DOCTOR OF PHILOSOPHY

The Biceps Femoris Long Head Muscle Structure: Implications on risk factors for hamstring strain injuries

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The Biceps Femoris Long Head Muscle Structure: Implications on risk factors for hamstring strain injuries

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BSc, MSc

Submitted in partial satisfaction of the requirements for the Degree of Doctor of Philosophy

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Published Chapters in Peer-Reviewed Journals:

- Chapter 2. **Yagiz G**, Akaras E, Kubis H-P, Owen JA. Heterogeneous effects of eccentric training and nordic hamstring exercise on the biceps femoris fascicle length based on ultrasound assessment and extrapolation methods: A systematic review of randomised controlled trials with meta-analyses. PLoS ONE. 2021 Nov 9;16(11). e0259821. https://doi.org/10.1371/journal.pone.0259821
- Chapter 3. **Yagiz G**, Shida N, Kuruma H, Furuta M, Morimoto K, Yamada M, Uchiyama T, Kubis H-P, Owen JA. Playing Rugby Leads to Longer Biceps Femoris Fascicles, but Stiffer Biceps Femoris, and Lower Knee Flexors to Extensors Muscle Volume Ratios in the Long-Term. International Journal of Sports Physiology and Performance. In press.
- Chapter 4. **Yagiz G**, Williams K, Owen J, Kubis H-P. Alterations in biceps femoris long head fascicle length, eccentric hamstring strength qualities and single-leg hop distance throughout the ninety minutes of TSAFT90 simulated football match. PLoS ONE. 2022 Dec 9;17(12):e0278222. e0278222. https://doi.org/10.1371/journal.pone.0278222
- Chapter 5. **Yagiz G**, Akaras E, Kubis H-P, Owen JA. The Effects of Resistance Training on Architecture and Volume of the Upper Extremity Muscles: A Systematic Review of Randomised Controlled Trials and Meta-Analyses. Applied Sciences. 2022 Feb 2;12(3). 1593. https://doi.org/10.3390/app12031593

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- Invited Speaker. **Yagiz G**. the Significance of Biceps Femoris Long Head Muscle Structure for Hamstring Strain Injuries. 1st International Congress of Selcuk Health Sciences, 2022, 1-2 Dec, Konya, Turkiye. Available from: http://isuhsc2022.selcuk.edu.tr/invited-speakers-2/.

Other Relevant Works Published During the PhD:

- Shida N, **Yagiz G**, Yamada T. The Effects of Exergames on Muscle Architecture: A Systematic Review and Meta-Analysis. Applied Sciences. 2021 Nov 3;11(21). 10325. https://doi.org/10.3390/app112110325

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List of Acronyms

AV……...Average

ACSA……..Anatomical cross-sectional area

ANOVA……..Analysis of variance

BFlh…….Biceps femoris long head

B-mode……Brightness mode

BFR……..Blood flow restricted

CI…….Confidence interval

CSA…….Cross-sectional area

CV……Coefficient of variation

DNA…….Deoxyribonucleic acid

D……...Dominant

EFOV……...Extended Field of View

ES…….Effect size

FL…….Fascicle length

HSIs……..Hamstring strain injuries

ICC……Intraclass correlation coefficient

KE……..Knee extensors

KF……..Knee flexors

LoE……Level of evidence

MD……Mean difference

MLE……..Manual linear extrapolation

MRI……...Magnetic resonance imaging

mRNA……...Messenger ribonucleic acid

MT…….Muscle thickness

MV…….Muscle volume

ND……..Non-dominant

NHE……Nordic hamstring exercise

PA……...Pennation angle

PCSA……..Physiological cross-sectional area

PhD…….Doctor of philosophy

PMS……Passive muscle stiffness

PRISMA…….....The Preferred Reporting Items for Systematic Reviews and Meta-analyses

RCT…….Randomised controlled trial

RevMan……...Review manager

RM……...Repetition maximum

RNA……..…Ribonucleic acid

SAFT^{45}…….the Soccer-specific Aerobic Field Test (45 minutes)

SAFT^{90}…….the Soccer-specific Aerobic Field Test (90 minutes)

SD……Standard deviation

SLHB……...Single-leg hamstring bridge

SLHD……...Single leg hop distance

SMD……..…Standardised mean difference

T-SAFT^{90}…….….the Technical Soccer-Specific Aerobic Field Test (90 minutes)

US……..…Ultrasound

vBFR…….Venous blood-flow restricted

%HRmax……...Mean percentage of maximal heart rate

ABSTRACT

The main focus of this thesis is the investigation of structural muscle parameters (i.e., fascicle length (FL) and passive muscle stiffness (PMS)) of the biceps femoris long head (BFlh) due to their relationship with hamstring injuries in sports. Chapters two, three and four contain two original experimental studies and one systematic review with meta-analysis focusing on the topic above. In the first systematic review with meta-analysis (chapter two), studies investigating the effects of eccentric training, including the Nordic hamstring exercise, have been screened and investigated based on the BFlh FL based on ultrasound assessment methods. The systematic review's findings indicated that eccentric training showed a large effect size on increasing the BFlh FL when it was measured using the trigonometric equation method. However, eccentric exercise did not largely increase the BFlh FL when measured using the manual linear extrapolation method or panoramic ultrasound scanning. Conclusions of the meta-analysis highlight that a "gold standard" measurement method is needed for comparable results between the studies investigating the effects of eccentric exercise on the BFlh FL. The first experimental study of this thesis (chapter three) compared the BFlh muscle structural parameters and knee extensors (KE) and knee flexors (KF) muscle volume ratios between rugby players and physically active non-athlete controls to explore the long-term effects of playing rugby on the mentioned muscular structure. The findings demonstrate that playing rugby and rugby-specific training led to increased BFlh PMS and lower BFlh FL/KE and KF/KE muscle volume ratios in the long term. Habitual rugby training and match-play lead to structural and morphological alterations in the KF and KE that may increase HSIs risk. Practitioners should administer long-term hamstring pre-habilitation training to reduce HSI risk in rugby players. The second experimental study of this thesis (chapter four) aimed to examine football-specific fatigue-induced alterations in risk factors of the HSIs, including biceps femoris long head fascicle length (BFlh FL), single-leg hop distance, hamstrings' maximal eccentric strength, and single-leg hamstring bridge test (SLHB) performance. Outcomes revealed significant decrements in SLHB performance and maximal eccentric hamstring strength immediately after ninety minutes of a simulated football match ($TSAFT^{90}$). However, in this study, we could not observe any significant change in the BFlh FL and single-leg hop distance immediately after half-time and full-time of the $TSAFT^{90}$. In conclusion, this study provided strong evidence for improving eccentric strength and SLHB performance in practitioners. In chapter five of this thesis, the systematic review – a meta-analysis of morphological effects of exercise on the upper limb muscles found that various

exercise types induced large effect sizes on increasing muscle size in distinct upper extremity muscles. At least four weeks of training were necessary to induce the forementioned hypertrophic responses.

Additional Information

This thesis was affected by the prolonged Covid-19 pandemic restrictions for about two years, making data collection very challenging for studies recruiting human participants. Initially, it was planned that the PhD studies would consist of entirely original investigations. However, the Covid-19 pandemic did not allow that. Several contingency studies were scheduled for the PhD, including randomised controlled trials. Consequently, two chapters consisted of two critical systematic reviews and meta-analyses of the literature instead of original investigations due to the Covid-19 pandemic, while the other two chapters consisted of original investigations. At the beginning of the pandemic, only one systematic review was planned to conduct for the thesis during the Covid-19 pandemic. However, an additional systematic review was conducted during the prolonged restrictions due to the Covid-19 pandemic.

Chapter 1. General Introduction

Hamstring strain injuries (HSIs) are endemic non-contact injuries in sports requiring high-speed running [1], such as Australian Rules football, American football, football, rugby, and track and field sports [2-6]. The HSIs accounted for 26% in track and field [7], 13.7% in Australian football [8], 24% in football [3], 12% in American football [4] and 6-15% of all injuries in rugby [9]. HSIs cause the most significant training and match time lost in Australian football [10] and rugby [9, 11] and increased absence of playing and training in soccer [12]. Moreover, the following high rate of reoccurrence has been detected: 32% in American football [13], 27% in Australian football [10], 21% in rugby [9] and 16% in soccer [12]. Furthermore, the recurrent HSIs are more severe than the first injuries and cause higher time loss [9]. Apart from these, recurrent hamstring injuries may lead to adhesion in the popliteal nerve, enthesopathy, problems in meniscuses of the knee, anomalies of the lumbar spine, abnormal quadriceps power, motor dysfunction of the nervus ischiadicus and the end of athletic career [14-16]. In the last two decades, scientists have shown an increased effort to provide an optimal injury-prevention technique for HSIs [17]. However, the HSIs have increased in comparison with the earlier epidemiologic data in high-speed running involving sports such as Australian Rules football, rugby union, and football [18]. For instance, a 4% annual increase was detected in HSIs between 2001 and 2014 in professional football [19]. Nowadays, 24% of all injuries are classified as HSIs in football [3].

Among the hamstrings, the biceps femoris long head (BFlh) has been pointed out as the most injured muscle (80% of all HSIs) [20]. HSIs generally occur during running, and running caused HSIs calculated as 100% in sprinting [14], more than 60% in soccer [21], 80% in Australian rules football [22], and 68% in rugby [9]. The most vulnerable time for the HSIs was detected as the late swing phase of running [23-25]. During this phase, the hamstrings eccentrically contract to decelerate the tibia and control the concentric antagonist contraction of the quadriceps femoris [26]. At this moment, the BFlh reaches about 110% of the length due to elongation, which is greater than semimembranosus (108.2%) and semitendinosus (107.5) [27]. HSIs commonly occur when the muscle fascicles cannot withstand this excessive tensile force [28]. For this reason, insufficient eccentric contraction of the hamstrings during the late swing phase of running was considered the leading cause of HSIs [25, 29]. In light of this information, researchers have focused on improving the insufficient eccentric contraction of hamstrings and proposed eccentric strength training, including the popular Nordic hamstring exercise (NHE) as an injury prevention strategy for HSIs [30-33].

Numerous risk factors for HSIs were previously pointed out by prospective studies [34], and the risk factors of HSIs were divided into two groups non-modifiable and modifiable risk factors [35]. Non-modifiable risk factors include, but are not limited to, age [36-38] and previous injury [37, 38]. Modifiable risk factors include, but are not restricted to, fatigue [13, 39], insufficient warm-up [40], strength imbalances [41, 42, 13, 43, 44], inadequate eccentric hamstring strength [45], increased hamstring passive muscle stiffness [46], and BFlh muscle architecture [45]. Muscle architecture is a broad term comprising fascicle geometry (fascicle length (FL) and pennation angle) and muscle size (anatomical and physiological cross-sectional areas, muscle thickness and muscle length) [47]. Among the architectural parameters, shorter BFlh fascicle length (shorter than 10.56 cm) was defined as a risk factor for the HSIs by increasing the risk of HSIs more than fourfold, and together with the increased hamstring stiffness, was defined as the structural risk factors for HSIs [34].

Since the proposal of BFlh fascicle length being a critical HSI risk, numerous studies have been published examining the effects of eccentric strength training, including NHE, on the biceps femoris FL. Additionally, three systematic reviews and meta-analyses reporting the impact of general eccentric strength training on the biceps femoris FL [48] or particularly the effects of the NHE [49, 50] on the biceps femoris FL have been published in the last three years. However, the previous meta-analyses [49, 48, 50] were run by ignoring whether the studies used ultrasound assessment or extrapolation methods. Furthermore, these meta-analyses [49, 48, 50] did not explain the underlying reason for their substantial to considerable statistical heterogeneities [51] that were detected by the I^2 statistics, which shows the percentage ratio of the variability in effect sizes caused by heterogeneity rather than chance [51]. However, Franchi et al. [52] have compared ultrasound assessment methods that include panoramic scanning (extended field of view (EFOV)), manual linear extrapolation (MLE) and trigonometric equations for estimating the BFlh FL; they demonstrated that equation methods from a single image significantly overestimate biceps femoris FL. Additionally, Franchi et al. [52] mentioned that the experimental studies employed the trigonometric equation method for measuring biceps femoris FL and reported a high magnitude of biceps femoris FL change comparing the other techniques. In the second chapter, this PhD thesis aimed to clarify previously mentioned effect sizes [49, 48, 50] of eccentric training, including the NHE, on BFlh FL based on the assessment methods involving trigonometric equation methods, the MLE and panoramic ultrasound scanning.

The muscle imbalances between knee flexors (KF) and knee extensors (KE) favouring the knee extensors were previously indicated as a risk factor for HSIs [94]. Additionally, shorter BFlh fascicle length [45] increased passive hamstring stiffness [46] and were also defined as risk factors for the HSIs. Revealing long-term adaptations of BFlh fascicle length, passive stiffness, the BFlh FL to KE muscle volume, and BFlh to KE, KF to KE and BFlh to KF muscle volume ratios to playing rugby can bring new insights into developments of rugby training programs. However, there is no comprehensive cross-sectional study examining the adaptations of the mentioned parameters to playing ruby in the long term that exists in the literature. Thus, this PhD thesis aimed to investigate long-term transformations of the morphology of the thigh muscles, BFlh FL and passive muscle stiffness in the third chapter of the thesis.

The HSIs show a higher incidence during football match play than football training (respectively 3.70 (3.43-3.99) vs 0.43 (0.39-0.47) per 1000 hours) [95]. The HSIs are more frequent in the last fifteen minutes of both halves of a football match [12, 96, 21]. It was suggested that increased muscular fatigue could play a substantial role in HSIs occurrence in football [97, 98]. Considering this information, studies [99-120] concentred on exploring interrelationships between football match-specific fatigue and HSIs risk factors are warranted. Previous studies [99-109, 111-113, 116-118, 120] examining the effects of an actual or simulated football match on alterations of the eccentric hamstring strength did not use specific strength assessment methods related to the risk for HSIs. None of the studies focused on changes in the other risk factors that BFlh FL [45] and single-leg hop distance (SLHD) [121] due to an actual or simulated football match. Therefore, this PhD thesis aimed to monitor alterations in the BFlh FL, SLHD, and eccentric hamstring strength parameters during a simulated football match play in chapter four of this thesis.

The architectural parameters and volumes of skeletal muscles identify the functional traits of a muscle [53]. Research has shown that muscle architectural parameters are significant predictors of athletic performance [54-65], athletic injuries [66-72, 45] and strength [73-84]. Architectural parameters and volume of the upper extremity muscles are essential predictors of athletic performance, rate of force development, strength, and power [85, 56, 86-93]. Screening effects of resistance modalities on the architectural parameters and volume of the upper extremity muscles can be a reference point for future conditioning and training regimens for athletes. Therefore, this PhD thesis aims to perform a comprehensive systematic review with meta-analyses to identify the effects of resistance training modalities on the

architectural parameters and muscle volumes of the upper extremity muscles in the fifth chapter.

The structure of the thesis is organised as follows:

- Chapter 2: Systematic review with meta-analyses 1- Heterogeneous effects of eccentric training and Nordic hamstring exercise on the biceps femoris fascicle length based on ultrasound assessment and extrapolation methods: A systematic review of randomised controlled trials with meta-analyses
- Chapter 3: Original investigation 1 - Playing rugby leads to longer biceps femoris fascicles, but stiffer biceps femoris, and lower biceps fascicle length to knee extensors and knee flexors to knee extensors muscle volume ratios in long-term
- Chapter 4: Original investigation 2- Alterations in biceps femoris long head fascicle length, Eccentric hamstring strength qualities and single-leg hop distance throughout the ninety minutes of TSAFT90 simulated football match
- Chapter 5: Systematic review with meta-analyses 2 - The effects of resistance training on architecture and volume of the upper extremity muscles: A systematic review of randomised controlled trials and meta-analyses
- Chapter 6: General discussion
- Chapter 7: General conclusions and future research suggestions

Chapters 2, 4, and 5 are published in peer-reviewed journals, and chapter 3 is in press in a peer-reviewed journal, as illustrated on page 8.

Chapter 2. Systematic Review with Meta-analyses 1.

Heterogeneous effects of eccentric training and Nordic hamstring exercise on the biceps femoris fascicle length based on ultrasound assessment and extrapolation methods: A systematic review of randomised controlled trials with meta-analyses

A version of this chapter has been published in the peer-reviewed journal "Plos ONE"

Yagiz G, Akaras E, Kubis HP, Owen JA (2021) Heterogeneous effects of eccentric training and nordic hamstring exercise on the biceps femoris fascicle length based on ultrasound assessment and extrapolation methods: A systematic review of randomised controlled trials with meta-analyses. PLOS ONE 16(11): e0259821. https://doi.org/10.1371/journal.pone.0259821

Abstract

Objective: To systematically review the effects of eccentric training based on biceps femoris long head fascicle length using ultrasound assessment and extrapolation methods. **Design:** Systematic review and meta-analysis of randomised controlled trials. **Data sources:** CENTRAL, CINAHL Plus with full text, PubMed and OpenGrey databases were searched on 6 July 2021. **Eligibility criteria:** for selecting studies Randomised controlled trials (RCTs) lasting at least four weeks and presenting data about biceps femoris long head (BFlh) fascicle length (FL) as an outcome. **Methods:** Searching databases, screening studies, performing risk of bias assessments and determining the level of evidence (LoE) for each meta-analysis were applied during the study. PRISMA 2020 statement and Cochrane Handbook for Systematic Reviews of Interventions were used as the guidelines of this systematic review. **Results:** Eight randomised controlled trials were included in meta-analyses. Based on the very low and low LoE, eccentric training has small (g = 0.29, 95% CI [-0.26, 0.85]), moderate (g = 0.72, 95% CI [0.17, 1.28]) and large (g = 2.20, 95% CI [0.99, 3.41]) effect sizes (ES) based on manual linear extrapolation (MLE), panoramic ultrasound scanning and trigonometric equation methods, respectively. Similarly, Nordic hamstring exercise (NHE) has small (g = 0.23 [-1.02, 1.47]), small (g = 0.38, 95% CI [-0.50, 1.27]) and large (g = 1.98, 95% CI [0.52, 3.44]) ES based on the MLE, panoramic ultrasound scanning and trigonometric equation methods, respectively. **Conclusions:** ES of eccentric training, including NHE, varies between the MLE, panoramic ultrasound scanning, and equation methods. The relevant scientific community should have a consensus on measurement standards of the BFlh FL measurements. Further studies can be conducted to compare the effects of eccentric training based on ultrasound assessment and extrapolation methods.

2.1. Introduction

Hamstring strain injuries (HSIs) appear as an endemic injury among non-contact injuries for the sports that require high-speed running, including Australian Rules football, rugby union and football [1–5]. Despite increased efforts by researchers to provide an optimal injury prevention technique in the last two decades, HSIs have increased based on earlier epidemiologic data in Australian Rules football, rugby union and football [6]. For instance, Ekstrand and coworkers [7] detected a 4% annual increase in HSIs between 2001 and 2014 in professional football. The biceps femoris long head (BFlh) appears to be the most frequently injured muscle among the hamstring muscles [8]. In addition, re-injuries are very frequent in this anatomical section in the event that an adequate rehabilitation process and an adequate instrumental evaluation have not been performed [9].

The hamstring muscles are important contributors to stabilizing the knee joint, and a more balanced hamstring-to-quadriceps force ratio is shown to reduce lower limb injury [10– 12]. The majority of HSIs occur during running activities [13, 14]. The late swing phase of running was defined as the most vulnerable time for hamstrings [15–17]. During the late swing phase of running, the hamstrings behave as an antagonist to the quadriceps femoris and produce eccentric contraction for controlling the quadriceps femoris muscle and for decelerating the tibia [18]. At this moment, the BFlh is exposed to the highest stretch and reaches about 110% of its length, which is greater than semimembranosus (108.2%) and semitendinosus (107.5) [19]. HSIs generally occur when the muscle fibres cannot resist the excessive tensile force [20]. For this reason, insufficient eccentric contraction of the hamstrings during the late swing phase of running was considered the leading cause of HSIs [15, 21]. In light of this information, researchers have focused on improving the stated insufficient eccentric contraction of hamstrings and proposed eccentric strength training, including the popular Nordic hamstring exercise (NHE) as an injury prevention strategy for HSIs [22–25]. It should also be noted that there is an ongoing debate about whether the hamstrings produce eccentric contraction or isometric contraction during the late swing phase of running [26, 27].

Shorter BFlh fascicle length (FL) has recently been proposed as a risk factor for HSIs in 2016 [28]. Timmins et al. [28] highlighted that a BFlh FL shorter than 10.56 cm increases the risk of an HSI more than fourfold. Since this date, the number of studies examining the effects of eccentric strength training, including NHE, on the BFlh FL has been increasing.

Additionally, three systematic reviews and meta-analyses reporting the effects of general eccentric strength training on the BFlh FL [29] or particularly the effects of the NHE [30, 31] on the BFlh FL have been published in the last two years.

In the previous systematic reviews and meta-analyses, Cuthbert et al. [30] claimed that the NHE has a very large effect size of more than 2.58 to increase BFlh FL; Medeiros, Marchiori and Baroni [31] reported a large effect size (0.97) for the effects of NHE on the same parameter, and Gérard et al. [29] calculated a 1.97 cm eccentric strength training-induced increment in the BFlh FL. However, the previous meta-analyses [29–31] did not perform subgroup analyses based on the ultrasound assessment methods for analysing their heterogeneities. Furthermore, none of the meta-analyses [29–31] explored the underlying reason for their substantial to considerable statistical heterogeneities [32] (I^2 = 88.03% [30], I^2 = 99% [29], I^2 = 71% [31]) that detected by the I^2 statistics, which indicates the percentage ratio of the variability in effect estimates caused by heterogeneity rather than chance [32].

Recently, Franchi et al. [33] have compared methods, including panoramic ultrasound scanning (extended field of view (EFOV)), manual linear extrapolation (MLE) and trigonometric equations for estimating BFlh FL; they demonstrated that equation methods from a single image significantly overestimate BFlh FL compared to the EFOV technique, while no significant difference between EFOV and MLE techniques was observed. Additionally, Franchi et al. [33] criticised the intervention studies that used the trigonometric equation method to calculate BFlh FL for effects of eccentric training and reported a high magnitude of BFlh FL change.

Despite lacking an intervention study comparing the effects of eccentric training on the BFlh FL based on estimations via trigonometric equation methods, MLE and panoramic ultrasound scanning, this systematic review aims to recalibrate effect sizes of eccentric training in general and, in particular, effect sizes of the NHE on the BFlh FL comparing the ultrasound assessment and extrapolation methods.

2.2. Methodology

The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) 2020 statement was used as the guideline for this study, which is designed on the basis of systematic reviews of randomised controlled trials consisting of a 27-item checklist [34].

2.2.1. Database search strategy

PubMed, CINAHL Plus with Full Text via Ebsco, The Cochrane Central Register of Controlled Trials (CENTRAL) and OpenGrey databases were searched for all the indicated date ranges. A combination of the following key terms were used for the database searches: 'Exercis*', 'Training*', 'Biceps Femoris', 'Hamstring*', 'Knee Flexors', 'Posterior Thigh', 'Semitendinosus', 'Semimembranosus', 'ACSA', 'Architectur*', 'Cross Sectional Area', 'Cross-sectional Area', 'Fascic*', 'Fiber Length', 'Fibre Length', 'Pennat*', 'Pinnat*', 'Muscle Thickness', 'Muscle Volume', 'Muscle Structure', 'Muscle Length' and 'PCSA'. When applicable, relevant MeSH terms for 'exercise' were added to the key terms during the database searches. When the "OR" bullion operator was employed within the key term groups, the "AND" bullion operator was used between the key term groups. The last search of the databases was conducted on 6 June 2021; all the database searches are shown in Supporting Information 2.1.

The first author performed the database searches. Once the searches of PubMed, CINAHL Plus with Full Text via Ebsco and The Cochrane Central Register of Controlled Trials (CENTRAL) database were completed, citations were exported to the Endnote^{x9} citation manager [35]. The first author automatically removed duplicate citations through the Endnote citation manager.

2.2.2. Study selection process and criteria

After removing duplicates, the citations were independently screened based on the title and abstracts by the first and second authors via Rayyan (http://rayyan.qcri.org), a free web and mobile app designed for screening eligible studies for systematic reviews [36]. Additionally, the OpenGrey database was independently screened online on its webpage by the first and second authors. During the study screening period, the first and second authors were blinded to each other's decisions about all the citations. After screening the studies for eligibility, disagreements regarding selecting eligible studies were resolved by a discussion between the first and second authors. The third and last authors were considered referees for unsolved discussions between the first and second authors for study selection. This process was also applied during the risk of bias assessment and data extraction processes when disagreements arose for selecting eligible studies. Once eligible studies were selected, the lead and second authors also screened reference lists of the included studies.

The following criteria were considered inclusion criteria: (1) being a randomised controlled trial (RCT), (2) eccentric hamstring interventions with at least four weeks of

exercise, which was employed by the previous relevant systematic reviews [29–31], (3) presenting effects of eccentric training on BFlh FL as an outcome. This systematic review included both sexes as the previous systematic reviews did [29–31], Behan et al. [37] pointed out that BFlh FL does not differ between the genders. Additionally, Medeiros, Marchiori and Baroni [31] mentioned that including both sexes is unlikely to impact their meta-analysis.

2.2.3. Outcome measures

Eccentric exercise-induced alterations in BFlh FL based on the ultrasound assessment and extrapolation methods.

2.2.4. Risk of bias assessments, data extraction and synthesis

The Cochrane Collaboration's tool for assessing the risk of bias in randomised trials [38] was independently used for determining the risk of bias in included studies by the first and second authors. By following instructions for risk of the bias assessment tool [38], eligible studies were investigated on the basis of random sequence generation (selection bias), allocation concealment (selection bias), blinding participants and personnel (performance bias), blinding outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other bias. Each category in this risk of bias assessment tool was graded as 'low risk of bias,' 'unclear risk of bias,' or 'high risk of bias' for each selected study. Afterwards, the decisions were entered into the RevMan computer program [39]. Any conflicts were resolved by the same discussion process for screening eligible studies. Data were independently extracted from included studies by the first and second authors. When a disagreement arose, it was solved through the same discussion mechanism used in the study selection section of this review. The extracted data comprised authors, years, participants' characteristics, characteristics of exercise interventions, details of ultrasound measurement techniques and results.

Meta-analyses were performed using the Review Manager (RevMan 5.4.1) program [39]. A non-training placebo or control group was considered a comparator for an exercising group in each study. The mean difference (MD) in cm and the standardised mean difference (SMD) in Hedge's (adjusted) g effect size were calculated for each meta-analysis as a summary statistic using RevMan [39]. The SMD used in the review was the effect size, namely, Hedges' (adjusted) g in the RevMan program [40]. Hedges' g differs from Cohen's d by adjusting effect size and correcting potentially biased estimates in the case of a small sample

(n < 20) [41]. The intervention effect size has been interpreted by the following classification: small (0.2), medium (0.5) or large (0.8), which are commonly used for Cohen's d [42] and Hedges' g [43] effect size interpretations [44].

The missing standard deviation (SD) is a common feature in studies presenting continuous outcome data [32]. The missing standard deviations of changes from the baseline for a group can be calculated using the following formula [32, 45]:

$$\mathrm{SDchange} = \sqrt{\mathrm{SD}^2\mathrm{baseline} + \mathrm{SD}^2\mathrm{final} - (2 \times \mathrm{r} \times \mathrm{SDbaseline} \times \mathrm{SDfinal})}$$

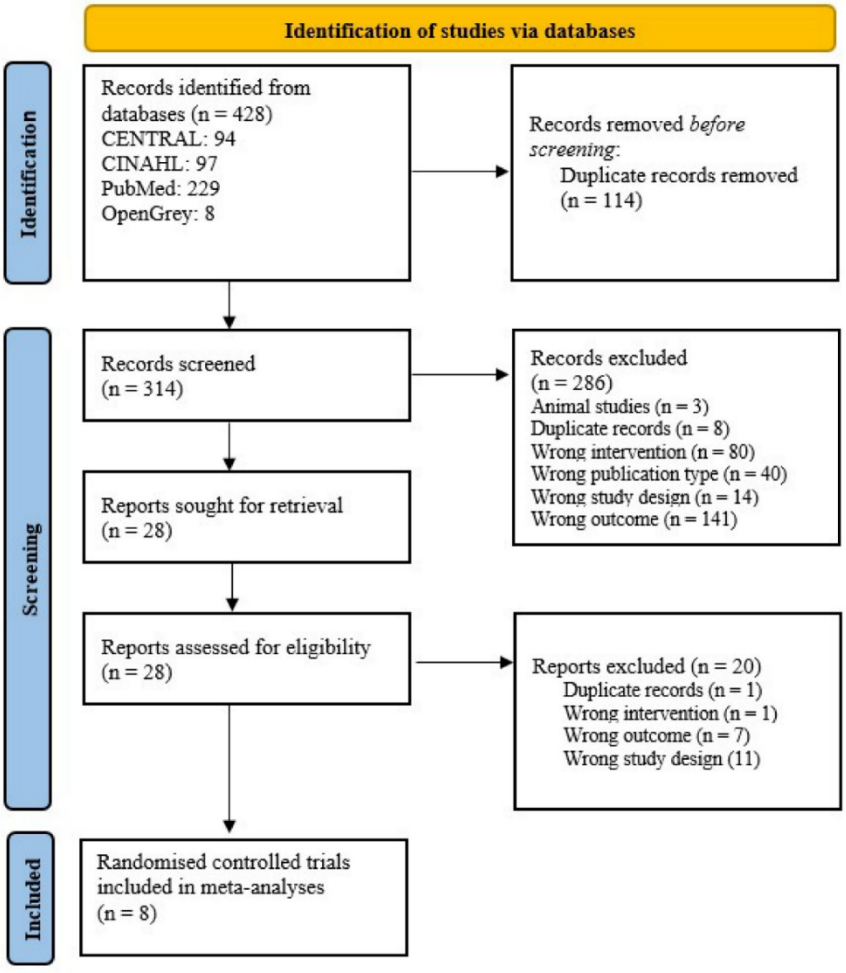

Figure 2.1. PRISMA 2020 flow diagram. This diagram illustrates the eligible study identification, screening, inclusion and exclusion processes of this systematic review.

Table 2.1. Characteristic of the eligible randomised controlled trials.

RCTs	Groups	Participants' physical activity level	Mean age	Eccentric training program	Total volume	Extrapolation and ultrasound measurement techniques	Reliability of ultrasound assessments	Post-pre mean (cm)± SD	Significance compared to control group (p-value)
Bourne et al.(51)	HE: 10 males NHE: 10 males CG: 10 males	Recreationally active	HE: 23.1± 4.1 NHE: 21.6± 3.2 CG: 21.3± 3.7	HE: 10-weeks of HE exercise NHE: 10-weeks of NHE	**596 reps (284 for the first 5-weeks)**	**Trigonometric equation**, single image from the mid-thigh	**NA** It is stated the assessor has previously shown > 0.90 ICC value elsewhere	**HE**: 1.328± 0.440676 (for the first 5-weeks: 0.75± 0.61857) **NHE**: 2.218± 0.732132 (for the first 5-weeks: 1.23± 0.461929) **CG**: -0.189± 0.548583 (for the first 5-weeks: -0.27± 0.359833)	HE: **Significant increase at post training** (p = 0.003) **and mid-training** (p = 0.011) NHE: **Significant increase at post training** (p = 0.001) **and mid-training** (p < 0.001)
Lovell et al.(52)	NHE-BT: 10 males NHE-AT: 14 males CG: 10 males	Amateur football players	23.6± 4.7	12-weeks of NHE	**684 reps**	**Trigonometric equation**, single image from the mid-thigh	**CV: 8.7%**	**NHE-BT**: 1.55034417± 1.1859943 **NHE-AT**: -0.627885264987804± 2.11626770438755 **CG**: -0.27138± 2.86589542	**Not specified**
Marušič et al.(53)	EG: 18 (12 males, 6 females) CG: 16 (12 males, 4 females)	Recreationally active	EG: 24.2 2.1 CG: 23.0 2.8	6- weeks of modified NHE (75º hip flexion) and glider exercise	**128 reps**	**Panoramic ultrasound**	**ICC: 0.92**	**EG:** 0.5722± 0.512 **CG:** 0.0313± 0.6074	**Significant increase** (p = 0.04)
Mendiguchia et al.(54)	NHE: 7 (gender is not specified) CG: 8 (gender is not specified)	Football players		6-weeks of NHE	**358 reps**	**Manual linear extrapolation**, single image from the mid-thigh	**ICC:** 0.989	**EG:** 0.73± 1.04882656 **CG:** -0.03± 0.4670603	**Not specified**

Potier et al.(55)	EG: 11 (7 females, 4 males) CG: 11 (9 females, 2 males)	NA	EG: 27± 0.8 CG: 29.6± 1.2	8-weeks of eccentric hamstring curls	**NA**	**Manual linear extrapolation**, single image, the exact location is not specified	**ICC: 0.95**	**EG:** 1.98± 1.1639 **CG:** 0.95± 1.6788	**No significant change** (p = 0.11)
Riberio-Alvares et al.(56)	NHE: 10 (7 females, 3 males) CG: 10 (7 females, 3 males)	Physically active	NHE: 23.7± 3.3 CG: 26± 2.7	4-weeks of NHE	**93 reps**	**trigonometric equation,** single image from the mid-thigh	**NA**	NHE: 1.8± 0.93 CG: 0.19± 0.68	**Not specified**
Seymore et al.(57)	NHE: 10 (6 females, 4 males) CG: 10 (8 females 2 males)	Recreationally active	NHE: 18.3± 0.5 CG: 19.9± 1.2	6-weeks of NHE	**358 reps**	**Panoramic ultrasound**	**ICC: 0.99**	NHE: 0.11± 0.9 CG: -0.18± 0.49	**No significant change** (p = 0.377)
Wiesinger et al.(58)	Eccentric IK: 10 Males NHE: 10 males CG: 10 males	Recreationally active	Eccentric IK: 25.9± 2.6 NHE: 25.0± 2.9 CG: 26.2± 2.3	Eccentric IK: 6-weeks of eccentric exercise at an isokinetic machine NHE: 6-weeks of NHE	**220 reps**	**Manual linear extrapolation**, single image from the mid-thigh	**NA**	**Eccentric IK:** 0.05± 0.07 **NHE:** -0.01± 0.13 **CG:** 0.04± 0.13	Eccentric IK: **No significant change** NHE: **No significant change** (for overall group x time interaction, p = 0.451)

Note: The mean changes and standard deviations of the mean changes presented in the table were obtained via contacting corresponding authors of the studies Bourne et al.(51), Lovell et al.(52), Marušič et al.(53), Riberio-Alvares et al.(56) and Seymore et al.(57) due to the missing standard deviations of the mean changes. The data presented for the study of Potier et al.(55) was able to be calculated based on the given in-text details via RevMan 5.4.1(39). There was no missing outcome data in the publications of Wiesinger et al.(58) and Mendiguchia et al.(54).

Abbreviations: CG, Control group, CV, Coefficient of variations, EG, Exercise group, ICC, Interclass correlation coefficient, IK, Isokinetic, HE, Hip extension, NA, Not applicable, NHE, Nordic hamstring exercise, NHE-AT, Nordic hamstring exercise after training, NHE-BT, Nordic hamstring exercise before training, RCTs: Randomised controlled trials, reps, repetitions.

SDchange corresponds to the SD of the mean changes from baseline, SDbaseline corresponds to the SD of the pre-test, SDfinal represents the SD of the post-test, and the r corresponds to the correlations between the SD baseline and SD final measurements; however, this correlation value is not generally presented in studies. Therefore, typically, it is not possible to calculate the SD of changes from baseline based on only having the SD baseline and SD post-intervention values. This systematic review followed the suggestions of the Cochrane Handbook for Systematic Reviews of Interventions from the starting point [32]. First, additional data, e.g., confidence intervals (CI), P values, t values, F values and standard errors, were checked and missing SD changes from baseline were calculated using the Review Manager RevMan 5.4.1) program when sufficient information was available [39]. However, due to insufficient information, this type of calculation was not possible in most studies in the systematic review. As a second step, the authors of the eligible studies were contacted and asked to share missing relevant data. Before the meta-analyses, FL data of eligible studies was converted into centimetres (cm) to avoid miscalculations of the mean difference changes in meta-analyses.

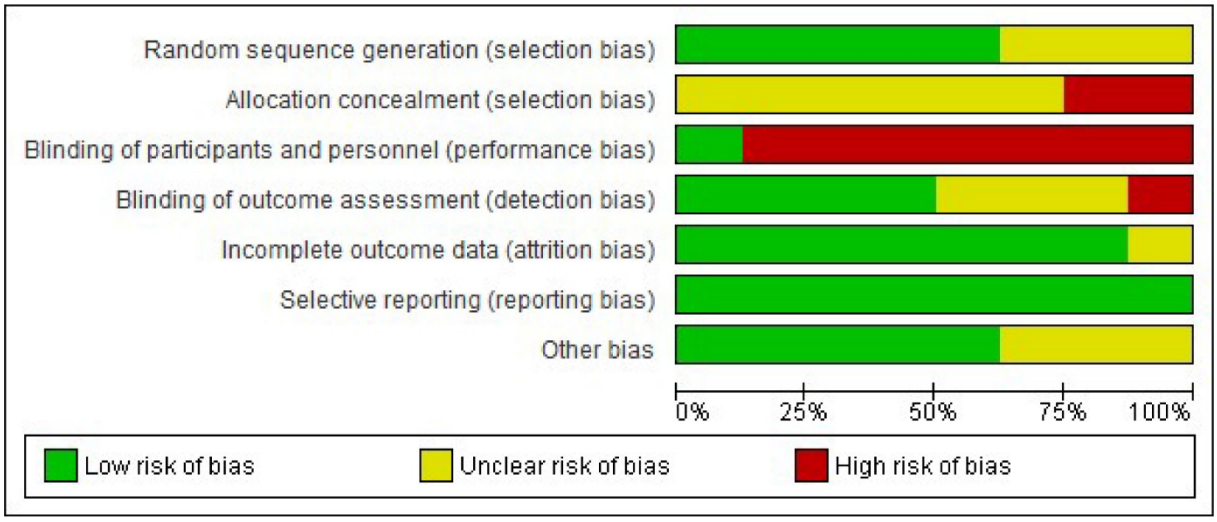

Figure 2.2. Risk of bias assessment graph. This graph shows the general percentage ratio of reviewer authors' judgements about the risk of bias of each bias item for all included studies (generated via RevMan 5.4.1)

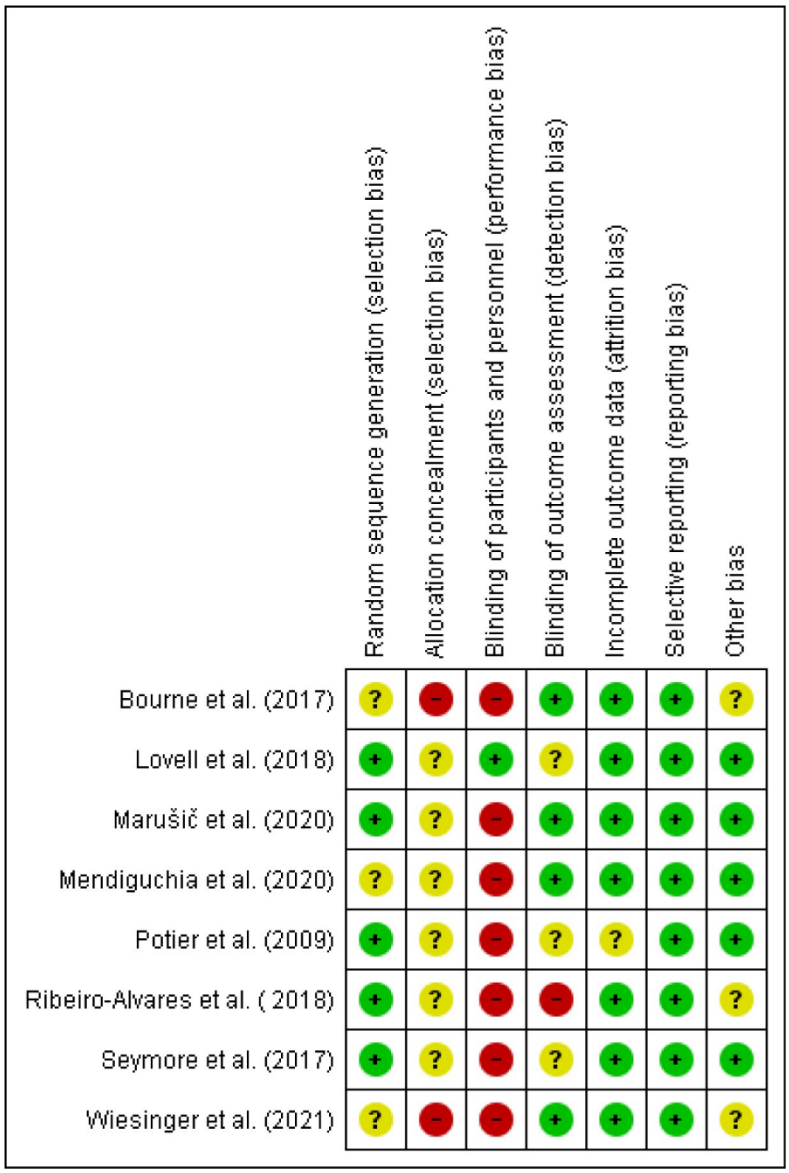

Figure 2.3. Review authors' judgements about each risk of bias item for included studies [51–58]. Positive (+) values represent a low risk of bias, question marks (?) represent an unclear risk of bias, and negative (-) values represent a high risk of bias (generated via RevMan 5.4.1).

When a meta-analysis was performed, heterogeneity was assessed by chi-squared ($\chi 2$, or Chi^2) statistics. The level of heterogeneity calculated by I^2 statistics indicates the percentage ratio of the variability in effect estimates caused by heterogeneity rather than chance [32]. 25%, 50%, and 75% I^2 results were grouped as low, moderate and high, respectively [46]. Meta-analyses were performed using a more conservative random effect (RE) model for continuous data, inverse variance and 95% CI [47]. The random effect model was considered to provide a better account for methodological and statistical heterogeneities in a recent systematic review [48].

After performing meta-analyses, the relevant data were exported to GRADEpro GDT software [49], and the level of a body of evidence (LoE) was assessed by applying the

GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach in the GRADE handbook [50]. The usage of the GRADE approach was recommended by the Cochrane Collaboration's tool for assessing the risk of bias in randomised trials [38] and the Cochrane Handbook for Systematic Reviews of Interventions [32] for clarifying the level of a body of evidence. The GRADE approach classifies the quality of a body of evidence as high, moderate, low and very low [50]. A GRADE evidence profile was assessed via the GRADEpro GDT software for the levels of the bodies of evidence in consideration of study design, risk of bias, inconsistency, indirectness, imprecision and publication bias.

2.3. Results

2.3.1. Database search results

Initially, 428 records were identified throughout the database searches. One hundred fourteen duplicate records were automatically removed via the Endnotex[9] citation manager [35]. The remaining 314 records were screened based on the title and abstracts via the Rayyan web program [36]. Afterwards, 28 records were included in the full-text screening. As a result, eight RCTs [51–58] were included in meta-analyses. The study selection process is illustrated in the PRISMA 2020 flow diagram (Figure 2.1.). Additionally, a PRISMA 2020 checklist is presented in Supporting Information 2.2.

