.6%)
Median Age		27
Median Height (m)		1.66 (IQR 0.07)
Median Weight (kg)		58 (IQR 11.0)
Median BMI (kg/m^2)		21.0 (IQR 4.31)
Smoker	Yes:	0 (0%)
	No:	9 (100%)

The median increase in hamstring strength on the right leg was 12.5 pounds (Interquartile Range, IQR = 5.9) (p= 0.13) and left leg was 12.5 pounds (IQR = 0) (p= 0.14). 2 participants did not show an increase in hamstring strength.

Hypertrophy of the tendons

The median increase in cross-sectional area for the left Semitendinosus was 0.02 mm^2 (IQR = 0.07) (p-value = 0.76). The median increase in cross-sectional area for the right Semitendinosus was 0.02 mm^2 (IQR =0.03) (p-value = 0.73). The median increase in cross-sectional area for the left Gracilis was 0.01 mm^2 (IQR = 0.02) (p-value = 0.44). There was a median decrease in cross-sectional area for the right Gracilis of 0.01 mm^2 (IQR = 0.03) (P-value = 0.54).

The following tables (Table 2 and 3) show the overall distribution for the change in respective tendon cross-sectional areas before and after intervention of each of the 9 participants.

Table 2: Pre-intervention and Post-intervention Cross-sectional Area of Semitendinosus Tendons

Participant	Pre-intervention (mm^2)	Post-intervention (mm^2)	Change (mm^2)
Left Semitendinosus			
Participant A	0.12	0.27	0.15
Participant B	0.09	0.09	0
Participant C	0.11	0.13	0.02
Participant D	0.09	0.14	0.05
Participant E	0.15	0.08	-0.07
Participant F	0.18	0.12	-0.06
Participant G	0.07	0.11	0.04
Participant H	0.13	0.1	-0.03
Participant I	0.09	0.11	0.02
Median Change			0.02
Right Semitendinosus			
Participant A	0.15	0.23	0.08
Participant B	0.08	0.09	0.01
Participant C	0.11	0.15	0.04
Participant D	0.08	0.11	0.03
Participant E	0.09	0.08	-0.01
Participant F	0.12	0.12	0
Participant G	0.15	0.08	-0.07
Participant H	0.1	0.1	0
Participant I	0.09	0.12	0.03
Median Change			0.02

Table 3: Pre-intervention and Post-intervention Cross-sectional Area of Gracilis Tendons

Participant	Pre-intervention (mm^2)	Post-intervention (mm^2)	Change (mm^2)
Left Gracilis			
Participant A	0.06	0.08	0.02
Participant B	0.05	0.05	0
Participant C	0.07	0.09	0.02
Participant D	0.07	0.09	0.02
Participant E	0.07	0.06	-0.01
Participant F	0.09	0.04	-0.05
Participant G	0.05	0.07	0.02
Participant H	0.05	0.06	0.01
Participant I	0.04	0.05	0.01
Median Change			0.01
Right Gracilis			
Participant A	0.05	0.08	0.03
Participant B	0.05	0.04	-0.01
Participant C	0.06	0.08	0.02
Participant D	0.09	0.09	0
Participant E	0.1	0.07	-0.03
Participant F	0.1	0.05	-0.05
Participant G	0.05	0.04	-0.01
Participant H	0.05	0.08	0.03
Participant I	0.05	0.04	-0.01
Median Change			-0.01

Biomechanical properties of the tendon

The Secondary Outcome measure of the study was tendon modulus, as measured via ultrasound elastography of each tendon, pre and post intervention.

Median changes in BA1 Stiffness coefficient before and after intervention is as follows: 0.01 for left Semitendinosus (p-value = 0.03), -0.06 for right Semitendinosus (p value = 0.31), -0.52 for left Gracilis (p value = 0.43), -0.02 for right Gracilis (p value = 0.13).