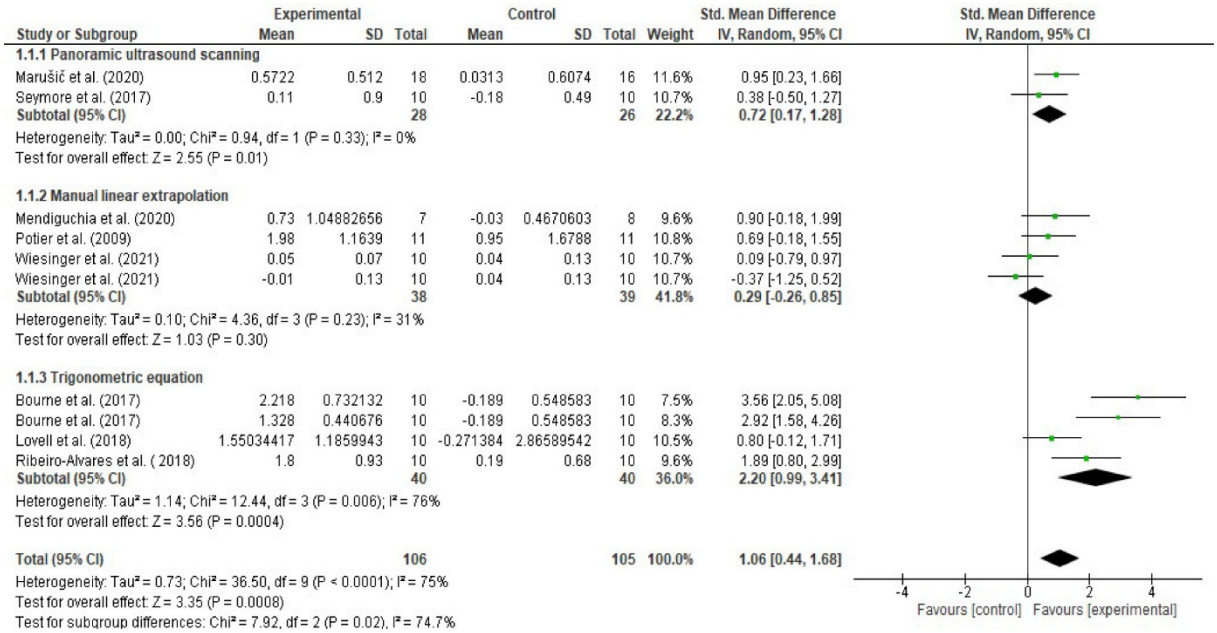

Figure 2.4. Forest plot effect sizes of eccentric training on biceps femoris long head fascicle length based on ultrasound assessment and extrapolation methods. Overall eccentric training has a large effect size on increasing biceps femoris long head FL (g = 1.06 [0.44, 1.68], I^2 = 75%). Eccentric training has a small effect based on the manual linear extrapolation method (g = 0.29 [-0.26, 0.85], I^2= 31%), a medium effect based on the panoramic ultrasound assessments (g = 0.72 [0.17, 1.28], I^2= 0%) and a large effect based on the trigonometric equation method (g = 2.20 [0.99, 3.41], I^2= 76%) (created via RevMan 5.4.1).

2.3.2. Characteristics of included studies

The study groups, participants' ages, genders, physical activity levels, training types, total volumes, ultrasound extrapolation techniques, reliability of ultrasound assessments, mean changes and standard deviations of the mean changes between post and pre-tests, and results are presented in Table 2.1.

2.3.3. Risk of bias assessments

The first and second authors independently completed risk of bias assessments for each included study via the Cochrane Collaboration's tool for assessing the risk of bias in randomised trials [38]. The low risk of bias scores of the studies in the seven sections [38] ranged from three [51, 55, 56, 58] to five [52, 53]. The risk of bias assessment graph (Figure 2.2.) and a table showing the authors' conclusions on each risk of bias parameter for each study (Figure 2.3.) were generated via RevMan [39] for future use to determine the level of evidence for meta-analyses via GRADEpro GDT software [49].

2.3.4. Evidence levels of the meta-analyses

The LoE of meta-analyses was determined using the GRADEpro GDT software based on the GRADE approach [50], which categorised the level of a body of evidence as high, moderate, low and very low [50]. The results for each meta-analysis are presented in Supporting Information 2.3.

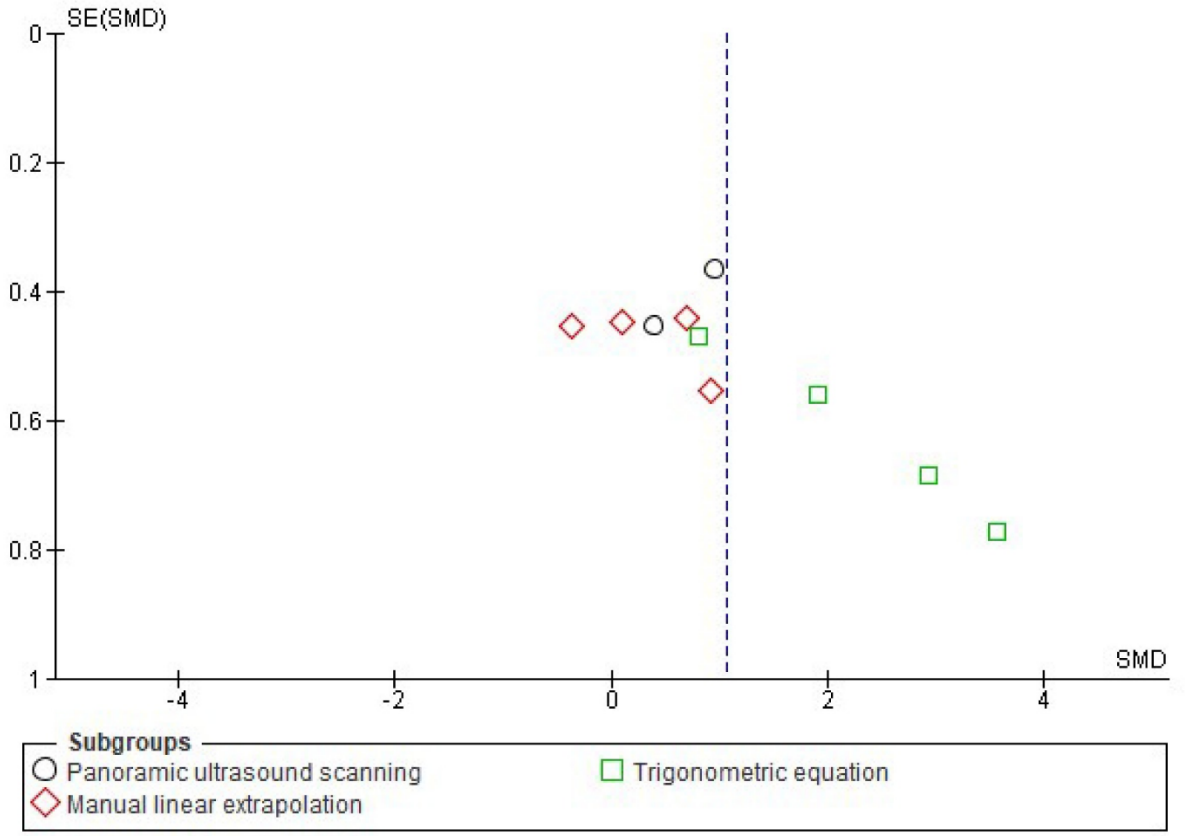

Figure 2.5. Funnel plot effect sizes of eccentric training on biceps femoris long head fascicle length based on the ultrasound assessment and extrapolation methods. Red coloured squares represent studies that used the manual linear extrapolation method, black coloured circles represent studies that used the panoramic ultrasound scanning method, and green coloured squares represent studies that used the trigonometric equation method (created via RevMan 5.4.1). Acronyms: SE(SMD), standard error of standardised mean differences; SMD, standardised mean difference.

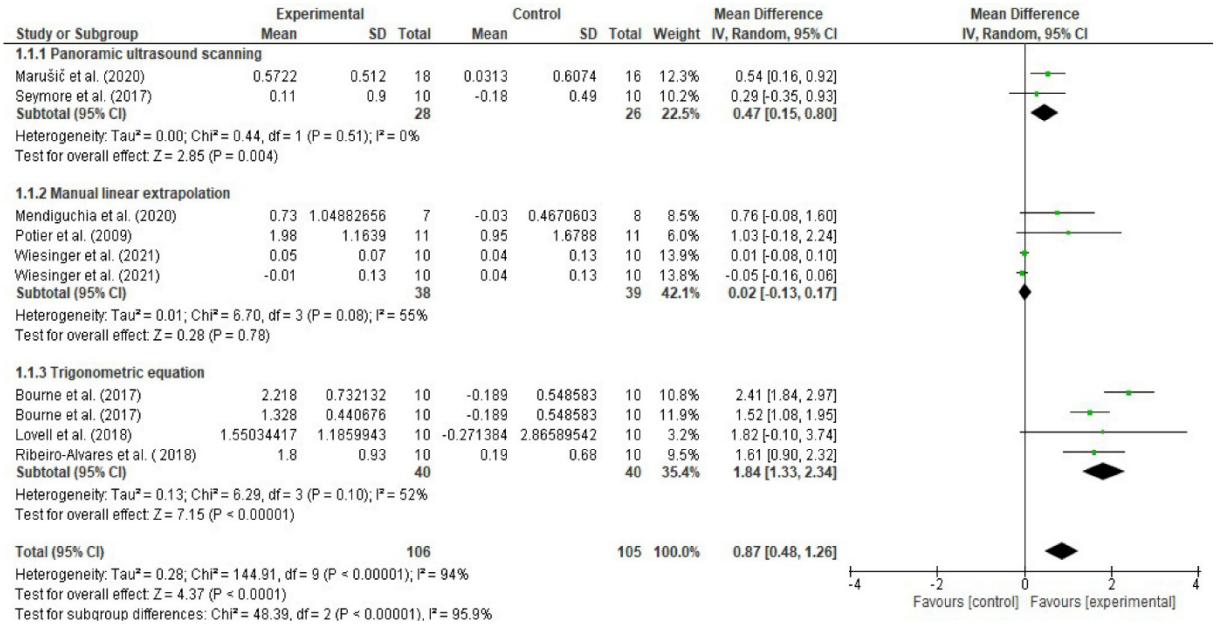

Figure 2.6. Forest plot eccentric training-induced mean (cm) changes in biceps femoris long head fascicle length based on the ultrasound assessment and extrapolation methods. Eccentric training leads to 0.02 cm ([-0.13, 0.17], I 2 = 55%), 0.47 cm ([0.15, 0.80], I 2 = 0%), and 1.84 cm ([1.33, 2.34], I 2 = 52%) increases in biceps femoris long head FL based on the MLE method, panoramic ultrasound scanning and trigonometric equation methods, respectively (created via RevMan 5.4.1)

2.3.5. Meta-analyses

In total, eight RCTs [51–58] were included in the meta-analyses for the effects of eccentric training on biceps femoris long head FL, and six RCTs [51, 52, 54, 56–58] were included in the meta-analyses for the effects of the NHE on biceps femoris long head FL. Concerning the study of Lovell et al. [52], the FL values of the after-training-NHE group were not included in meta-analyses to maintain methodological homogeneity among the studies. The other pooled studies [51, 54, 56–58] in the meta-analyses investigating the effects of Nordic hamstring exercise on the biceps femoris long head muscle architecture did not perform the NHE after sports training. In support, the FIFA 11+ program has prescribed the Nordic hamstring exercise before training [59].

2.3.6. Effects of the eccentric training based on the ultrasound assessment and extrapolation methods

Eight RCTs [51–58] were included in the meta-analysis assessing the effects of eccentric training on the BFlh FL. In future subgroup analyses, three [51, 52, 56] of the RCTs were included in the trigonometric equation subgroup. Three RCTs [54, 55, 58] were included in the manual linear extrapolation (MLE) subgroup, and the remaining two RCTs [53, 57] were included in the panoramic ultrasound scanning subgroup. Hedge's (adjusted) g effect sizes were calculated for the random effect model and 95% CI for the overall effects of eccentric training, effects of eccentric training based on ultrasound equation, linear extrapolation and panoramic ultrasound assessment methods (Figs 2.4 and 2.5). Additionally, mean (cm) changes in BFlh FL for overall eccentric training and for the same subgroups were calculated and presented in Figures 2.6 and 2.7.

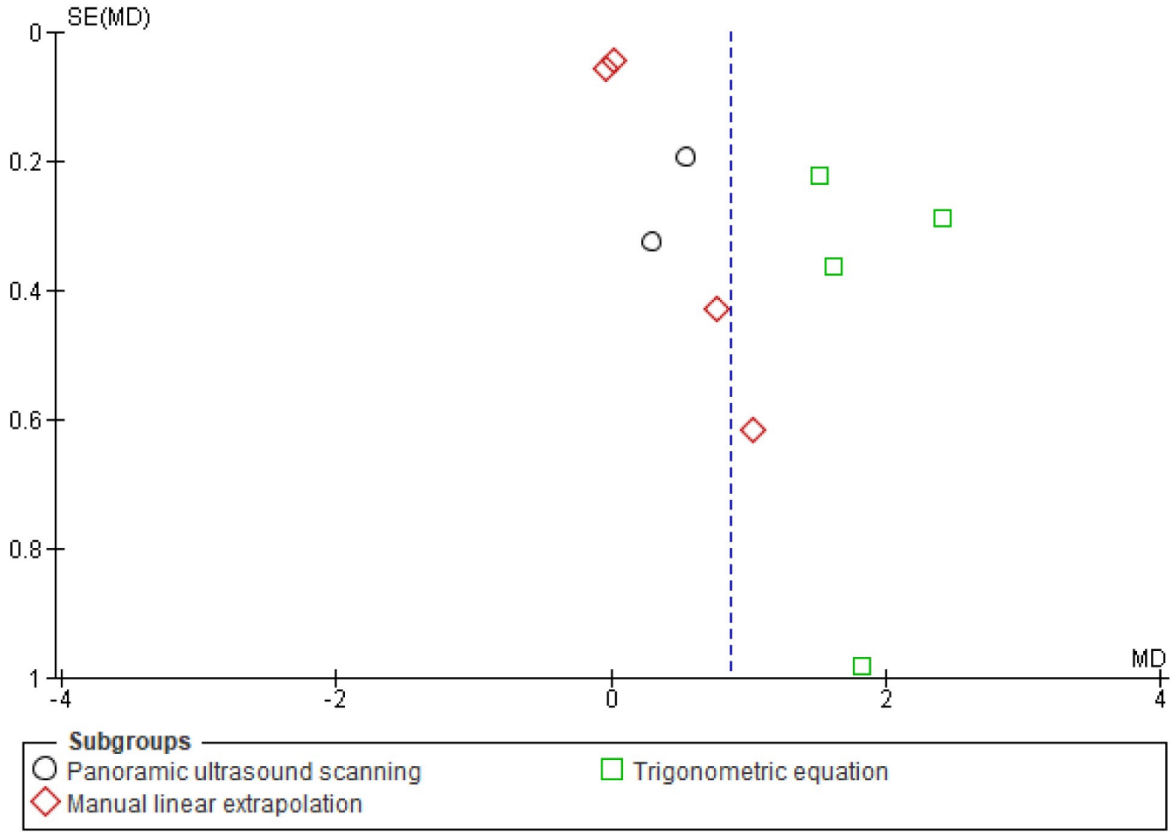

Figure 2.7. Funnel plot eccentric training-induced mean (cm) changes in BFlh fascicle length based on the ultrasound assessment and extrapolation methods. Red coloured squares represent studies that used the manual linear extrapolation method, black coloured circles represent studies that used the panoramic ultrasound scanning method, and green coloured squares represent studies that used the trigonometric equation method (created via RevMan 5.4.1). Acronyms: SE(MD), standard error of mean differences; MD, mean difference.

Meta-analyses revealed that overall eccentric training has a large effect size on increasing BFlh FL (g = 1.06 [0.44, 1.68], I 2 = 75%, LoE = very low). However, subgroup analyses suggested that the effect size of eccentric training on the BFlh FL differs from each other based on the ultrasound assessment and extrapolation methods (I^2 = 74.7%) (Fig 2.4), ranging from small to large based on the ultrasound assessment and extrapolation methods for

assessing BFlh FL (Figure 2.4.). Meta-analyses results showed that eccentric training has a small effect based on the MLE method (g = 0.29 [-0.26, 0.85], I^2 = 31%, LoE = low), a medium effect based on the panoramic ultrasound assessments (g = 0.72 [0.17, 1.28]), I^2 = 0%, LoE = low) and a large effect based on the trigonometric equation method (g = 2.20 [0.99, 3.41], I^2 = 76%, LoE = very low) (Figure 2.4.).

Likewise, meta-analyses that were carried out to assess eccentric training-induced MDs (cm) detected differences in the eccentric training-induced cm changes in BFlh FL between the ultrasound assessments and extrapolations (I^2 = 95.9) (Figure 2.6.). Subgroup analyses indicated that eccentric training leads 0.02 cm ([-0.13, 0.17], I^2 = 55%), 0.47 cm ([0.15, 0.80], I^2 = 0%), and 1.84 cm ([1.33, 2.34], I^2 = 52%) increases in BFlh FL based on the MLE method, panoramic ultrasound scanning and trigonometric equation methods, respectively (Figures 2.6. and 2.7.).

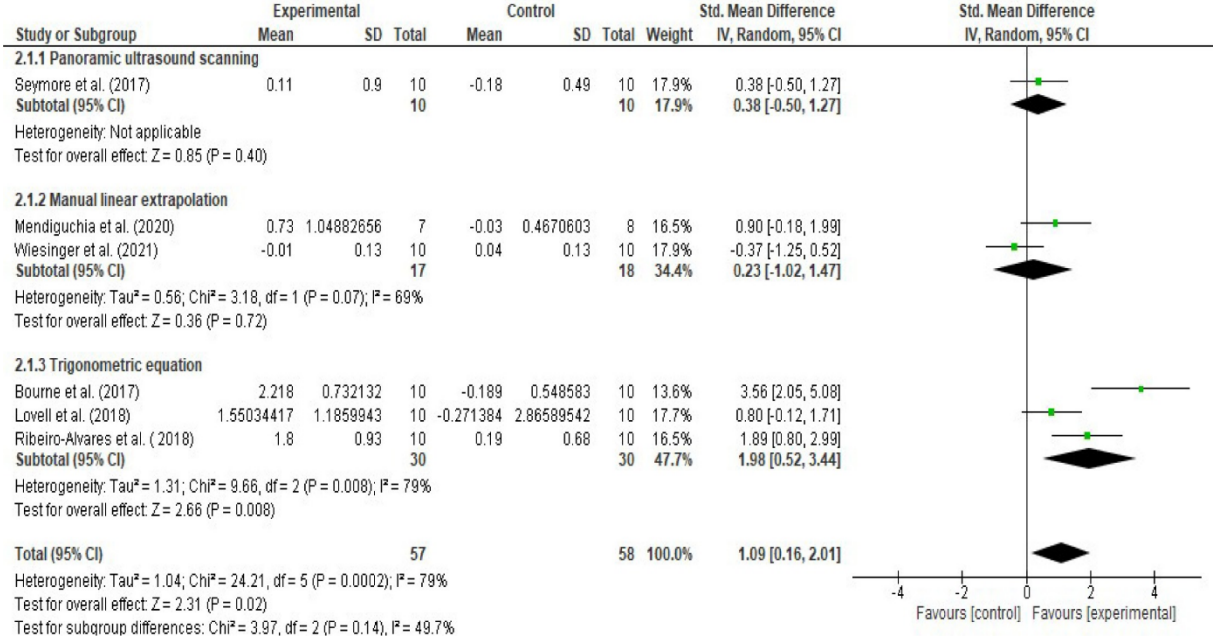

Figure 2.8. Forest plot effect sizes Nordic Hamstring Exercise (NHE) on biceps femoris long head fascicle length based on the ultrasound assessment and extrapolation methods. The overall effect size of the NHE on increasing biceps femoris long head FL was large (g = 1.09 [0.16, 2.01], I^2 = 79%). NHE has a small effect size on increasing the biceps femoris long head FL based on the MLE method (g =, 0.23 [-1.02, 1.47], I^2 = 69%), has a small effect size on increasing biceps femoris long head FL based on the panoramic ultrasound scanning (g = 0.38 [-0.50, 1.27]), and has a large effect on increasing biceps femoris long head FL based on the equation methods (g = 1.98 [0.52, 3.44], I^2 = 79%) (created via RevMan 5.4.1).

2.3.7. Effects of the NHE based on the ultrasound assessment and extrapolation methods

Six RCTs [51, 52, 54, 56–58] were included in the meta-analyses that examine the effects of NHE on the BFlh FL. A subgroup analysis was performed for the same parameters as the meta-analyses for eccentric training. The overall effect size of the NHE on increasing BFlh FL was large (g = 1.09 [0.16, 2.01], I^2 = 79%, LoE = very low) (Fig 2.8). However, the

subgroup analysis suggests a difference between the values of the ultrasound assessment and extrapolation methods (Figures 2.8. and 2.9.). In particular, NHE has a small effect size on increasing the BFlh FL based on the MLE method (g =, 0.23 [-1.02, 1.47], I^2 = 69%, LoE = very low), has a small effect size on increasing BFlh FL based on the panoramic ultrasound scanning (g = 0.38 [-0.50, 1.27], LoE = low), and has a large effect on increasing BFlh FL based on the equation methods (g = 1.98 [0.52, 3.44], I^2 = 79%, LoE = very low) (Figure 2.8.).

Moreover, the meta-analyses performed to detect the NHE-induced mean (cm) changes found that the NHE leads to a 1.08 cm increment ([0.09, 2.07], I^2 = 95%) in the BFlh FL (Figures 2.10. and 2.11.). However, subgroup analysis indicated considerable differences between the study groups applied equation, MLE and panoramic ultrasound techniques (I^2 = 90.2%) (Fig 2.10). Subgroup analysis showed that the NHE do leads to 0.24 cm ([-0.52, 1.01], I^2 = 71%), 0.29 cm ([-0.35, 0.93]) and 2.04 cm ([1.45, 2.63], I^2= 34%) increases in the BFlh fascicle length based on the MLE, panoramic ultrasound scanning and trigonometric equation methods, respectively (Figure 2.10.).

2.3.8. Effects of 4–6 weeks of NHE on the biceps femoris long head FL based on ultrasound assessment and extrapolation methods

Four studies [51, 56–58] with 4–6 weeks duration and with similar participants' physical activity levels pooled in a meta-analysis in different subgroups based on the ultrasound assessment and extrapolation method for a better understanding of the possible effects of the total volume of the NHE and on the effect size estimation of the NHE on BFlh FL, As a difference, the mid-training data (5 weeks of NHE training and the control group) of Bourne et al. [51] employed this time in the meta-analysis for having closer total volumes between the studies. A forest plot in Figure 2.12. and a funnel plot in Figure 2.13. show the studies' effect sizes. Despite the similar physical activity levels of the participants, four weeks [56] and five weeks [51] of NHE interventions used trigonometric equation methods for estimating the FL showed large effects sizes on increasing BFlh FL, while the six weeks of NHE interventions using the MLE [58] or panoramic ultrasound scanning [57] methods were not showing even medium effect sizes on increasing BFlh FL.

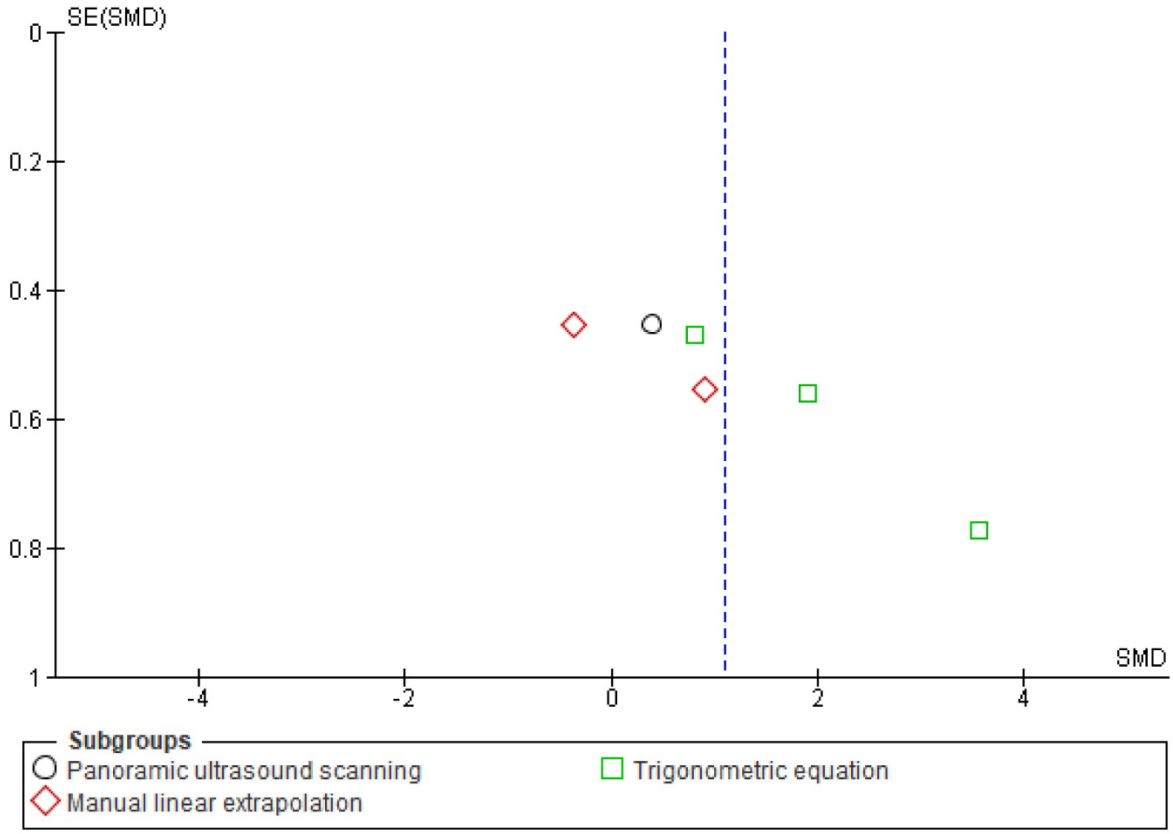

Figure 2.9. Funnel plot effect sizes Nordic hamstring exercise on biceps femoris long head fascicle length based on the ultrasound assessment and extrapolation methods. Red coloured squares represent studies that used the manual linear extrapolation method, black coloured circles represent studies that used the panoramic ultrasound scanning method, and green coloured squares represent studies that used the trigonometric equation method (created via RevMan 5.4.1). Acronyms: SE(SMD), standard error of standardised mean differences; SMD, standardised mean difference.

2.4. Discussion

To the best of our knowledge, this was the first systematic review performing meta-analyses that compared the effects of eccentric exercise, including NHE, on BFlh FL between the RCTs based on an equation method, the MLE method and panoramic ultrasound scanning for estimating BFlh fascicle length. Among the previous meta-analyses, Cuthbert et al. [30] reported that NHE has a very large effect size ($g \geq 2.58$) on increasing BFlh FL. Later, Medeiros, Marchiori and Baroni [31] estimated the effect size of the NHE as 0.97 ([-0.46, 1.48]). Additionally, Gérard et al. [29] found that eccentric strength training leads to a 1.97 cm ([1.48, 2.46] increment in BFlh FL. However, the findings of this meta-analysis differ from previous reviews. First, the effect sizes of the NHE were small (g = 0.23 [-1.02, 1.47], small (g = 0.38 [-0.50, 1.27]) and large (g = 1.98 [0.52, 3.44]) based on the MLE, panoramic ultrasound scanning and equation methods, respectively. Second, eccentric training leads 0.02 cm ([-0.13, 0.17], $I^2 = 55\%$), 0.47 cm ([0.15, 0.80], $I^2 = 0\%$), and 1.84 cm ([1.33, 2.34], $I^2 = 52\%$) increase in BFlh FL based on the MLE, panoramic ultrasound scanning and

trigonometric equation methods, respectively. Additionally, eccentric training has a small effect based on the MLE method (g = 0.29 [-0.26, 0.85]), a medium effect based on the panoramic ultrasound assessments (g = 0.72 [0.17, 1.28])) and a large effect based on the trigonometric equation method (g = 2.20 [0.99, 3.41]).

Despite the fact that the equation method is validated by Kellis et al. [60] for estimating BFlh FL, Franchi et al. [33] have recently pointed out that the trigonometric equation method [60] overestimates 1.91 ± 2.1 cm BFlh FL compared to panoramic ultrasound (extended field of view) images. In contrast, the manual MLE method and panoramic ultrasound images had no significant differences between them [33]. In the case of this systematic review, three [51, 52, 56] of the eight RCTs used the trigonometric equation method [60]; three RCTs used the manual MLE method [54, 55, 58] and two RCTs employed panoramic ultrasound scanning [53, 57] for calculating the BFlh FL. Although initially large effect sizes for the eccentric training and NHE were found to increase BFlh FL without considering the calculation methods, subgroup analyses of this review detected differences between the ultrasound scanning and extrapolation methods. This systematic review detected large effect sizes only for those studies that applied trigonometric equation methods to estimate BFlh FL when considering the methods. The meta-analyses and subgroup analyses results showed that the eccentric strength training, including NHE, did not show any large effect on the size of BFlh FL based on the studies that applied the MLE method and panoramic ultrasound scanning. Additionally, a previous study found a poor agreement between ultrasound assessments using a trigonometric equation method for estimating BFlh FL and diffusion tensor MRI measurements on the BFlh FL [61]. However, more comparisons between the existing ultrasound and MRI measurement techniques are needed to have an overall idea about the agreement level between MRI and ultrasound assessments of BFlh FL. Furthermore, developing a gold standard measurement method, e.g. freehand three-dimensional ultrasound scanning, for BFlh FL measurements, is needed, as stated by Franchi and colleagues [33].

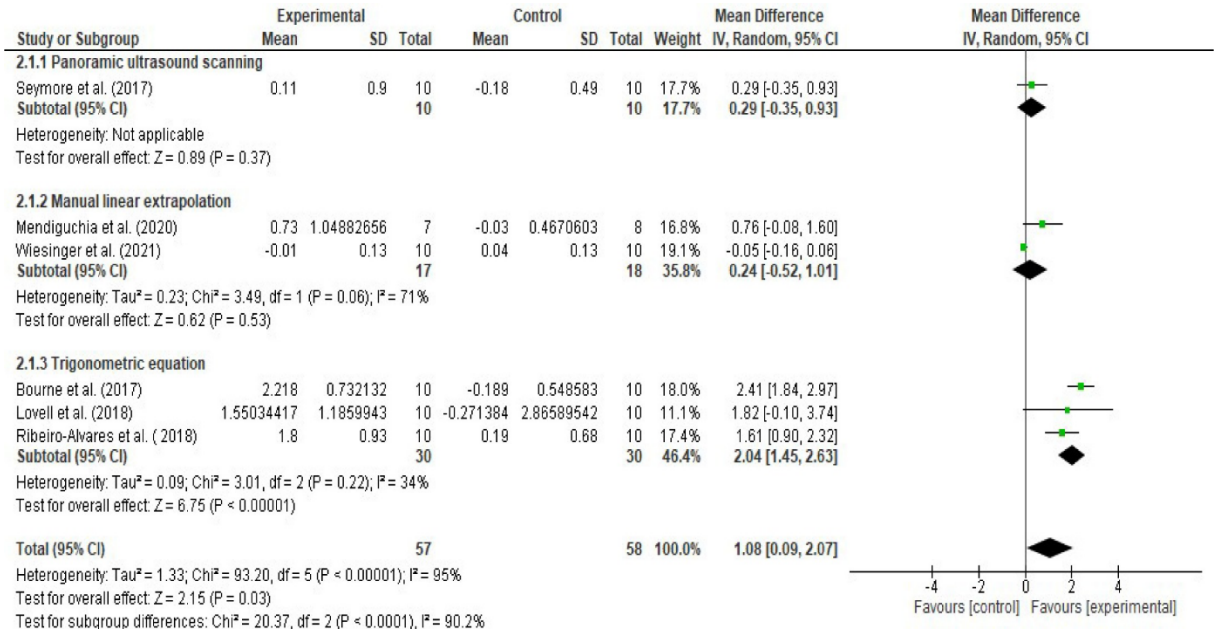

Figure 2.10. Forest plot Nordic hamstring exercise-induced mean (cm) changes in biceps femoris fascicle length based on the ultrasound assessment and extrapolation methods. Overall, NHE leads to a 1.08 cm increment ([0.09, 2.07], I^2 = 95%). NHE do leads to 0.24 cm ([-0.52, 1.01], I^2 = 71%), 0.29 cm ([-0.35, 0.93]) and 2.04 cm ([1.45, 2.63], I^2= 34%) increases in the biceps femoris fascicle length based on the MLE, panoramic ultrasound scanning and trigonometric equation methods, respectively (created via RevMan 5.4.1).

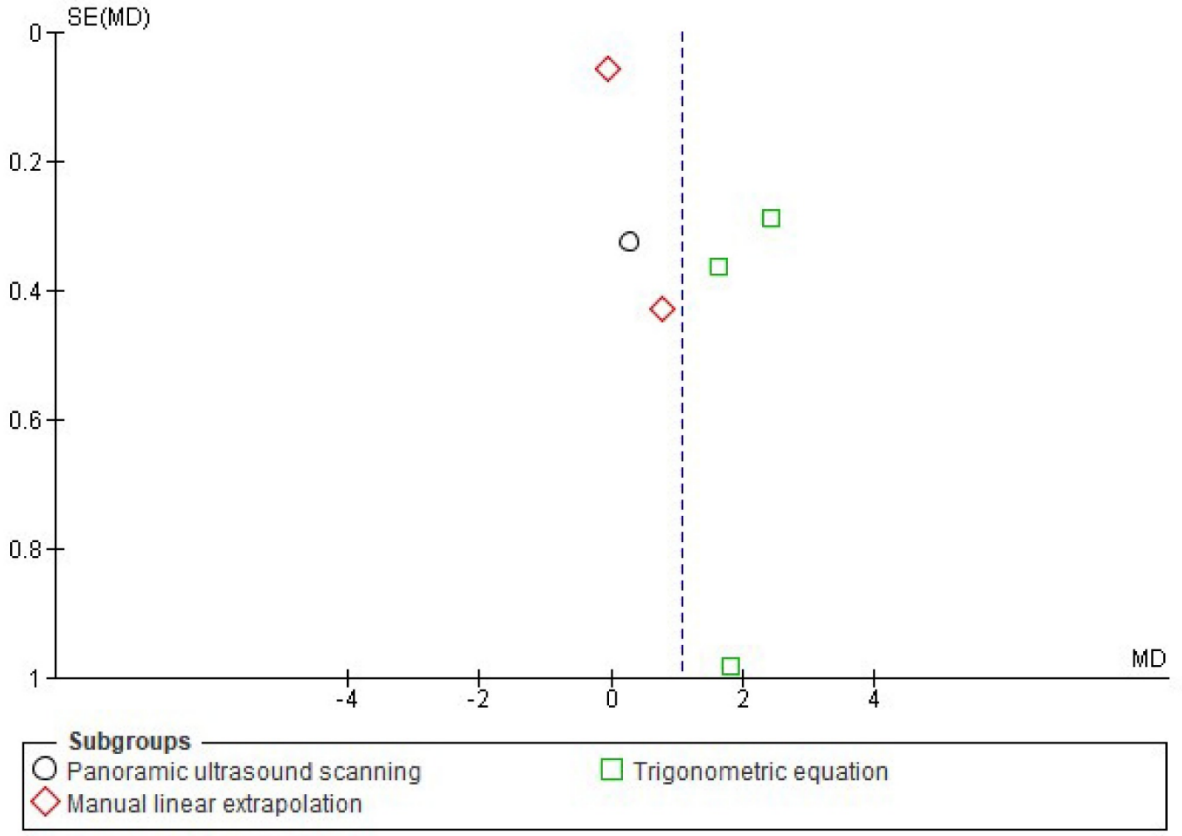

Figure 2.11. Funnel plot Nordic hamstring exercise-induced mean (cm) changes in biceps femoris long head fascicle length based on the ultrasound assessment and extrapolation methods. Red coloured squares represent studies that used the manual linear extrapolation method, black coloured circles represent studies that used the panoramic ultrasound scanning method, and green coloured squares represent studies that used the trigonometric equation method (created via RevMan 5.4.1). Acronyms: SE(MD), standard error of mean differences; MD, mean difference.

There might be a possible underlying overestimation of the effect sizes reported by those studies that used the equation method for estimating the BFlh FL compared to the MLE and panoramic ultrasound scanning methods. However, this argument still needs evidence. Further studies might be conducted to compare the effects of eccentric training based on ultrasound assessment and extrapolation methods. Additionally, the relevant scientific community could consider reaching a consensus for BFlh FL measurements to assess the

impacts of training on this parameter by providing more comparable results between interventions.

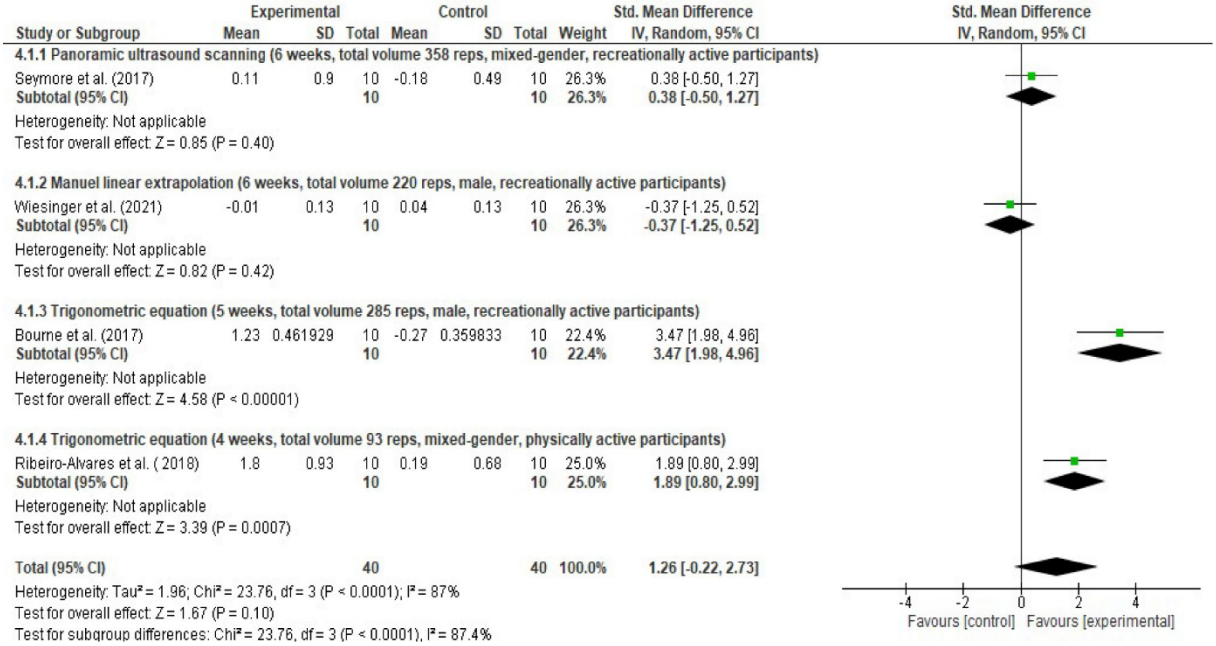

Figure 2.12. Forest plot effects of 4–6 weeks of Nordic hamstring exercise on the biceps femoris long head FL based on ultrasound assessment and extrapolation methods. NHE interventions used trigonometric equation methods for estimating the FL showed large effects sizes (g = 1.89–3.47) on increasing biceps femoris long head FL, while the six weeks of NHE interventions using the MLE (g = -0.37) or panoramic ultrasound scanning (g = 0.38) methods were not showing even medium effect sizes on increasing biceps femoris long head FL (created via RevMan 5.4.1).

In addition to these issues, missing standard deviations of the mean changes from baseline is critical when performing a meta-analysis of RCTs. A lower SD can produce a higher effect size or vice versa. The Cochrane handbook for Systematic Reviews of Interventions [32] describes missing SDs of the mean changes from baseline as a common feature in the literature, and the same handbook identifies the importance of obtaining the SDs. The formula for calculating the SD changes from baseline, and it is difficult to obtain this missing outcome, as explained in the 'data extraction, analysis and synthesis' section of this systematic review. Previously, a survey reported that 68% of Cochrane reviewers who were aiming to run a meta-analysis for a continuous outcome faced the missing mean or SD value problems, and 85% of the reviewers finally asked the authors of the studies to share their missing outcome data, 76% of whom eventually did not pool the studies with missing outcome data [62]. This systematic review followed the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions [32]. Among the eight RCTs [51–58], only two RCTs [54, 58] reported the required mean change and SDs of the mean changes from baseline. Among the remaining six RCTs, the required data could be calculated from the in-text information that exact P values and standard errors of only one RCT [55] via the Calculator of the RevMan program (RevMan 5.4.1) [55]. The required data for the remaining five studies [51–53, 56, 57] were obtained by contacting the corresponding authors of the

studies. Starting from this point, the methodology of this systematic review for obtaining precise data differs from previous meta-analyses that investigated the effects of eccentric strength training [29] or NHE [30, 31] on BFlh FL.

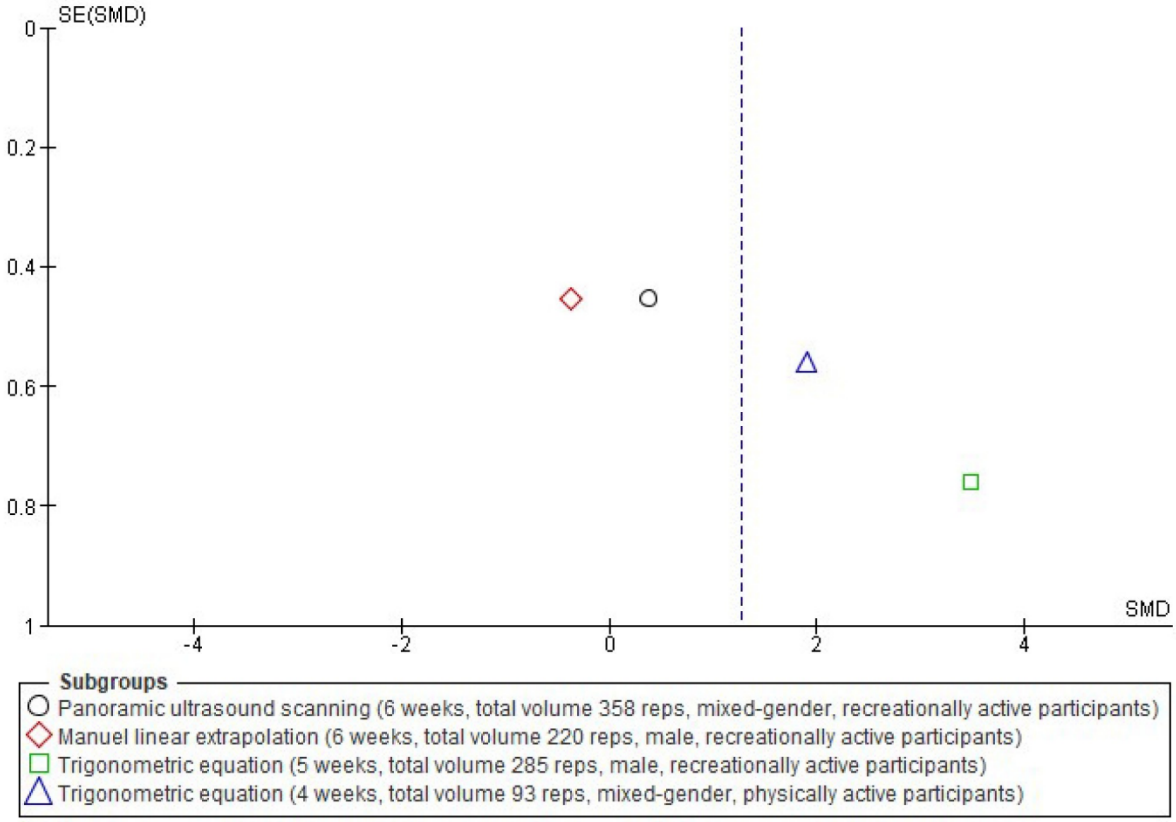

Figure 2.13. Funnel plot effects of 4–6 weeks of Nordic hamstring exercise on the BFlh FL based on ultrasound assessment and extrapolation methods. The red coloured square represents a study that used the manual linear extrapolation method, the black coloured circle represent a study that used the panoramic ultrasound scanning method, and the green coloured square and blue coloured triangle represent studies that used the trigonometric equation method (created via RevMan 5.4.1). Acronyms: SE(SMD), standard error of standardised mean differences; SMD, standardised mean difference

Cuthbert and colleagues' method [30] for meta-analysis differed from this systematic review and other relevant systematic reviews in methods to calculate the effect size of the NHE on BFlh FL. Nevertheless, the remaining two systematic reviews [29, 31] conducted meta-analyses based on the mean changes and SDs of the mean changes from baseline for intervention and control groups, allowing a comparison of the results with those of this review [29, 31]. Four meta-analyses were carried out using the common studies among the present systematic review and recent systematic reviews [29, 31] for all cases of continuous data of MD (cm), 95% CI, fixed effect (FE); MD (cm), 95% CI, RE; SMD (effect size: Hedge's (adjusted) g), 95% CI, FE; and SMD (effect size: Hedge's (adjusted) g), 95% CI for establishing the proposed comparisons. All the results are shown in four funnel plots and four forest plots created by the RevMan computer program in Supporting Information 2.4.