Median changes in BA2 Stiffness coefficient before and after intervention is as follow: -4.58 for left Semitendinosus (p value = 0.03), -3.32 for right Semitendinosus (p value = 0.13), 0.7 for left Gracilis (p value = 1), -0.03 for right Gracilis (p value = 0.66).

The relative changes of both stiffness coefficient for each muscle group is illustrated in Figure 2.

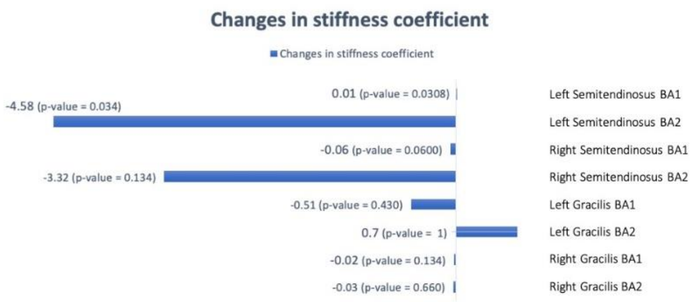


Figure 2: Changes in stiffness coefficient

DISCUSSION

This is the first study to investigate the hypertrophy of hamstring tendon sizes in the Asian population. Asians have been shown to have a smaller body composition, and therefore smaller graft sizes with mean hamstring graft sizes of 7.7 mm. This may predispose this population to poor graft outcomes following ACL reconstruction, and warrants further studies looking into increasing the hamstring tendon sizes pre-ACL intervention.

Our study found that 12 weeks of resistance training did not significantly increase the ultrasound measured cross sectional areas of the hamstring tendons. Although there was an increase in tendon cross sectional area in 3 of the 4 studied tendons, these findings were not significant.

Previous studies have reported similar effects of resistance training on the human patellar tendon, in which knee extension resistance exercises had produced increases in the mean patellar tendon cross-sectional area [6, 9]. Another study examined the patellar tendon size in 12 participants who had asymmetrical knee extensor strength on both legs as a result of frequent sport-specific loading on a dominant leg. It was found that the dominant leg had a greater proximal and distal patellar tendon cross-sectional area than the non-dominant one, thus providing further evidence for the phenomenon of tendon hypertrophy in response to chronic loading [10]. The difference in the degree of tendon hypertrophy compared to our study might have been limited by the short duration of the resistance training, as previous studies by Kongsgaard *et al*. had demonstrated only a very small magnitude of tendon hypertrophy after 12 weeks of strength training. This suggests that while some degree of tendon hypertrophy was achieved in the twelve weeks of resistance training in this study, it may take a longer duration of loading to achieve a larger extent of hypertrophy [6, 10]. However, we must take into consideration that in the circumstances surround the ACL injured athlete, a prolonged preoperative training time may not be practical and may be poorly received.

This study also found that post-intervention, there were decreases in BA1 stiffness coefficient for the right semitendinosus, left and right gracilis; as well as decreases in BA2 stiffness coefficient for left semitendinosus, right semitendinosus and right gracilis. However, it was also noted post-intervention that there was an increase in BA1 stiffness coefficient for left semitendinosus and an increase in BA2 stiffness coefficient for left gracilis. Hence we were unable to draw any conclusion for change in stiffness coefficients post-intervention.

Proposed mechanisms of action for the positive correlation between resistance training and cross sectional area of the semitendinosus tendon include increased rates of human tendon collagen and skeletal muscle synthesis. The increased anabolic activity of the musculotendinous unit may be attributed to the coordinated responses of muscle and tendon fibroblasts and muscle fibres to mechanical signals during contractile activity. Such a theory is plausible as muscle fibre hypertrophy would only be practical if accompanied by a concomitant remodeling of connective tissue around them, including the tendon [11]. Another study reported elevated procollagen type-1 C-terminal propeptide (PICP) levels after exercise in peritendinous tissue and circulating blood, thereby corroborating that acute exercise induces increased biosynthesis of collagen and promotes tendon hypertrophy [12]. Mechanical adaptations of the tendon accompany muscular hypertrophy, resulting in the ability of the musculotendinous units to collectively bear greater loads [9].