Additionally, Table 2.2. demonstrates the meta-analyses results based on the data of this review and the systematic reviews of Gérard et al. [29] and Medeiros, Marchiori& Baroni [31] for common studies. Based on the results, the reported data of previous systematic reviews [29, 31] produced results that were close to the actual centimetre changes in BFlh FL for common individual eligible studies [51, 55–57]. However, the reported data of both meta-analyses [29, 31] failed to precisely estimate actual effect sizes of the eccentric strength training or NHE on the BFlh FL due to miscalculations of the SDs of mean changes from the baseline. Therefore, this strongly suggests that future meta-analyses for continuous outcomes of RCTs related to the effects of eccentric exercise interventions on the BFlh FL should follow the recommendations of the Cochrane Handbooks for Systematic Reviews of Interventions [32], which includes contacting the corresponding authors of eligible studies to obtain mean changes and SDs of the mean changes from the baseline for precise results. Conversely, one limitation of the present review might be the small number of eligible studies pooled in meta-analyses. Nevertheless, this systematic review included eight studies in the quantitative syntheses, more than the previous systematic reviews that included five [29, 30] or four [31] studies. Additionally, a further confounder in the analysis of this review is the heterogeneity of training interventions, which adds non-accountable variability to the outcomes measures.

Table 2.2. Comparisons of effect sizes and mean changes of each study based on the given in-text data between meta-analyses investigating effects of eccentric strength training on biceps femoris fascicle length.

Study												
	MD (cm), FE, 95% CI			**MD (cm), RE, 95% CI**			**SMD (Effect size: Hedge's (adjusted) g), FE, 95% CI**			**SMD (Effect size: Hedge's (adjusted) g), RE, 95% CI**		
	Present SR	**Gérard et al.[29]**	**Medeiros, Marchiori& Baroni[31]**	**Present SR**	**Gérard et al.[29]**	**Medeiros, Marchiori& Baroni[31]**	**Present SR**	**Gérard et al.[29]**	**Medeiros, Marchiori& Baroni[31]**	**Present SR**	**Gérard et al.[29]**	**Medeiros, Marchiori& Baroni[31]**
Bourne et al.[51] (NHE vs control)	**2.41** [1.84, 2.97]	**2.47** [2.36, 2.58]	**2.40** [1.66, 3.14]	**2.41** [1.84, 2.97]	**2.47** [2.36, 2.58]	**2.40** [1.66, 3.14]	**3.56** [2.05, 5.08]	**18.79** [12.23, 25.35]	**2.73** [1.44, 4.02]	**3.56** [2.05, 5.08]	**18.79** [12.23, 25.35]	**2.73** [1.44, 4.02]
Bourne et al.[51] (HE vs control)	**1.52** [1.08, 1.95]	**1.58** [1.47, 1.69]	NA	**1.52** [1.08, 1.95]	**1.58** [1.47, 1.69]	NA	**2.92** [1.58, 4.26]	**11.61** [7.50, 15.71]	NA	**2.92** [1.58, 4.26]	**11.61** [7.50, 15.71]	NA
Mendiguchia et al.[54]	**0.76** [-0.08, 1.60]	NA	**0.76** [-0.27, 1.79]	**0.76** [-0.08, 1.60]	NA	**0.76** [-0.27, 1.79]	**0.90** [-0.18, 1.99]	NA	**0.71** [-0.35, 1.77]	**0.90** [-0.18, 1.99]	NA	**0.71** [-0.35, 1.77]
Potier et al.[55]	**1.03** [-0.18, 2.24]	**1.03** [0.91, 1.15]	NA	**1.03** [-0.18, 2.24]	**1.03** [0.91, 1.15]	NA	**0.69** [-0.18, 1.55]	**6.83** [4.45, 9.21]	NA	**0.69** [-0.18, 1.55]	**6.83** [4.45, 9.21]	NA
Riberio-Alvares et al.[56]	**1.61** [0.90, 2.32]	**1.63** [1.07, 2.19]	**1.63** [0.37, 2.89]	**1.61** [0.90, 2.32]	**1.63** [1.07, 2.19]	**1.63** [0.37, 2.89]	**1.89** [0.80, 2.99]	**2.44** [1.22, 3.66]	**1.09** [0.13, 2.04]	**1.89** [0.80, 2.99]	**2.44** [1.22, 3.66]	**1.09** [0.13, 2.04]
Seymore et al.[57]	**0.29** [-0.35, 0.93]	**0.29** [-0.18, 0.76]	**0.29** [-0.80, 1.38]	**0.29** [-0.35, 0.93]	**0.29** [-0.18, 0.76]	**0.29** [-0.80, 1.38]	**0.38** [-0.50, 1.27]	**0.51** [-0.38, 1.41]	**0.22** [-0.66, 1.10]	**0.38** [-0.50, 1.27]	**0.51** [-0.38, 1.41]	**0.22** [-0.66, 1.10]

Abbreviations: CG, Control Group, EG, Exercise Group, FE: Fixed Effect Model, MD, Mean Difference, NA, Not Applicable, RCT, Randomised Controlled Trial, RE: Random Effect Model, SMD, Standardised Mean Difference, SR, systematic review

2.5. Conclusions

Based on the meta-analyses and subgroup analyses of this systematic review, effect sizes on the eccentric strength training vary from small to large among the MLE, panoramic ultrasound scanning, and trigonometric equation methods. The only large effect size was detected in the subgroup consisting of the studies that used the trigonometric equation method for estimating BFlh FL. Likewise, the effect size of the NHE was large in the subgroup of the studies that used the trigonometric equation method for estimating BFlh FL. A consensus on ultrasound scanning techniques and BFlh FL estimation might provide comparable results between the exercise interventions targeting BFlh FL. Additionally, a future study can be conducted to compare the effects of eccentric training, which includes the NHE, based on the ultrasound assessment and extrapolation methods.

Chapter 3. Original Investigation 1. Playing rugby leads to longer biceps femoris fascicles, but stiffer biceps femoris, and lower knee flexors to knee extensors muscle volume ratios in long-term

A version of this chapter is in press in the peer-reviewed journal "International Journal of Sports Physiology and Performance"

Yagiz G, Shida N, Kuruma H, Furuta M, Morimoto K, Yamada M, Uchiyama T, Kubis H-P, Owen JA (2023). Playing rugby leads to longer biceps femoris fascicles, but stiffer biceps femoris, and lower knee flexors to knee extensors muscle volume ratios in long-term. International Journal of Sports Physiology and Performance. Under Review.

Abstract

Purpose: Shorter biceps femoris long head (BFlh) fascicle length (FL), increased hamstring passive muscle stiffness (PMS), and lower knee flexor (KF) to knee extensor (KE) ratios are suggested risk factors for hamstring strain injuries (HSIs). This study aimed to determine if HSI risk factors related to muscle structure and morphology were different between rugby union players and controls. **Methods:** BFlh fascicle length (FL), passive muscle stiffness (PMS), relative and absolute muscle volume (MV) of knee flexor (KF) and extensors (KE) were measured via B-mode ultrasound, shear-wave elastography and magnetic resonance imaging, in 21 rugby players from the top division of the university rugby league of Japan and 21 physically active non-athletes. **Results:** The BFlh FL was longer ($P < 0.001$), and BFlh PMS was higher in rugby players ($P= 0.001$-0.009). The absolute BFlh, KF, and KE MVs were also higher in rugby players ($P < 0.001$). There were no differences in the relative BFlh and KF MVs while the relative KE MVs were higher in rugby players ($P = 0.027$-0.028), whilst the percentage BFlh fascicle length/KE, BFlh/KE, and KF/KE values of the rugby players were significantly lower than the control group ($P = 0.001$-0.02). The mean BFlh MV significantly correlated with the FL ($R = 0.57$), and PMS ($R = 0.42$). **Conclusion:** Habitual rugby training and match-play lead to structural and morphological alterations in the KF and KE that may increase HSIs risk. Practitioners should administer long-term hamstring pre-habilitation training to reduce HSI risk in rugby players.

3.1. Introduction

Hamstring strain injuries (HSIs) are common in team sports and cause the greatest time lost to playing and training in rugby union [1, 2]. The effect of HSI on player availability is further compounded by the high proportion of recurrent injuries [3], suggesting that this injury is difficult to rehabilitate effectively [4]. Therefore, scientists have focused on identifying risk factors for HSIs over the last two decades to develop optimal hamstring injury prevention strategies.

The biceps femoris long head (BFlh) is the most susceptible to injury among the hamstrings muscle group, accounting for more than 80% of all HSIs [5]. The late swing phase of running is the most vulnerable time for hamstring injuries [6, 7]. During this phase of running, the hamstrings behave as an antagonist to the quadriceps femoris and contract eccentrically to control the quadriceps femoris muscle during tibial deceleration [8]. At this moment, the BFlh is exposed to the highest stretch, reaching about 110% of its length [9]. HSIs generally occur when the muscle fascicles cannot resist these excessive tensile forces [10]. Besides high-speed running, the most severe HSIs in rugby union [2] happen during the kicking activities during concentric muscle actions of the antagonists of the hamstrings [11]. Despite the multifactorial nature of HSIs [12], muscle imbalance, particularly insufficient hamstring strength in comparison with the quadriceps, has been strongly suggested as a risk factor for HSIs [13]. Muscle structural and morphological risk factors for the HSIs have also been proposed in recent years [14-16], including shorter BFlh fascicle length [15] and increased passive hamstring stiffness [16]. Whether the nature of rugby union match play or training leads to alterations in these risk factors and a potential increase in the risk of HSIs incidence and recurrence is unclear.

Therefore, the primary aim of this study was to compare BFlh fascicle length, passive stiffness, and thigh muscles' morphology in male rugby union players and healthy active controls. The secondary aim was to assess relationships between the BFlh muscle volume, fascicle length and passive muscle stiffness. We hypothesised that rugby players would have 1) greater muscle volume due to long-term training and competition, 2) longer BFlh fascicle length due to the potentially larger muscle size, 3) higher BFlh passive stiffness due to the potentially higher muscle volume, 4) lower BFlh fascicle length/KE, BFlh/KE and KF/KE muscle volume ratios due to potentially higher knee extensor activities compared with healthy controls.

3.2. Methods

3.2.1. Subjects

Participants were recruited via email and verbal advertisements among the rugby teams in Tokyo and the university population of Tokyo Metropolitan University. Inclusion criteria for the rugby group were a) being healthy and actively playing rugby in the Japanese university division 1 rugby union competition, b) absence of an acute lower extremity injury, c) absence of a known hamstring injury and traumatic knee injury history such as anterior cruciate ligament injury, d) being between 18-35 years old. Inclusion criteria for the control group were: a) being healthy, b) not having a totally sedentary lifestyle to minimise the adverse effects of a sedentary lifestyle on our measures, c) not performing any regular strength, power sports, and any sports discipline-specific training, d) absence of an acute lower extremity injury, e) absence of a known hamstring injury and traumatic knee injury history such as anterior cruciate ligament injury, f) being between 18-35 years old. Training regimens, training and injury histories of the rugby group were recorded via a written questionnaire. The physical activity status of the control group was measured using the International Physical Activity Questionnaire short form (IPAQ-sf) [17]. The dominant thigh was determined as the preferred kicking leg. The Tokyo Metropolitan University, Arakawa campus ethics committee provided ethical approval (code: 20067) according to the Declaration of Helsinki (World Medical Association, 2013). Written informed consent, health screening questionnaires, and a standard magnetic resonance imaging (MRI) questionnaire were read and signed by the participants before study enrolment.

3.2.2. Design

A cross-sectional study design was used in this study to compare those habituated to rugby participation and the active control group. A priori sample size calculation was calculated for knee flexors to knee extensors muscle size ratio [18] using G*Power software [19] for 0.8 effect size, 80% statistical power and 0.05 alpha level in a total of forty-two participants were equally divided for both groups (twenty-one rugby group and twenty-one for the control group (1:1 allocation ratio). Additionally, the required sample size of reliability assessments for the BFlh fascicle length and stiffness measurements of this study were calculated by referring to the intraclass correlation coefficient (ICC) values of previous reliability studies investigating ultrasound-measured BFlh fascicle length and ultrasound-based shear wave elastography measured stiffness [20, 21]. The lowest ICC value for the BFlh fascicle length and stiffness measurements in these studies was 0.81. Therefore, the required sample size for

this reliability was calculated based on a 0.8 ICC value, which is lower than the lowest reliability value among the mentioned BFlh fascicle length and stiffness reliability assessments [20, 21]. In light of guidelines [22] for ICC reliability studies, the required sample size was estimated as seven for two measurements, 0.8 ICC value and 80% statistical power.

3.2.3. Measurements

Both groups underwent BFlh fascicle length measurements via B-mode ultrasonography, the BFlh passive stiffness assessments via ultrasound-based shear-wave elastography, and thigh muscles' volume measurements via magnetic resonance imaging (MRI). Additionally, measures of BFlh fascicle length and passive stiffness measurements were repeated twice on different days in seven participants to calculate the reliability of the measurements. The same researcher (M.F.), who was experienced in musculoskeletal ultrasound imaging, performed the scanning during all fascicle length and passive muscle stiffness measurements alongside another experienced researcher (G.Y.) [23]. The MRI scanning was performed by H.K., an experienced researcher in MRI measures for musculoskeletal assessments. The first author (G.Y.) completed the fascicle length digitisations and boundary tracings of the muscles for calculating the BFlh fascicle lengths and BFlh, KE and KF muscle volumes.

3.2.3.1. Biceps Femoris Long Head Fascicle Length

A linear array transducer of a two-dimensional B-mode ultrasound (i18LX5 (46 mm width), Applio i800, Canon Medical Systems) was used to assess the BFlh fascicle length in both thighs by following the methodology of a recent study [23]. Participants laid down on a standard medical bed without performing any voluntary muscle contraction. An ultrasound image of the BFlh fascicles along the BFlh muscle orientation was taken from the 50% distance between the trochanter major and popliteal crease (Figure 3.1). The fascicle length was calculated via the manual linear extrapolation method (MLE) in light of a recent study [23] by using the ImageJ software (National Institutes of Health, Bethesda, Maryland, USA).

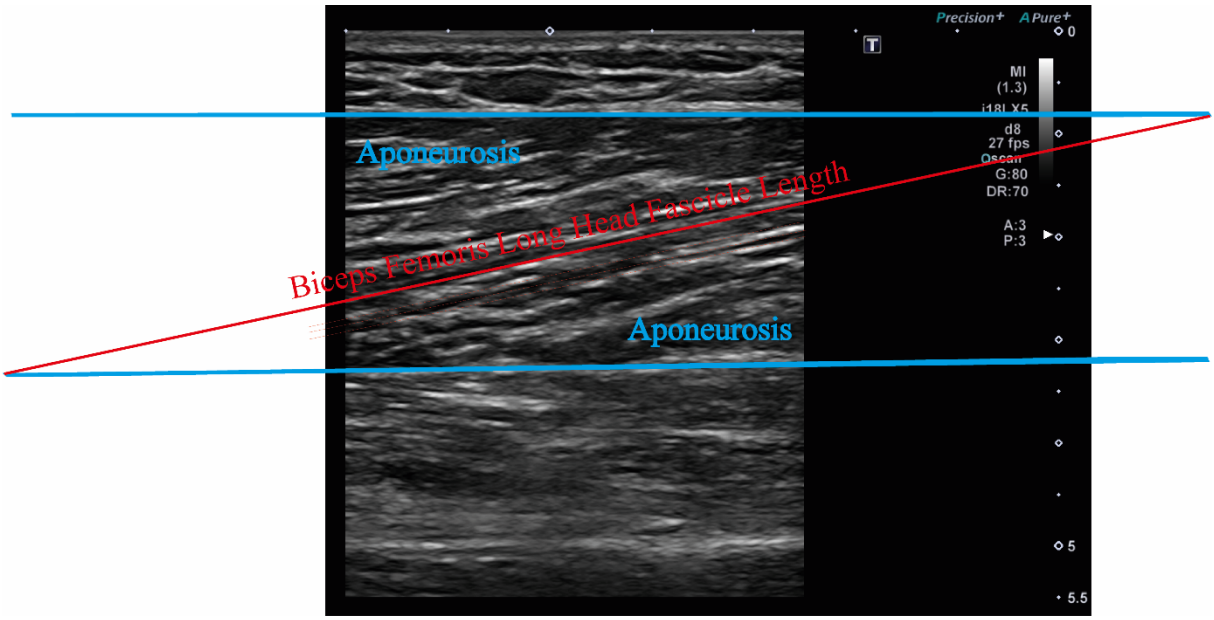

Figure 3.1. Example of biceps femoris long head fascicle length measurements via B-mode ultrasound. The fascicle length was calculated based on the manual linear extrapolation method by following the methodology of a recent study [23].

3.2.3.2. Biceps Femoris Long Head Passive Muscle Stiffness

The BFlh muscle stiffness was measured by using the same ultrasound machine and transducer as for the BFlh fascicle length measurement by using the validated procedure for passive stiffness of individual muscles via the shear-wave elastography function of the ultrasound machine [24]. Precisely the same procedure for the BFlh fascicle length was followed during the BFlh muscle stiffness measurements of both legs with an addition that a 10-mm elastogram was taken from the central region of the BFlh muscle belly to determine the passive muscle stiffness of the BFlh (Figure 3.2).

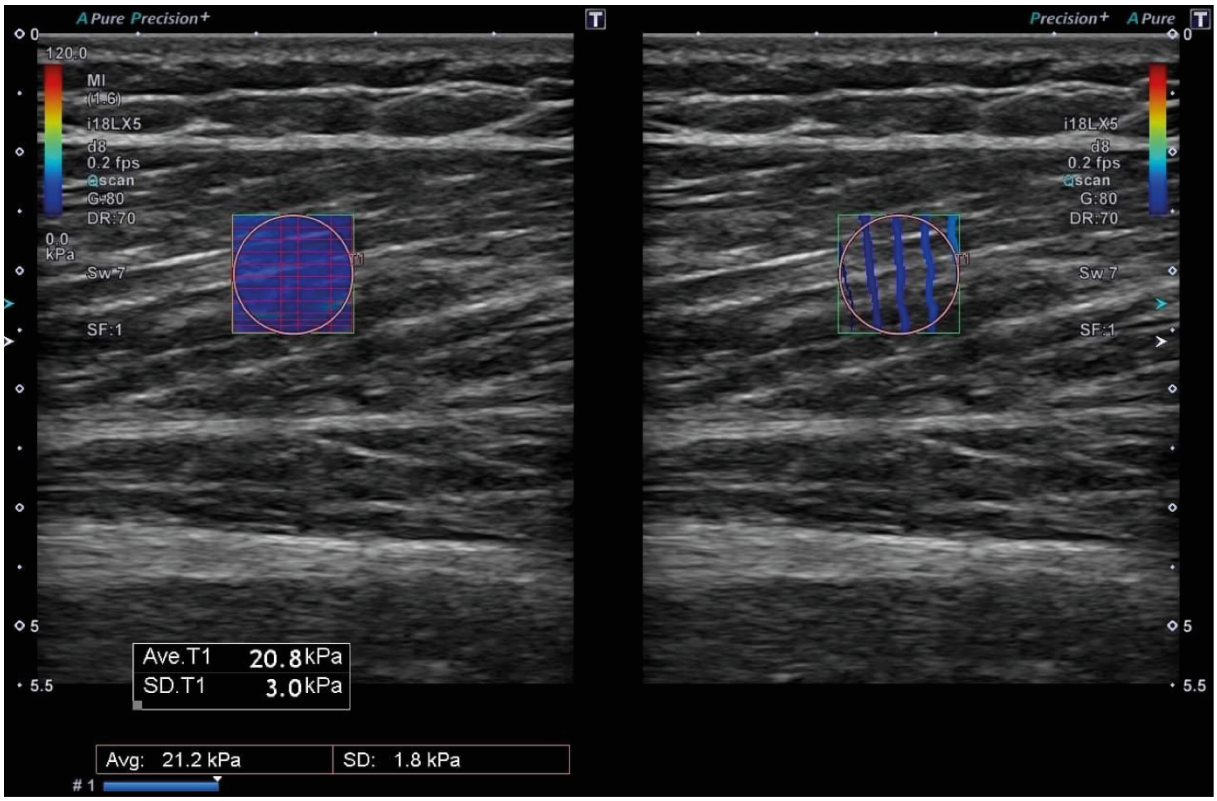

Figure 3.2. Example of a biceps femoris long head passive muscle stiffness measurement via ultrasound-based shear wave elastography. A 10-mm elastogram was taken from the central region of the biceps femoris long head muscle belly.

3.2.3.3. Muscle Volume Measurements

The MRI scans and further muscle volume calculations were completed using a 3-Tesla (3T) MRI imaging system with air coil technology (SIGNA Premier 3.0T; GE Healthcare, Chicago, IL). Participants assumed a supine position with neutral hips, and extended knees in the magnet bore with a strap on both limbs to prevent unwanted movements. T-1 weighted contiguous axial MRI scans of both legs were recorded starting from the iliac crest and finishing at the tibial condyles (field of view 420mm x 420mm, slice thickness: 10 mm, interslice thickness: 0 mm). The KF and KE muscle boundaries were manually traced using OsiriX MD software (version 13.0.1, Pixmeo SARL, Bernex, Switzerland). All the visible cross-sectional areas of the KE and KF muscles were outlined in each axial MRI image (Figure 3.3). To calculate the absolute BFlh, KE (rectus femoris, vastus intermedius, vastus medialis, and vastus lateralis) and KF (the biceps femoris short and long heads, gracilis, Sartorius, semimembranosus and semitendinosus) muscle volumes, their cross-sectional areas were summed and multiplied by the slice thickness [25]. Relative muscle volumes were

calculated by dividing the absolute muscle volume values by the individual participants' body mass (cm^3/kg).

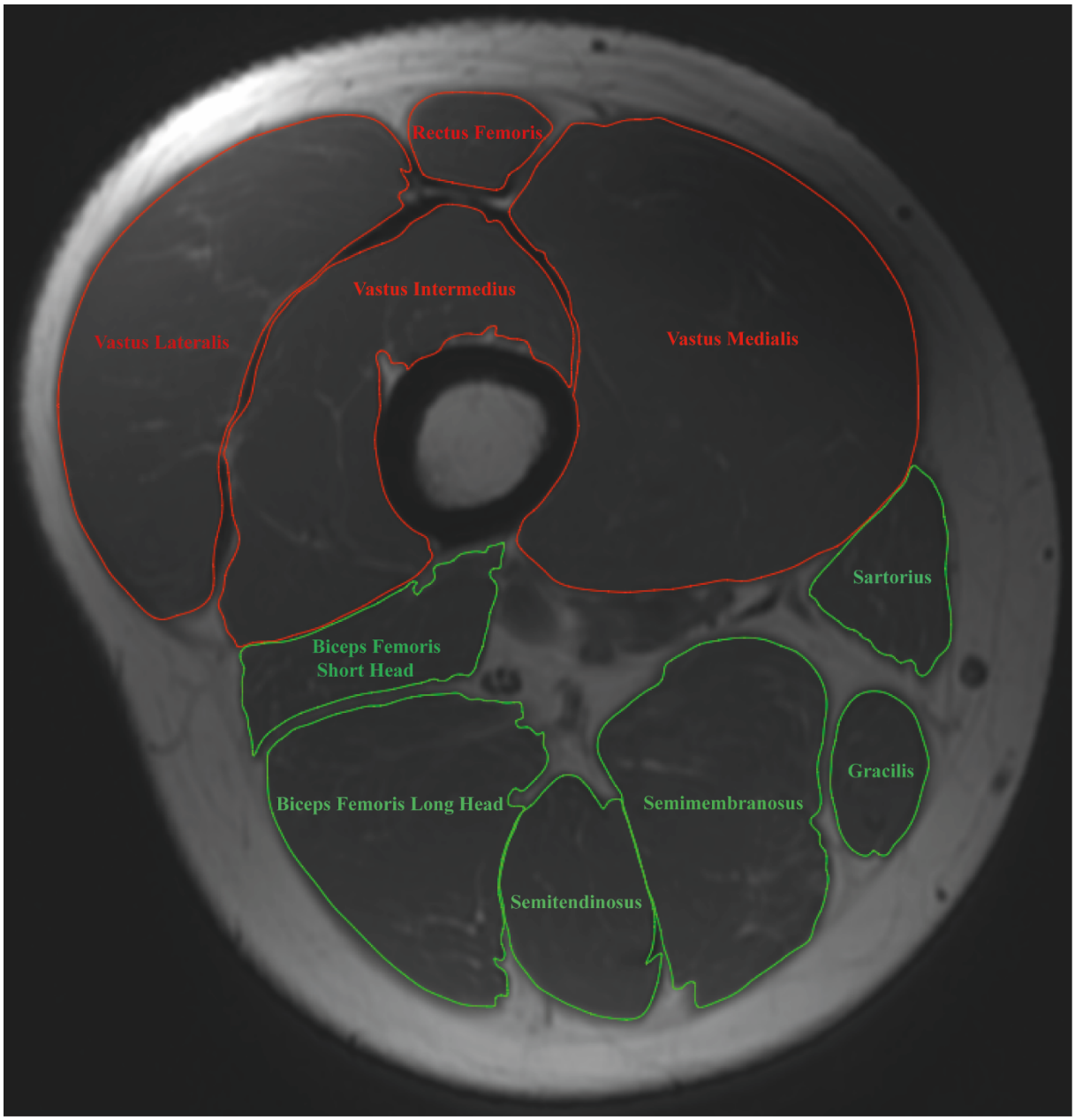

Figure 3.3. An example cross-sectional MRI image of the right thigh to show knee flexor and extensor muscles cross-sectional areas for future usage for muscle volume calculations. The muscles outlined in red represent the knee extensors at the thigh, while those outlined in green show the knee flexors.

3.2.4. Statistical Analyses

The SPSS software (Version 27, IBM Corporation, Chicago, Illinois) was used for statistical analyses of this study. The BFlh fascicle length, passive muscle stiffness, absolute and relative muscle volume of the BFlh, overall KE and KF of both legs and average of both

legs were compared by using the one-way analysis of variance (ANOVA) between the groups. The homogeneity of variances was tested via Levene statistics. The reliability of the BFlh fascicle length and passive muscle stiffness measurements were assessed via ICC analysis for both legs based on two-way random absolute agreement. An ICC value lower than 0.5, 0.5-0.75, 0.75-0.9, and over 0.9 were accepted as poor, moderate, high and very high reliabilities, respectively. In addition, linear regression analyses were performed to find out relationships between the BFlh muscle volume, fascicle length and passive muscle stiffness. The correlation coefficient values $R \leq 0.3$, R = 0.3-05, R= 0.5-0.7, R = 0.7-0.9, and $R \geq 0.9$ were considered very weak, weak, moderate, strong, and very strong. The alpha level for the statistical significance was set at 0.05 for all the statistical analyses of this study.

3.3. Results

Initially, forty-seven participants were recruited for the study. However, four participants did not meet the inclusion criteria of this study on the pre-screening forms, and one participant did not attend all the measurements. Therefore, five participants were excluded from the study, and forty-two participants (twenty-one for the rugby and twenty-one for the control group) completed the study. Participants' physical and training characteristics are shown in Table 3.1.

Table 3.1. Physical Features and Training Characteristics of Participants (mean ± SD)

	Rugby group	**Control group**	**P-value for homogeneity of variances**	**P-value for mean difference**
Age (years)	20.38 ± 1.16	22.05 ± 1.07	0.45	**P < 0.001**
Height (cm)	173.04 ± 4.64	170.49 ± 6.14	0.47	P = 0.14
Body mass (kg)	87.44 ± 10.87	63.76 ± 7.78	0.26	**P < 0.001**
Total Years of Rugby-Specific Training	9.07 ± 3.4	-	-	-
Rugby Training hours and sessions per week	18.43 ± 3.94 hours, 5.57 ± 1.08 sessions	-	-	-

Rugby Match Frequency per week	1.29 ± 0.72	-	-	-
Training intensity and hours of CG per week	-	0.8 ± 1.29 vigorous intensity, 2.37 ± 3.24 moderate intensity, and 5.27 ± 6.24 low intensity	-	-
Abbreviations: CG, control group; RG, rugby group; SD, standard deviation.				

Seven participants underwent intra-tester and inter-day reliability assessments across two separate sessions on different days. As a result, the BFlh fascicle length and passive muscle stiffness measurements were graded as very highly reliable for both legs (Table 3.2).

Table 3.2. Reliability assessment results of the BFlh FL and passive muscle stiffness measurements for both legs based on two-way random absolute agreements (ICC, 95% CI).

	Dominant leg	**Non-dominant leg**
BFlh FL	0.97 [0.78, 0.99]	0.97 [0.855, 0.99]
BFlh passive muscle stiffness	0.91 [0.42, 0.98]	0.94 [0.66, 0.99]
Abbreviations: BFlh, the biceps femoris long head; FL, fascicle length.		

Statistical analyses showed that rugby players exhibited significantly longer BFlh fascicles, higher BFlh passive muscle stiffness and higher BFlh absolute muscle volume in both thighs (Table 3.3). However, there were no differences in the relative muscle volume values of both thighs between the groups (Table 3.3). The fascicle lengths of six participants (three from the rugby and three from the control group) were not calculated due to unclear fascicular paths in the images.

Table 3.3. The biceps femoris long head's fascicle length, passive muscle stiffness, and absolute and relative muscle volume results of the groups.

	Rugby group	**Control group**	**P-value for homogeneity of variances**	**P-value for mean difference**

D BFlh FL (cm)	10.68 ± 1.15**	9.1 ± 1.11	0.912	**P < 0.001**
ND BFlh FL (cm)	10.6 ± 1.21**	9 ± 1.25	1	**P < 0.001**
AV BFlh FL (cm)	10.64 ± 1.16**	9.05 ± 1.16	0.889	**P < 0.001**
D BFlh passive muscle stiffness (kPa)	24.65 ± 10.46*	16.85 ± 7.61	0.094	**P = 0.009**
ND BFlh passive muscle stiffness (kPa)	25.14 ± 11.92*	14.9 ± 4.79	**0.003**	**P = 0.001**
AV BFlh passive muscle stiffness(kPa)	24.89 ± 8.52**	15.87 ± 5.58	**0.017**	**P < 0.001**
D absolute BFlh MV (cm^3)	288.03 ± 41.22 **	216.17 ± 45.31	0.611	**P < 0.001**
ND absolute BFlh MV(cm^3)	287.98 ± 45.49 **	214.58 ± 49.08	0.961	**P < 0.001**
AV absolute BFlh MV (cm^3)	288.01 ± 42.84 **	215.38 ± 45	0.977	**P < 0.001**
D relative BFlh MV (cm^3/kg)	3.31 ± 0.36	3.4 ± 0.7	**0.049**	P = 0.573
ND relative BFlh MV (cm^3/kg)	3.3 ± 0.4	3.39 ± 0.81	**0.044**	P = 0.662
AV relative BFlh MV (cm^3/kg)	3.3 ± 0.37	3.4 ± 0.72	0.053	P = 0.605
Abbreviations: AV, average; BFlh, biceps femoris long head; D, dominant; FL, fascicle length; MV, muscle volume; ND, non-dominant;, *significantly higher than the other group (P < 0.05); **significantly higher than the other group (P < 0.001).				

Based on the absolute muscle volume comparisons between the groups, KE and KF muscle volumes of both thighs were significantly higher in the RG than the CG (Table 3.4). However, the RG only demonstrated higher relative KE muscle volumes than the CG (Table 3.4). There were no significant differences in relative KF muscle volumes of both legs between the groups (Table 3.4).

Table 3.4. Absolute and relative total muscle volumes of the knee extensors and knee flexors based on the groups.

	Rugby group	**Control group**	**P-value for homogeneity of variances**	**P-value for mean difference**
D absolute KE (cm^3)	3017.39 ± 429.3**	2061.11 ± 310.37	0.136	**P < 0.001**
ND absolute KE (cm^3)	3004.9 ± 422.13**	2027.96 ± 320.84	0.868	**P < 0.001**
AV absolute KE (cm^3)	3011.14 ± 423.64**	2042.17 ± 312.78	0.167	**P < 0.001**
D relative KE (cm^3/kg)	34.55 ± 2.8*	32.31 ± 3.49	0.464	**P = 0.027**
ND relative KE (cm^3/kg)	34.44 ± 3.1*	31.83 ± 4.21	0.397	**P = 0.028**
AV relative KE (cm^3/kg)	34.49 ± 2.91*	32.07 ± 3.76	0.453	**P = 0.025**
D absolute KF (cm^3)	1374.23 ± 205.58**	1041.93 ± 192.75	0.874	**P < 0.001**
ND absolute KF (cm^3)	1373.39 ± 196.62**	1010.07 ± 192.41	0.868	**P < 0.001**
AV absolute KF (cm^3)	1373.81 ± 198.63**	1026 ± 187.44	0.858	**P < 0.001**
D relative KF (cm^3/kg)	15.73 ± 1.29	16.34 ± 2.45	**0.032**	P = 0.32
ND relative KF (cm^3/kg)	15.72 ± 1.25	15.86 ± 2.64	**0.006**	P = 0.831
AV relative KF (cm^3/kg)	15.73 ± 1.22	16.1 ± 2.45	**0.022**	P = 0.536

Abbreviations: AV, average; D, dominant; KE, knee extensors; KF, knee flexors; ND, non-dominant; *significantly higher than the other group (P < 0.05); **significantly higher than the other group (P < 0.001).

The percentage BFlh/KE, BFlh/KF and KF/KE muscle volume ratios of both legs were compared between the groups. In consequence, the RG displayed significantly lower percentage BFlh/KE and KF/KE muscle volumes in both thighs (Table 3.5). However, there were no significant differences in BFlh/KF muscle volume ratios in both legs between the groups (Table 3.5).

Table 3.5. Knee flexors to knee extensors percentage muscle volume ratios, biceps femoris long head to knee extensors percentage muscle volume ratios, and biceps femoris long head fascicle length to knee extensors percentage muscle volume ratios of the groups.

	Rugby group	**Control group**	**P-value for homogeneity of variances**	**P-value for mean difference**
D KF/KE%	45.7 ± 4.12	50.55 ± 4.78*	0.185	**P = 0.001**
ND KF/KE%	45.87 ± 4.03	49.8 ± 4.27*	0.393	**P = 0.004**
AV KF/KE%	45.78 ± 3.9	50.27 ± 4.47*	0.268	**P = 0.001**
D BFlh/KE%	9.59 ± 0.91	10.5 ± 1.45*	**0.044**	**P = 0.019**
ND BFlh/KE%	9.61 ± 0.98	10.59 ± 1.57*	**0.039**	**P = 0.02**
AV BFlh/KE%	9.6 ± 0.91	10.56 ± 1.41*	0.121	**P = 0.012**
D BFlh/KF%	21.04 ± 1.8	20.76 ± 1.93	0.603	P = 0.637
ND BFlh/KF%	20.99 ± 1.8	21.26 ± 2.4	0.277	P = 0.683
AV BFlh/KF%	21 ± 1.7	21.01 ± 1.95	0.667	P = 0.997
D BFlh FL/KE %	0.36 ± 0.6	0.45 ± 0.11*	0.346	**P = 0.004**
ND BFlh FL/KE %	0.36 ± 0.61	0.45 ± 0.12*	0.342	**P = 0.005**
AV BFlh FL/KE %	0.36 ± 0.61	0.45 ± 0.11*	0.327	**P = 0.004**

Abbreviations: AV, average; BFlh, biceps femoris long head; D, dominant; FL, fascicle length; KE, knee extensors; KF, knee flexors; MV, muscle volume; ND, non-dominant; *significantly higher than the other group ($P < 0.05$); **significantly higher than the other group ($P < 0.001$).

The BFlh muscle volume exhibited significant, moderate, positive correlations with the BFlh dominant, non-dominant and average fascicle length values (Table 3.6). Additionally, the BFlh muscle volume illustrated significant, weak, positive correlations with the dominant and average BFlh passive muscle stiffness (Table 3.7).

Table 3.6. Correlations between the biceps femoris fascicle length, muscle volume and passive muscle stiffness.

	BFlh MV	**BFlh passive muscle stiffness**
D BFlh FL	D BFlh MV** ($R = 0.588$, $R^2 = 0.345$, **$P < 0.001$**)	D BFlh passive stiffness* ($R = 0.341$, $R^2 = 0.116$, **$P = 0.021$**)
ND BFlh FL	ND BFlh MV* ($R = 0.496$, $R^2 = 0.323$, **$P = 0.001$**)	ND BFlh passive stiffness ($R = 0.249$, $R^2 = 0.062$, $P = 0.072$)
AV BFlh FL	AV BFlh MV** ($R = 0.568$, $R^2 = 0.345$, **$P < 0.001$**)	AV BFlh passive stiffness* ($R = 0.369$, $R^2 = 0.136$, **$P = 0.027$**)

Abbreviations: AV, the average value of both thighs; BFlh, biceps femoris long head; D, dominant thigh; FL, fascicle length; KE, knee extensors; KF, knee flexors; MV, muscle volume; ND, non-dominant thigh; *significantly correlated ($P < 0.05$); **significantly correlated ($P < 0.001$).

Table 3.7. Correlations between the biceps femoris passive muscle stiffness, muscle volume and fascicle length.

	BFlh MV	**BFlh FL**
D BFlh passive muscle stiffness	D BFlh MV* ($R = 0.461$, $R^2 = 0.212$, **$P = 0.002$**)	D BFlh FL* ($R = 0.341$, $R^2 = 0.116$, **$P = 0.042$**)
ND BFlh passive muscle stiffness	ND BFlh MV ($R = 0.218$, $R^2 = 0.047$, $P = 0.166$)	ND BFlh FL ($R = 0.249$, $R^2 = 0.062$, $p = 0.143$)
AV BFlh passive muscle stiffness	AV BFlh MV*: $R = 0.416$, $R^2 = 0.173$, **$P = 0.006$**	AV BFlh FL*: $R = 0.369$, $R^2 = 0.136$, **$P = 0.027$**

Abbreviations: AV, the average value of both thighs; BFlh, biceps femoris long head; D, dominant thigh; FL, fascicle length; KE, knee extensors; KF, knee flexors; MV, muscle volume; ND, non-dominant thigh; *significantly correlated ($P < 0.05$).

3.4. Discussion

To the authors' knowledge, this is the first study to compare BFlh fascicle length, passive muscle stiffness, and the BFlh, KE and KF muscle volumes between rugby players and healthy, physically active controls to assess the potential long-term adaptations of these structures to rugby-specific training and match-play, and specifically whether these alterations may affect HSIs risk. The main findings of the study showed that long-term exposure to rugby-specific training and competition led to greater absolute muscle volume of the KE and KF, an increase in BFlh stiffness and BFlh fascicle length. Notably, KE muscle volume relative to body mass was also greater in rugby players, which contributed to lower KF to KE ratios and lower ratios for BFlh fascicle length/KE muscle volume and BFlh to KE muscle volume. Suggestive of a potential increase in HSIs risk based on previous research in this field [13,15,16]. The rugby group in this study played in the top Japanese university rugby competition (division 1) with 9.07 ± 3.4 years of rugby-specific training history. The control group included non-sedentary non-athletes who were weekly performing 0.8 ± 1.29 vigorous intensity, 2.37 ± 3.24 moderate intensity, and 5.27 ± 6.24 low-intensity non-sport-specific exercise such as running and walking. By recruiting this control group, it aimed to minimise the potential adverse effects of sedentary lifestyles and minimise any sport-specific alterations in the outcome measures.

Our Study has revealed that playing rugby led to significantly longer BFlh fascicles in both thighs (dominant (D): 10.68 cm vs 9.1 cm, non-dominant (ND): 10.6 cm vs 9 cm). However, playing rugby leads to lower percentage BFlh fascicle length/KE muscle volume ratios (D and ND: 0.36 vs 0.45), lower KF to KE percentage ratios in both thighs (D: 45.7% vs 50.55%, ND: 45.87% vs 49.8%), lower BFlh to KE percentage muscle volume ratios in both legs of the rugby players (D: 9.59% vs 10.5%, ND: 9.61% vs 10.59%). Likewise, rugby players showed higher KE muscle volume values relative to body mass (dominant: 34.55 cm^3/kg vs 32.21 cm^3/kg, non-dominant: 34.44 cm^3/kg vs 31.83 cm^3/kg). However, they did not show differences in KF muscle volume values relative to body mass in both legs compared to controls (dominant:15.73 cm^3/kg vs 16.34 cm^3/kg, non-dominant: 15.72 cm^3/kg vs 15.86 cm^3/kg for the RG and CG, respectively). Another important finding from this study was that long-term rugby-specific training and match play increased the BFlh muscle stiffness.

In their prospective study, Timmins and colleagues highlighted BFlh fascicle length as a risk factor for HSIs [15]. However, one of the limitations of this study was not assessing the architectural characteristics of the hamstrings relative to knee extensors. The knee extensors contribute to the increased tensile force during the eccentric action of the hamstrings by behaving as an antagonist. Indeed, our study found significantly lower percentage ratios of BFlh fascicle length/KE muscle volume in both legs for the rugby group compared to the control (dominant and non-dominant: 0.36 vs 0.45). These results may indicate that rugby-specific adaptations in the BFlh fascicle length/KE muscle volume can increase the tensile force in the series of sarcomeres in the BFlh fascicle length and might increase the risk of HSIs. The regression analysis showed that BFlh muscle volume explained 35% ($R = 0.568$, $R^2 = 0.345$, $P < 0.001$) of the variances in the increased BFlh fascicle length. These results suggest that rugby players may consider focusing more on increasing BFlh muscle volume through specific hypertrophy training.

Overall, these results indicate that long-term rugby-specific training and match play lead to unbalanced hypertrophy in favour of the knee extensors. When considering that KE muscle volume is one of the strongest predictors of concentric muscle power [26], this alteration might increase the tensile force on the BFlh fascicles during the late swing phase of running due to the antagonist behaviour of the KE and might increase the vulnerability of the muscle. Unfortunately, this argument requires further investigation due to the lack of prospective and retrospective studies addressing the predictive abilities of architectural and morphological parameters of the hamstrings relative to KE for the HSIs. Therefore, future prospective studies should examine whether there are threshold values in the BFlh fascicle length/KE muscle volume, BFlh/KE and KF/KE muscle volume ratios for predicting HSIs.
Additionally, this study has shown that long-term rugby-specific training and match play led to higher BFlh passive muscle stiffness in both legs (D: 24.65 vs 16.85 kPa; ND: 25.14 vs 14.9 kPa). This observation might further compound HSIs risk, as evidence has suggested that increased hamstring stiffness is a risk factor for the HSIs [16]. However, much of the previous research on passive muscle stiffness have adopted techniques, including measuring the whole muscle-tendon complex of the agonist's muscles. These techniques are limited by not being capable of evaluating the stiffness of the individual muscles [27]. However, the use of shear-wave elastography in this study has allowed an accurate assessment of passive stiffness [24]. Our findings revealed that long-term rugby participation leads to increases in passive muscle stiffness of the BFlh in both thighs. However, previous research [16] showing that increased hamstring stiffness is a risk factor for HSIs employed less valid assessments free oscillation

technique to assess the passive stiffness of the muscle and tendon of all knee flexors rather than measuring the passive stiffness of the individual muscles. Therefore, new prospective studies are needed to assess the predictive ability of the BFlh passive muscle stiffness and determine if there is a predictive threshold value for the HSIs using the updated technology [24], namely shear wave elastography. Despite the overall high-reliability results for the passive muscle stiffness measurements of this study, the confidence intervals of the results were wide. Therefore, the reliability results for the passive muscle stiffness measurements should be interpreted cautiously. The small sample size of the reliability assessments could cause these large confidence intervals, which can be considered a limitation of this study. Additionally, the reliability assessments comprised only intra-tester reliability measurements. Not performing inter-tester reliability measurements is another limitation of this study. Future reliability studies should be conducted by recruiting a larger sample size and inter-tester reliability measurements too.

Our study employed the "gold standard" measurement of MRI for muscle volume assessments [28]. However, no "gold standard" measurement method of the BFlh fascicle length exists in the literature [20]. Additionally, the effect size of exercise can vary between the ultrasound assessment methods, such as the trigonometric equation method potentially leads to overestimated BFlh fascicle length [20] and size of exercise effect on the BFlh fascicle length compared to MLE, panoramic ultrasound scanning [29] or diffusion-tensor MRI[30]. Despite this study using the MLE method, which doesn't significantly overestimate the BFlh fascicle length [20] and effects of exercise on the BFlh fascicle length [29], using this method is still a limitation of this study due to lacking a "gold standard" method for the BFlh fascicle length assessments [20]. This study measured the muscle volume of the major knee flexors naturally located at the thigh. However, lateral and medial gastrocnemius, popliteus, and soleus muscles also contribute to knee flexion, despite not being their primary activity. Thus, not measuring the volume of these muscles can be another confounding factor of this study. Additionally, the vast majority of the rugby players were recruited from the same team, which might decrease the generalisability of the findings to all rugby players in the same league. Lastly, this study recruited players from the top Japanese university rugby league (division 1) with 9.07 ± 3.4 years of rugby-specific training history. Still, this study could not recruit players competing at the top-level international leagues, which may be another limitation. It also should be noted that the fascicles of six participants could not be calculated due to unclear ultrasound images, which failed to show fascicular paths. Unclear fascicular paths are not uncommon in fascicle length measurements [4]. However, not

successfully measuring the fascicle length of six participants is defined as another limitation of this study.

3.5. Practical Applications

The findings of this study suggest that habitual participation in rugby union training and competition results in an alteration in the structure and morphology of the thigh musculature, which may increase the risk of HSIs. These alterations include an increase in knee extensor muscle volume relative to the knee flexors and an increase in bicep femoris passive muscle stiffness. Coaches and athletes are advised to maintain balanced developments between the knee flexors and extensors by adjusting rugby-training regimens. Specifically, they focus more on the development of muscle hypertrophy, strength qualities and mobility in the hamstrings muscle group as part of a pre-habilitation routine. Based on these findings, future prospective studies should investigate whether measures such as the BFlh fascicle length/KE, BFlh/KE, and KF/KE muscle volume ratios predict HSIs.

3.6. Conclusions

This study reveals that long-term rugby-specific training and match play may lead to an increased risk of HSIs compared to active controls, based on imbalanced developments favouring the knee extensor muscles. Specifically considering hamstring strain injury mechanism, exposure to rugby leads to increased BFlh passive muscle stiffness and smaller BFlh fascicle length/KE ratios. Moreover, playing rugby did not increase the KF muscle volume relative to body mass.

Chapter 4. Original Investigation 2. Alterations in biceps femoris long head fascicle length, Eccentric hamstring strength qualities and single-leg hop distance throughout the ninety minutes of TSAFT^{90} simulated football match

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Abstract

Introduction: Football matches show higher hamstring strain injuries (HSIs) than football training. The occurrence of HSIs increases in the last fifteen minutes of both halves of football matches and shows an incremental trend towards the end of the ninety minutes. **Objectives:** This study aimed to examine football-specific fatigue-induced alterations in risk factors of the HSIs, including biceps femoris long head fascicle length via ultrasonography (BFlh FL), single-leg hop distance, hamstrings' maximal eccentric strength, and single-leg hamstring bridge test (SLHB) performance. **Methodology:** During ninety minutes of the $TSAFT^{90}$ football simulation, the BFlh FL and single-leg hop distance were measured three times (before, at half-time and after 90 minutes of simulated match-play), and maximal hamstrings eccentric strength and SLHB test scores were recorded twice (before and after simulated match-play) for both legs in physically active participants (n = 15). **Results:** Maximal eccentric hamstrings' strength (dominant leg (D): $p < 0.001$, Hedges' (adjusted) *g* effect size = -0.969; non-dominant leg (ND): $p < 0.001$, $g = -0.929$) and the SLHB performance (D: $p < 0.001$, $g = -1.249$; ND: $p < 0.001$, $g = -1.108$) showed large decrements immediately after the $TSAFT^{90}$ intervention. There were no significant alterations in the BFlh FL and the single-leg hop distance. **Conclusions:** Maximal eccentric strength and the SLHB performance of hamstrings are reduced after 90 minutes of simulated football match play. Practitioners may consider focusing on improving eccentric strength and SLHB performance. Future studies should examine alterations in the BFlh fascicles' dynamic lengthening and shortening ability during a football match.

4.1. Introduction

Hamstring strain injuries (HSIs) are the most common non-contact injuries in football, representing 12% of all injuries [1]. The typical prevalence of HSIs is reported to be in the region of 5 to 6 injuries per season in a football team composed of 25 players [2]. Additionally, hamstring strain re-injuries are higher (16%) [1], more severe, and cause greater time loss than the initial HSIs in football [3]. Moreover, HSIs in football have shown a 4.1% annual increase [4] despite scientists' increasing efforts to provide an optimal injury prevention method in the last two decades.

Match-caused HSIs show a higher incidence than training-caused HSIs in football (respectively 3.70 (3.43–3.99) vs 0.43 (0.39–0.47) per 1000 hours) [5]. Match-induced HSIs are more frequent in the last fifteen minutes of each half of football matches [1,6,7]. Suggestive that increased muscular fatigue might play a substantial role in multifactorial causations of the HSIs in football [8,9]. From this viewpoint, studies [10–31] focused on exploring interrelationships between ninety minutes of football match-induced fatigue and modifiable risk factors of HSIs are warranted.

Researchers have identified various risk factors for hamstring strain injuries, which were previously divided into modifiable and non-modifiable risk factors [32–34]. Non-modifiable risk factors of HSIs include older age [35–40] and previous lower extremity injuries [40–44]. Modifiable risk factors include, but are not restricted to, decreased eccentric hamstring strength qualities [45–48], lower single-leg hop distance (SLHD) [47], and structural risk factors of hamstrings [33] (shorter biceps femoris long head fascicle lengths (BFlh FL) [40], higher hamstring stiffness [49]).

The vast majority of the previous studies [10–20,22–24,27–29,31] investigating a 90-minute football match or simulated-football match-induced changes in hamstring strength used isokinetic strength assessments except for one study [10], which used a Nordic hamstring exercise device for assessing hamstrings eccentric strength. However, the most recent meta-analysis recalibrating risk factors for HSIs suggested that isokinetic strength values were not a risk factor for future HSIs [33]. Additionally, the meta-analytic evidence [33] also suggests that eccentric strength assessments using Nordic hamstring devices are unrelated to future HSIs. Consequently, studies investigating the immediate effects of 90-

minute football or simulated football match on the hamstring strength parameters did not use the specific strength assessments associated with risks for future HSIs.

Conversely, the single-leg hamstring bridge test (SLHB), which assesses the capacity of repetitive high-force production of the hamstrings [46] and eccentric hamstring strength assessed via a handheld dynamometer [47], has been shown to be associated with initial HSIs [33]. To date, no study examining the effect of soccer match-play on HSIs risk has utilised this test for evaluating football match-induced changes in the SLHB performance, and eccentric hamstring strength exists. In addition, no study has investigated the immediate effects of a 90-minute actual or simulated football match on BFlh FL and SLHD, which are significantly associated with future HSIs [33]. Previously, a shorter passive BFlh FL was defined as an independent risk factor for future HSIs by increasing the injury risk more than fourfold (risk ratio: 4.1) [40]. Similarly, a lower SLHD score was defined as a risk factor for future HSIs (odds ratio: 0.884) [47].

Many researchers have adopted simulated soccer match protocols when examining changes in modifiable HSI risk factors during and immediately after soccer match-play due to the problems associated with measurement during actual match-play. A recent systematic review examining the efficacy of soccer match-play simulations concluded that these simulations do not precisely represent the biochemical strains of an actual football match [50]. In response to these findings, da Silva and Lovell [51] designed and validated a 90-minute soccer-specific aerobic field test (T-SAFT^{90}), which mimics the mechanical and physiological, immune, endocrine and muscle damage responses of an actual 90-minutes football match. However, no study has adopted the T-SAFT^{90}-when examining alterations in risk factors of HSIs.

Therefore, investigating the immediate effects of ninety minutes of the TSAFT^{90}-generated fatigue-induced alterations in the risk factors for hamstring strain injuries might bring new insights for improving post-match recovery strategies and preparing optimal injury prevention programs for hamstring strains for football players. Therefore, this study aimed to explore the immediate alterations in the modifiable risk factors of HSIs [33] after TSAFT^{90} by measuring the SLHB performance, eccentric hamstring strength via handheld dynamometer, BFlh FL, and SLHD [40,46,47]. Additionally, the mean percentage of maximal heart rate (%HRmax) for every fifteen minutes of the 90-minute TSAFT^{90} simulated football match was measured as a secondary measurement.

The late-swing phase of running was pointed out as the most vulnerable time of the hamstring muscles [52–54]. At the late-swing phase of running, hamstrings eccentrically contract to decelerate the tibia and to control the antagonist quadriceps femoris muscles' concentric force [55]. The BFlh reaches 110% of its length at the late swing phase of running [56]. The HSIs most commonly occur when the muscle fascicles cannot resist an excessive elongation during the late-swing phase of running [57]. Therefore, shorter BFlh fascicles [40] and insufficient eccentric hamstring contractions were considered risk factors for HSIs [40,52,53].

It has recently been revealed the BFlh fascicles actively lengthen during eccentric contraction [58]. Additionally, it has previously been pointed out that hamstrings undergo elongations with eccentric contraction during the late-swing phase of running [56]. During this time, an excessive antagonist force higher than the eccentric force of the hamstrings elongates the hamstrings and can lead to damage and strains in BFlh fascicles [40,52,53]. Accordingly, a shorter BFlh fascicle length was defined as a risk factor for HSIs because of a possible lesser ability to be stretched and possible greater damage due to lesser sarcomeres in the series of the BFlh fascicles than longer fascicles during the eccentric muscle activation of the hamstrings [40]. A football match includes around 1687 metres of running and 170 metres of sprinting [59]. Based on these, the present study hypothesised that BFlh FL would increase after each half of the 90-minute TSAFT^{90} simulated football match due to exposure due to the repetitive eccentric elongation and a possible eccentric overload in the hamstrings muscles during a football match that may lead to potential damage in the hamstrings' muscle fascicles [40], which could negatively affect the shortening ability of the BFlh fascicles could lead increments in the length of the fascicles.

Regarding eccentric hamstring strength, previous studies either used a Nordic hamstring exercise execution device [10] or an isokinetic device [11,14,19,20,29] to assess eccentric hamstring strength and reported significant decreases after a football match intervention. Accordingly, the present research hypotheses that maximal eccentric strength and SLHB performance will significantly decrease after the simulated football match. Similarly, single-leg hop distance will decrease immediately after halftime and the full-time 90-minute TSAFT^{90} simulated football match due to fatigue-led strength decrements. Lastly, the %HRmax for every 15 minutes of simulated football intervention will increase throughout the time points.

4.2. Methodology

4.2.1. Study design

A quasi-experimental one-group repeated measures study design was used in the present study. Ethical approval was obtained from the local ethics committee of the School of Human and Behavioural Sciences at Bangor University (code: 2022–17105) according to the declaration of Helsinki (World Medical Association, 2013).

On the first day, the first BFlh FL measurements of the reliability assessments, approximately fifteen minutes of a warm-up, baseline measurements of SLHD via single-leg hop test, eccentric maximal hamstrings' strength via handheld dynamometer, and SLHB tests were completed for both thighs based on the given order in Figure 4.1. After at least two days of waiting, the TSAFT^{90} intervention was applied to the participants. Most recently, Bueno et al. [10] measured maximal eccentric hamstring strength with 24-hour separations between pre-test and post-test after a football match. However, the present study allowed a longer time (at least two days, mean: 5 days) to eliminate possible negative effects of the strength measurements on the post-test. Moreover, the soreness status of the hamstrings was requested from the participants before the second-day measurements, and if the participant mentioned any soreness in the hamstrings, the second-day measurement was postponed to a different day until the participant mentioned a full self-reported recovery of the hamstrings.

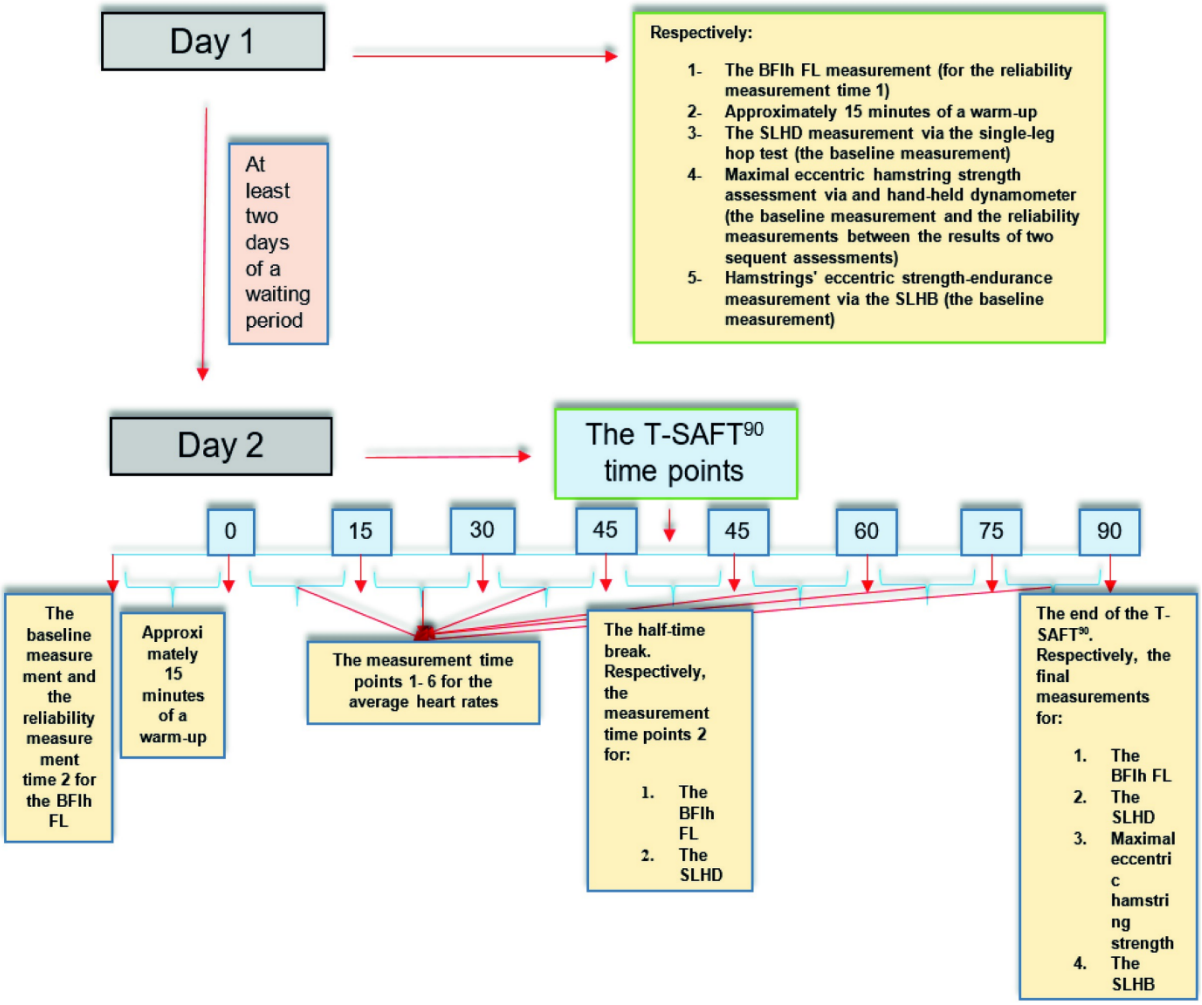

Figure 4.1. Study flow diagram. This diagram shows the actions taken in the first and second sessions of the study.

During the intervention day, baseline measurements of the BFlh FL for both thighs (which were also second measurements for inter-day intra-rater reliability assessments), approximately fifteen minutes of a warm-up, and ninety minutes of the TSAFT^{90} football simulations were implemented corresponding to the order given in Figure 5.1. At the half-time of the TSAFT^{90}, the BFlh FL and the SLHD were respectively measured for the second time for both thighs (Figure 4.1) After the ninety minutes of the TSAFT^{90} intervention, the BFlh FL (third and final measurement), the SLHD (third and last measurement), eccentric maximal hamstring strength (second and final measurement), and the SLHB (second and final measurement) were measured for both thighs based on the order given in Figure.4.1. For detecting the immediate effects of the simulated football match, all the second-day measurements were completed less than five minutes after half-time and less than ten minutes after full-time, according to the order given in Figure 4.1. Additionally, the %HRmax of each

15 minutes of the 90 minutes of football simulation was calculated. The tests were completed by the first author (GY), an experienced sports physiotherapist in the use of ultrasonography for muscle structure assessments, strength measurements via handheld dynamometry, and SLHB test measurements.

4.2.2. Sample size

The required sample size for this study was calculated using G*Power software version 3.1.9.7 [60]. Effects size (ES = 1.10) was referred from a recent study [10] that investigated the effects of a 90-minutes soccer match on eccentric hamstring strength. However, to ensure the required sample size, the present study chose a 0.5 effect size during the sample size calculation. Additionally, the following parameters were utilised during the sample size calculation: 0.05 alpha level, 0.80 power, one group, two measurement points, 0.5 correlation among repeated measurements, and one epsilon value that represents the level of sphericity and accepted as 1 for one group repeated measures design. As a result, the required quantity of sample size was calculated as ten participants. However, this study aimed to recruit at least fifteen participants to increase statistical power.

Reliability studies require a different sample size calculation from the one-group repeated measures design sample size calculation above. The required sample size was calculated in light of the intraclass correlation (ICC) value (BFlh FL= 0.98 [61]) for the manual linear extrapolation method (MLE), and the lowest single measure ICC (SIMC = 0.837 [47]) value for the same methodology with this study for the maximal eccentric hamstring strength measurement via handheld dynamometry. However, this study chose an ICC value of 0.8 to ensure an adequate sample size for the reliability study. Afterwards, the required sample size was calculated as 7 for two measurements, 0.05 alpha level and 0.80 power, by following the guideline of Bujang and Baharum [62]. However, this study aimed to measure all fifteen participants to minimise the adverse effects of possible dropouts or measurement errors.

4.2.3. Participants

Physically active male participants were recruited via advertisements, e-mail and verbal announcements. Inclusion criteria were considered as a) being male, physically active, healthy and habitually performing at least 75 minutes of vigorous-intensity or 150 minutes of moderate-intensity exercise per week [63], which was assessed via the International Physical

Activity Questionnaire short form (IPAQ-sf) [64], b) being free from an acute lower extremity injury, c) being at least 18 years old and maximum 39 years old.

The intervention and testing procedures were verbally explained to the participants before the intervention, and written informed consent was provided to participants on the intervention day. Participants were asked to fill and sign the required forms, e.g. questionnaires and informed consent, before the study. Moreover, participants were advised not to perform exhaustive exercises 48 hours before the TSAFT^{90} intervention and tests [29].

4.2.4. Simulated soccer match protocol (TSAFT^{90})

da Silva and Lovell [51] recently designed the TSAFT^{90} soccer simulation, which includes technical and jumping activities as an addition to the SAFT^{90}, and they validated that TSAFT^{90} mimics mechanical and physiological, immune, endocrine and muscle damage responses of a 90-minutes soccer match. The additional technical activities of TSAFT^{90} include passes, shoots, and ball drilling [51]. The T-SAFT^{90} consists of six random and intermittent activities within a 15-minute period completed three times for each of two 45-minute halves and separated by 15 minutes of a passive resting period, representing a 90-minute soccer match [65]. Performing the activities and arranging the intensity of the activities were maintained via an audio file containing verbal signals obtained from da Silva and Lovell [51].

4.2.5. Warm-up

Approximately fifteen minutes of a warm-up program was performed after BFlh FL measurements on both study days (Figure 4.1). This warm-up program was completed on a 20-m shuttle on a football pitch. It consisted of twelve football-related exercises: light jogging, side stepping, backwards jogging, forward and backwards skipping with arm circles, jumping jacks, high kicks, high knees, dynamic hamstring stretching, walking lunges, sprints, and high knees at higher speeds.

4.2.6. Testing procedures

Before starting the assessments, participants' height (cm) and body mass (kg) were recorded. The preferred leg for kicking the ball was accepted as the dominant leg. The study procedures were explained verbally, visually and in writing to the participants before the

baseline tests and intervention. The testing order and times are defined in the study design section and illustrated in Figure 4.1. The sequencing of the legs was left to right during all the measurements.

To increase commitment during the single-leg hop test, eccentric maximal hamstrings' strength measurement and the SLHB test, it was announced to the participants before the tests that certain cash prizes would be given to the first three average scores of the pre- mid- and post-tests of both legs.

4.2.6.1. Biceps femoris long head fascicle length measurement

A two-dimensional B-mode ultrasound (US) (Esaote, MyLab 50, the Esaote Group, Genova, Italy) was used to measure the BFlh FL for the dominant and non-dominant limbs of the participants. Participants laid prone on a standard medical bed, as shown in Figure 4.2A [66], and were asked not to perform any voluntary muscle contractions during the measurements. Two US images of the BFlh FL were taken from the mid-point distance between the popliteal crease and the trochanter major when the BFlh was passive [40,66] (Figure 4.2A). Previously, the passive BFlh FL was defined as a risk factor for HSIs [40]. Therefore, this study measured the BFlh FL without voluntary contraction, namely at a passive position, as previously described [40].

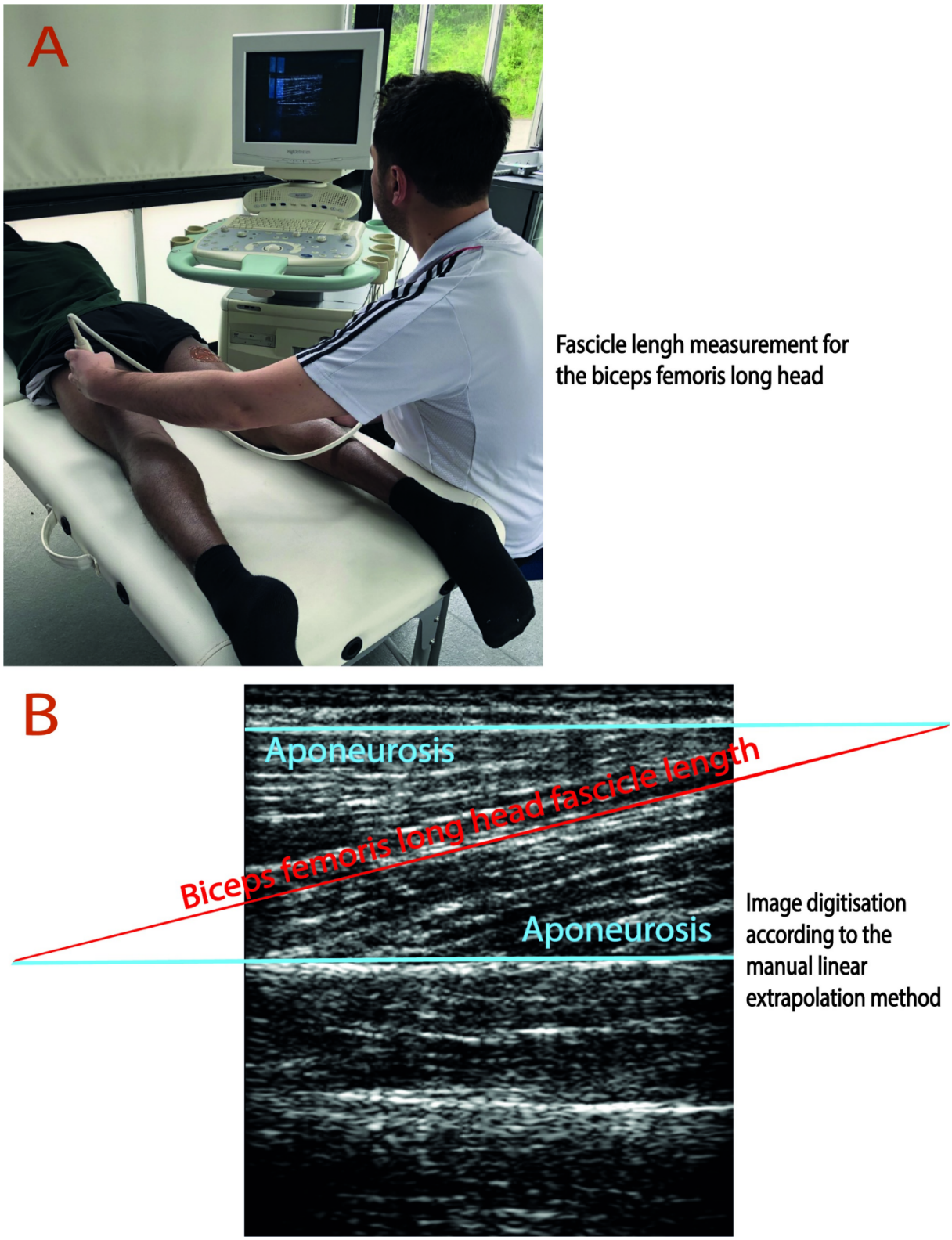

Figure 4.2. The biceps femoris long head fascicle length measurement and digitisation. A: 2-dimensional ultrasound images were taken from the mid-thigh for both legs. B: Digitisation for the biceps femoris long head fascicle length according to the manual linear extrapolation

method. The individual pictured in Figure 4.2. has provided written informed consent (as outlined in the PLOS consent form) to publish their image alongside the manuscript.
US measurement was performed using a linear array ultrasound probe (LA523E, 7.5–12 MHz, the field of view: 5 cm depth x 4.7 cm width) (Figure 4.2A). During the measurements, a minimum pressure was applied to minimise the possible effects of the pressure on the BFlh FL measurements [67]. Firstly, the US probe was placed transverse to the BFlh to monitor the cross-sectional area of the BFlh. After ensuring the correctness of the location of the BFlh, the US probe was turned in a parallel orientation with the BFlh muscle orientation. At this position, slight ultrasound probe adjustments were applied to visualise the aponeuroses. Then, two longitudinal BFlh muscle architecture images were taken (Figure 4.2A) The mean values for the BFlh FL of these two images were calculated as the fascicle length [68]. External markers (e.g. scars, freckles and the distance of the features to the measurement points) [69] and internal markers (subcutaneous adipose tissue and markers between fascicles) [70] of the first US measurements were referred to ensure the reproducibility and correctness of the measurement places of the BFlh FL in the sequent assessment time points.

The ImageJ software (ImageJ, National Institutes of Health, Bethesda, Maryland, USA) was used for calculating the length of the BFlh FL by using the MLE method described by Potier et al. [68]. Before the ImageJ calculations, the architectural features of the BFlh were drawn using Adobe Illustrator software, which was also previously used for scientific digitisations [71,72], according to the MLE method [68]. The superficial and intermediate aponeuroses were drawn and extended over their visible lengths (Figure 4.2B) Then, the visible part of the BFlh FL was drawn and extended until reaching the extensions of the aponeuroses (Figure 4.2b). After setting the scale of the measurement units in the ImageJ software, the BFlh FL was calculated as the mean of the two US pictures for each assessment. Additionally, the BFlh FL measurement reliability assessment was performed for both legs between the BFlh FL measurements in the first session and baseline measurements in the second session.

4.2.6.2. Eccentric hamstring strength measurement

Hamstrings' maximal eccentric strength was measured using a handheld dynamometer (CSD 300 Strength Dynamometer, Chatillon, Largo, Florida) following the protocol suggested by Goossens et al. [47]. Participants laid down in a prone position on a standard medical bed for the test. The knee-joint angles were measured by using a goniometer. Participants' legs were positioned at the start position (Figure 4.3A), and the participants were asked to hold and

resist the pressure applied by the assessor via the handheld dynamometer (Figure 4.3A and 4.3B). Additionally, participants were informed that the assessor would eventually pull the lower leg down [47] (Figure 4.3B). For each leg, two measurements were completed, and the highest measure was accepted as the maximal eccentric strength of the hamstrings [47]. Additionally, using the results of the two measurements, intra-tester reliability was assessed. The starting point of the measurement (Figure 4.3A) and the finishing point of the assessment (Figure 4.3B) are shown in Figure 5.3. Each test was finished in about five seconds, and the tester accordingly applied pressure to allow the participants to produce their maximal eccentric hamstring force in a similar time and similar velocity.

Figure 4.3. Hamstrings' eccentric maximum strength measurements by handheld dynamometry. The hip joints were neutral (0 degrees of hip extension) during the measurements. A: The starting point of the measurement was when the knee was approximately 60º flexed and when the handheld dynamometer was on the two centimetres proximal to the malleolus of the ankle. B: The ending position of the hamstrings' maximum eccentric strength measurement. The individual pictured in Figure 4.3 has provided written informed consent (as outlined in the PLOS consent form) to publish their image alongside the manuscript.

4.2.6.3. Single-leg hamstring bridge performance

The capacity of repetitive high-force production of the hamstrings was assessed using the SLHB test, as suggested by Freckleton and colleagues [46]. The single-leg hamstring bridge test is a reliable test [73,74] and mimics the functional capacity of the hamstring as similar to the late swing phase of running [46].

To perform the single-leg hamstring bridge test, participants laid down on the floor and put one heel on a box at 60 cm height [46]. The arms of the participants were crossed on their chests [46]. The leg, which would be tested, was at around twenty degrees of knee flexion as defined previously [46]. Then, participants pushed down their tested heels and lifted their bottoms off the floor [46]. Participants were asked to maintain the movements by touching the ground by their bottom and reaching 0º of hip extension by lifting their bottom without resting [46]. The other leg was in a vertical position as stationary to eliminate any momentums that might be provided by swinging the leg [46]. Participants were advised to aim to do as much as possible to repeat the same movement until failure [46]. Feedback was given consistently to ensure the correct technique's achievement over the test [46]. In the case of losing the proper form, participants were warned once, and a subsequent fault in the technique led to the ceasing of the test [46]. Maximum repetitions were recorded as the outcome of the tested leg, and the same test was applied to the other leg [46]. The SLHB testing position has illustrated the Figure 5.4.

Figure 4.4. Single Leg Hamstring Bridge (SLHB) test. Participants were asked to perform movements by touching the ground by their bottom and reach 0º of hip extension by lifting

their bottom respectively and without resting with the help of a 60-cm high box. The other leg was in a vertical position as inactive and stationary to eliminate any momentums that might be provided by swinging the leg. Participants were advised to aim to perform as much as they could repeat the same movement until failure. The individual pictured in Figure 4.4 has provided written informed consent (as outlined in the PLOS consent form) to publish their image alongside the manuscript.

4.2.6.4. Single-leg hop distance measurement

The SLHD measurements were completed via the single-leg hop test by following the instructions of Goossens et al. [47], who modified the hop test described by Munro and Herrington [75]. Participants performed three successful single-leg jumps as far as possible, maintaining the landing position on the same footprint for three seconds. Subsequently, each leg's best scores were accepted as the single-leg hop distance [47]. During the test, the usage of arms was not restricted, and participants wore sports shoes [47].

4.2.6.5. The mean percentage of maximal heart rate

The %HRmax was measured every 15 minutes of the TSAFT^{90} by using a heart rate tracking system (Activio Telemetry Heart Rate System, Activio International AB, Bastad, Sweden).

4.2.7. Statistical analyses

Primary statistical analyses of the results were performed using the SPSS software (IBM Corporation, Chicago, Illinois). Participants' characteristics (age, height and weight) were given in means and standard deviations. One-way repeated measures ANOVA and Bonferroni posthoc test were employed for analysing the following dependent variables: %HRmax, the BFlh FL, eccentric maximal hamstring strength, the SLHB score and the SLHD variables for one group and between two to six measurement points depending on the variable. The ICC values were calculated for two-way random, absolute agreements for single measures for the reliability analyses [76]. It has been interpreted that an ICC value less than 0.5 indicate poor reliability, an ICC value between 0.5 and 0.75 represents moderate reliability, an ICC value between 0.75 and 0.9 means high reliability, and an ICC value over 0.9 is indicative of very high reliability [77]. Moreover, the Hedges' (adjusted) *g* effect sizes were automatically calculated for one group repeated measures design by entering the means and SDs of the pre-tests and post-tests, correlations between pre-tests and post-tests, and sample size to the

Comprehensive Meta-Analysis software (CMA, version 3.0, Biostat, Englewood, New Jersey) [78]. The main difference between Hedges' (adjusted) *g* and Cohen's d is the better estimation of Hedges' g by adjusting potentially biased estimates than Cohen's d for sample sizes smaller than twenty participants [79]. The Hedges' g effect sizes were interpreted as small (0.2), medium (0.5) or large (0.8) [80].

4.3. Results

Eighteen participants were initially recruited. One participant did not meet the inclusion criteria. Two participants did not attend the second session of the study. In short, seventeen participants attended the first session. However, only fifteen participants completed the study (n = 15, age = 25.73 ± 5.98 years, height = 172.45 ± 5.17 cm, weight = 72.27 ± 7.22 kg). The dominant leg was detected as the right side in all participants. Participants mentioned that they perform weekly 7.14 ± 5.07 hours of vigorous physical activity and 5.18 ± 3.14 years of sports-specific training history (from recreationally active to a professional level: eight participants were football players, two participants were cricket players, one participant was a sprinter, one participant was a boxer, one participant was a kickboxer, one participant was a volleyball player, one participant was a kayaker). None of the participants mentioned a lower extremity injury history.

4.3.1. The mean percentage of maximal heart rate

One participant's %HRmax measurement was not completed due to a technical error. Therefore, the %HRmax measurements were completed for fourteen participants every fifteen minutes throughout the ninety minutes TSAFT^{90} football simulation. Based on the results, the %HRmax of the last 15 minutes of the TSAFT^{90} was significantly higher than the rest of the time points, and there was no significant difference between the rest of the measurement time points (Figure 4.5).

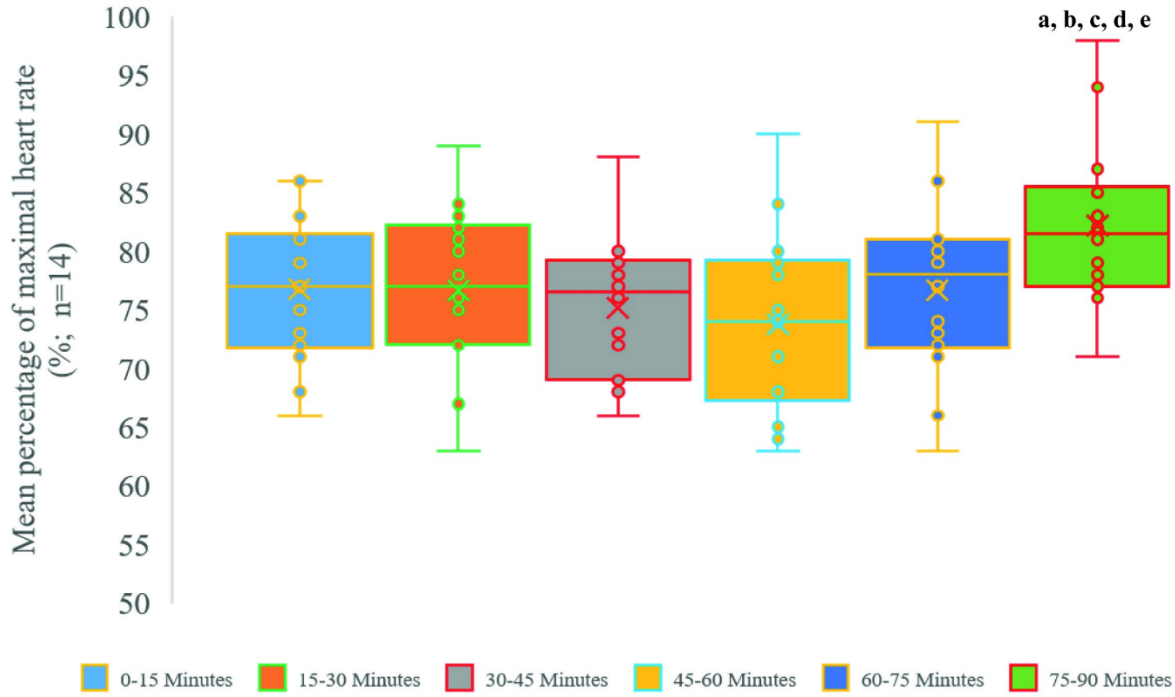

Figure 4.5. Box & Whisker plots show the mean percentage of maximal heart rate of each fifteen minutes across ninety minutes of the TSAFT^{90} football simulation. The first box with blue colour represents the mean percentage of maximal heart rate of 0–15 minutes, the second box with the orange colour indicates the mean percentage of maximal heart rate of 15–30 minutes, the third box with grey colour refers to the mean percentage of maximal heart rate of the 30–45 minutes, the fourth box with yellow colour points out the mean percentage of maximal heart rate of the 45–60 minutes, the fifth box with navy blue colour demonstrates the mean percentage of maximal heart rate of the 60–75 minutes, and the sixth box with green colour shows the mean percentage of maximal heart rate of the 75–90 minutes of the TSAFT^{90} football simulation. Abbreviations: a, significantly higher than 0–15 minutes ($p = 0.021$); b, significantly higher than 15–30 minutes ($p = 0.014$); c, significantly higher than 30–45 minutes ($p < 0.001$); d, significantly higher than 45–60 minutes ($p = 0.001$); e, significantly higher than 60–75 minutes ($p = 0.013$). Abbreviations: n, sample size.

4.3.2. Alterations in the biceps femoris long head fascicle length

For both thighs, BFlh FL measurements showed very high-reliability results (n = 15, dominant ICC = 0.982, 95% CI [0.946, 0.994], percentage coefficient of variation (CV %) = 2%; non-dominant ICC = 0.987, 95% CI [0.961, 0.995], CV % = 1.7%) (Figure 4.6). However, no significant differences were detected between measurement time points for both legs' BFlh FL and the average BFlh FL of the legs due to the ninety minutes TSAFT^{90} simulation (Table 4.1).

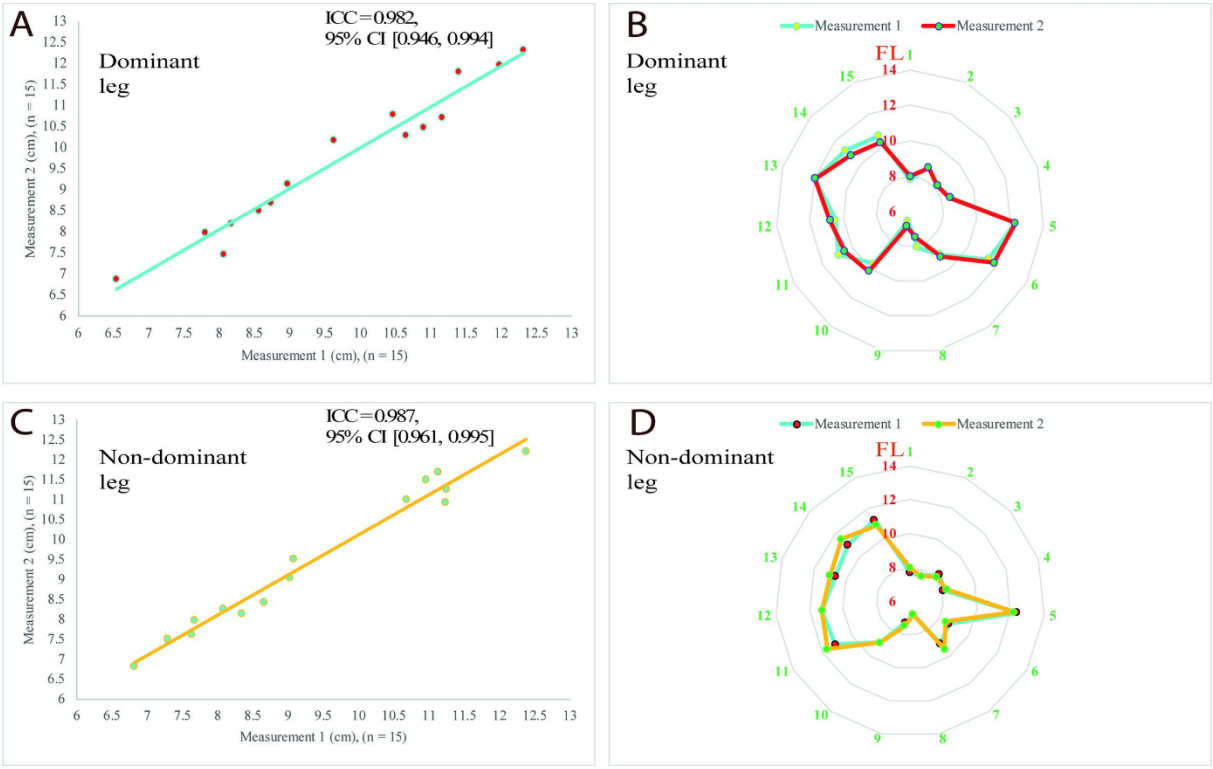

Figure 4.6. Reliability results of the biceps femoris long head fascicle length measurements for both legs. A: Scatter plots with a regression line for the dominant leg reliability measurements, B: Radar chart for the dominant leg reliability measurements shows agreements between measurements for each participant from 1 to 15, C: Scatter plots with a regression line for the non-dominant leg reliability measurements, D: Radar chart for the non-dominant leg reliability measurements shows agreements between measurements for each participant from 1 to 15. Abbreviations: CI, confidence interval; FL, fascicle length; ICC: Intraclass correlation coefficient; n, sample size.

Table 4.1. Alterations in the biceps femoris long head fascicle length (n = 15).

Thigh	Baseline (mean ± SD) (cm)	Half-time (mean ± SD) (cm)	Full-time (mean ± SD) (cm)	Mean ± SD change (half-time vs baseline) (cm)	Mean ± SD change (full-time vs baseline) (cm)	Mean ± SD change (full-time vs half-time) (cm)	p-value (half-time vs baseline)	p-value (full-time vs baseline)	p-value (full-time vs half-time)	Effect size (half-time vs baseline) (Hedges' (adjusted) *g*)	Effect size (full-time vs baseline) (Hedges' (adjusted) *g*)	Effect size (full-time vs half-time) (Hedges' (adjusted) *g*)
Dominant	9.69 ± 1.71	9.76 ± 1.49	9.82± 1.75	0.07 ± 0.85	0.13 ± 0.81	0.06 ± 0.94	**p = 1.0**	**p = 1.0**	**p = 1.0**	**0.044 (trivial)**	**0.07 (trivial)**	**0.03 (trivial)**
Non-dominant	9.46± 1.80	9.53 ± 1.76	9.57 ± 1.65	0.07 ± 0.87	0.11 ± 0.8	0.04 ± 0.97	**p = 1.0**	**p = 1.0**	**p = 1.0**	**0.037 (trivial)**	**0.058 (trivial)**	**0.021 (trivial)**
Average of both	9.57 ± 1.66	9.65± 1.4	9.69 ± 1.61	0.08 ± 0.7	0.12 ± 0.63	0.04 ± 0.6	**p = 1.0**	**p = 1.0**	**p = 1.0**	**0.044 (trivial)**	**0.07 (trivial)**	**0.027 (trivial)**

Abbreviations: n, Sample size; N, Newton; SD, Standard Deviation.

4.3.3. Changes in the maximal eccentric hamstring strength

High to very high-reliability results were observed for the maximal eccentric hamstring strength by the handheld dynamometry for both legs (n = 17, dominant ICC = 0.947, 95% CI [0.862, 0.981], CV % = 2.1%; non-dominant ICC = 0.95, 95% CI [0.868, 0.982], CV % = 2.8%) (Figure 4.7). There were significantly large reductions in the maximal eccentric hamstring strength for both legs and the average of both legs following the 90 minutes TSAFT^{90} simulation ($p < 0.001$, g = from -0.969 to 0.929) (Table 4.2).

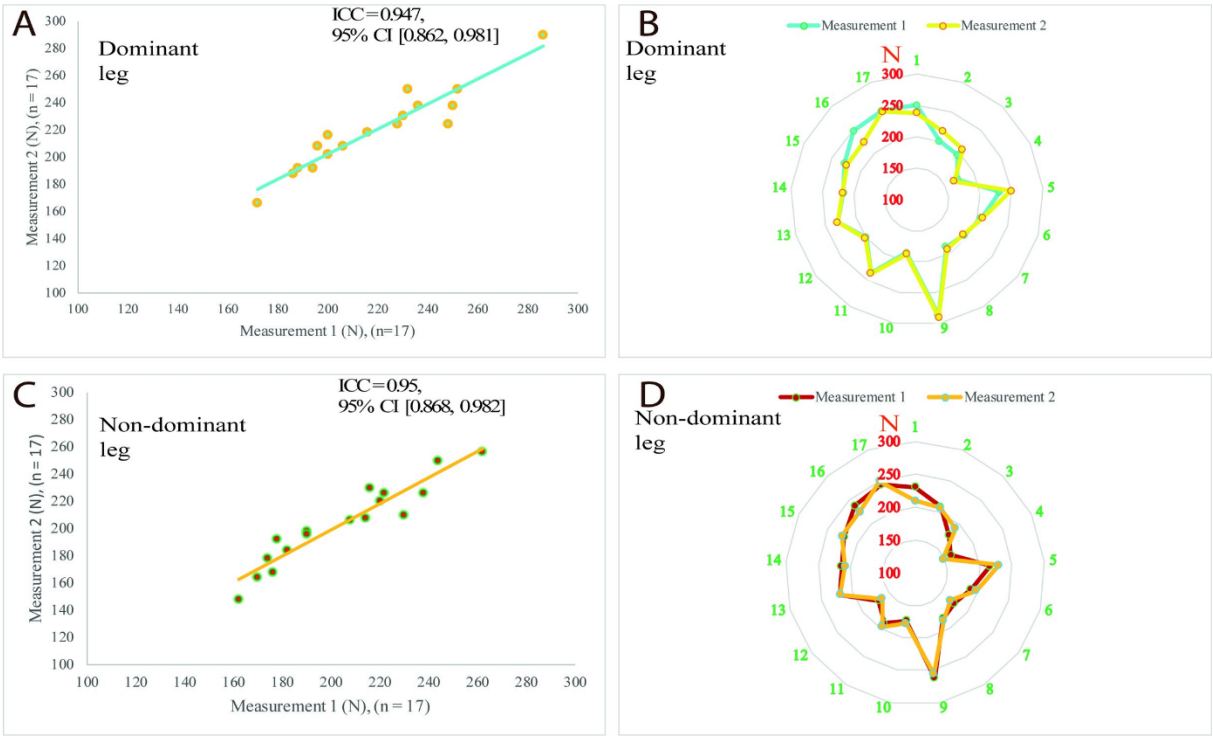

Figure 4.7. Reliability results from the maximal eccentric hamstring strength measurements for both legs via handheld dynamometry. A: Scatter plots with a regression line for the dominant leg reliability measurements, B: Radar chart for the dominant leg reliability measurements shows agreements between measurements for each participant from 1 to 17, C: Scatter plots with a regression line for the non-dominant leg reliability measurements, D: Radar chart for the non-dominant leg reliability measurements shows agreements between measurements for each participant from 1 to 17. Abbreviations: CI, confidence interval; ICC: Intraclass correlation coefficient; N, Newton; n, sample size.