We note that this study has exhibited trends in keeping with existing literature in the increased cross sectional area of semitendinosus. These findings are clinically significant because they imply that it is possible to increase the diameter and hence cross-sectional area of the semitendinosus tendon through resistance training induced hypertrophy, thus increasing their mechanical strength which would make them stronger grafts for ACL reconstruction. The relationship between cross-sectional area and graft strength has been elucidated in previous studies [13, 14]. Additionally, small increases in the tendon size can be clinically significant because the graft is quadrupled intraoperatively (folded onto itself to form a 4 strand graft). The small increases in median cross-sectional area of the semitendinosus tendons translate to considerable increments in the diameters of the final graft. Within twelve weeks, resistance training was able to achieve measurable increases in the diameters of the left semitendinosus, right semitendinosus and right gracilis tendons.

However, the results were non-significant due to the small numbers in the trial and we note that the cohort size is similar to previous studies. Hence, this study provides the basis for a larger-scale randomized control trial of the effect of preoperative resistance training on ACL reconstruction graft strength. In the future, preoperative resistance training could be implemented for ACL reconstruction patients, in order to produce stronger and more viable autografts from the semitendinosus and gracilis tendons.

Limitations

This study was underpowered to detect significant change due to a small sample size as well as the drop-out rate.

This also predispose the study to a higher degree of random error. There was an incongruous decrease in median cross-sectional area of the right gracilis, as well as increases in BA1 of the left semitendinosus and BA2 of the left gracilis, indicating decreases in the stiffness of these tendons. These increments contradict existing literature as well as the general trends of increased median cross-sectional area and tendon stiffness post-intervention that had been demonstrated in this study. It is possible that these inconsistencies stem from random error. To follow up on this study, a larger scale study should be conducted to confirm the cause-effect relationship between resistance training and tendon hypertrophy.

CONCLUSION

In conclusion, this is the first human intervention study which reports resistance-training induced hypertrophy of the semitendinosus tendon intended for producing stronger ACL autografts. We found statistically insignificant but potentially clinically significant increases in the median cross-sectional area of the tendons as measured on ultrasound. Future large-scale studies on ACL injured patients may be considered to measure the true intraoperative graft sizes after intervention.

Conflict of Interest

The authors report no declarations of interest.

Authors' Contribution

Dr Michael Yam – Conceptualising study design, analysis and interpretation of data