Table 4.2. Changes in the eccentric maximal hamstring strength were measured by handheld dynamometry (n = 15).

Thigh	**Baseline (mean ± SD) (N)**	**Full-time (mean ± SD) (N)**	**Mean ± SD change (full-time vs baseline) (N)**	**p-value**	**Effect size (full-time vs baseline) (Hedges' (adjusted) *g*)**

Dominant	219 ± 25	179 ± 42	-40 ± 31	**p < 0.001**	**-0.969 (large)**
Non-dominant	206 ± 25	165 ± 43	-41 ± 30	**p < 0.001**	**-0.929 (large)**
Average of both	213 ± 25	172 ± 42	-41 ± 30	**p < 0.001**	**-0.952 (large)**
Abbreviations: n, Sample size; N, Newton; SD, Standard Deviation.					

4.3.4. Alterations in the single-leg hamstring bridge test performance

There were significantly large reductions in the SLHB performance based on the SLHB scores for both legs and the average of both legs ($p < 0.001$, g = from -1.249 to -1.108) (Table 5.3).

Table 4.3. Alterations in the SLHB performance (n = 15).

Thigh	**Baseline (mean ± SD) (reps)**	**Full-time (mean ± SD) (reps)**	**Mean ± SD change (full-time vs baseline) (reps)**	**p-value**	**Effect size (full-time vs baseline) (Hedges' (adjusted) *g*)**
Dominant	29 ± 6	20 ± 7	-9 ± 4	**p < 0.001**	**-1.249 (large)**
Non-dominant	27 ± 6	19 ± 6	-8 ± 4	**p < 0.001**	**-1.108 (large)**
Average	28 ± 6	19 ± 7	-9 ± 4	**p < 0.001**	**-1.193 (large)**
Abbreviations: n, Sample size; reps, repetitions; SD, Standard Deviation; SLHB, Single-leg hamstring bridge test.					

4.3.5. Alterations in the single-leg hop distance

No significant differences were observed between measurement time points of the SLHD for both legs and the average SLHD results due to the ninety minutes TSAFT^{90} simulation (Table 5.4).

Table 4.4. Changes in single-leg hop distance (n = 15).

Leg	Baseline (mean ± SD) (cm)	Half-time (mean ± SD) (cm)	Full-time (mean ± SD) (cm)	Mean ± SD change (half-time vs baseline) (cm)	Mean ± SD change (full-time vs baseline) (cm)	Mean ± SD change (full-time vs half-time) (cm)	p-value (half-time vs baseline)	p-value (full-time vs baseline)	p-value (full-time vs half-time)	Effect size (half-time vs baseline) (Hedges' (adjusted) *g*)	Effect size (full-time vs baseline) (Hedges' (adjusted) *g*)	Effect size (full-time vs half-time) (Hedges' (adjusted) *g*)
Dominant	184 ± 27.67	187.8 ± 20.33	188.4 ± 22.95	3.8 ± 13.39	4.4 ± 12.68	0.6 ± 7.19	**p = 0.871**	**p = 0.601**	**p = 1.0**	**0.127 (trivial)**	**0.153 (trivial)**	**0.024 (trivial)**
Non-dominant	180.01 ± 22.59	180.14 ± 23.38	179.17 ± 24.81	0.13 ± 14.81	-0.85 ± 12.45	-0.97± 11.54	**p = 1.0**	**p = 1.0**	**p = 1.0**	**0.005 (trivial)**	**-0.033 (trivial)**	**-0.038 (trivial)**
Average of both	182 ± 24.05	183.57 ± 21.37	183.78 ± 22.51	1.57 ± 10.27	1.78 ± 9.61	0.21 ± 7.05	**p = 1.0**	**p = 1.0**	**p = 1.0**	**0.063 (trivial)**	**0.071 (trivial)**	**0.009 (trivial)**

Abbreviations: n, Sample size; SD, Standard Deviation.

4.4.Discussion

To the authors' knowledge, this study is the first study that examined changes in the SLHD and the BFlh FL throughout a ninety minutes simulated football match. Additionally, this study differs from the previous simulated football studies in terms of methods of maximal eccentric hamstring strength and the SLHB performance measurements by using predictive methods for HSIs [46, 47]. There were no significant alterations in the SLHD and BFlh FL after 45 minutes and 90 minutes of $TSAFT^{90}$. However, the $TSAFT^{90}$ simulated football match led to significantly large decrements in the maximal eccentric strength. Additionally, the mean percentage of maximal heart rate was significantly higher in the last fifteen minutes of the simulated football match than in the rest of the measurement points.

The passive BFlh FL is defined as the architectural risk factor for future HSIs [40]. In addition to this, there was no study that examined alterations in the architectural risk factor of HSIs after ninety minutes of a football match. Therefore, this study aimed to observe whether there would be an alteration in the architectural risk factor of the HSIs or not. It has been stated that BFlh fascicles actively lengthen during eccentric contraction [58]. However, the effects of eccentric training on the BFlh FL are controversial depending on the ultrasound measurement methods [81-84]. This contradiction could be caused by the absence of a gold standard for the BFlh FL measurements [61], which might be a limitation of the present study. Regarding the immediate effects of playing football on the BFlh FL, Gonçalves (2017) [85] examined the influence of a forty-five minutes football simulation ($SAFT^{45}$) on the BFlh FL. They detected no changes in the fascicle length; however, no study has investigated alterations in the BFlh FL following ninety minutes of simulated or an actual football match. Accordingly, this study confirms the findings of Gonçalves (2017) [85] that there are no changes in the BFlh FL after forty-five minutes of a simulated football match and adds that there are no alterations in the BFlh FL after ninety minutes of the $TSAFT^{90}$ football

simulation. Future studies can examine the association between football-induced fatigue and BFlh fascicles' lengthening-shortening ability.

From the perspective of changes in maximal eccentric hamstring strength and hamstrings' SLHB performance parameters, the present study reported large reductions (g = from -0.969 to -0.929) after the ninety minutes of a TSAFT^{90} football simulation. Moreover, this study detected larger reductions in the hamstrings' strength qualities measured by the SLHB test (g = from -1.249 to -1.108) compared with maximal eccentric strength reductions measured via handheld dynamometry (g = from -0.969 to -0.929). Similarly, Bueno et al. (2021) [10] have recently observed large decrements in hamstrings' eccentric strength after a real football match (Cohen's d = -1.1). The present study confirms the findings of Bueno et al. (2021) [10].

Based on the results of the present study, both hamstrings' capacity to produce repetitive high force and maximal eccentric hamstrings strength showed large decrements after performing the TSAFT^{90} football simulation. However, decrements in the SLHB scores were relatively higher than the decrease in their maximal eccentric strength. The SLHB is a test that uses a constant external force obtained by a portion of the participant's body weight and assesses maximum repetitions against the same force. The SLHB test could represent hamstrings' repetitive high force production capacity rather than the maximal eccentric strength or eccentric peak torque. Improving hamstrings' repetitive high-force production capacity via the SLHB should be targeted together with improving the hamstrings' eccentric strength in the vulnerable population of athletes for HSIs.

This study used the MLE method for calculating the BFlh FL. The MLE method did not significantly differ from panoramic ultrasound scanning, while trigonometric equations were significantly overestimating the BFlh FL [61]. Nevertheless, using the MLE method can be considered a limitation of this study due to the absence of a "gold standard" method for BFlh FL measurements in the literature. Another confounding factor might be not only including

professional football players in the study. Despite the high to very high intra-tester reproducibility of maximal eccentric strength measurements of the present study, using a handheld dynamometer can be another limitation because of its user dependence which requires experience and high physical power; these requirements might lead to inter-tester differences. Additionally, the TSAFT^{90} interventions were completed in outdoor conditions, which can add uncountable variability to the results. However, the outcome measurements were conducted under indoor conditions in the same room. The football simulation interventions of this study were completed on weekdays between the 13th of May 2022 and the 17th of June 2022, when the highest daytime temperatures of weekdays were retrospectively analysed, it was seen that the mean temperature was 15.9 ± 1.3 degrees, the minimum temperature was 13 degrees of Celsius, and maximum temperature was 18 degrees of Celsius based on the previous meteorology records of www.accuweather.com. However, not recording environmental factors during the TSAFT^{90} interventions is a limitation of this study. Future studies are needed to clarify whether environmental factors alter the outcome measures of this study or not.

4.5.Conclusions

The ninety minutes of the TSAFT^{90} football simulation leads to large decrements in the hamstrings' maximal eccentric strength and the SLHB performance in both legs. However, the TSAFT^{90} football simulation doesn't significantly alter the passive mid-BFlh FL and doesn't alter the single-leg hop distance after half-time and full-time of the match. Therefore, scientists, conditioners, physiotherapists etc., should focus on improving hamstrings' eccentric strength and repetitive high-force production ability via the SLHB. Future studies can examine changes in lengthening-shortening abilities of the BFlh FL during a ninety minutes football match to bring insights into the prevention strategies of the HSIs.

Chapter 5. Systematic Review with Meta-analyses 2.

The Effects of Resistance Training on Architecture and Volume of the Upper Extremity Muscles: A Systematic Review of Randomised Controlled Trials and Meta-Analyses.

A version of this chapter has been published in the peer-reviewed journal "Applied Sciences"

Yagiz G, Akaras E, Kubis H-P, Owen JA (2022) The Effects of Resistance Training on Architecture and Volume of the Upper Extremity Muscles: A Systematic Review of Randomised Controlled Trials and Meta-Analyses. Applied Sciences 12:1593

Abstract

To systematically review the effects of exercise on fascicle geometry and muscle size parameters of the upper extremity muscles, the CENTRAL, CINAHL, PubMed and OpenGrey databases were searched on 31 July 2021. Finally, 17 randomised controlled trials (RCTs) were included in this systematic review. High-intensity bench press training (g = 1.03) and 12 RM bench press exercises (g = 1.21) showed a large effect size on increasing pectoralis major muscle size. In the elbow extensors, large effects were reported for an increase in muscle size with isometric maximal voluntary co-contraction training (g = 1.97), lying triceps extension exercise (g = 1.25), and nonlinear periodised resistance training (g = 2.07). In addition, further large effects were achieved in the elbow flexors via traditional elbow flexion exercises (g = 0.93), concentric low-load forearm flexion-extension training (g = 0.94, g = 1), isometric maximal voluntary co-contraction training (g = 1.01), concentric low-load forearm flexion-extension training with blood flow restriction (g = 1.02, g = 1.07), and nonlinear periodised resistance training (g = 1.13, g = 1.34). Regarding the forearm muscles, isometric ulnar deviation training showed a large effect (g = 2.22) on increasing the flexor carpi ulnaris and radialis muscle size. Results show that these training modalities are suitable for gaining hypertrophy in the relevant muscles with at least four weeks of training duration. Future RCTs should investigate the effects of exercise modalities on the triceps brachii fascicle geometry, the infraspinatus muscle thickness (MT) and the subscapular MT due to their associations with sports performance.

5.1. Introduction

Training-induced muscle adaptations are one of the core elements in training strategies for players, coaches, sports teams, sports federations or non-athletes. The number of studies focusing on muscle architecture has increased due to increasing access to technology for non-invasive muscle visualisation methods, e.g., magnetic resonance imaging (MRI) and ultrasound measurements. For example, investigating relationships between muscle architectural parameters and sports performance, muscle strength or sports injuries, and adaptations resulting from training, detraining, bed rest or micro-gravity has received attention from researchers. Approximately 65% of PubMed database records containing the term "muscle architecture" have been published in the last decade (Supporting table 3.1).

The term muscle architecture has a broad definition in the literature and includes the anatomical cross-sectional area (ACSA) and physiological cross-sectional areas (PCSA) of muscles, fascicle length (FL), muscle thickness (MT), muscle length and pennation angle (PA) [1]. These skeletal muscle architectural parameters identify the functional traits of a muscle [2]. Studies revealed that muscle architectural parameters are predictors of strength [3,4,5,6,7,8,9,10,11,12,13,14], athletic performance [15,16,17,18,19,20,21,22,23,24,25,26] and athletic injuries [27,28,29,30,31,32,33,34].

The upper extremity muscles include muscles involving shoulder joint movements, e.g., rotator cuff muscles, the pectoralis major muscle, and the deltoid muscle; arm muscles, e.g., biceps brachii and triceps brachii; forearm muscles, e.g., flexor and extensor carpi ulnaris, flexor and extensor carpi radialis; and hand and wrist muscles, such as palmaris brevis, lumbrical muscles, hypothenar and thenar muscles [35]. Muscle size parameters of the upper extremity muscles are strongly correlated with better lifting ($r = 0.77–0.91$) [17], swimming ($r = −0.56$) [36], rowing ($r^2 = 0.195$) [37], and shot put performances ($r = 0.68$) [38]. Additionally, the upper extremity muscle sizes are significantly correlated with the upper extremity strength parameters such as elbow joint torque ($r = 0.705–0.945$) [39], elbow flexion maximal power ($r = 0.81$) [40], elbow extensor strength ($r = 0.7–0.78$) [41], finger extension force ($r_s = 0.85$) [42], bench press strength ($r = 0.866$) and bench throw peak power ($r = 0.821$) [43], and shoulder external rotation strength ($r = 0.287$) [44]. Regarding the upper extremity muscles' fascicle geometry, the triceps brachii FL is one of the best predictors of better 200 -m front crawl swimming time ($r^2 = 0.392$) [36] and significantly correlated with better swimming ($r = −0.64$)

[36] and lifting performances (r = 0.45–0.52) [17]. The triceps brachii PA was significantly correlated with elbow extension strength parameters (r = 0.471–0.563) [45].

Training-induced muscle architectural changes may depend on the exercise's contraction type. Eccentric (lengthening) and concentric (shortening), and isometric training can lead to comparable hypertrophic responses in skeletal muscles [46,47]. Kawakami et al. [48] noted muscle size increments are accompanied by pennation angle increases in hypertrophied muscles. By comparison, Franchi, Reeves, and Narici [46] highlighted that the underlying myogenic and molecular responses might be different in eccentric and concentric muscle actions because eccentric training is considered to favour increases in fascicle length, and concentric training to favour higher increments of pennation angle [46]. A recent study by Pincheira et al. [49] showed that eccentric training could increase fascicle length by increasing sarcomere lengths. Another study stated that concentric, eccentric and isometric exercises could lead to similar increases in total DNA and RNA quantities, which are representative of muscle hypertrophy; however, concentric and isometric training increases muscle insulin-like growth factor 1 mRNA levels, whereas eccentric training does not increase these levels [46]. In short, there may be different underlying myogenic and molecular mechanisms of different training-induced muscle adaptations depending on the contraction type.

In consideration of the importance of the architectural parameters of upper extremity muscles for strength, power, rate of force development and sports performance, screening training-induced adaptations in the architecture of the upper extremity muscles may be a reference point for future training and conditioning directions for both athletes and non-athletes who target the upper extremities. Therefore, this systematic review with meta-analyses aimed to screen and reveal the effects of exercise on all available upper extremity muscles' volumes and architectural parameters that include fascicle geometry and muscle size variables.

5.2. Materials and Methods

This review followed the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [50]. The PRISMA 2020 checklist includes a 27-item checklist for all sections of a systematic review. The PRISMA 2020 checklist is shown in Supporting Information 5.1. Before this systematic review, a review protocol was registered on INSPLASY (INPLASY202050074) [51].

5.2.1. Information Sources and Database Search Strategy

On 31 July 2021, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, PubMed, and OpenGrey database searches were completed by using a combination of the key terms of 'Exercis*', 'Training*', 'Architectur*', 'Fascic*', 'Fiber Length', 'Fibre Length', 'Pennat*', 'Pinnat*', 'Morphology', 'Muscle Thickness', 'Cross Sectional Area', 'Cross-sectional Area', 'Muscle Volume', 'Muscle Structure', and 'Muscle Length' without any time, language, study type etc. restrictions. Detailed search strategies for each database are presented in Supporting Information 5.2.

5.2.2. Eligibility Criteria and Study Selection Process

Firstly, the duplicate records were automatically removed via the EndNote X^9 computer [52] program by the first author. Then, the remaining citations were imported to the Rayyan web application [53], which was designed for screening eligible studies for systematic reviews. The first and second authors independently screened the citations for eligibility, and they were blinded to decisions until the end of the screening process. Any conflicts that arose about the inclusion of the studies were firstly solved by discussion between the first and second authors. The third and fourth authors were considered referees if there were unresolved discussions. This conflict -solving mechanism was also applied during the risk of bias assessment and data extraction processes. Bangor University libraries retrieved non-available full-texts.

The following inclusion criteria were considered (1) being a randomised controlled trial, (2) being a full-text journal article in the English language, (3) exercise interventions lasting at least four weeks in healthy adults between 18 and 50 years old, (4) solely investigating exercise interventions, (5) using a non-invasive imaging technique (i.e., magnetic resonance imaging (MRI), ultrasonography) to assess muscle architectural parameters of a defined muscle or muscle groups of the upper extremities; and (6) presenting outcomes related to at least one muscle architectural parameter.

5.2.3. Outcome Measures

Changes in architectural parameters involving cross-sectional areas, fascicle length, muscle thickness, muscle volume and pennation angle of upper extremity muscles due to an exercise intervention were the outcome measures of this systematic review and meta-analysis.

5.2.4. Risk of Bias Assessments of Eligible Studies

For assessing the risk of bias in the included studies, the Cochrane Collaboration's tool for assessing the risk of bias in randomised trials [54] was employed. The first and second authors independently assessed the risk of bias for each eligible study regarding random sequence generation (selection bias), allocation concealment (selection bias), blinding participants and personnel (performance bias), blinding outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other biases. Risk of bias categories were marked as "high risk of bias", "unclear risk of bias", and "low risk of bias".

5.2.5. Data Extraction

Information for groups, age, gender, number and physical activity levels of participants, type of exercises allocated for groups, the materials used during the exercise, exercising procedure, duration, number of sessions, sets and repetitions, targeted muscle or muscle groups, measurement device and region, type of muscle architectural parameters, pre-test and post-test values, statistical analyses and results were independently extracted from eligible studies by the first and second authors.

5.2.6. Meta-Analyses

Meta-analyses of this review were conducted via the Review Manager computer program (RevMan 5.4.1) [55]. A non-training control of the placebo group was considered the comparator for this systematic review. RevMan automatically calculates Hedges' (adjusted) g effects size (standardised mean difference (SMD)) using the mean difference (MD) from baseline and the standard deviation (SD) of these mean differences for exercise and control groups [56]. The difference between Hedges' g and Cohen's d is the adjustments of Hedges' g effect size calculations for a small sample having fewer than 20 participants [57]. Effect size interpretation was considered the commonly used interpretation for both Hedge's g [58] and Cohen's d [59] that small (0.2), medium (0.5) or large (0.8) [60].

The standard deviations of the mean changes from baseline are defined as a common missing outcome data [61], and difficulties for running a meta-analysis without missing SDs explained by previous systematic reviews [62,63]. For calculating missing SDs, a formula was defined as [64,65]:

$$\mathrm{SDchange} = \sqrt{\mathrm{SD^2baseline} + \mathrm{SD^2final} - (2 \times \mathrm{r} \times \mathrm{SDbaseline} \times \mathrm{SDfinal})}$$

SDchange means the SD of the mean changes from baseline, SDbaseline represents the SD of the pre-test, SDfinal corresponds to the SD of the post-test, and the r symbolises the correlations between the baseline and final measurements; this correlation value is not generally presented in the studies. For instance, among the studies eligible for this systematic review, none demonstrate this r-value. Based on this, this systematic review employed the following process for obtaining the missing outcome data: Firstly, given additional data, e.g., confidence intervals, p-values, t-values, F-values, and standard errors were controlled, and missing SDchanges from baseline were estimated using RevMan [55]. However, the first step could not be applied due to the lack of information in the included studies. As a second step, corresponding authors of the included studies were contacted to request their data -sets or the mean and SDchanges from baseline values, as previously recommended [61,62,63]. Thirdly, if the corresponding authors did not share their data with this systematic review, and the SDbaseline and SDfinal values were known, the SDchange value was calculated by assigning a value of 0.7 to the r in the formula [64,65] to provide a conservative estimate [66] as undertaken by previous systematic reviews [67,68,69,70]. Finally, if there were still missing outcome data, the study was not included in the meta-analysis and is mentioned separately in the -text.

The heterogeneity of a meta-analysis was measured by the chi-squared (χ^2 or Chi^2) statistic, and the level of heterogeneity was estimated by the I^2 statistic, which indicates the percentage ratio of the variability in effect estimates caused by heterogeneity rather than chance [71]. I^2 results were interpreted as low (25%), moderate (50%) and high (75%) [72]. When statistical heterogeneity was absent ($p > 0.05$ in the Chi^2 statistics), a meta-analysis was performed for continuous data, inverse variance, fixed-effect model [73] and a 95% confidence interval (95% CI). However, when statistical heterogeneity was observed, a meta-analysis was performed using a more conservative random effect model for continuous data, inverse variance and a 95% CI [73].

5.2.7. Level of Evidence of the Meta-Analyses

Each meta-analysis result in RevMan was exported to GRADEpro GDT software [74], and the level of evidence (LoE) of meta-analyses was graded by applying the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) method as described in the GRADE handbook [75], and recommended by the Cochrane Collaboration's tool for assessing the risk of bias in randomised trials [54], and the Cochrane Handbook for Systematic Reviews of Interventions [61]. The GRADE approach categorises the LoE of each

meta-analysis as high, moderate, low and very low [75]. The GRADEpro GDT software measures the LoE of meta-analyses based on the study design, risk of bias, inconsistency, indirectness, imprecision and publication bias features.

5.3. Results

5.3.1. Study Screening and Selection

Initially, 8388 records were identified from database searches. After removing duplicates, 6524 records were screened based on titles and abstracts, and 6460 of these records were excluded according to pre-determined exclusion criteria. Finally, 64 records were examined based on the full-texts, and 17 randomised controlled trials (RCTs) [76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92] were included in this systematic review. The study screening and selection process is illustrated in a PRISMA 2020 flow diagram (Figure 5.1).

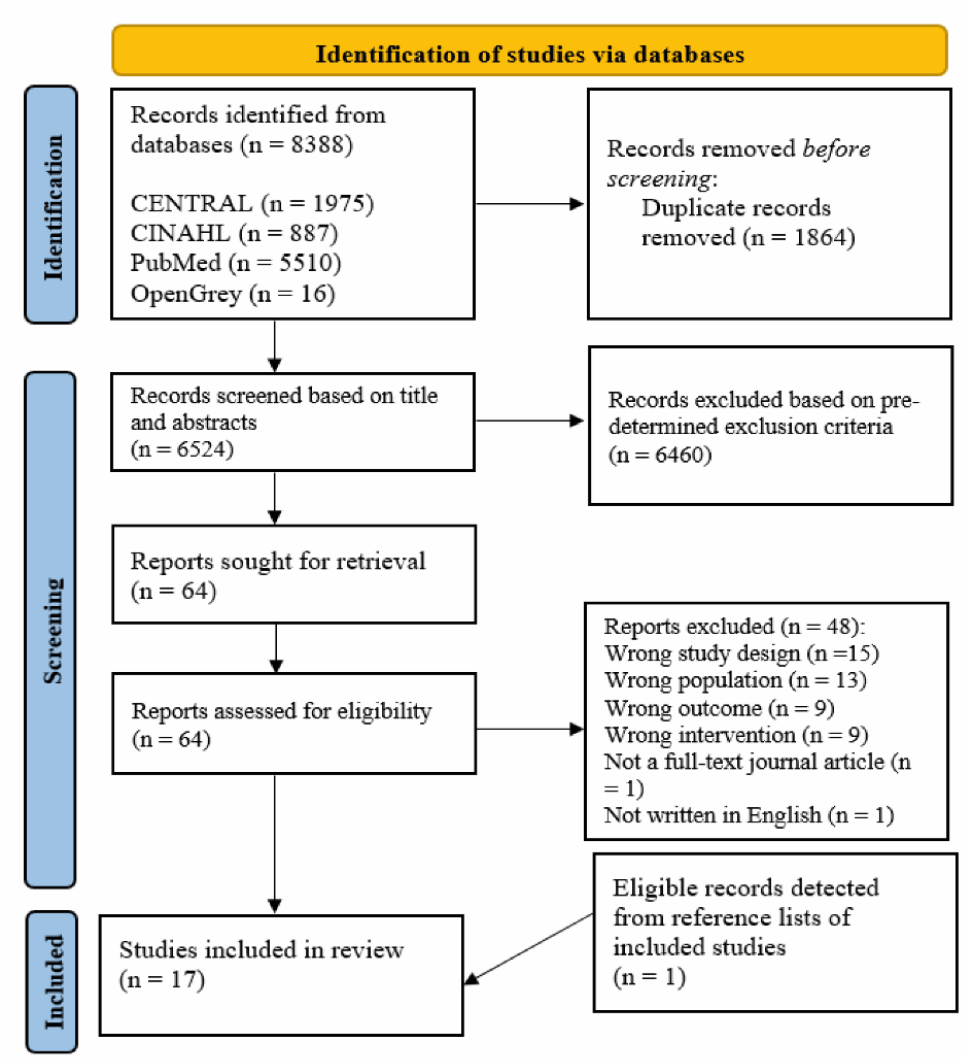

Figure 5.1. PRISMA 2020 flow diagram.

5.3.2. Risk of Bias Assessments

The low risk of bias scores ranges from two [92] to five [77] of seven sections of the Cochrane Collaboration's tool for assessing the risk of bias in randomised trials [54] among the included RCTs [76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92]. A risk of bias summary figure, which the shows review authors' judgements about each risk of bias item for each included study (Figure 5.2), and a risk of bias graph, which shows the review authors' conclusions about each risk of bias item presented as percentages across all included studies (Figure 5.3) were created via RevMan for further use in determining the level of evidence of meta-analyses using GRADEpro GDT software [74].

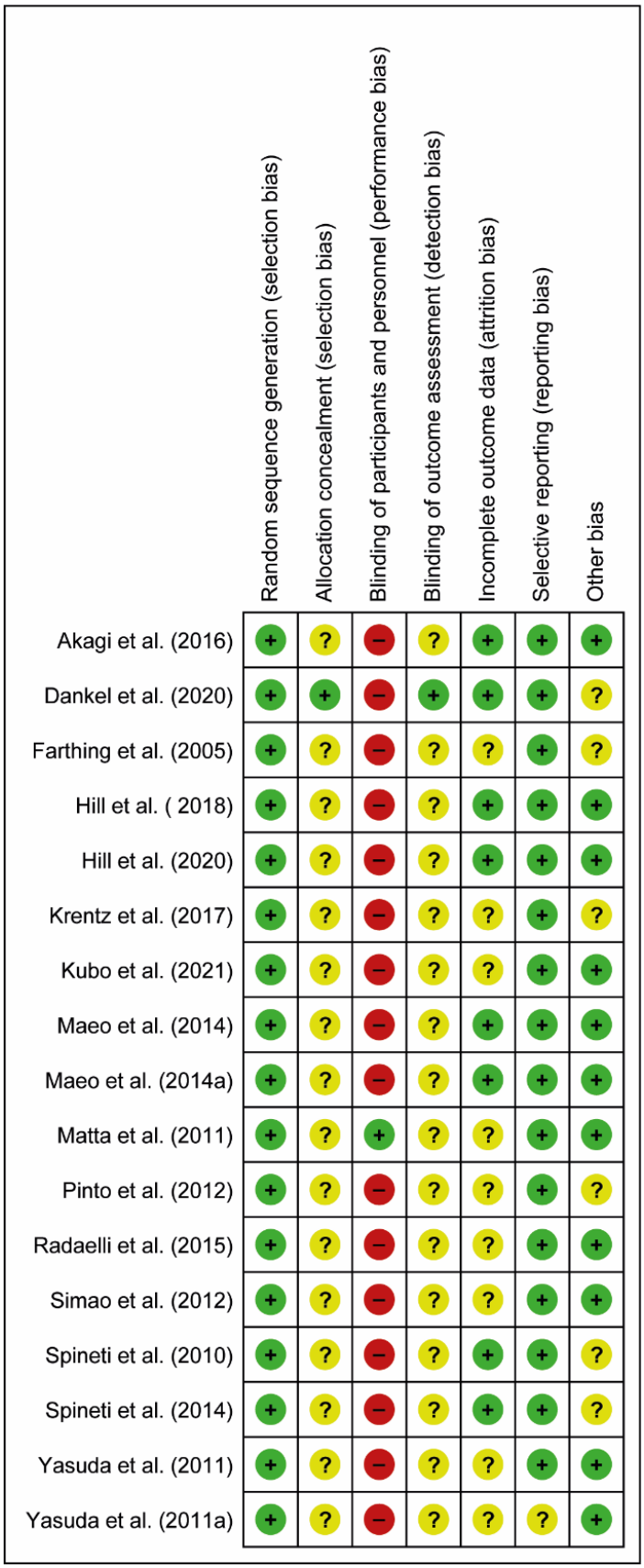

Figure 5.2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study. References for the studies in the table with the same publication year are

Maeo et al. (2014) [83], Maeo et al. (2014a) [84], Yasuda et al. (2011) [91] and Yasuda et al. (2011a) [92].

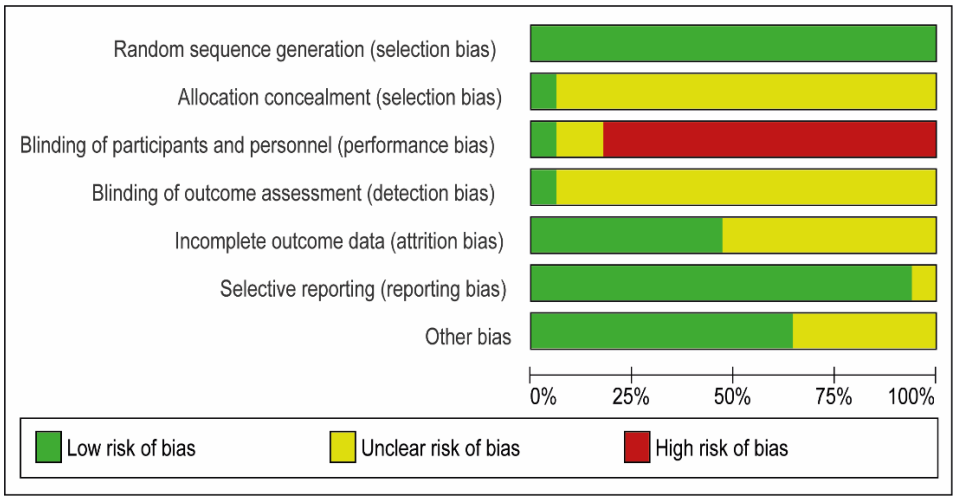

Figure 5.3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

5.3.3. Characteristics of the Participants and Intervention in the Included Studies

Participants' characteristics in the eligible studies, including age, gender, sample size and physical activity level of participants, are presented in Supporting Table 5.1. Additionally, intervention characteristics of the included studies that involve the type of exercises allocated for groups, exercise material, exercising procedure, total weeks, sessions, sets and repetitions, targeted muscle or muscle groups, measurement device and region, type of muscle architectural parameters, pre-test and post-test values, statistical analyses and results are shown in Supporting Table 5.2.

5.3.4. Meta-Analyses

None of the included 17 RCTs [76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92] showed the required SD changes from baseline to allow a meta-analysis to be performed. Additionally, in-text information provided by the included studies was not enough to calculate these missing SDs from baseline using the RevMan calculator [55]. Therefore, the corresponding authors of the eligible studies were contacted to obtain the required data. Missing outcome data of seven RCTs [76,77,79,83,84,89,90] were collected in this way. As a second step, if the corresponding authors did not share their data with this systematic review, and the SDbaseline and SDfinal values were known, the SDchange value was calculated by assigning a value of 0.7 to the r in the formula [64,65], to provide a conservative estimate [66]

as used by previous systematic reviews [67,68,69,70]. Four additional RCTs [78,82,88,91] were included in quantitative analyses by using this method. In total, eleven RCTs [76,77,78,79,82,83,84,88,89,90,91] were included in the meta-analyses of this systematic review. Due to insufficient outcome data, six RCTs [80,81,85,86,87,92] were not included in a meta-analysis. However, participants and intervention characteristics and the results of these studies are presented in Supporting Tables 3.1 and 3.2.

5.3.4.1. The Chest

Ten weeks of 12RM resistance bench press training [82] showed a large effect on increasing the pectoralis major MV (g = 1.21 [0.21, 2.21]), whereas ten weeks of 4RM and 8RM resistance bench press training [82] showed a medium effect on increasing the same parameter (g = 0.61 [−0.29, 1.51], g = 0.64 [−0.23, 1.5], respectively) (Figure 5.4). Overall, the bench press training showed a large effect (g = 0.79 [0.26, 1.32], LoE = low) on increasing the pectoralis major muscle volume. Six weeks of high-intensity bench press training [91] led to large increments in the pectoralis major muscle CSA (g = 1.03 [0.09, 1.98], LoE = very low) (Figure 5.5). Additionally, 6-weeks of low-intensity bench press training with BFR [91] led to medium increments in the pectoralis major muscle CSA (g = 0.63 [−0.27, 1.54], LoE = very low) (Figure 5.6).

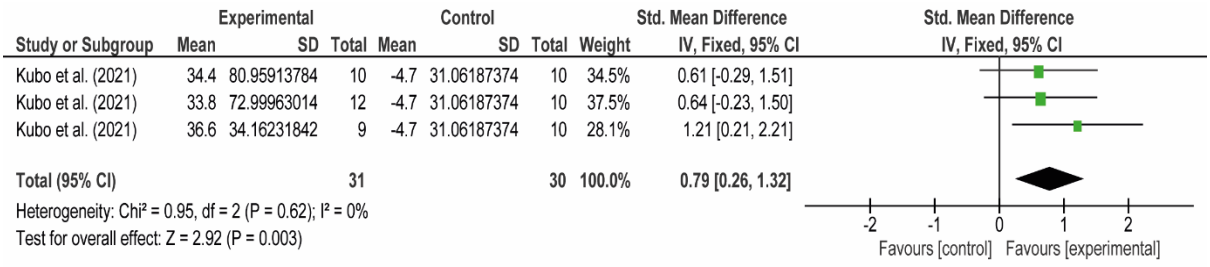

Figure 5.4. The effect size of 10 weeks of resistance training on increasing the pectoralis major MV. The lines respectively correspond to 4RM, 8RM and 12RM training groups.

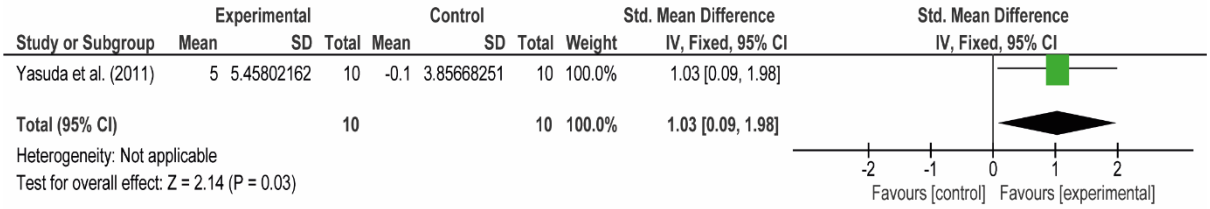

Figure 5.5. The effect size of 6 weeks of high-intensity resistance training on the pectoralis major muscle CSA.

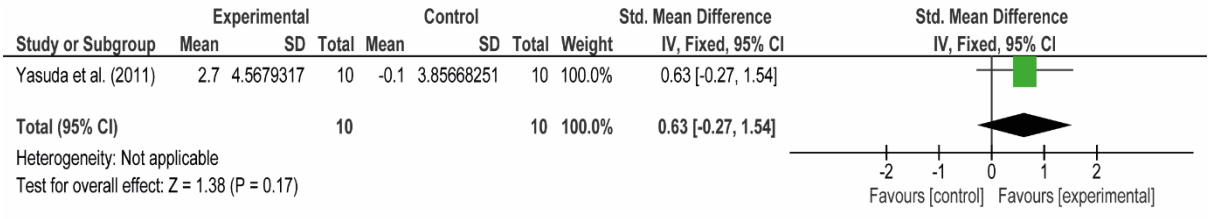

Figure 5.6. The effect size of low-intensity bench press training with blood-flow restriction on the pectoralis major CSA.

5.3.4.2. The Posterior Arm

Six weeks of lying triceps extension exercise [76], which was performed via a dumbbell adjusted at 80% of 1 repetition maximum (RM), showed a large effect size (g = 1.25 [0.33, 2.16], LoE = moderate) to increase the triceps brachii long head MT (Figure 5.7). Six weeks of high-intensity bench press training [91] showed a medium effect size on increasing the triceps brachii muscle CSA (g = 0.72 [−0.19, 1.63], LoE = very low) (Figure 5.8). Six weeks of low-intensity bench press training with BFR [91] showed a small effect on increasing the triceps brachii muscle CSA (g = 0.41 [−0.48, 1.3], LoE = very low) (Figure 5.9). Twelve weeks of linear periodised resistance training [88,90] showed a trivial effect on increasing the triceps brachii MT (g = 0.15 [−0.40, 0.7], LoE = very low) (Figure 5.10). Twelve weeks of nonlinear periodised resistance training [88,90] showed a small effect on increasing the triceps brachii MT (g = 0.33 [0.56, 1.7], LoE = very low) (Figure 5.11). On the contrary, 12 weeks of nonlinear periodised resistance training [89] illustrated a large effect size on increasing the triceps brachii MV (g = 2.07 [1.26, 2.89], LoE = high) (Figure 5.12). The isometric maximal voluntary co-contraction training [83,84] (4 and 12 weeks of study duration combinations) showed a large effect on increasing the MT of the elbow extensors (g = 1.97 [−0.63, 4.56], LoE = moderate) (Figure 5.13).

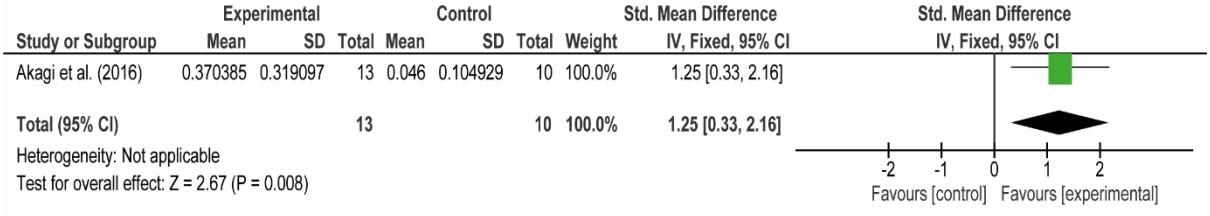

Figure 5.7. The effect size of 6 weeks of lying triceps extension exercise (sequential concentric and eccentric elbow extensions) on the triceps brachii long head MT.

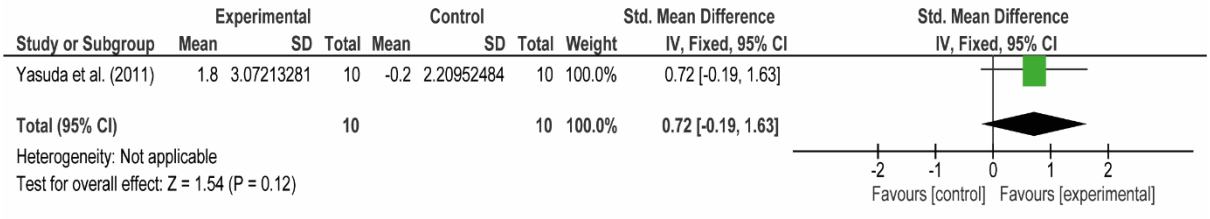

Figure 5.8. The effect size of 6 weeks of high-intensity training on the triceps brachii muscle CSA.

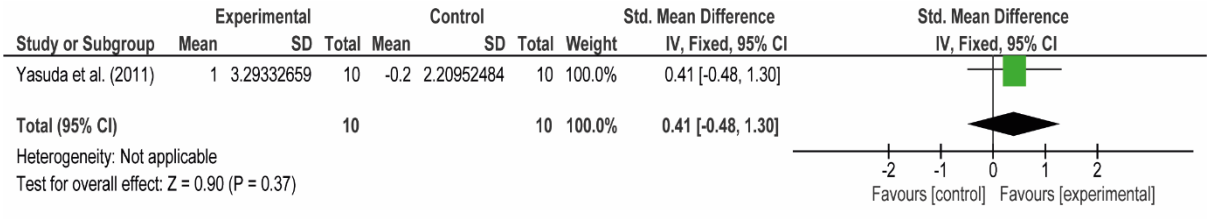

Figure 5.9. The effect size of low-intensity bench press training with blood-flow restriction on the triceps brachii CSA.

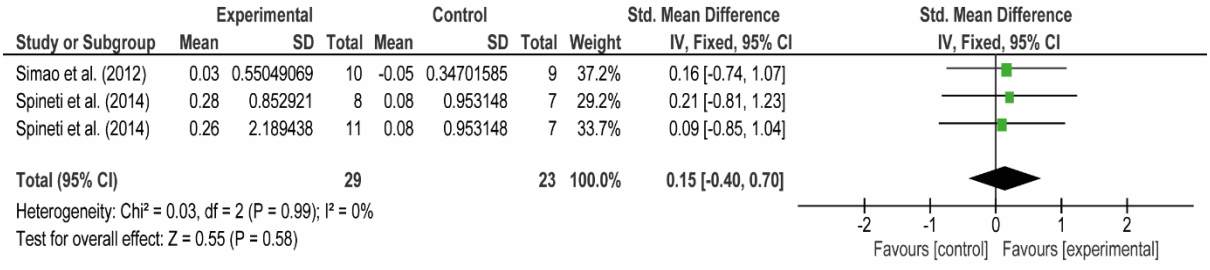

Figure 5.10. The effect size of 12 weeks of linear periodised resistance training on increasing the triceps brachii MT. The lines for Spineti et al. [90] respectively represent linear periodised large-to-small muscle training and small-to-large muscle training groups.

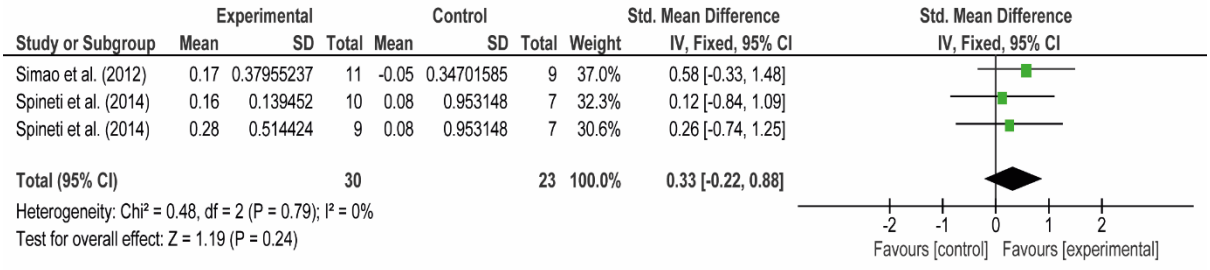

Figure 5.11. The effect size of 12 weeks of nonlinear periodised resistance training on increasing the triceps brachii MT. The lines for Spineti et al. [90] respectively represent nonlinear periodised large-to-small muscle training and small-to-large muscle training groups.

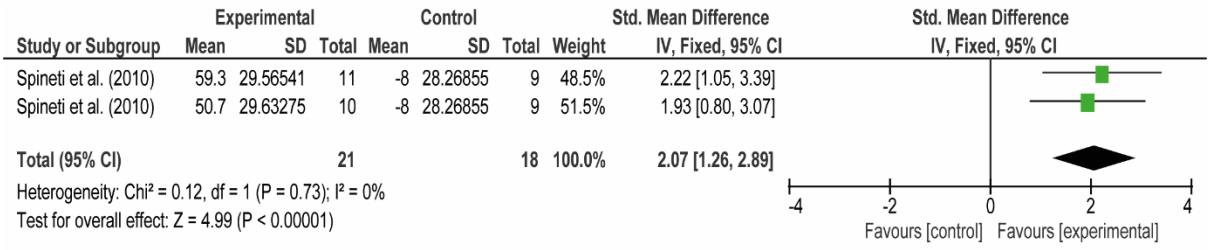

Figure 5.12. The effect size of 12 weeks of nonlinear periodised resistance training on increasing the triceps brachii MV. The lines for Spineti et al. [89] respectively represent nonlinear periodised large-to-small muscle training and small-to-large muscle training groups.

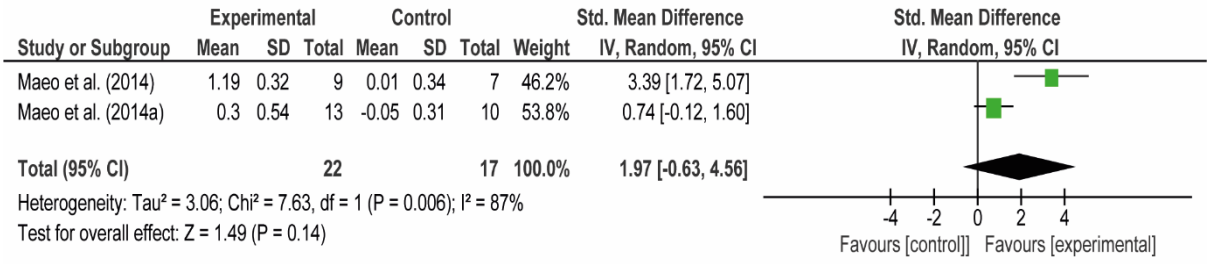

Figure 5.13. The effect size of isometric maximal voluntary co-contraction training on the elbow extensors MT. References for the studies in the table with the same publication year are Maeo et al. (2014) [83] and Maeo et al. (2014a) [84].

5.3.4.3. The Anterior Arm

Four weeks of concentric low-load (at 30% of concentric elbow flexion peak torque) forearm flexion-extension training with vBFR (40% of lowest pressure needed to restrict brachial artery) [79] showed a large effect size on increasing the biceps brachii MT (g = 1.07 [0.12, 2.02], LoE = low) (Figure 5.14), and on increasing the biceps brachii CSA (g = 1.02 [0.07, 1.96], LoE = low) (Figure 5.15). Additionally, four weeks of concentric low-load (at 30% of concentric elbow flexion peak torque) forearm flexion-extension training [79] showed a large effect size on increasing the biceps brachii MT (g = 0.94 [0.01, 1.87], LoE = low) (Figure 5.16), and on increasing the biceps brachii CSA (g = 1 [0.06, 1.94], LoE = low) (Figure 5.17). Twelve weeks of linear periodised resistance training [88,90] showed a medium effect on increasing the biceps brachii MT (g = 0.73 [0.18, 1.28], LoE = very low) (Figure 5.18). In contrast, 12 weeks of nonlinear periodised resistance training [88,90] showed a large effect on increasing the biceps brachii MT (g = 1.13 [0.56, 1.7], LoE = low) (Figure 5.19). Similarly, 12 weeks of nonlinear periodised resistance training [89] illustrated a large effect size on increasing the biceps brachii MV (g = 1.34 [0.63, 2.06], LoE = moderate) (Figure 5.20). Six weeks of

traditional elbow flexion exercises [77] using a dumbbell showed a large effect size on increasing the elbow flexors MT (g = 0.93 [0.69, 1.17], LoE = high) (Figure 5.21), whereas heavy training [77] showed a small effect on the same parameter (g = 0.38 [0.15, 0.6], LoE = high) (Figure 5.22). Finally, the isometric maximal voluntary co-contraction training [83,84] (4 and 12 weeks of study duration combinations) showed a large effect on increasing the MT of the elbow flexors (g = 1.01 [0.33, 1.69], LoE = moderate) (Figure 5.23).

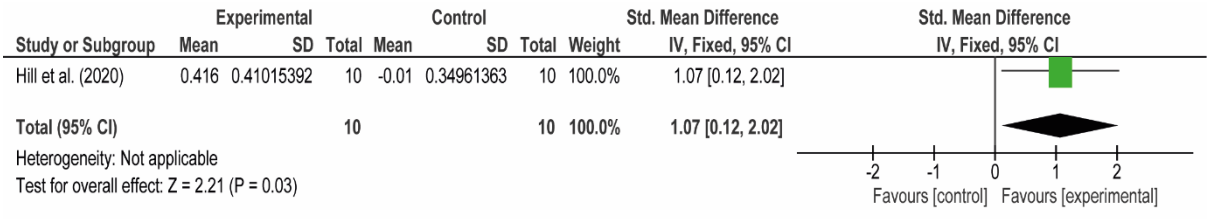

Figure 5.14. The effect size of 4 weeks of concentric low-load (at 30% of concentric elbow flexion peak torque) forearm flexion-extension training with vBFR (40% of lowest pressure needed to restrict brachial artery) on increasing the biceps brachii MT.

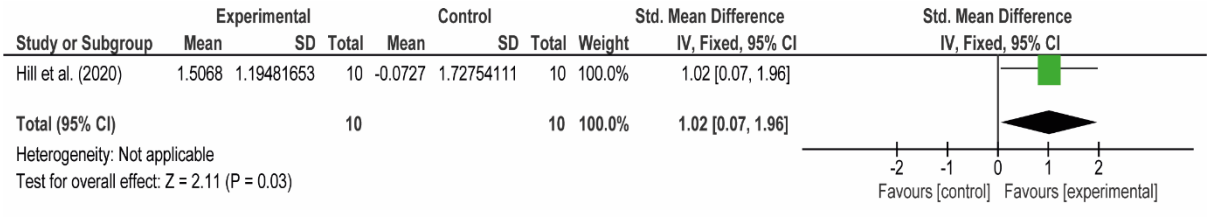

Figure 5.15. The effect size of 4 weeks of concentric low-load (at 30% of concentric elbow flexion peak torque) forearm flexion-extension training with vBFR (40% of lowest pressure needed to restrict brachial artery) on increasing the biceps brachii CSA.

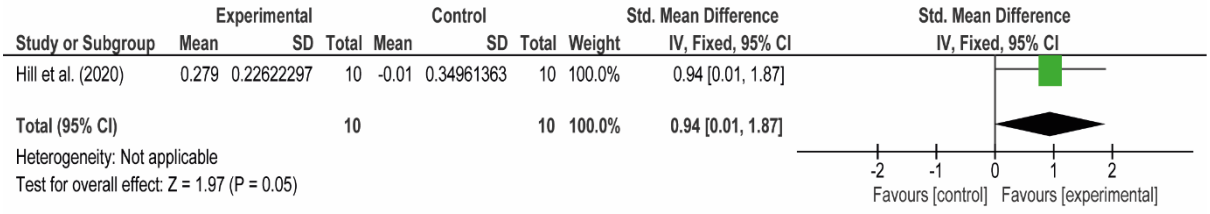

Figure 5.16. The effect size of 4 weeks of concentric low-load (at 30% of concentric elbow flexion peak torque) forearm flexion-extension training on increasing the biceps brachii MT.

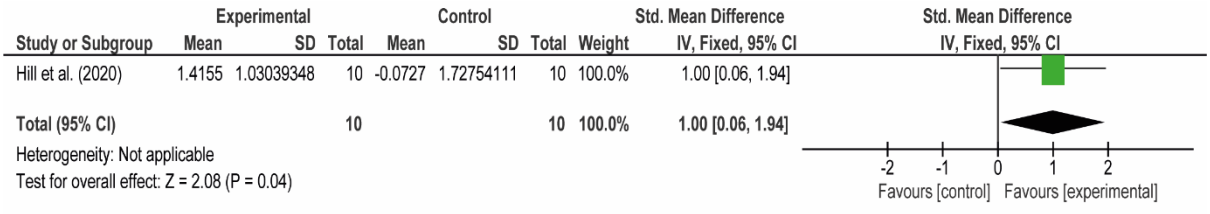

Figure 5.17. The effect size of 4 weeks of concentric low-load (at 30% of concentric elbow flexion peak torque) forearm flexion-extension training on increasing the biceps brachii CSA.

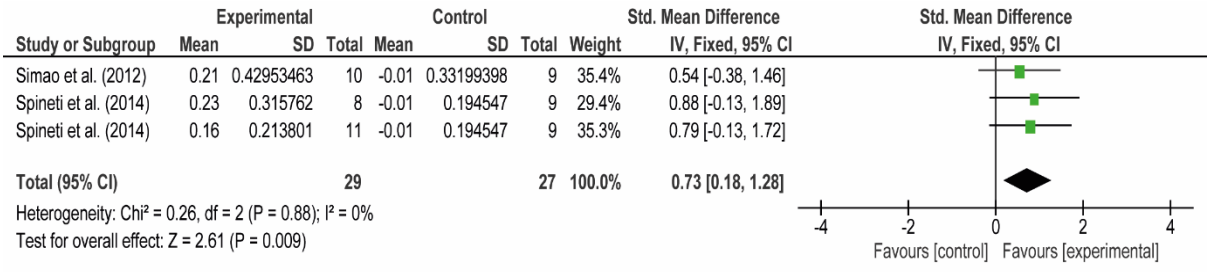

Figure 5.18. The effect size of 12 weeks of linear periodised resistance training on increasing the biceps brachii MT. The lines for Spineti et al. [90] respectively represent linear periodised large-to-small muscle training and small-to-large muscle training groups.

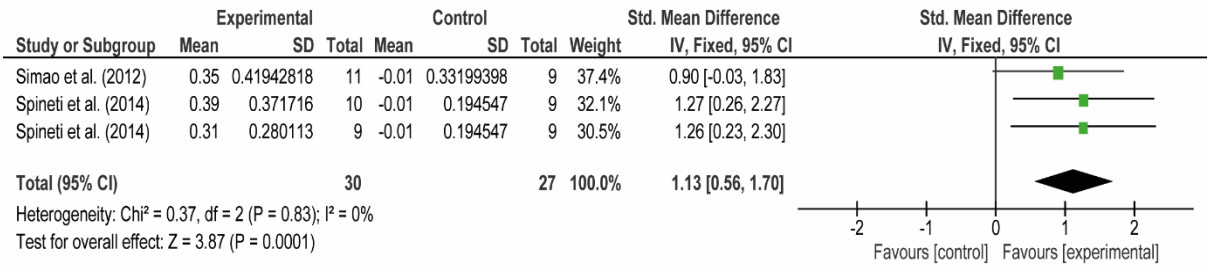

Figure 5.19. The effect size of 12 weeks of nonlinear periodised resistance training on increasing the biceps brachii MT. The lines for Spineti et al. [90] respectively represent nonlinear periodised large-to-small muscle training and small-to-large muscle training groups.

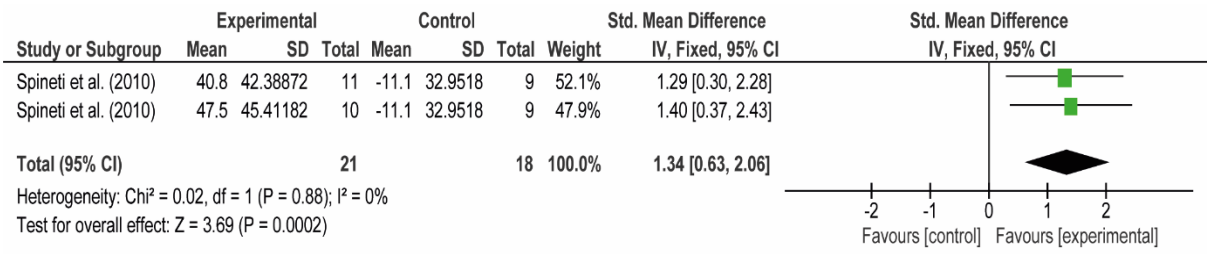

Figure 5.20. The effect size of 12 weeks of nonlinear periodised resistance training on increasing the biceps brachii MV. The lines for Spineti et al. [89] respectively represent nonlinear periodised large-to-small muscle training and small-to-large muscle training groups.

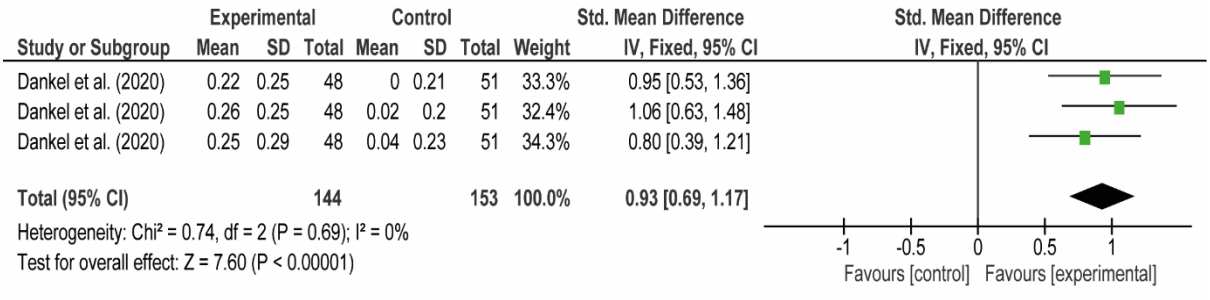

Figure 5.21. The effect size of 6 weeks of traditional elbow flexion exercise on the elbow flexors' MT. The lines respectively represent 50%, 60% and 70% measurement levels of elbow flexors' MT.

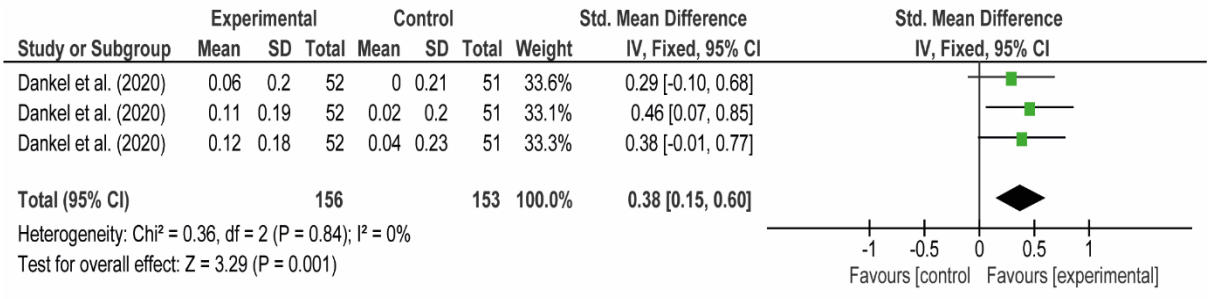

Figure 5.22. The effect size of 6 weeks of heavy elbow flexion exercise on the elbow flexors' MT. The lines respectively represent 50%, 60% and 70% measurement levels of elbow flexors' MT.

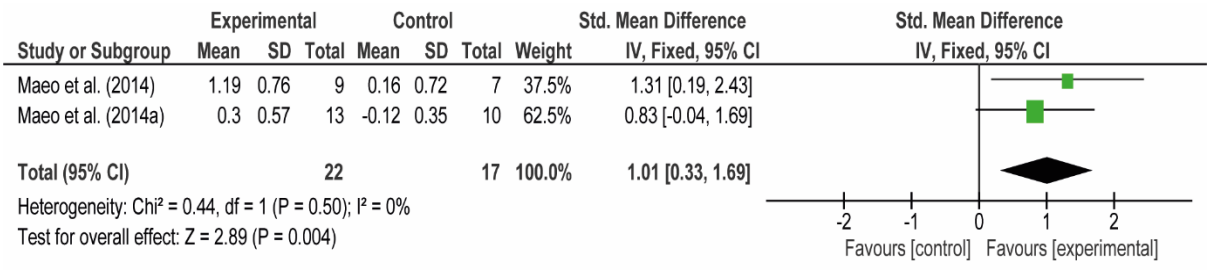

Figure 5.23. The effect size of isometric maximal voluntary co-contraction training on the elbow flexors MT. References for the studies in the table with the same publication year are Maeo et al. (2014) [83] and Maeo et al. (2014a) [84].

5.3.4.4. Forearm

Six weeks of isometric ulnar deviation training [78] showed a large effect (g = 2.22 [−0.9, 5.33], LoE = very low) on increasing the flexor carpi ulnaris and radialis MT of the trained right and left hands (Figure 5.24).

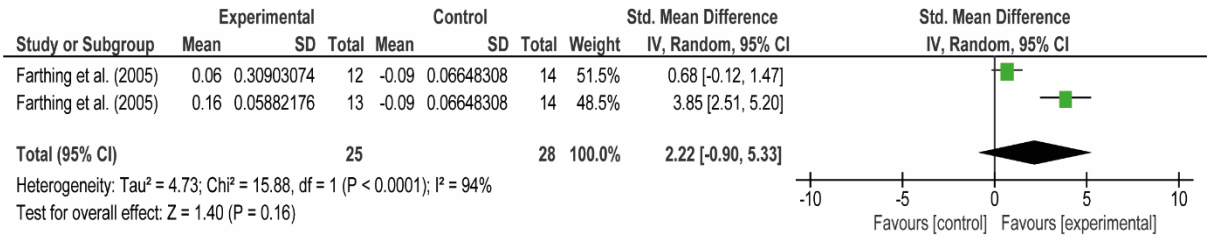

Figure 5.24. The effect size of 6 weeks of isometric ulnar deviation training [78] on flexor carpi ulnaris and radialis MT of the trained right and left hands. The first line represents the right-hand (dominant) trained group, and the second line represents the left-hand (non-dominant) trained group.

5.3.4.5. Level of Evidence of the Meta-Analyses

The LoE of each meta-analysis was determined using the GRADEpro GDT software [74] according to the GRADE handbook [75] as described in the methodology section of this systematic review. The LoE values of meta-analyses ranged from very low to high. The LoE of each meta-analysis is presented in Supporting information 5.3.

5.4. Discussion

To the authors' knowledge, this systematic review with meta-analyses is the first screening of RCTs for the effects of all types of exercises on the architecture of upper extremity muscles. This systematic review with meta-analyses aimed to overview the effects of exercise interventions on improving the architecture of upper extremity muscles. The meta-analyses of this systematic review revealed that most exercise interventions with at least 4-weeks of exercise duration showed large effect sizes for increasing the size of individual upper extremity muscle or muscle groups (Figure 5.25, Figure 5.26, Figure 5.27 and Figure 5.28). In summary, the following exercises showed large effects on increasing the size of the targeted muscles: high-intensity concentrically-biased bench press training for the pectoralis major; lying concentrically-biased triceps extension, isometric maximal voluntary co-contraction training, and nonlinear periodised resistance training for the triceps brachii; traditional concentric elbow flexion exercise, low-load concentric forearm flexion-extension training without and with blood-flow restriction, isometric maximal voluntary co-contraction training, and nonlinear periodised resistance training for the biceps brachii; and isometric ulnar deviation training for the flexor carpi ulnaris and radialis.

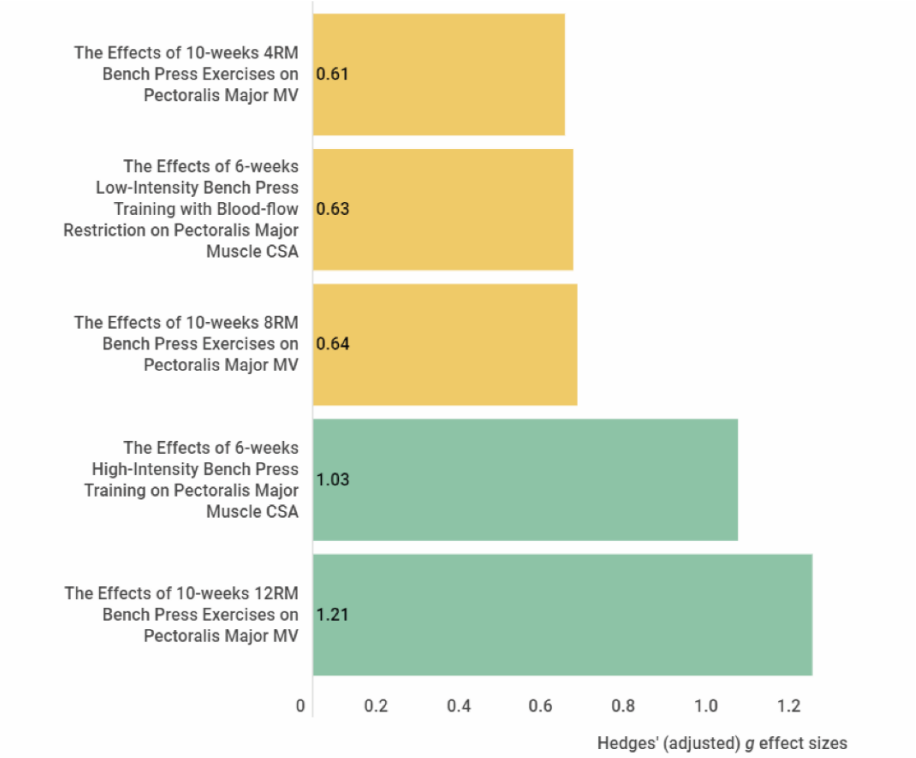

Figure 5.25. The effect size of the exercise interventions on the pectoralis major muscle cross-sectional area and volume. The yellow colour indicates a medium effect size, and the green colour indicates a large effect size. Abbreviations: CSA, cross-sectional area, MV, muscle volume.

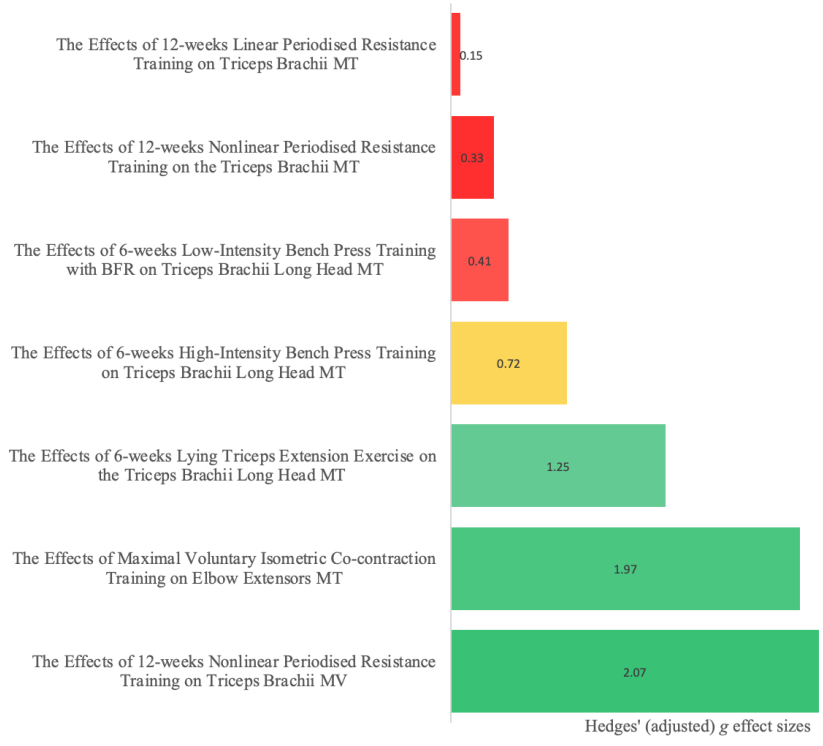

Figure 5.26. The effect size of the exercise interventions on the elbow extensor muscle thickness, cross-sectional muscle area and muscle volume. The red colour indicates a small or trivial effect size, the yellow colour indicates a medium effect size, and the green colour indicates a large effect size. Abbreviations: CSA, cross-sectional area; MT, muscle thickness; MV, muscle volume.

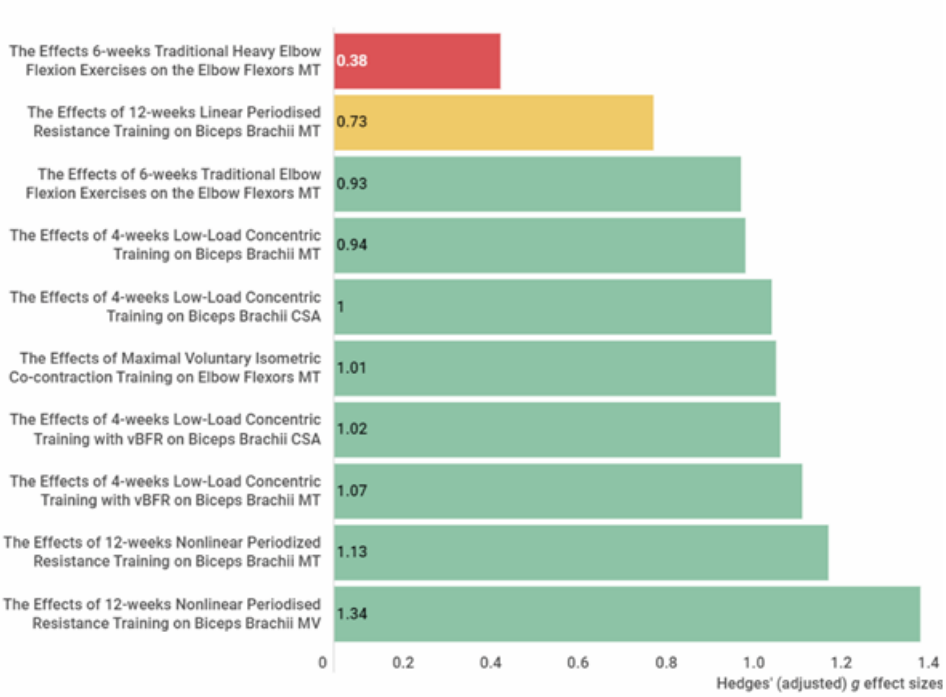

Figure 5.27. The effect size of the exercise interventions on the elbow flexors muscle thickness, muscle cross-sectional area and muscle volume. The red colour indicates a small or trivial effect size, the yellow colour indicates a medium effect size, and the green colour indicates a large effect size. Abbreviations: CSA, cross-sectional area; MT, muscle thickness; MV, muscle volume.

Figure 5.28. The effect size of the exercise interventions on the forearm flexors muscle thickness. The green colour indicates a large effect size. Abbreviations: MT, muscle thickness.

In addition to the training modalities included in the meta-analyses, six RCTs [75,76,80,81,82,87] were not included in the meta-analyses due to missing outcome data. The findings and intervention characteristics of the RCTs are presented in Supporting Table 5.3.

Among these RCTs, Matta et al. [85] investigated the effects of a nonlinear periodised strength training program on biceps brachii and triceps brachii MT and the triceps brachii long head PA and reported significant alterations in the outcome measures depending on the arm sites. The study of Matta et al. [85] was the only RCT that measured the PA of a muscle, which is a fascicle geometry component, among the eligible RCTs. The triceps brachii long-head PA was significantly correlated with the strength parameters of the elbow extensors [45]. By comparison, the triceps brachii long head FL was one of the best predictors of better swimming performance [36] and significantly correlated with lifting performance parameters [17]. However, there was no RCT that investigated the effects of an exercise intervention on the FL of the triceps brachii long head. Although it did not meet the inclusion criteria of this systematic review, a recent uncontrolled trial [93] compared the effects of concentrically-biased cable push-down and cable overhead extension exercises, and Stasinaki and colleagues [93] did not report significant alterations in the FL of the triceps brachii long head even when the concentric elbow extension starts from a fascicle lengthened position. This may be due to the effects of concentric training. A future RCT should examine the impacts of eccentric training on the FL of the triceps brachii long head.

In terms of the muscle size parameters, the triceps brachii MT has been found to be strongly correlated with elbow extension strength [41]. Additionally, the triceps brachii MT was stated as being significantly correlated with better swimming performance ($r = -0.56$) [36]. Moreover, elbow extensors' and flexors' muscle size parameters (ACSA, PCSA and MV) showed significant strong correlations with elbow joint torque ($r = 0.705–0.945$) [39]. Furthermore, the elbow extensors' cross-sectional muscle area (CSA) was correlated with rowing performance and was the significant best predictor of arm pull during the rowing activity in rowers ($r^2 = 0.195$) [37]. Elbow flexors CSA showed a strong correlation with elbow flexion maximal power ($r = 0.81$) [40]. Arm muscle CSA has significantly correlated with the shot put performance ($r = 0.68$) [38]. The pectoralis major muscle CSA was strongly correlated with bench press strength ($r = 0.866$), and muscle volume was strongly correlated with bench throw peak power ($r = 0.821$) [43]. Either concentric, isometric, eccentric or blood-flow-restricted resistance training modalities led to significant muscle hypertrophies. Based on these findings, athletes, healthy individuals aiming to increase their related performance or muscle strength parameters, astronauts after a space mission [94] and patients experiencing muscle atrophies after bedrest [95,96], which were mentioned above, may refer to the training regimens that showed large effects sizes on increasing the pectoralis major, arm and forearm muscles' size

parameters. However, exercise selection should cautiously be made due to the small number of studies included in each meta-analysis.

Additionally, the infraspinatus MT was significantly correlated with shoulder external rotation strength in professional baseball pitchers (r = 0.287) [44]. The subscapular MT was the best single predictor for powerlifting performance in professional powerlifters [17]. However, this systematic review did not detect any RCTs focusing on exercise-induced alterations in these muscle architectural parameters. Future RCTs may be conducted to investigate exercise-induced alteration in these muscle architectural parameters in the relevant samples, such as exercise-induced alterations in the infraspinatus MT in baseball pitchers, in the subscapular MT in powerlifters, and in the fascicle geometry of the triceps brachii in swimmers.

Regarding the effect size calculations of the RCTs, initially, none of the RCTs reported the required SDs of the mean changes from baseline for exercise and control groups. The difficulties associated with conducting a meta-analysis without this variable are well described in the literature [61,62,63]. Therefore, this systematic review strongly suggests that future RCTs should share their raw data, or mean changes from baseline and SDs of the mean changes from baseline, with their publications for more comparable future studies and meta-analyses. Additionally, for the effect sizes reported in individual RCTs, the calculations were generally in respect of the baseline and post-test scores of the intervention groups of post-test scores of the intervention and control groups. Both approaches may lead to wrong interpretations and fewer comparisons between the RCTs. Therefore, this systematic review strongly suggests that future RCTs should calculate the effect sizes based on the mean changes from baseline and their SD in an intervention group, comparing the same parameters with a control group, as calculated in this systematic review. Finally, random allocation, and blinding of participants and assessors, were the most common risks of bias among the RCTs. Thus, following the CONSORT statement [97] for parallel-group randomised trials may reduce the risk of biases caused by the methodology, and this can be recommended for future RCTs.

A limitation of this study may be the small number of the RCTs included in each meta-analysis. A further limitation of our review is the inclusion of only English-language articles, which may have led to the omittance of some data in the analysis. Similar to previous relevant meta-analytic studies that included both genders in the meta-analyses [62,63,98], this systematic review did not address the question of the influence of sex for a differential response to training in the meta-analyses, which adds a limitation to the outcomes provided. More RCTs

may have led to stronger conclusions in this systematic review. Another limitation is not being able to perform assessments of meta-regression or publication bias, which are not suitable for performing each meta-analysis due to the few RCTs [61] included in the meta-analyses of this systematic review. An additional confounding factor is a difference between training interventions, which can lead to uncountable variability in the results of the meta-analyses.

5.5. Conclusions

Regarding the pectoralis major muscle size, six weeks of high-intensity bench press training [91] and ten weeks of 12 RM bench press exercises [82] can be applied for hypertrophy in this muscle. To achieve hypertrophy in elbow extensors, six weeks of lying triceps extension exercise [76], isometric maximal voluntary co-contraction training [83,84], and 12 weeks of nonlinear periodised resistance training [89] may be a suitable intervention. From the perspectives of elbow flexors, 6-weeks of traditional elbow flexion exercises [77], 4-weeks of concentric low-load forearm flexion-extension training [79], isometric maximal voluntary co-contraction training [83,84], 4-weeks of concentric low-load forearm flexion-extension training with vBFR [79], or 12-weeks of nonlinear periodised resistance training [88,90] can be applied to gain hypertrophies in the elbow extensors. Finally, six weeks of isometric ulnar deviation training can be used to increase the flexor carpi ulnaris and radialis muscle size [78].

However, these results should be cautiously interpreted due to the small number of RCTs included in each meta-analysis. More RCTs are needed to provide more precise and robust conclusions about the effects of exercise on the architecture of the upper extremity muscles. Additionally, all the eligible studies of this systematic review were restricted to muscle size measurements and did not expand towards the fascicle geometry, such as the FL of the triceps brachii long head. Future RCTs can examine the effects of exercise on the triceps brachii FL and PA, the infraspinatus MT and the subscapular MT due to their associations with sports performance.

Chapter 6: General Discussion

Chapter two of this thesis was the first meta-analytic study performing effect size calculations of eccentric exercise on increasing the biceps femoris long head fascicle length (BFlh) by subgrouping studies based on ultrasound assessment methods of the BFlh FL. Among previous meta-analyses, Cuthbert et al. [1] reported that NHE has a very large effect size (ES) ($g \geq 2.58$) on increasing biceps femoris FL. However, Cuthbert et al. [1] did not use a comparator such as a placebo or a non-training control group in their meta-analysis. Instead, Cuthbert et al. [1] pooled exercise and control groups separately, which did not allow observing changes in the BFlh FL relative to the control group. Additionally, included studies of Cuthbert et al. [1] were not homogenous in terms of the study design, such as non-controlled and controlled studies. Furthermore, Medeiros, Marchiori and Baroni [2] estimated the effect size of the NHE as 0.97 ([-0.46, 1.48]). However, the "r" value estimations for calculating standard deviations of changes from the baseline of the study [2] were not obtained by the authors of the included studies, and the "r" value estimations led to different ES calculations from the actual values (Table 2.2.). Although Gérard et al. [3] did not mention any effect size of eccentric exercise of the BFlh FL, they mentioned 1.97 cm ([1.48, 2.46] increment in BFlh FL. However, Gérard et al. [3] also miscalculated the "r" values, which leads to overestimated sizes of the eccentric training effects of the BFlh FL (Table 2.2.). Moreover, no previous meta-analyses performed a subgroup analysis to assess their substantial to considerable statistical heterogeneities. However, this systematic review obtained missing outcome data by contacting authors for more precise results and included only randomised controlled trials to analyse more homogenous studies regarding study design. Additionally, the findings of this meta-analytic study differ from previous studies. First, the only large effect sizes of eccentric training, including the Nordic hamstring exercise (NHE), were observed when measured using the trigonometric equation method for the BFlh FL calculation (eccentric training ES = 2.2; NHE ES = 1.98). However, there were no large effects detected for eccentric training, including NHE, when the BFlh FL measurements were performed based on the manual linear extrapolation (MLE) or extended field of view (EFOV) methods (eccentric training: MLE = 0.29, EFOV = 0.72; NHE: MLE = 0.23, EFOV: 0.38).

Franchi et al. [4] revealed that the trigonometric equation method overestimates 1.91 ± 2.1 cm biceps femoris FL compared with panoramic ultrasound (extended field of view) images. In contrast, the manual MLE method and panoramic ultrasound images had no significant differences [4]. When considering the findings of this meta-analysis together with the findings of Franchi et al. [4], there might be a potential underlying overestimation of the ES reported by those studies that used the equation method for estimating the biceps femoris FL compared

with the MLE and panoramic ultrasound scanning methods to calculate the BFlh FL. However, this argument still needs evidence. Future research should compare the effects of eccentric training based on ultrasound assessment and extrapolation methods and should clarify whether the effect size of eccentric training changes between the ultrasound assessment methods or not.

Additionally, the relevant scientific community should reach a consensus for a "gold standard" measurement for the BFlh FL to assess the ES of the training interventions on the BFlh FL for homogenous and comparable results between studies. One limitation of the present review might be the small number of eligible studies pooled in meta-analyses. Nevertheless, this systematic review included eight studies in the quantitative syntheses, more than the previous systematic reviews that included five [1, 3] or four [2] studies. Additionally, a further confounder in the analysis of this review is the heterogeneity of eccentric training interventions, which adds non-accountable variability to the outcome measures. Therefore, future studies should consider the apply same training protocols to have more comparable results.

Chapter three of this thesis was the first comprehensive cross-sectional study, which compared the BFlh fascicle length, passive muscle stiffness, and the BFlh, KE and KF muscle volumes between rugby players and healthy, physically active controls to understand long-term adaptations of these structures to rugby-specific training and match play. This study's RG group played in the top Japanese university rugby league (division 1) with 9.07 ± 3.4 years of rugby-specific training history. The control group consisted of non-sedentary non-athletes who were weekly performing 0.8 ± 1.29 vigorous intensity, 2.37 ± 3.24 moderate intensity, and 5.27 ± 6.24 low-intensity non-sport-specific exercise such as running and walking. By recruiting this control group, it aimed to minimise potential adverse effects of the sedentary lifestyle and minimise any sport-specific alterations in the outcome measures.

Based on the findings of this study, playing rugby led to significantly longer BFlh fascicles in both thighs (dominant: 10.68 cm vs 9.1 cm, non-dominant: 10.6 cm vs 9 cm). One of the main limitations of the prospective study [5], which suggested the BFlh fascicle length as a risk factor for HSIs, was not to investigate the predictive ability architectural characteristics of the hamstrings relative to knee extensors. The knee extensors contribute to the increased tensile force during the eccentric action of the hamstrings by behaving as an antagonist. Indeed, our study investigated the BFlh fascicle length/KE muscle volume ratio and detected

lower percentage ratios in both legs for the RG compared to CG (dominant and non-dominant: 0.36 vs 0.45). These results may indicate that rugby-specific adaptations in the BFlh fascicle length/KE muscle volume can increase the tensile force in the series of sarcomeres in the BFlh fascicle length and might increase the risk of HSIs. The regression analysis showed that the increased BFlh muscle volume explains 35% ($R = 0.568$, $R^2 = 0.345$, $P < 0.001$) of the increased BFlh fascicle length variances. These results suggest that rugby players may consider increasing their BFlh muscle volumes. Our study has revealed that playing rugby leads to lower KF to KE percentage ratios in both thighs (dominant: 45.7% vs 50.55%, non-dominant 45.87% vs 49.8%). Likewise, lower BFlh to KE percentage muscle volume ratios were observed in both legs of the rugby players compared to controls (D: 9.59% vs 10.5%, ND: 9.61% vs 10.59%). Likewise, rugby players showed significantly higher KE muscle volume values relative to body mass (dominant: 34.55 cm^3/kg vs 32.21 cm^3/kg, non-dominant: 34.44 cm^3/kg vs 31.83 cm^3/kg); however, they did not show a significant difference in KF muscle volume values relative to body mass in both legs compared to controls (dominant:15.73 cm^3/kg vs 16.34 cm^3/kg, non-dominant: 15.72 cm^3/kg vs 15.86 cm^3/kg for the RG and CG, respectively).

Altogether, these results indicate that rugby-specific training and match-play lead to unbalanced hypertrophies in favour of the knee extensors in the long term. When considering the KE muscle volume is one of the strongest predictors of concentric muscle power [6], this unbalanced increment in favour of the KE might increase the tensile force on the BFlh fascicles during the late swing phase of running due to the antagonist behaviour of the KE and might increase the vulnerability of the muscle. Unfortunately, this argument needs evidence due to lacking prospective and retrospective studies addressing the predictive abilities of architectural and morphological parameters of the hamstrings relative to KE for the HSI. Thus, future prospective studies can examine whether there are and threshold values in the BFlh fascicle length/KE muscle volume, BFlh/KE and KF/KE muscle volume ratios for predicting the HSIs or not.

Based on the findings of this study, rugby-specific training and match play increased the BFlh muscle stiffness in the long term. This increase might be relevant to the increased risk for the HSIs due to the prospective study that indicates increased hamstring stiffness as a risk factor for the HSIs. However, previous techniques assessing passive muscle stiffness included all the muscle-tendon of whole agonist muscles in the measurements, and these techniques were not capable of evaluating the stiffness of the individual muscles [7]. However,

technological developments allowed assessments of the passive stiffness of individual muscles using shear-wave elastography [8]. In this way, our study could measure the passive muscle stiffness of the BFlh, the most frequently injured muscle among the hamstrings, by using the shear-wave elastography technology and revealed that playing rugby leads to increments in passive muscle stiffness of the BFlh in both thighs. However, the prospective study [9] illustrated increased hamstring stiffness as a risk factor for HSIs was employed one of the old technological assessments called the free oscillation technique, which assesses the passive stiffness of the muscle and tendon of all knee flexors rather than measuring the passive stiffness of the individual muscles. Therefore, future studies are needed to assess the predictive ability of the BFlh passive muscle stiffness and determine if there is a predictive threshold value for the HSIs using the updated technology [8], namely shear wave elastography.

Our study employed the "gold standard" measurement of MRI for the muscle volume assessments of the participants [10]. However, no "gold standard" measurement method of the BFlh fascicle length exists in the literature [4]. Additionally, the effect size of exercise can vary between the ultrasound assessment methods, such as the trigonometric equation method potentially leads to overestimated BFlh fascicle length [4] and size of exercise effect on the BFlh fascicle length compared to MLE, panoramic ultrasound scanning [11] or diffusion-tensor MRI [12]. Despite this study using the MLE method, which doesn't significantly overestimate the BFlh fascicle length [4] and effects of exercise on the BFlh fascicle length [11], using this method is still a limitation of this study due to lacking a "gold standard" method for the BFlh fascicle length assessments [4]. This study measured the muscle volume of the major knee flexors naturally located at the thigh. However, lateral and medial gastrocnemius, popliteus, and soleus muscles also contribute to knee flexion, despite not being their primary activity. Thus, not measuring the volume of these muscles can be another confounding factor of this study. Lastly, this study recruited players from the top Japanese university rugby league (division 1) with 9.07 ± 3.4 years of rugby-specific training history. Still, this study could not recruit players competing at the top-level international leagues, which can be another limitation of this study. Despite the overall high-reliability results for the passive muscle stiffness measurements of this study, the confidence intervals of the results were wide. Therefore, the reliability results for the passive muscle stiffness measurements should be interpreted cautiously. The small sample size of the reliability assessments could cause these large confidence intervals, which can be considered a limitation of this study.

Additionally, the reliability assessments comprised only intra-tester reliability measurements. Not performing inter-tester reliability measurements is another limitation of this study. Future reliability studies should be conducted by recruiting a larger sample size and inter-tester reliability measurements too. Regarding the fascicle length calculations, the fascicles of six participants could not be calculated due to unclear ultrasound images which failed to show fascicular paths. Unclear fascicular paths are not uncommon in fascicle length measurements [4]. However, not successfully measuring the fascicle length of six participants is defined as another limitation of this study.

Chapter four of this thesis was the first study that investigated alterations in the single-leg hop distance (SLHD) and the BFlh FL during the 90 minutes of a simulated football match. In addition, this study employed predictive maximal eccentric hamstring strength and single-leg bridge performance (SLHB) assessment methods for HSIs [13, 14], which differs from previous similar studies. Based on the findings of this study, the SLHD and BFlh FL did not change after the half-time and full-time of the simulated football match. However, significant large decrements were observed in the maximal eccentric hamstring strength ($g = 0.95$) and SLHB performance ($g = -1.2$) after the full-time football simulation. In addition, the mean percentage of maximal heart rate was significantly higher during the last fifteen minutes of the football simulation in comparison with the rest of the simulated football match.