Jason Kok Kiong Chia – Acquisition of data

Jia Yen Wong – Acquisition of data

Nicholas Jiajie Leong – Revision of article

Elisabeth Ker Hsuen Tan – Drafting of article

Yao Hao Teo – Drafting of article

Yu Kit Jaron Yong – Drafting of article

Ernest Kwek – Supervisor, approval of final version

Keng Thiam Lee – Supervisor, approval of final version

REFERENCES

1. Mall NA, Chalmers PN, Moric M, Tanaka MJ, Cole BJ, Bach BR, Jr., *et al*. Incidence and trends of anterior cruciate ligament reconstruction in the United States. Am J Sports Med. 2014; 42(10):2363-70.
2. Lee YHD, Kuroda R, Chan KM. Anterior Cruciate Ligament Reconstruction: A 2015 global perspective of the Magellan Society. Asia Pac J Sports Med Arthrosc Rehabil Technol. 2015; 2(4):122-128.
3. Cerulli G, Placella G, Sebastiani E, Tei MM, Speziali A, Manfreda F. ACL Reconstruction: Choosing the Graft. Joints. 2013; 1(1):18-24.
4. Conte EJ, Hyatt AE, Gatt CJ, Jr., Dhawan A. Hamstring autograft size can be predicted and is a potential risk factor for anterior cruciate ligament reconstruction failure. Arthroscopy. 2014; 30(7):882-90.
5. Suggs J, Wang C, Li G. The effect of graft stiffness on knee joint biomechanics after ACL reconstruction--a 3D computational simulation. Clin Biomech (Bristol, Avon). 2003; 18(1):35-43.
6. Kongsgaard M, Reitelseder S, Pedersen TG, Holm L, Aagaard P, Kjaer M, *et al*. Region specific patellar tendon hypertrophy in humans following resistance training. Acta Physiol (Oxf). 2007; 191(2):111-121.
7. Ying M, Yeung E, Li B, Li W, Lui M, Tsoi CW. Sonographic evaluation of the size of Achilles tendon: the effect of exercise and dominance of the ankle. Ultrasound Med Biol. 2003; 29(5):637-42.
8. Chiquet M. Regulation of extracellular matrix gene expression by mechanical stress. Matrix Biol. 1999; 18(5):417-26.
9. Seynnes OR, Erskine RM, Maganaris CN, Longo S, Simoneau EM, Grosset JF, *et al*. Training-induced changes in structural and mechanical properties of the patellar tendon are related to muscle hypertrophy but not to strength gains. J Appl Physiol (1985). 2009; 107(2):523-30.
10. Couppe C, Kongsgaard M, Aagaard P, Hansen P, Bojsen-Moller J, Kjaer M, *et al*. Habitual loading results in tendon hypertrophy and increased stiffness of the human patellar tendon. J Appl Physiol (1985). 2008; 105(3):805-10.
11. Miller BF, Olesen JL, Hansen M, Dossing S, Crameri RM, Welling RJ, *et al*. Coordinated collagen and muscle protein synthesis in human patella tendon and quadriceps muscle after exercise. J Physiol. 2005; 567(Pt 3):1021-33.
12. Langberg H, Skovgaard D, Petersen LJ, Bulow J, Kjaer M. Type I collagen synthesis and degradation in peritendinous tissue after exercise determined by microdialysis in humans. J Physiol. 1999; 521 Pt 1:299-306.
13. Pichler W, Tesch NP, Schwantzer G, Fronhofer G, Boldin C, Hausleitner L, *et al*. Differences in length and cross-section of semitendinosus and gracilis tendons and their effect on anterior cruciate ligament reconstruction: a cadaver study. J Bone Joint Surg Br. 2008; 90(4):516-9.
14. Noyes FR, Butler DL, Grood ES, Zernicke RF, Hefzy MS. Biomechanical analysis of human ligament grafts used in knee-ligament repairs and reconstructions. J Bone Joint Surg Am. 1984; 66(3):344-52
15. Sepulveda F, Sanchez L, Amy E, Micheo W. Anterior Cruciate Ligament Injury: Return to Play, Function and Long-Term Considerations. Curr Sports Med Rep. 2017; 16(3):172-8.
16. Grassi A, Ardern CL, Marcheggiani Muccioli GM, Neri MP, Marcacci M, Zaffagnini S. Does revision ACL reconstruction measure up to primary surgery? A meta-analysis comparing patient-reported and clinician-reported outcomes, and radiographic results. Br J Sports Med. 2016; 50(12):716-24.
17. Challa S, Satyaprasad J. Hamstring graft size and anthropometry in south Indian population. J Clin Orthop Trauma. 2013; 4(3):135-8.
18. Khayyeri H, Blomgran P, Hammerman M, Turunen MJ, Löwgren A, Guizar-Sicairos M, *et al*. Achilles tendon compositional and structural properties are altered after unloading by botox. Sci Rep. 2017; 7(1):13067.
19. Kubo K, Kanehisa H, Fukunaga T. Effects of resistance and stretching training programmes on the viscoelastic properties of human tendon structures in vivo. J Physiol. 2002; 538(Pt 1):219-26.