The passive BFlh FL is defined as the architectural risk factor for future HSIs [15]. No study investigated changes in the BFlh FL after ninety minutes of a football match. Thus, chapter five of this thesis aimed to determine whether there was a change in the passive BFlh FL during a simulated football match. It was pointed out that the BFlh fascicles actively lengthen during the hamstrings' eccentric action [16]. Initially, chapter five of the thesis hypothesised that the BFlh fascicles might be lengthened after the simulated football match due to repetitive eccentric exposure during the match. However, this study could not observe any significant changes in the passive BFlh FL after the half-time and full-time of the football simulation. Likewise, Gonçalves [17] examined the influence of a forty-five minutes football simulation ($SAFT^{45}$) on the BFlh FL and could not detect any changes in the BFlh FL after forty-five minutes of football simulation ($SAFT^{45}$). Chapter five of this thesis confirms the findings of Gonçalves [16] and adds that there are no alterations in the passive BFlh FL even after ninety minutes of the $TSAFT^{90}$ football simulation. When considering the mechanism of the HSIs, examining alterations in the lengthening, and shortening abilities of the BFlh fascicles might bring new insights to HSIs due to repetitive elongations in the hamstrings

during eccentric contractions throughout ninety minutes of a football match. Future studies can examine if there are any alterations in the lengthening-shortening ability of the BFlh fascicles during a football match.

Regarding the alterations in maximal eccentric hamstring strength and hamstrings' SLHB performance, chapter five of this thesis reported large decrements after the ninety minutes of a TSAFT^{90} simulated football match. Similarly, Bueno et al. (2021) [17] have recently observed large decrements in hamstrings' eccentric strength after an actual football match. The present study confirms the outcomes of Bueno et al. (2021) [17]. Decrements in the SLHB scores were relatively higher than the decrease in their maximal eccentric strength. The SLHB test uses a constant external force obtained by a portion of the participant's body weight and assesses maximum repetitions against the same force. The SLHB test could represent hamstrings' repetitive high force production capacity rather than the maximal eccentric strength or eccentric peak torque. Improving the hamstrings' maximal eccentric strength and SLHB performance should be targeted in the vulnerable population of athletes for HSIs.

This study used the MLE method for calculating the BFlh FL. The MLE method did not significantly differ from panoramic ultrasound scanning, while trigonometric equations significantly overestimated the BFlh FL [4]. In addition, the effects of eccentric training on the BFlh FL are controversial depending on the ultrasound measurement methods [18-20, 11]. This contradiction could be caused by the absence of a gold standard for the BFlh FL measurements [4], which might be a limitation of the present study. Another limitation was not only including professional football players in the study. Additionally, using a handheld dynamometer can be another limitation because its user dependence requires experience and high physical power; the former could lead to inter-tester differences despite the high to very high intra-tester reproducibility of maximal eccentric strength measurements of the present study. Moreover, the TSAFT^{90} interventions were completed outdoors, which could have added unaccounted variability to the results. TSAFT^{90} interventions were completed on weekdays between the 13th of May 2022 and the 17th of June 2022; when the highest daytime temperatures of weekdays were retrospectively analysed, it was seen that the mean temperature was 15.9 ± 1.3 degrees, the minimum temperature was 13 degrees of Celsius, and maximum temperature was 18 degrees of Celsius based on the previous meteorology records of www.accuweather.com. However, not recording environmental factors during the TSAFT90 interventions is a limitation of this study. Future studies are needed to clarify whether environmental factors alter the risk factors of HSIs or not.

Chapter five of this thesis was the first meta-analytic study, especially screening impacts of all the types of resistance training modalities on the upper extremity muscles' architecture and volume. From the perspectives of chest muscles, six weeks of high-intensity bench press training (g = 1.03) [21] and ten weeks of 12 RM bench press exercises (g = 1.21) [22] led to large increments in the pectoralis major size. However, the other exercises showed medium effects (g = 0.61-0.64) on increasing pectoralis major muscle size (Figure 5.25). Regarding the elbow extensors, six weeks of lying triceps extension exercise [23] (g = 1.25), the isometric maximal voluntary co-contraction training [24, 25] (4 weeks and 12 weeks study duration combinations) (g = 1.97), 12-weeks nonlinear periodised resistance training [26] (g = 2.07) largely increased the size of elbow extensors when the rest of the exercises were not showing any large effects on increasing the elbow flexors muscle size (g = 0.15-0.72) (Figure 5.26). From the aspects of elbow flexors, six weeks of traditional elbow flexion exercises (g = 0.93) [27], four weeks of concentric low-load forearm flexion-extension training (g = 0.94) [28], 4-weeks of concentric low-load) forearm flexion-extension training (g = 1) [28], isometric maximal voluntary co-contraction training [26, 27] (4 weeks and 12 weeks study duration combinations) (g = 1.01), 4-weeks concentric low-load forearm flexion-extension training with vBFR (g = 1.02) [28], 4-weeks concentric low-load (at 30% of concentric elbow flexion peak torque) forearm flexion-extension training with vBFR (g = 1.07) [28], 12-weeks nonlinear periodised resistance training (g = 1.13) [29, 30], and 12-weeks nonlinear periodised resistance training (g =1.34) [26] exhibited large effects on increasing the size of elbow flexors (Figure 5.27). Lastly, six weeks of isometric ulnar deviation training has presented a large impact (g = 2.22) on leading hypertrophy in the flexor carpi ulnaris and radialis MT [31] (Figure 5.28). Based on these, athletes or healthy individuals aiming to gain hypertrophy might refer to the relevant training regimens that showed large effect sizes on increasing the pectoralis major, arm and forearm muscle size parameters. However, exercise should be cautiously selected to the small numbers of the included studies in each meta-analysis.

Except for these muscle size parameters mentioned in the paragraph above, the triceps brachii fascicle geometry was significantly correlated with angular velocity (r = 0.563), maximal joint power (r = 0.519) and maximal isometric torque (r = 0.471) of elbow extension [32], swimming performance (r = -0.64), bench lift (r = 0.52), deadlift (r = 0.56) and squat lift (r = 0.45) performances [33]. The triceps brachii fascicle geometry was the best predictor of better 200-m front crawl swimming time (r^2 = 0.392) [34]. Further, infraspinatus MT was

significantly correlated with shoulder external rotation strength in professional baseball pitchers (r = 0.287) [35]. The subscapular MT was the best single predictor for powerlifting performance in professional powerlifters [33]. However, this systematic did not observe any RCTs focusing on resistance training-leading changes in the fascicle geometry of triceps brachii, infraspinatus MT, and supraspinatus MT. Future RCTs should investigate the impacts of resistance training modalities in these mentioned muscle architectural parameters in the relevant sports disciplines, such as infraspinatus MT in baseball pitchers, subscapular MT in powerlifters, and fascicle geometry of the triceps brachii in swimmers. A limitation of this study was including a small number of randomised controlled trials (RCTs) in each meta-analysis. Another limitation was not being able to perform further analyses such as meta-regression or assessing the included studies in a meta-analysis due to the small number of RCTs in each meta-analysis [36]. A further confounding factor was inter-differences of the training interventions that can lead to uncountable variability in the results of the meta-analyses.

Chapter 7: General Conclusions and Future Research Suggestions

Chapter two of this thesis was a systematic review with meta-analyses, and it aimed to compare the effect size of eccentric training, including the Nordic hamstring exercise (NHE), on the biceps femoris long head (BFlh) fascicle length (FL) based on different ultrasound assessment methods. Based on the findings of chapter two of this thesis, the effect size of eccentric exercise, including the NHE, on increasing the BFlh FL vary between ultrasound examination methods: Manual linear extrapolation, panoramic ultrasound scanning and trigonometric equation methods. A "gold standard" measurement method is needed for comparable results between the studies investigating the effects of eccentric exercise on the biceps femoris long head fascicle length. A future randomised controlled trial should compare the size of the eccentric exercise effect between the ultrasound assessment methods to clarify if there is a significant difference between the effect sizes based on the ultrasound assessment methods on the same sample exposed to the same intervention.

Chapter three of this thesis was a cross-sectional study, and it aimed to compare BFlh fascicle length, passive stiffness, and thigh muscles' morphology in male rugby union players and healthy active controls for understanding the long-term effects of playing rugby on the mentioned muscular structures. In light of the findings of chapter four of this thesis, long-term rugby-specific training and match play may lead to an increased risk of HSI compared to active controls, based on imbalanced developments favouring the knee extensor muscles. Specifically considering hamstring strain injury mechanism, exposure to rugby leads to increased BFlh passive muscle stiffness and smaller BFlh fascicle length/KE ratios. Moreover, playing rugby did not increase the KF muscle volume relative to body mass. In conclusion, habitual rugby training and match-play lead to structural and morphological alterations in the KF and KE that may increase HSI risk. Practitioners should administer long-term hamstring pre-habilitation training to reduce HSI risk in rugby players. Future prospective studies should examine whether there are threshold values in the BFlh fascicle length/KE muscle volume, BFlh/KE and KF/KE muscle volume ratios for predicting HSIs.

Chapter four of this thesis had a one-group repeated measures study design, and it aimed to investigate immediate changes in selected modifiable risk factors of hamstring strain injuries that are BFlh FL, maximal eccentric hamstring strength, single leg hamstring bridge (SLHB) performance and single-leg hop distance, as specified by chapter five of this thesis, maximal eccentric strength and the SLHB performance of hamstrings are reduced after 90 minutes of simulated football match play. Practitioners may consider focusing on improving

eccentric strength and SLHB performance. Future studies should examine alterations in the BFlh fascicles' dynamic lengthening and shortening ability during a football match.

Chapter five of this thesis was a systematic review with meta-analyses, and it aimed to screen studies focusing on the impacts of resistance training on the upper extremity muscles' architectural parameters and volumes. According to the findings of chapter three of this thesis, high-intensity bench press training, 12 RM bench press exercises, isometric maximal voluntary co-contraction training, lying triceps extension exercise, nonlinear periodised resistance training, traditional elbow flexion exercises, concentric low-load forearm flexion-extension training, concentric low-load forearm flexion-extension training with blood flow restriction, and isometric ulnar deviation training showed large effects on increasing muscle size of the relevant upper extremity muscles. Results show that these training modalities are suitable for gaining hypertrophy in the relevant muscles with at least four weeks of training duration. Future RCTs should investigate the effects of exercise modalities on the triceps brachii fascicle geometry, the infraspinatus muscle thickness (MT) and the subscapular MT due to their associations with sports performance.

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Appendices

Appendix I - Ethical Approval Documents

I.a. Ethical approval for Chapter 4 (Original Investigation 1).

別記第2号様式(第6条関係)

2都立大荒管第782号
令和　3年　1月　5日

信太　奈美　様

東京都立大学大学院人間健康科学研究科
研究科長　渡邊　賢　印

研究倫理審査の判定結果について(通知)

2020年12月8日付で申請のあった研究計画(受理番号:20067)に係る標記の件について、研究倫理委員会において下記のとおり判定されましたので、通知します。

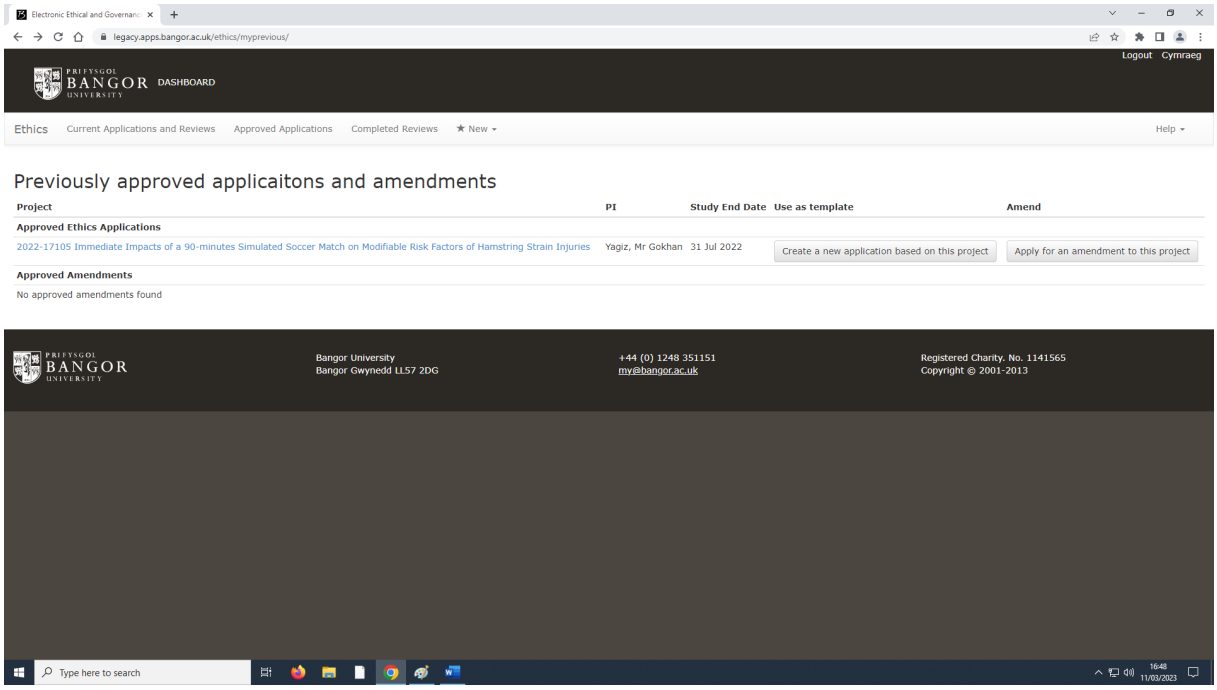
記

承認番号	20067

区　分		所属・職名 (学生は学修番号を記入)	氏　名
1. 申請者		人間健康科学研究科　理学療法科学域　准教授	信太　奈美
2. 研究者	(1) 研究代表者	人間健康科学研究科　理学療法科学域　准教授	信太　奈美
	(2) 共同(又は分担)研究者	来間　弘展、安田　透、Gokhan Yagiz, Julian Andrew Owen, Hans-Peter Kubis	
	(3) 指導教員		
3. 研究課題名		Differences in hamstrings muscle architecture, elasticity and hamstrings-quadriceps morphology between athletes from the sports carrying high hamstring strain injury incidence and age-matched sedentary controls.	
4. 判定		承　認(付記あり)　・　条件付承認　・　変更の勧告 不承認　・　該当せず(委員会開催　2020年12月18日)	
5. 理由又は勧告		(付記)　別紙参照	

注1　委員会の判定に対して異議がある場合は、この通知を受けた日の翌日から起算して2週間以内に再審査を請求することができます。
注2　委員会の判定が「変更の勧告」となった場合は、勧告に基づき変更した研究計画により、この通知を受けた日の翌日から起算して1か月以内に再申請することができます。
注3　委員会の判定が「条件付承認」となった場合は、付した条件に基づき速やかに書類を修正し、迅速審査の申請を行ってください。
注4　「承認」で付記事項がある場合は、修正した修正箇所を赤字にした書類一式の電子データをメールにてrinri-hs@tmu.ac.jpに送付し、研究倫理審査申請書(別記第1号様式)の原本を管理課企画担当(学務課窓口)に提出してください。
注5　研究が終了しましたら、研究倫理報告書(別記第4号様式)を提出してください。

I.b. Ethical approval for Chapter 5 (Original Investigation 2).



URL: https://legacy.apps.bangor.ac.uk/ethics/myprevious/

Accessed on 11/03/2023

Appendix II- Conference abstracts specifically relating to this thesis

OA34

CHANGES IN RISK FACTORS OF HAMSTRING STRAIN INJURIES FOLLOWING SIMULATED SOCCER MATCH-PLAY (TSAFT90)

[1]GÖKHAN YAĞIZ, [1]VINAY KUMAR DAYALA, [1]KEVIN WILLIAMS, [1]JULIAN ANDREW OWEN, [1]HANS-PETER KUBIS

[1]Bangor University, Institute For Applied Human Physiology, School of Human and Behavioural Sciences, Bangor, UK

The occurrence of hamstring strain injuries (HSIs) during a football match is greater than the occurrence during football training. The last fifteen minutes of each forty-five minutes of a football match are the most vulnerable time for the hamstrings, based on the increasing incidence of injuries towards the end of a match. This study investigated changes in the HSIs risk factors in an athletic population (n = 15), including the biceps femoris fascicle length (BFlh FL), single-leg hop distance, maximal eccentric hamstring strength, and eccentric hamstring endurance, during the TSAFT90 simulated soccer match. The BFlh FL (via ultrasonography) and single-leg hop distance (via single-leg hop test) were measured before, at half-time and immediately after the TSAFT90. The maximal eccentric hamstring strength (via handheld dynamometry) and eccentric hamstring endurance (via single-leg hamstring bridge test) were assessed twice before and immediately after the TSAFT90. As a secondary measurement, the average percentage heart rate (%HRmax) was estimated for every fifteen minutes of the T-SAFT90 soccer simulation. Significant large decrements were observed in the hamstrings' eccentric endurance (dominant leg (D): $p < 0.001$, Hedges' (adjusted) g effect size = -1.249; non- dominant leg (ND): $p < 0.001$, $g = -1.108$), and hamstrings' maximal eccentric strength (D: $p < 0.001$, $g = -0.969$; ND: $p < 0.001$, $g = -0.929$). The %HRmax of the last fifteen minutes was significantly higher than the rest of each fifteen minutes of the TSAFT90. There were no significant changes in the BFlh FL and single-leg hop distance. Outcomes show that HSIs risk factors such as eccentric endurance and strength are mostly affected by TSAFT90. Specialists should focus on increasing hamstrings' eccentric endurance and strength to reduce the risk of HSIs during football match-play.

Keywords: Muscle architecture - posterior thigh - knee flexors - lower extremity - strain injury

Appendix III. Supporting Information and Supporting Tables.

III.a. Supporting information 2.1. Database searches.

Figure A. CINAHL Plus with full-text.

EBSCOhost

Tuesday, July 06, 2021 1:41:42 PM

#	Query	Limiters/Expanders	Last Run Via	Results
S4	S1 AND S2 AND S3	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	97
S3	AB ACSA OR Architectur* OR "Cross Sectional Area" OR "Cross-sectional Area" OR Fascic* OR "Fiber Length" OR "Fibre Length" OR Pennat* OR Pinnat* OR "Muscle Thickness" OR "Muscle Volume" OR "Muscle Structure" OR "Muscle Length" OR PCSA	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	16,888
S2	AB "Biceps Femoris" OR Hamstring* OR "Knee flexors" OR "Posterior Thigh" OR Semitendinosus OR Semimembranosus	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	6,251
S1	AB Exercis* OR Training*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	252,301

Table A. The Cochrane Central Register of Controlled Trials (CENTRAL).

Search Name:

Date Run: 06/07/2021 13:44:44

Comment:

ID Search Hits

#1 MeSH descriptor: [Exercise] explode all trees 25883

#2 Exercis* OR Training* 177668

#3 "Biceps Femoris" OR Hamstring* OR "Knee Flexors" OR "Posterior Thigh" OR Semitendinosus OR Semimembranosus 3185

#4 ACSA OR Architectur* OR "Cross Sectional Area" OR "Cross-sectional Area" OR Fascic* OR "Fiber Length" OR "Fibre Length" OR Pennat* OR Pinnat* OR "Muscle Thickness" OR "Muscle Volume" OR "Muscle Structure" OR "Muscle Length" OR PCSA 6018

#5 #1 AND #2 24238

#6 #3 AND #4 AND 5 in Trials 94

Table B. PubMed.

Search number	Query	Sort By	Filters	Results	Time
6	#3 AND #4 AND #5	Most Recent		229	09:03:44
5	#1 OR #2	Most Recent		813,191	09:02:35
4	ACSA OR Architectur* OR "Cross Sectional Area"[Title/Abstract] OR "Cross-sectional Area"[Title/Abstract] OR Fascic* OR "Fiber Length"[Title/Abstract] OR "Fibre Length"[Title/Abstract] OR Pennat* OR Pinnat* OR "Muscle Thickness"[Title/Abstract] OR "Muscle Volume"[Title/Abstract] OR "Muscle Structure"[Title/Abstract] OR "Muscle Length"[Title/Abstract] OR PCSA	Most Recent		243,366	09:01:44
3	"Biceps Femoris"[Title/Abstract] OR Hamstring*[Title/Abstract] OR "Knee flexors"[Title/Abstract] OR "Posterior Thigh"[Title/Abstract] OR Semitendinosus[Title/Abstract] OR Semimembranosus[Title/Abstract]	Most Recent		16,555	08:59:55

	Exercis*[Title/Abstract] OR			
2	Training*[Title/Abstract]	Most Recent	716,114	08:51:32
1	"Exercise"[Mesh]	Most Recent	212,935	08:50:22

Figure B. OpenGrey.

III.b. Supporting information 2.2. PRISMA 2020 checklist.

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Pages 3-5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Pages 4, 5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Pages 6, 7
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Pages 5, 6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supporting File S1

Section and Topic	Item #	Checklist item	Location where item is reported
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Pages 6, 7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Pages 6-9
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Pages 10-13, 20-22, Table 1
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 7, 13
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Pages 13-22
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Pages 13-22
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Pages 7-10, 13-23, Table 1, Supporting Information S4
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Pages 7-10, 13-23
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Pages 13-23
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Pages 13-23
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	No missing results
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 13, Supporting Information S3
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Pages 9, 10, Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1

Section and Topic	Item #	Checklist item	Location where item is reported
Study characteristics	17	Cite each included study and present its characteristics.	Page 10, table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Figures 2, 3
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Figures 4-13, Tables 1,2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Supporting Information S3
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Figures 4-13, Table 2, Supporting Information S4
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Figures 4-13, Supporting Information S4
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NA
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	No missing results
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Supporting Information S3.
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pages 18-23
	23b	Discuss any limitations of the evidence included in the review.	Pages 18-23
	23c	Discuss any limitations of the review processes used.	Page 22
	23d	Discuss implications of the results for practice, policy, and future research.	Pages 18-23
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	NA
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	NA
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Pages 24, 25
Competing interests	26	Declare any competing interests of review authors.	Page 24
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 24

Abbreviations: NA, not applicable

III.c. Supporting information 2.3. Level of evidence of the meta-analyses.

Table A. Eccentric training (created via GRADEpro GDT).

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Effects of eccentric training on the biceps femoris fascicle length based on the ultrasound extrapolation methods	placebo	Relative (95% CI)	Absolute (95% CI)		
Effects of eccentric training on the biceps femoris fascicle length based on the ultrasound extrapolation methods												
8	randomised trials	serious [a]	very serious [b]	not serious	serious [c]	publication bias strongly suspected very strong association [d]	106	105	-	SMD **1.06 higher** (0.44 higher to 1.68 higher)	⨁◯◯◯ VERY LOW	
Effects of eccentric training on the biceps femoris fascicle length based on the ultrasound extrapolation methods - Panoramic ultrasound scanning												
2	randomised trials	serious [e]	not serious	not serious	serious [c]	none	28	26	-	SMD **0.72 higher** (0.17 higher to 1.28 higher)	⨁⨁◯◯ LOW	
Effects of eccentric training on the biceps femoris fascicle length based on the ultrasound extrapolation methods - Manual linear extrapolation												
3	randomised trials	serious [f]	not serious	not serious	serious [c]	none	38	39	-	SMD **0.29 higher** (0.26 lower to 0.85 higher)	⨁⨁◯◯ LOW	
Effects of eccentric training on the biceps femoris fascicle length based on the ultrasound extrapolation methods - Trigonometric equation												
3	randomised trials	serious [g]	very serious [b]	not serious	serious [c]	publication bias strongly suspected very strong association [h]	40	40	-	SMD **2.2 higher** (0.99 higher to 3.41 higher)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **SMD:** Standardised mean difference

Explanations

a. None of the 8 RCTs mentioned allocation concealment. Only one study performed participant blinded assessment. Three studies did not perform an assessor-blinded intervention. Three studies did not perform a reliability study.

b. I2 ≥ 75%

c. Large CI, low sample size

d. Detected in the funnel plot

e. No concealment, no blinded participants, no assessor-blinded in a study

f. No concealment in 3 studies, no reliability in one study, no blinded participants, no assessor-blinded in one study, no reliability in one study.

g. No concealment in 3 studies. No participants were blinded in 2 studies, no assessor-blinded in 1 study, no reliability was performed in 2 studies.

h. Possible overestimation was seen in funnel plots.

Table B. Nordic hamstring exercise (created via GRADEpro GDT).

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Effects of Nordic hamstring exercise on the biceps femoris fascicle length based on the ultrasound extrapolation methods	placebo	Relative (95% CI)	Absolute (95% CI)		
Effects of Nordic hamstring exercise on the biceps femoris fascicle length based on the ultrasound extrapolation methods												
6	randomised trials	serious [a]	very serious [b]	not serious	serious [c]	publication bias strongly suspected strong association [d]	57	58	-	SMD **1.09 higher** (0.16 higher to 2.01 higher)	⨁◯◯◯ VERY LOW	
Effects of Nordic hamstring exercise on the biceps femoris fascicle length based on the ultrasound extrapolation methods - Panoramic ultrasound scanning												
1	randomised trials	serious [e]	not serious	not serious	serious [c]	none	10	10	-	SMD **0.38 higher** (0.5 lower to 1.27 higher)	⨁⨁◯◯ LOW	
Effects of Nordic hamstring exercise on the biceps femoris fascicle length based on the ultrasound extrapolation methods - Manual linear extrapolation												
2	randomised trials	serious [f]	serious [g]	not serious	serious [c]	none	17	18	-	SMD **0.23 higher** (1.02 lower to 1.47 higher)	⨁◯◯◯ VERY LOW	
Effects of Nordic hamstring exercise on the biceps femoris fascicle length based on the ultrasound extrapolation methods - Trigonometric equation												
3	randomised trials	serious [h]	very serious [b]	not serious	serious [c]	publication bias strongly suspected very strong association [i]	30	30	-	SMD **1.98 higher** (0.52 higher to 3.44 higher)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **SMD:** Standardised mean difference

Explanations

a. No allocation concealment, no blinded participants in 5 studies, no reliability performed for three studies, no assessor-blinded in 3 studies.

b. I2 ≥ 75%

c. Large CI, low sample size

d. Was seen in the funnel plot

e. No blinded assessor or participants,

f. No allocation concealment in 2 studies, no blinded participants in two studies, no reliability performed in one study.

g. I2 ≥ 50%

h. No allocation concealment in 3 studies, no participants blinded in 2 studies, no assessors blinded in 2 studies, no reliability performed for one study

i. Possible overestimations were seen in the funnel plot

III.d. Supporting information 2.4. Comparisons.

Comparisons between this meta-analysis and previous meta-analyses[1 2]

Figure A. Funnel plot for mean difference (cm), 95% confidence interval, fixed effect.

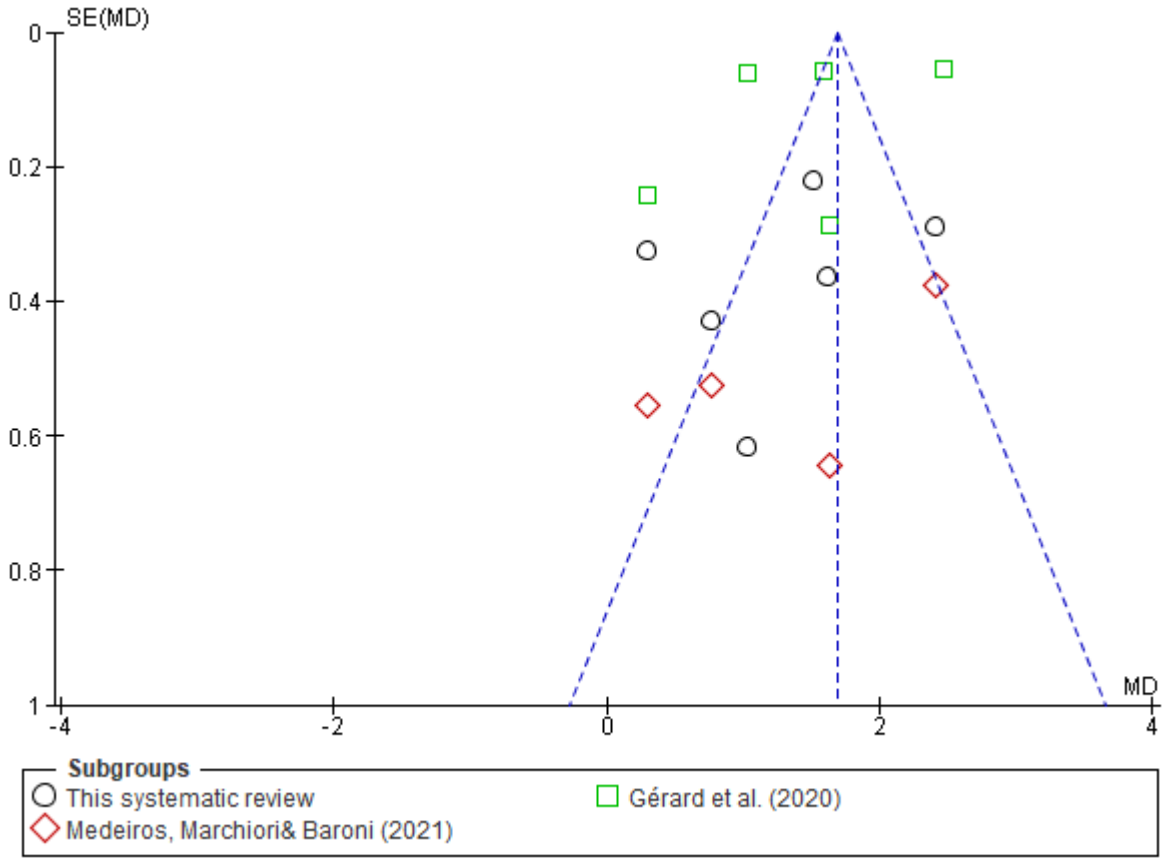


Figure B. Forest plot for mean difference (cm), 95% confidence interval, fixed effect.

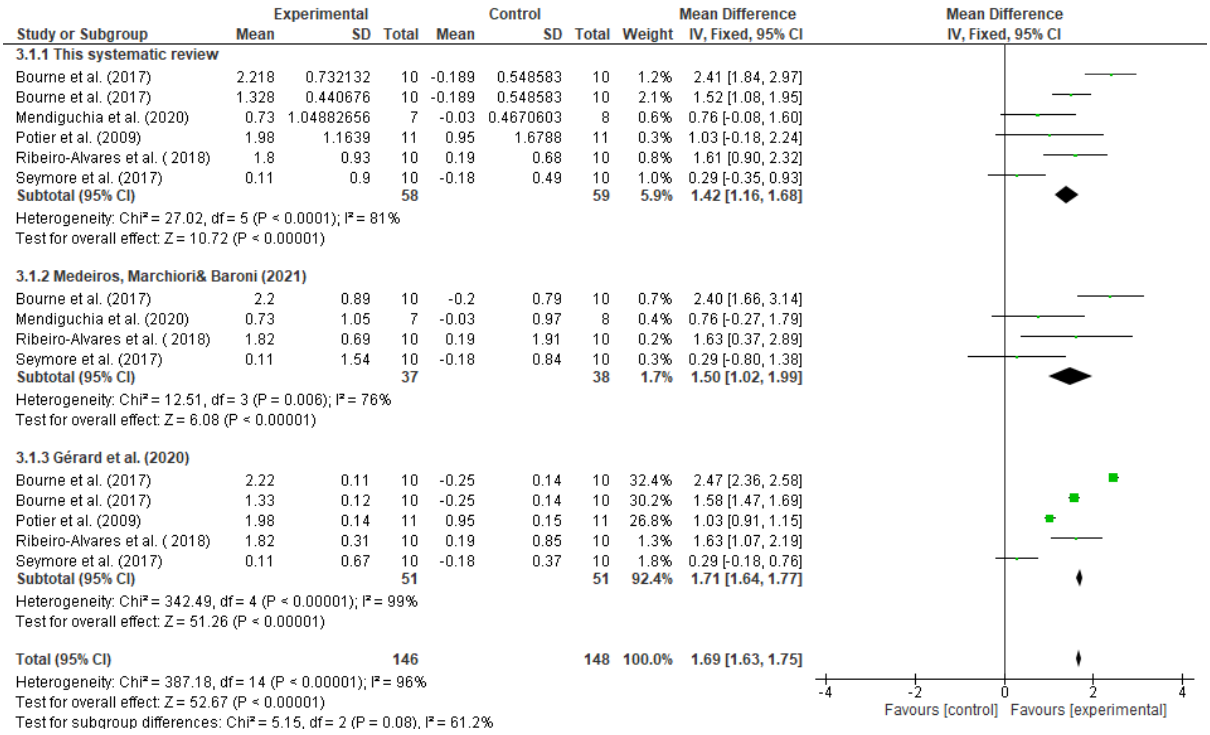


Figure C. Funnel plot for mean difference (cm), 95% confidence interval, random effect.

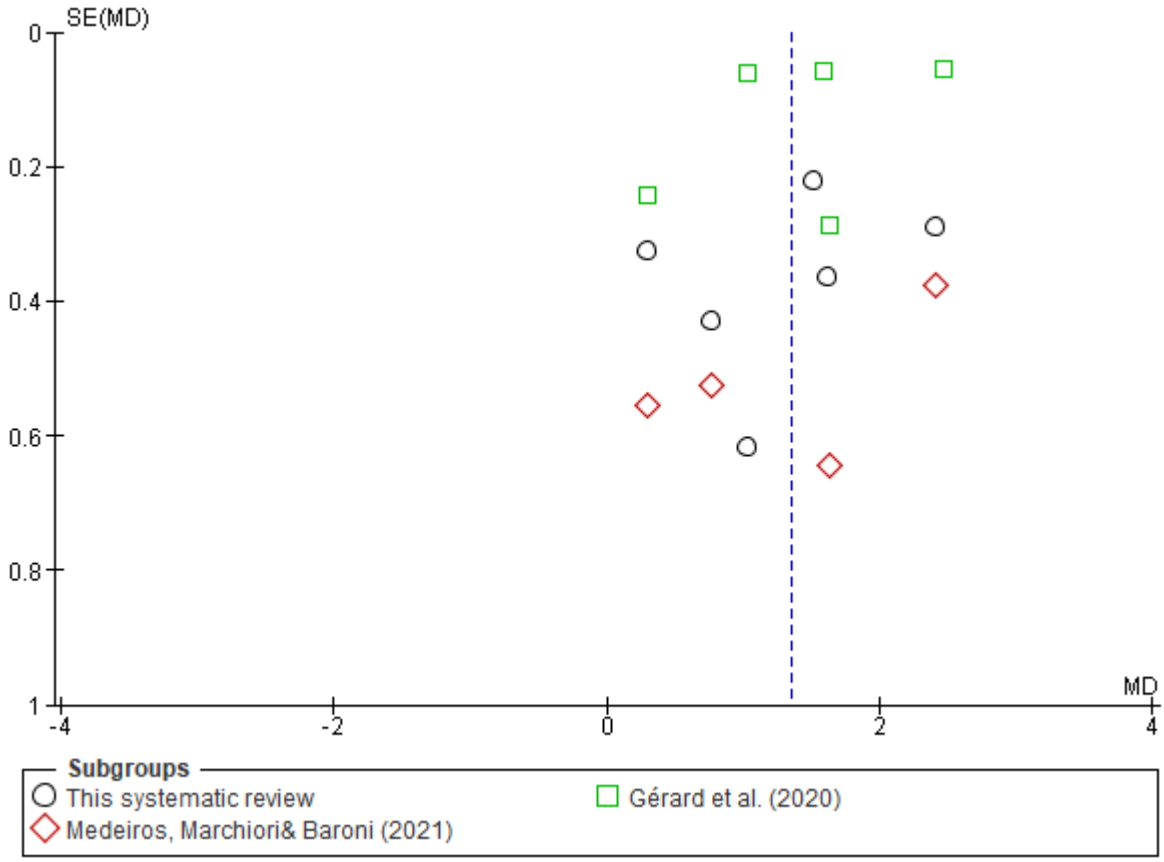


Figure D. Forest plot for mean difference (cm), 95% confidence interval, random effect.

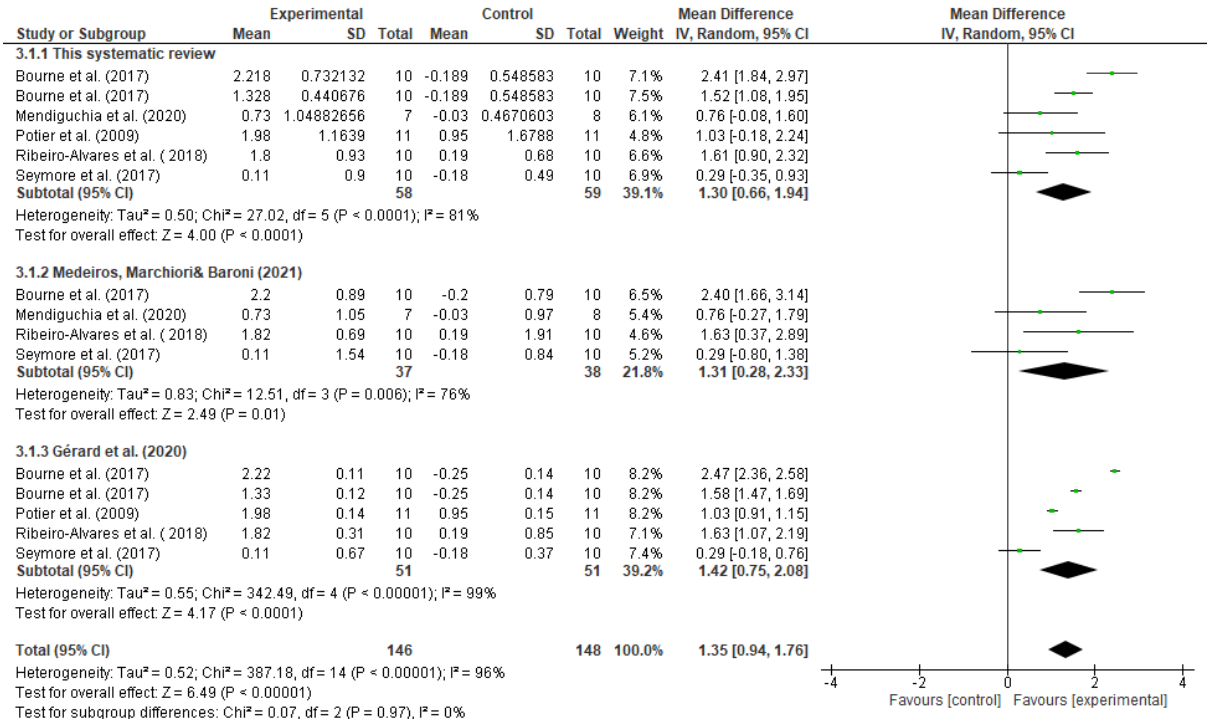


Figure E. Funnel plot for standardised mean difference (effect size (Hedge's (adjusted) g)), 95% confidence interval, fixed effect.

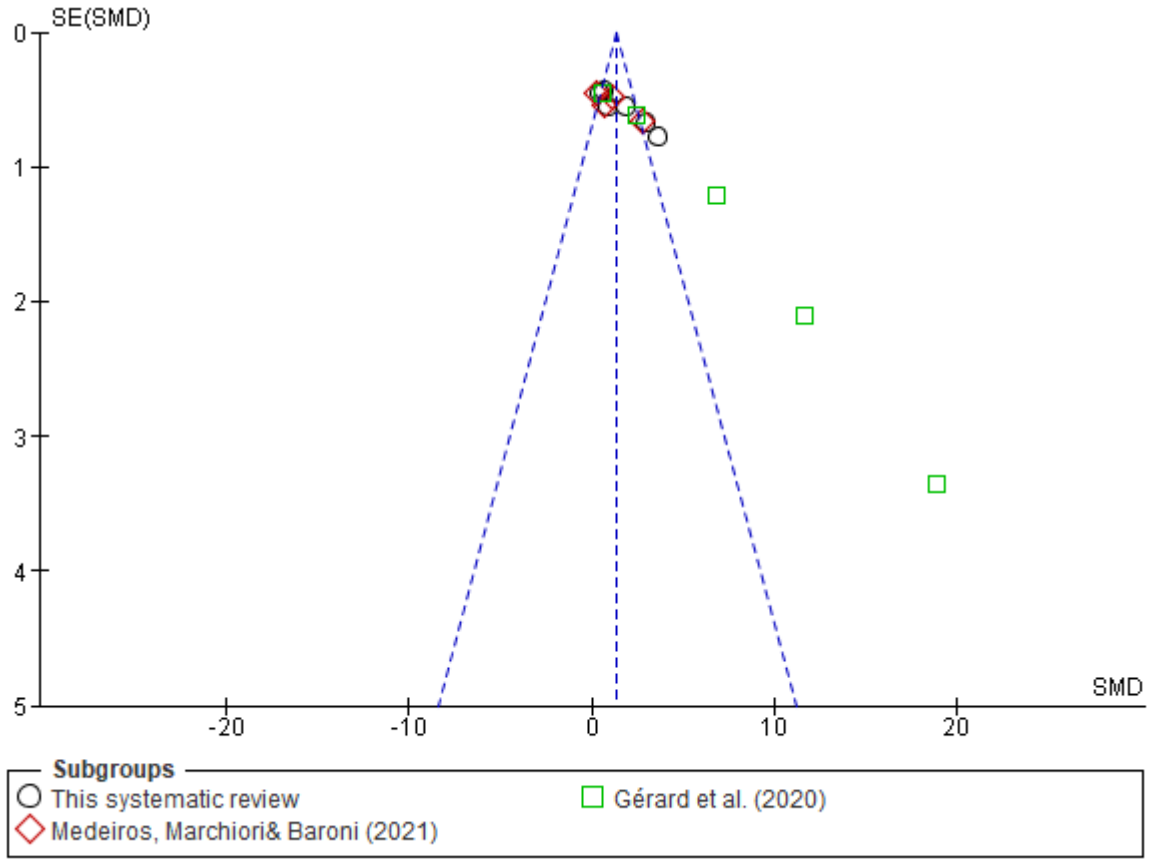


Figure F. Forest plot for standardised mean difference (effect size (Hedge's (adjusted) g)), 95% confidence interval, fixed effect.

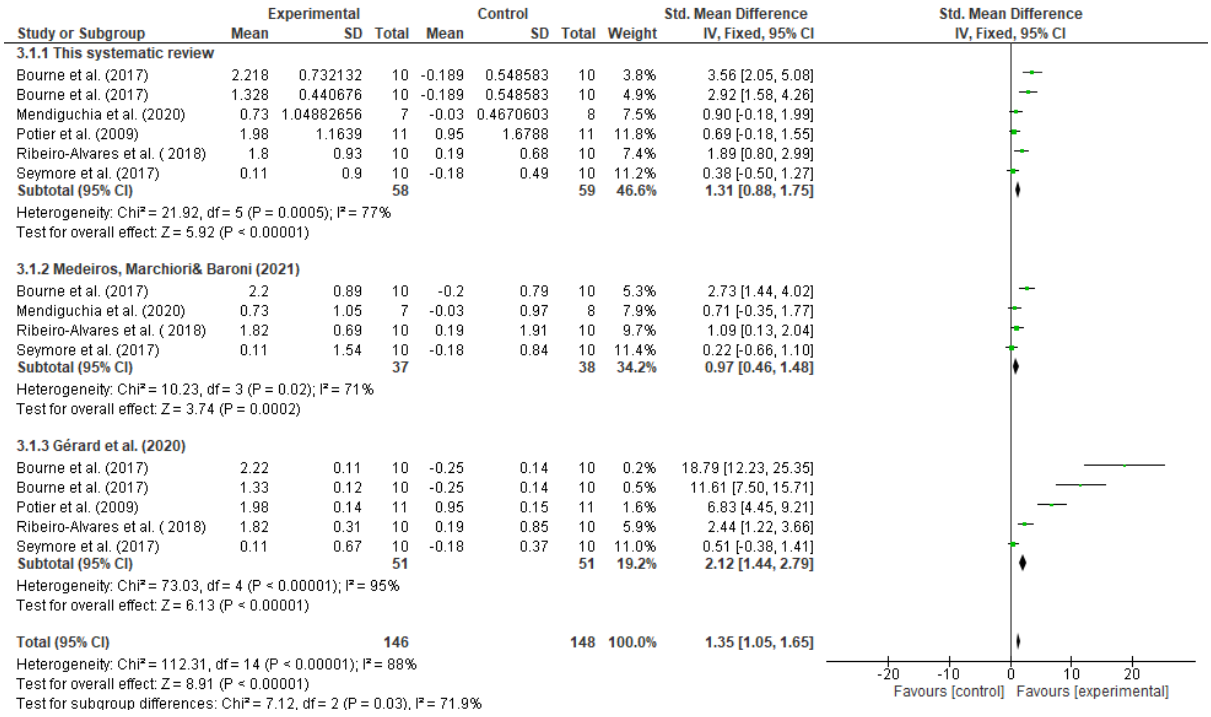


Figure G. Funnel plot for standardised mean difference (effect size (Hedge's (adjusted) g)), 95% confidence interval, random effect.

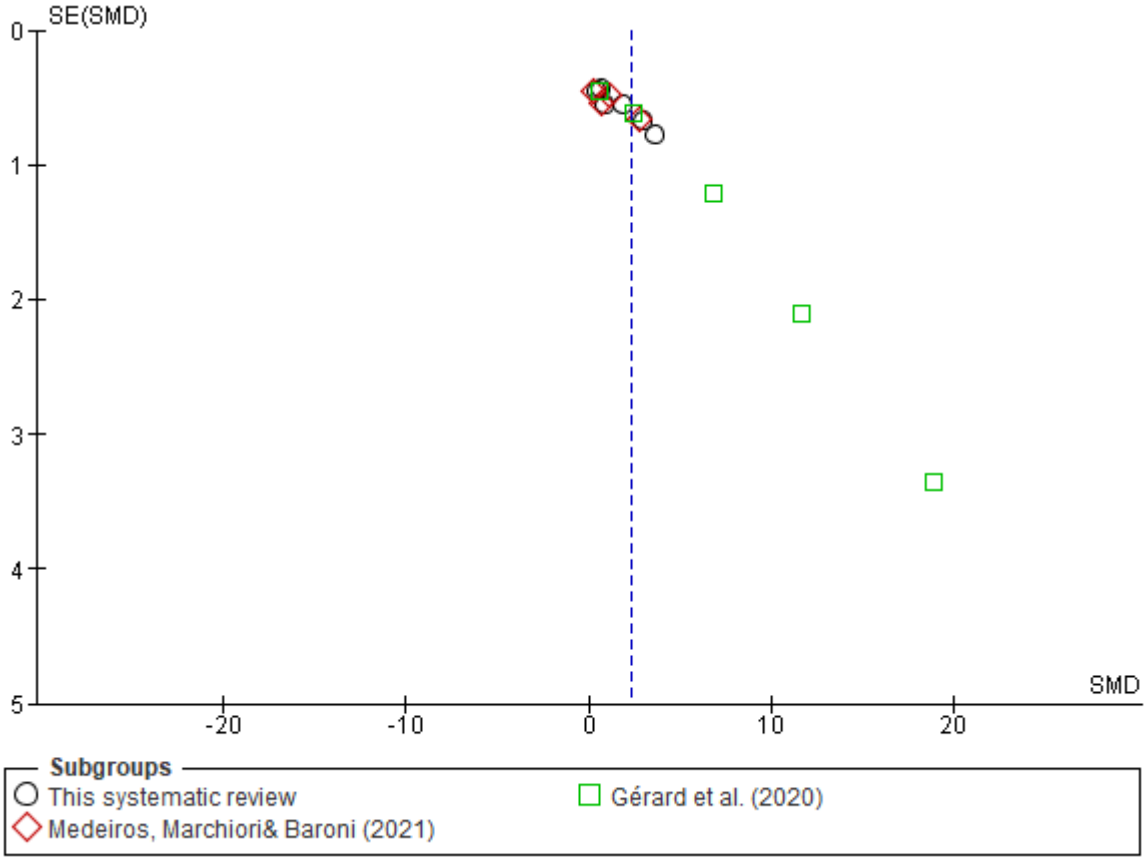
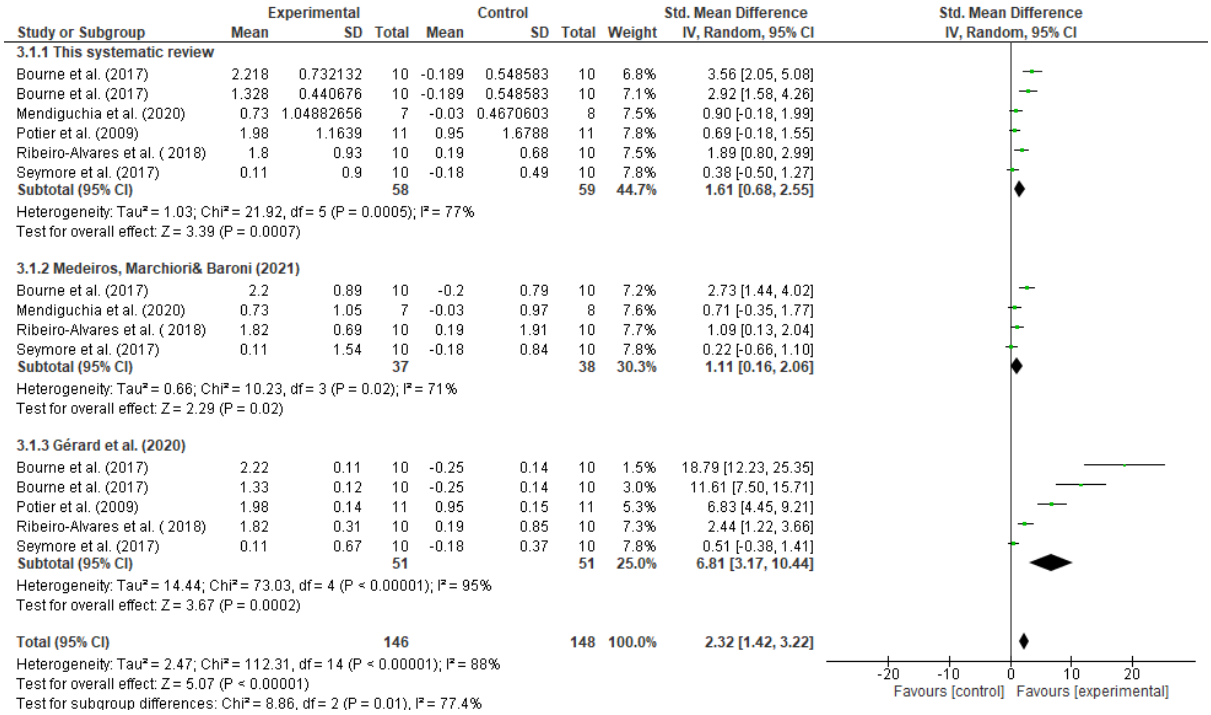


Figure H. Forest plot for standardised mean difference (effect size (Hedge's (adjusted) g)), 95% confidence interval, random effect.



III.e. Supporting information 5.1. PRISMA 2020 Cheklist.

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Pages 1, 2
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Pages 1, 2
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 3
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 2, 3, Supplementary File S3
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary File S3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Pages 3, 4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming	Pages 3-5

Section and Topic	Item #	Checklist item	Location where item is reported
		data from study investigators, and if applicable, details of automation tools used in the process.	
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Pages 3-5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Pages 3-5
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 3
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Pages 3-5
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Pages 3-5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Pages 3-5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Pages 3-5
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Pages 3-5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 20
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 20
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 20
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 5
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 5, Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 5, Figure 6
Study characteristics	17	Cite each included study and present its characteristics.	Page 5, Supplementary Table S3, Supplementary Table S3
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Figures 2, 3
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its	Figures 4-25

Section and Topic	Item #	Checklist item	Location where item is reported
		precision (e.g. confidence/credible interval), ideally using structured tables or plots.	
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Supplementary File S3
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Figures 4-25
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 20
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page 20
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Supplementary File S3
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Supplementary File S3
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pages 16-20
	23b	Discuss any limitations of the evidence included in the review.	Pages 16-20
	23c	Discuss any limitations of the review processes used.	Pages 16-20
	23d	Discuss implications of the results for practice, policy, and future research.	Pages 16-20
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 2
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 2
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Page 2
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 21
Competing interests	26	Declare any competing interests of review authors.	Page 21
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 21

III.f. Supporting information 5.2. Database searches.

1- CENTRAL (Cochrane Library)

Search Name:

Date Run: 31/07/2021 18:48:20

Comment:

ID Search Hits

#1 MeSH descriptor: [Exercise] explode all trees 26197

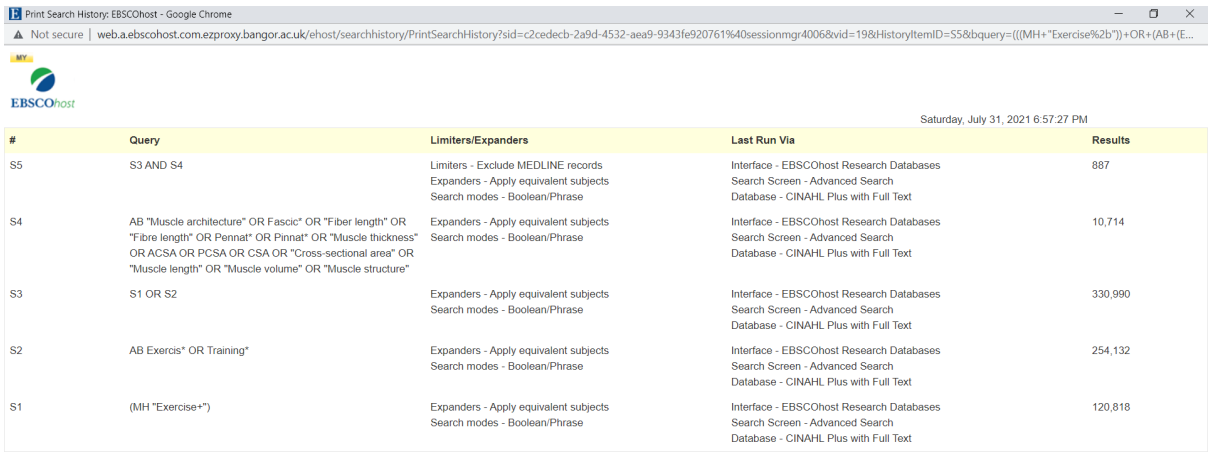
#2 Exercis* OR Training* 179395

#3 #1 OR #2 181046

#4 "Muscle architecture" OR Fascic* OR "Fiber length" OR "Fibre length" OR Pennat* OR Pinnat* OR "Muscle thickness" OR ACSA OR PCSA OR CSA OR "Cross-sectional area" OR "Muscle length" OR "Muscle volume" OR "Muscle structure" 6596

#5 #3 AND #4 in Trials1975

2- CINAHL Plus with Full-Text



Print Search History: EBSCOhost - Google Chrome

Not secure | web.a.ebscohost.com.ezproxy.bangor.ac.uk/ehost/searchhistory/PrintSearchHistory?sid=c2cedecb-2a9d-4532-aea9-9343fe920761%40sessionmgr4006&vid=19&HistoryItemID=S5&bquery=(((MH+"Exercise%2b"))+OR+(AB+(E...

EBSCOhost

Saturday, July 31, 2021 6:57:27 PM

#	Query	Limiters/Expanders	Last Run Via	Results
S5	S3 AND S4	Limiters - Exclude MEDLINE records Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	887
S4	AB "Muscle architecture" OR Fascic* OR "Fiber length" OR "Fibre length" OR Pennat* OR Pinnat* OR "Muscle thickness" OR ACSA OR PCSA OR CSA OR "Cross-sectional area" OR "Muscle length" OR "Muscle volume" OR "Muscle structure"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	10,714
S3	S1 OR S2	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	330,990
S2	AB Exercis* OR Training*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	254,132
S1	(MH "Exercise+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	120,818

Type here to search

16°C Cloudy

19:57
31/07/2021

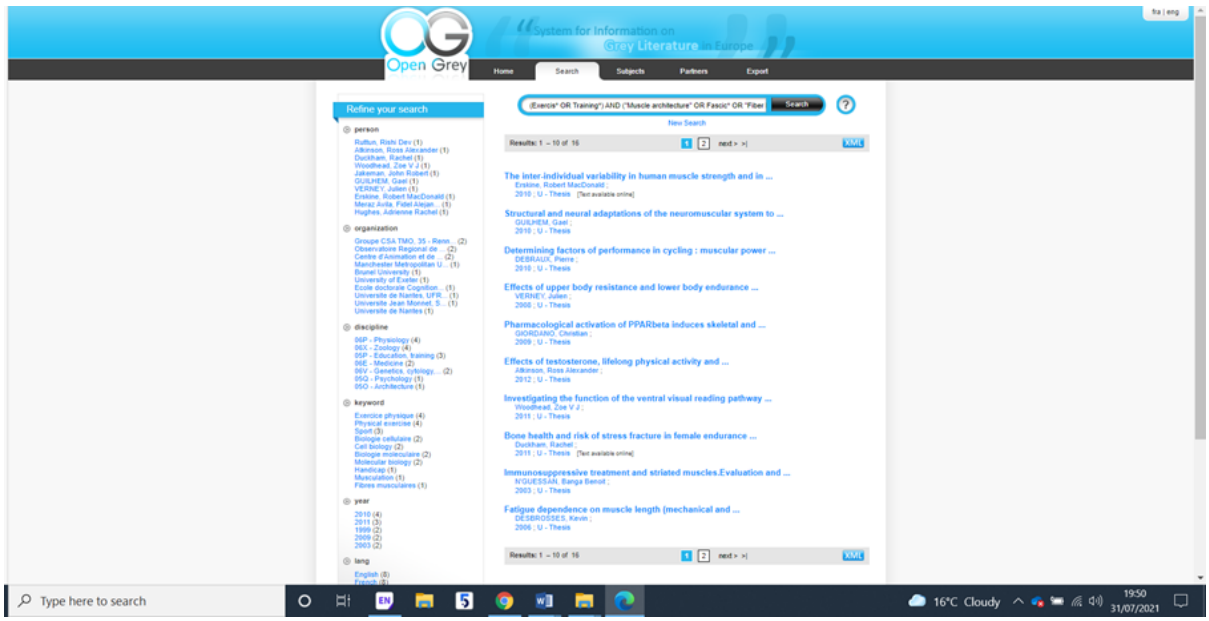
3- PubMed

Search number	Query	Sort By	Filters	Search Details	Results	Time
5	#3 AND #4	Most Recent		("Exercise"[MeSH Terms] OR ("exercis*"[Title/Abstract] OR "training*"[Title/Abstract])) AND ("Muscle architecture"[Title/Abstract] OR "fascic*"[All Fields] OR "Fiber	5,510	14:40:34

			length"[Title/Abstract] OR "Fibre length"[Title/Abstract] OR "pennat*"[All Fields] OR "pinnat*"[All Fields] OR "Muscle thickness"[Title/Abstract] OR "ACSA"[All Fields] OR "PCSA"[All Fields] OR "CSA"[All Fields] OR "Cross-sectional area"[Title/Abstract] OR "Muscle length"[Title/Abstract] OR "Muscle volume"[Title/Abstract] OR "Muscle structure"[Title/Abstract])		
4	"Muscle architecture"[Title/Abstract] OR Fascic* OR "Fiber length"[Title/Abstract] OR "Fibre length"[Title/Abstract] OR Pennat* OR Pinnat* OR "Muscle thickness"[Title/Abstract] OR ACSA OR PCSA OR CSA OR "Cross-sectional area"[Title/Abstract] OR "Muscle length"[Title/Abstract] OR "Muscle volume"[Title/Abstract] OR "Muscle structure"[Title/Abstract]	Most Recent	"Muscle architecture"[Title/Abstract] OR "fascic*"[All Fields] OR "Fiber length"[Title/Abstract] OR "Fibre length"[Title/Abstract] OR "pennat*"[All Fields] OR "pinnat*"[All Fields] OR "Muscle thickness"[Title/Abstract] OR "ACSA"[All Fields] OR "PCSA"[All Fields] OR "CSA"[All Fields] OR "Cross-sectional area"[Title/Abstract] OR "Muscle length"[Title/Abstract] OR "Muscle volume"[Title/Abstract] OR "Muscle structure"[Title/Abstract]	96,697	14:40:15
3	#1 OR #2	Most Recent	"Exercise"[MeSH Terms] OR "exercis*"[Title/Abstr	818,107	14:39:29

			act] OR "training*"[Title/Abstract]		
2	Exercis*[Title/Abstract] OR Training*[Title/Abstract]	Most Recent	"exercis*"[Title/Abstract] OR "training*"[Title/Abstract]	720,293	14:39:09
1	"Exercise"[Mesh]	Most Recent	"Exercise"[MeSH Terms]	214,469	14:38:43

4- OpenGrey



III.g. Supporting Information 5.3. Level of Evidence of the Meta-analyses.

. 1- The effect of 6-weeks of Lying Triceps Extension Exercise (Sequential Concentric and Eccentric Elbow Extensions) on the Triceps Brachii Long Head MT compared to placebo for [health problem]

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The effect of 6-weeks of Lying Triceps Extension Exercise (Sequential Concentric and Eccentric Elbow Extensions) on the Triceps Brachii Long Head MT	placebo	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious [a]	not serious	not serious	serious [b]	strong association	13	10	-	SMD **1.25 higher** (0.33 higher to 2.16 higher)	⨁⨁⨁◯ Moderate	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors

b. Small sample size, large confidence interval

2- The Effects of 6-weeks of Traditional Concentric Traditional Elbow Flexion Exercises on the Elbow Flexors MT compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of 6-weeks of Traditional Concentric Traditional Elbow Flexion Exercises on the Elbow Flexors MT	placebo	Relative (95% CI)	Absolute (95% CI)		

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of 6-weeks of Traditional Concentric Traditional Elbow Flexion Exercises on the Elbow Flexors MT	placebo	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	not serious	not serious	not serious	serious[a]	strong association	144	153	-	SMD **0.93 higher** (0.69 higher to 1.17 higher)	⨁⨁⨁⨁ High	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Small sample size, large confidence interval

3- The Effects of 6-weeks of Concentric Heavy (80-85% of 1RM) Elbow Flexion Exercises on the Elbow Flexors MT compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of 6-weeks of Concentric Heavy (80-85% of 1RM) Elbow Flexion Exercises on the Elbow Flexors MT	placebo	Relative (95% CI)	Absolute (95% CI)		

1.1.1. The Effects of 6-weeks of Concentric Heavy (80-85% of 1RM) Elbow Flexion Exercises on the Elbow Flexors MT

1	randomised trials	not serious	not serious	not serious	not serious	none	156	153	-	SMD **0.38 higher** (0.15 higher to 0.6 higher)	⨁⨁⨁⨁ High	

CI: confidence interval; **SMD:** standardised mean difference

4- The Effects of 6-weeks Unilateral Isometric Ulnar Deviation Training on Flexor Carpi Ulnaris and Flexor Carpi Radialis MT compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of 6-weeks Unilateral Isometric Ulnar Deviation Training on Flexor Carpi Ulnaris and Flexor Carpi Radialis MT	placebo	Relative (95% CI)	Absolute (95% CI)		
1.1.1. The Effects of 6-weeks Unilateral Isometric Ulnar Deviation Training on Flexor Carpi Ulnaris and Flexor Carpi Radialis MT												
1	randomised trials	very serious[a]	very serious[b]	not serious	serious[c]	very strong association	25	28	-	SMD **2.22 higher** (0.9 lower to 5.33 higher)	⨁◯◯◯ Very low	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors, incomplete outcome data

b. I2 = 94%

c. Small sample size, large confidence interval

5- The Effects of 4-weeks Venous Blood-flow Restricted (vBFR) Concentric Training on Biceps Brachii MT compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	The Effects of 4-weeks Venous Blood-flow Restricted (vBFR) Concentric Training on Biceps Brachii MT	placebo	Relative (95% CI)	Absolute (95% CI)		
The Effects of 4-weeks Venous Blood-flow Restricted (vBFR) Concentric Training on Biceps Brachii MT												
1	randomised trials	serious [a]	not serious	not serious	very serious[b]	strong association	10	10	-	SMD **1.07 higher** (0.12 higher to 2.02 higher)	⨁⨁◯◯ Low	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors

b. Small sample size, large confidence interva

6- The Effects of 4-weeks Venous Blood-flow Restricted (vBFR) Concentric Training on Biceps Brachii CSA compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	The Effects of 4-weeks Venous Blood-flow Restricted (vBFR) Concentric Training on Biceps Brachii CSA	placebo	Relative (95% CI)	Absolute (95% CI)		
The Effects of 4-weeks Venous Blood-flow Restricted (vBFR) Concentric Training on Biceps Brachii CSA												
1	randomised trials	serious [a]	not serious	not serious	very serious[b]	strong association	10	10	-	SMD **1.02 higher** (0.07 higher to 1.96 higher)	⨁⨁◯◯ Low	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors

b. Small sample size, large confidence interval

7- The Effects of 4-weeks Low-Load Concentric Training on Biceps Brachii MT compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	The Effects of 4-weeks Low-Load Concentric Training on Biceps Brachii MT	placebo	Relative (95% CI)	Absolute (95% CI)		
The Effects of 4-weeks Low-Load Concentric Training on Biceps Brachii MT and CSA												
1	randomised trials	serious [a]	not serious	not serious	very serious[b]	strong association	10	10	-	SMD **0.94 higher** (0.01 higher to 1.87 higher)	⨁⨁◯◯ Low	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors

b. Small sample size, large confidence interval

8- The Effects of 4-weeks Low-Load Concentric Training on Biceps Brachii CSA compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	The Effects of 4-weeks Low-Load Concentric Training on Biceps Brachii CSA	placebo	Relative (95% CI)	Absolute (95% CI)		
The Effects of 4-weeks Low-Load Concentric Training on Biceps Brachii CSA												
1	randomised trials	serious [a]	not serious	not serious	very serious[b]	strong association	10	10	-	SMD **1 higher** (0.06 higher to 1.94 higher)	⨁⨁◯◯ Low	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors

b. Small sample size, large confidence interval

9- The Effects of Bench Press Exercises on Pectoralis Major Muscle Volume compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of Bench Press Exercises on Pectoralis Major Muscle Volume	placebo	Relative (95% CI)	Absolute (95% CI)		
1.1.1. The Effects of Bench Press Exercises on Pectoralis Major Muscle Volume												
1	randomised trials	very serious [a]	not serious	not serious	serious[b]	strong association	31	30	-	SMD **0.79 higher** (0.26 higher to 1.32 higher)	⨁⨁◯◯ Low	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors, incomplete outcome data

b. Small sample size, large confidence interval

10 - The Effects of High Intensity Bench Press Training on Pectoralis Major Muscle CSA compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of High Intensity Bench Press Training on Pectoralis Major Muscle CSA	placebo	Relative (95% CI)	Absolute (95% CI)		
1.1.1. The Effects of High Intensity Bench Press Training on Pectoralis Major Muscle CSA												
1	randomised trials	very serious [a]	not serious	not serious	very serious [b]	strong association	10	10	-	SMD **1.03 higher** (0.09 higher to 1.98 higher)	⨁◯◯◯ Very low	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors, incomplete outcome data

b. Small sample size, large confidence interval

11. The Effects of Low Intensity Bench Press Training with blood-flow restriction (BFR) on Pectoralis Major Muscle CSA compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of Low Intensity Bench Press Training with blood-flow restriction (BFR) on Pectoralis Major Muscle CSA	placebo	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	10	10	-	SMD **0.63 higher** (0.27 lower to 1.54 higher)	⨁◯◯◯ Very low	

1.1.1. The Effects of Low Intensity Bench Press Training with blood-flow restriction (BFR) on Pectoralis Major Muscle CSA

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors, incomplete outcome data

b. Small sample size, large confidence interval

12- The Effects of High Intensity Bench Press Training on Triceps Brachii Muscle CSA compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of High Intensity Bench Press Training on Triceps Brachii Muscle CSA	placebo	Relative (95% CI)	Absolute (95% CI)		

1.1.1. The Effects of High Intensity Bench Press Training on Triceps Brachii Muscle CSA

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of High Intensity Bench Press Training on Triceps Brachii Muscle CSA	placebo	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	10	10	-	SMD **0.72 higher** (0.19 lower to 1.63 higher)	⨁◯◯◯ Very low	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors, incomplete outcome data

b. Small sample size, large confidence interval

13- The Effects of Low Intensity Bench Press Training with blood-flow restriction (BFR) on Triceps Brachii Muscle CSA compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of Low Intensity Bench Press Training with blood-flow restriction (BFR) on Triceps Brachii Muscle CSA	placebo	Relative (95% CI)	Absolute (95% CI)		

1.1.1. The Effects of Low Intensity Bench Press Training with blood-flow restriction (BFR) on Triceps Brachii Muscle CSA

1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	10	10	-	SMD **0.41 higher** (0.48 lower to 1.3 higher)	⨁◯◯◯ Very low	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors, incomplete outcome data

b. Low sample size, large confidence interval

14- The Effects of Maximal Voluntary Isometric Co-contraction Training on Elbow Extensors MT compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of Maximal Voluntary Isometric Co-contraction Training on Elbow Extensors MT	placebo	Relative (95% CI)	Absolute (95% CI)		
1.1.1. The Effects of Maximal Voluntary Isometric Co-contraction Training on Elbow Extensors MT												
2	randomised trials	serious [a]	not serious	not serious	serious[b]	publication bias strongly suspected very strong association[c]	22	17	-	SMD **1.97 higher** (0.63 lower to 4.56 higher)	⨁⨁⨁◯ Moderate	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants and assessors

b. Low sample size, large confidence interval

c. I2 = 87%

15- The Effects of Maximal Voluntary Isometric Co-contraction Training on Elbow Flexors MT compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of Maximal Voluntary Isometric Co-contraction Training on Elbow Flexors MT	placebo	Relative (95% CI)	Absolute (95% CI)		
1.1.1. The Effects of Maximal Voluntary Isometric Co-contraction Training on Elbow Flexors MT												
2	randomised trials	serious [a]	not serious	not serious	serious[b]	strong association	22	17	-	SMD **1.01 higher** (0.33 higher to 1.69 higher)	⨁⨁⨁◯ Moderate	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors

b. Small sample, large confidence interval

16- The Effects of Linear Periodized Resistance Training on Biceps Brachii MT compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of Linear Periodized Resistance Training on Biceps Brachii MT	placebo	Relative (95% CI)	Absolute (95% CI)		
1.1.1. The Effects of Linear Periodized Resistance Training on Biceps Brachii MT												
2	randomised trials	very serious [a]	not serious	not serious	serious[b]	none	29	27	-	SMD **0.73 higher** (0.18 higher to 1.28 higher)	⨁◯◯◯ Very low	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors, incomplete outcome data

b. Small sample size, large confidence interval

17- The Effects of Linear Periodized Resistance Training on Triceps Brachii MT compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of Linear Periodized Resistance Training on Triceps Brachii MT	placebo	Relative (95% CI)	Absolute (95% CI)		
1.1.1. The Effects of Linear Periodized Resistance Training on Triceps Brachii MT												
2	randomised trials	very serious [a]	not serious	not serious	serious[b]	none	29	23	-	SMD **0.15 higher** (0.4 lower to 0.7 higher)	⨁◯◯◯ Very low	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors, incomplete outcome data

b. Small sample size, large confidence interval

18- The Effects of Nonlinear Periodized Resistance Training on Biceps Brachii MT compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of Nonlinear Periodized Resistance Training on Biceps Brachii MT	placebo	Relative (95% CI)	Absolute (95% CI)		
1.1.1. The Effects of Nonlinear Periodized Resistance Training on Biceps Brachii MT												
2	randomised trials	very serious[a]	not serious	not serious	serious[b]	strong association	30	27	-	SMD **1.13 higher** (0.56 higher to 1.7 higher)	⨁⨁◯◯ Low	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors, incomplete outcome data

b. Small sample size, large confidence interval

19- The Effects of Nonlinear Periodized Resistance Training on Triceps Brachii MT compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of Nonlinear Periodized Resistance Training on Triceps Brachii MT	placebo	Relative (95% CI)	Absolute (95% CI)		
1.1.1. The Effects of Nonlinear Periodized Resistance Training on Triceps Brachii MT												
2	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	30	23	-	SMD **0.33 higher** (0.22 lower to 0.88 higher)	⨁◯◯◯ Very low	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors, incomplete outcome data

b. Small sample size, large confidence interval

20- The Effects of Nonlinear Periodized Resistance Training on Briceps Brachii MV compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of Nonlinear Periodized Resistance Training on Briceps Brachii MV	placebo	Relative (95% CI)	Absolute (95% CI)		
1.1.1. The Effects of Nonlinear Periodized Resistance Training on Briceps Brachii MV												
1	randomised trials	serious [a]	not serious	not serious	serious [b]	strong association	21	18	-	SMD **1.34 higher** (0.63 higher to 2.06 higher)	⨁⨁⨁◯ Moderate	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors

b. Small sample size, large confidence interval

21- The Effects of Nonlinear Periodized Resistance Training on Triceps Brachii MV compared to placebo for [health problem]

Setting:

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1.1.1. The Effects of Nonlinear Periodized Resistance Training on Triceps Brachii MV	placebo	Relative (95% CI)	Absolute (95% CI)		
1.1.1. The Effects of Nonlinear Periodized Resistance Training on Triceps Brachii MV												
1	randomised trials	serious [a]	not serious	not serious	serious[b]	very strong association	21	18	-	SMD **2.07 higher** (1.26 higher to 2.89 higher)	⨁⨁⨁⨁ High	

CI: confidence interval; **SMD:** standardised mean difference

Explanations

a. Allocation concealment, blinding participants, blinding assessors

b. Small sample size, large confidence interval

III.h. Supporting Table 5.1. Search for key term "muscle architecture" in PubMed database.

Search number	Query	Sort By	Filters	Search Details	Results	Time
2	"muscle architecture"			"muscle architecture"[All Fields]	984	09:57:06
1	"muscle architecture"		in the last 10 years	("muscle architecture"[All Fields]) AND (y_10[Filter])	636	09:57:02

III.i. Supporting Table 5.2. Participants' Characteristics in the Eligible Randomised Controlled Trials.

Study	Groups	Number of Participants	Gender	Age (year), Mean± SD	Level of Physical Activity
Akagi et al. (2016) [1]	Intervention Control	13 10	Male Male	22± 1.2 22.2± 1.0	Sedentary or Physically active

Dankel et al. (2020) [2]	Intervention (Traditional training group) Intervention (1RM training group) Control	48 52 51	29 females, 19 males 33 females, 19 males 32 females, 19 males	21± 2 20± 1 21± 3	Not specified
Farthing et al. (2005) [3]	Intervention (left training group) Intervention (right training group) Control	13 12 14	Female Female Female	Overall age: 20.8± 0.4	Not specified
Hill et al. (2018) [4]	Intervention (Ecc-vBFR) Intervention (Con-vBFR) Control	12 12 12	Female Female Female	21.7± 1.0 22.1± 1.7 23.3± 2.0	Recreationally active
Hill et al. (2020) [5]	Intervention (RT+BFR) Intervention (RT) Control	10 10 10	Female Female Female	22± 2 21± 1 23± 3	Recreationally active
Krentz et al. (2017) [6]	Intervention (ECC110 group) Intervention (ECC80 group) Control	8 9 15	3 females, 5 males 2 females, 7 males 8 females, 7 males	26.3± 6.7 23.3± 7.4 21.7± 3.2	Had varied training experiences
Kubo et al (2021) [7]	Intervention (4RM group) Intervention (8RM group) Intervention (12RM group) Control	10 12 9 10	Male Male Male Male	20.9± 0.4 20.9± 1.6 20.8± 0.8 21.1± 1.1	Physically active
Maeo et al. (2014a) [8]	Intervention Control	13 10	Male Male	21.8± 1.6 21.9± 1.6	Physically active
Maeo et al. (2014) [9]	Intervention Control	9 7	Male Male	21.4± 1.2 22.0± 1.8	Physically active
Matta et al. (2011) [10]	Intervention Control	40 9	Male Male	29.90± 1.72 25.89± 3.59	Physically active
Pinto et al. (2012) [11]	Intervention (FULL ROM group) Intervention (PARTIAL ROM group)	15 15 10	Male Male Male	21.7± 3.5 21.7± 3.3 24.5± 2.9	Not specified

	Control				
Radaelli et al. (2015) [12]	Intervention (1 SET group) Intervention (3 SETS group) Intervention (5 SETS group) Control	12 13 13 10	Male Male Male Male	24.1± 0.8 24.1± 1.2 24.7± 1.0 24.8± 0.6	Physically active
Simão et al. (2012) [13]	Intervention (NLP group) Intervention (LP group) Control	11 10 9	Male Male Male	30.2± 1.1 29.8± 1.9 25.9± 3.6	Physically active
Spineti et al. (2010) [14]	Intervention (LG-SM group) Intervention (SM-LG group) Control	11 10 9	Male Male Male	29.7± 1 30.5± 1.7 25.8± 3.6	Physically active
Spineti et al. (2014) [15]	Intervention (LG-OP) Intervention (SM-OP) Intervention (LG-LP) Intervention (SM-LP) Control	11 10 10 13 9	Male Male Male Male Male	30.2 ± 1.1 30.5 ± 1.8 29.8 ± 1.9 29.2 ± 2.9 25.9 ± 3.6	Physically active
Yasuda et al. (2011a) [16]	Intervention (HI-RT group) Intervention (LI-BFR group) Intervention (CB-RT group) Control	10 10 10 10	Male Male Male Male	Age range: 22-32	Recreationally active
Yasuda et al. (2011) [17]	Intervention (HIT group) Intervention (LI-BFR group) Control	10 10 10	Male Male Male	25.3± 2.9 23.4± 1.3 23.6± 1.6	Physically active
Abbreviations; BFR, Blood-flow restriction; CB-RT, Combined resistance training; Con-vBFR, concentric venous blood flow restriction; Control, Control group; Ecc-vBFR, Eccentric venous blood-flow restriction; HIT, high-intensity resistance training, HI-RT, High-intensity blood-flow restriction; LG-LP, large-linear; LG-SM, Large group-small group; LG-OP, large- undulatory; LI-BFR, Low-intensity blood-flow restriction; LP, Linear periodised; LTG, Left training group; NLP, Nonlinear periodised; RM, Repetition maximum; RTG, Right training group; RT, Resistance training; SM-LG, Small group-large group; SM-LP, small-linear; SM-OP, small- undulatory.					

III.j. Supporting Table 5.3. **Intervention characteristics of included randomised controlled trials.**

Study (year)	Groups, number of participants (n), Type of exercises allocated for groups	Material (s) for exercise (s)	The exercising procedure, total weeks, sessions, sets and repetitions	Target muscle (s) or muscle group for architectural measurements	The measurement device, measured region	Type of muscle architectural parameter(s)	Baseline values (mean± SD)	Post-test values (mean± SD)	Method of statistical analysis applied in the study	Alpa level	Results
Akagi et al. (2016) [1]	Training group (n=13): Lying triceps extension exercise (sequential concentric and eccentric elbow extensions) Control group (n=10): Did not train	A dumbbell adjusted to 80% of 1RM	6 wk, 3 sessions pw, 5 sets of 8 reps	Long head of the triceps brachii	2D B-mode US, proximal 70% point of upper arm length	MT (cm)	TG: 1.32± 0.35 CG: 1.29± 0.34	TG: 1.69 ± 0.30 CG: 1.34 ± 0.33	2-way ANOVA	0.05	-At interaction test time x experimental group: p= 0.006, ES (partial eta-squared)= 0.3 - Baseline vs post-test in TG: p< 0.001, ES (partial eta-squared)= 0.575 - Baseline vs post-test in the CG: p=0.564, ES (partial eta-squared)= 0.016

Dankel et al. (2020) [2]	Traditional training group (n=48): Elbow flexion exercise 1RM training group (n=52): Elbow flexion exercise Control group (n=51): Did not train	A dumbbell	6 wk, 3 sessions pw, Traditional training group performed 4 sets 8-12 reps until volitional failure 1RM group performed up to 5 heavy single repetitions (80%-85% of 1 RM)	Elbow flexors	2D B-mode US, 50%, 60% and 70% of the distance between acromion process and lateral epicondyle	MT (cm)	Traditional training: 50% length: 2.79± 0.67, 60% length: 2.99± 0.57, 70% length: 3.32± 0.61 1RM training: 50% length: 2.72± 0.57, 60% length: 2.92± 0.56, 70% length: 3.27± 0.60, Control group: 50% length: 2.61± 0.60, 60% length: 2.88± 0.56, 70% length: 3.22± 0.57,	Not mentioned	Bayesian ANCOVA	-	- Traditional training group was the group that showed increases in muscle size among the groups

Farthing et al. (2005) [3]	Right-training group (n=12): Unilateral isometric ulnar deviation training, trained only their right hand Left-training group (n=13): Unilateral isometric ulnar deviation training, trained only their left hand Control group (n=14): Did not train	An isokinetic dynamometer	6 wk, total 24 sessions, 2-6 sets of 8 reps	Flexor carpi ulnaris and flexor digitorum superficialis	2D B-mode US, 1/5 distance from the olecranon process to the distal head of ulna	MT (cm)	RTG: Trained hand: 2.93± 0.10 LTG: Trained arm: 3.00± 0.08 CG: Trained arm: 2.99± 0.09	RTG: Trained hand: 2.99 0.09 LTG: Trained arm: 3.16 ± 0.07 CG: Trained arm: 2.90 ± 0.08	Univariate ANOVA	0.05	The combined percentage increment of the MT in the training arms of the training groups (4.1± 2.0%) was significantly higher than the combined MT of control arms 4.0± 1.4%, $p<0.01$). The percentage difference for the combined MT of untrained arms (3.1± 1.2%) was not different from the combined MT of control arms.
Hill et al. (201	Ecc-vBFR group (n=12):	KAAT SU resistance band,	4 wk, 3 sessions, 4 sets (1 x 30, 3 x15).	Biceps brachii	2D B-mode ultrasound, 66% of	MT	All participants' baseli	Not mentioned	Mixed factorial ANOVA,	0.05	-There was a significant time x

8) [4]	Performed eccentric training with venous blood-flow restriction Con-vBFR group (n=12): Performed concentric training with venous blood-flow restriction CG (n=12): Received no intervention	an isokinetic dynamometer	Totally, 75 reps of eccentric or concentric muscle actions of the forearm flexors -40% of the lowest amount for completely occlude brachial artery		the distance from the medial acromion of the scapula to the fossa cubit		ne: 2.21± 0.24 (cm)		independent or dependent samples t-tests with Bonferroni correction.		group interaction ($p<0.001$) -In the Ecc-vBFR group, the MT increased from baseline and 0 week to 4th week (14.6% and 12.8%) -In Con-vBFR group, the MT increased from baseline and 0 week to 4th week (10.7% and 9.9%) -At the end of the 4-week the MT was greater in Ecc-vBFR (2.44 cm) and in Ecc-vBFR (2.35 cm) comparing the CG (2.15 cm)
Hill et	RT+BFR	KAATSU	4 wk, 3 sessions	Biceps Brachii	2D B-mode	MT(cm),	All partic	Not ment	Mixed factori	0.05	-For the

al. (2020) [5]	group (n=10): Performed reciprocal concentric forearm flexion-extension resistance training with venous blood-flow restriction RT group (n=10): Performed reciprocal concentric forearm flexion-extension resistance training CG (n=10):	resistance band, an isokinetic dynamometer	pw, , 4 sets (1 x 30, 3 x15). Totally, 75 reps of isokinetic muscle actions of the forearm flexors. -40% of the lowest amount for completely occlude brachial artery		ultrasound, mid-way of the distance from the medial acromion of the scapula to the fossa cubit for the biceps brachii	CSA(cm^2)	ipants' baseline CSA: 7.06± 1.93. MT: 2.13± 0.41	ioned	al ANCOVA, mixed factorial ANOVA, depended sample t-test with Bonferroni correction		MT, there was significant group x time interaction, RT and RT-BFR > CG (p<.001). The MT increased after 4 weeks in RT+BFR group (18.7%) and RT group (19%). The MT was grater after 4 weeks in RT+BFR (2.53 cm) and RT (2.52 cm) in comparison with the CG (2.16 cm). -There was a significant time x group interaction for the CSA. The

											biceps brachii CSA increased 21.9% for the RT-BFR group and 20% fo the RT group after 4 weeks. -No changes observed for the CG -After 4 weeks, the CSA in the RT-BFR group (8.44 cm^2) and RT group (8.48 cm^2) was higher than the CG (6.73 cm^2)
Krentz et al. (2017) [6]	ECC110 group (n= 8): Performed eccentric training at 110% of concentric 1RM	A dumbell	8 wk, 2-3 sessions pw, until volitional fatigue	Elbow flexors	2D B-mode ultrasound, the thickest point of the elbow flexors at relaxed position. Approximately, 33%	MT	Not mentioned	Not mentioned	MANCOVA	0.05	- Increments in ECC110 (3.82 cm) and ECC80 (3.78 cm) were higher than the control group

	ECC80 group (n=9): Performed eccentric training at 80% of concentric 1RM Control group (n=15): Did not train				distance from the fossa cubit.						(3.56 cm) (p<0.01)
Kubo et al. (2021) [7]	4RM group (n=10): Bench press 8RM group (n=12): Bench press 12RM group (n=9): Bench press Control group (n=10): Did not train	A barbell	10 wk, 2 sessions pw, 4RM group: 7 sets, 8RM group: 4 sets, 12RM group: 3 sets	Pectoralis major	T1 weighted MRI cross-sectional images of pectoralis major	MV (cm^3)	4RM group: 329.2 ± 104.9 8RM group: 345.6 ± 92.4 12RM group: 336.4 ± 46.2 Control group: 338.4 ± 40.2	4RM group: 363.6± 103.8 8RM group: 379.4± 95.6 12RM group: 373± 41.2 Control group: 333.7± 40	Kolmogorov–Smirnov test, Kruskal-Wallis test, Wilcoxon signed-rank test, Mann–Whitney test	0.05	-All of the exercise groups showed significant increases in pectoralis major muscle volume (p<0.001)
Maeo et al. (2014a) [8]	TG (n=13): Maximal voluntary isomet	-	4 wk, 3 sessions pw, 5 sets of 10 reps	Elbow flexors (biceps brachii + brachialis), elbow	2D B-mode ultrasound, 60% distance from the	MT (mm)	TG: Elbow flexors: 32.7± 3.5,	TG: Elbow flexors: 33.0 ± 3.5,	2-way repeated-measures ANOVA, paired	0.05	No significant change was detected for MT

	ric contractions of elbow flexors and extensors at 90º flexion of the elbow joint. CG (n=10): -			extensors (long and medial heads of triceps brachii)	acromial process of the scapula to the lateral epicondyle of the humerus		Elbow extensors: 32.2± 5.0 CG: Elbow flexors: 34.0± 2.2, Elbow extensors: 34.3± 3.0	Elbow extensors: 32.5 ± 4.8 CG: Elbow flexors: 33.9 ± 2.2, Elbow extensors: 34.2 ± 3.1	Student's t-test with Bonferroni correction, 3-way ANOVA		
Maeo et al. (2014) [9]	TG: Maximal voluntary isometric contractions of elbow flexors and extensors at 90º flexion of the elbow joint. CG: -	-	12 wk, 3 sessions pw, 5 sets of 10 reps	Elbow flexors (biceps brachii + brachialis), elbow extensors (long and medial heads of triceps brachii)	2D B-mode ultrasound, 60% distance from the acromial process of the scapula to the lateral epicondyle of the humerus	MT	Not mentioned	Not mentioned	2-way repeated-measures ANOVA, one way repeated measures ANOVA, Bonferroni post hoc test, unpaired Student's t-test	0.05	- There was significant group x time interaction for the elbow flexors and extensors -After 12 weeks, there were significant increment comparing baseline. Elbow flexors MT= +4%, p=0.009, r= 0.830), elbow extensors MT= +4%,

											p=0.001, r=0.943
Matta et al. (2011) [10]	TG (n=40): Performed a nonlinear periodised resistance training program CG (n=9): Kept their habitual activities	A barbell, lat pull-down machine	12 wk, 2 sessions pw, in 1 session: 4 sets of 12-15 reps (light intensity), in the next session: 3 sets of 8-10 reps (moderate intensity)machine lat pull-down, triceps extension in lat pull-down, free-weight bench press, and standing free-weight biceps curl with a straight bar	Biceps brachii, triceps brachii	2D B-mode ultrasound, 50%, 60%, 70% distances between the posterior crista of the acromion and the olecranon of the elbow joint	MT: Biceps brachii and triceps brachii at proximal, middle and distal sites PA: Triceps brachii at proximal, middle and distal sites	Not mentioned	Not mentioned	Multivariate repeated-measures ANOVA, the Tukey post hoc test, 2-way ANOVA	0.05	-There was a significant interaction between the training and MT measurement sites (p=0.025). The biceps brachii MT increased at the proximal site p<0.05, middle site p<0.05 and the distal site (p=0.03). The MT at the proximal site was significantly lower than the distal site at the pre-test and post-test (p<0.05). The increm

											ent for the biceps brachii MT was approximately 12% for the proximal site and 5% for the distal site -The triceps brachii MT significantly increased at the middle site (p=0.019) and distal site (p=0.009). -The triceps brachii PA significantly increased at the proximal site (p<0.05), middle site (p=0.002) and distal site (p=0.008). There were no

											significant differences for the triceps brachii PA between the 3 measurement sites at the pre- and post-test. The hypertrophy of the triceps brachii was statistically homogenous between the 3 measurement sites (for MT: p= 0.229, for the PA: p= 0.849)
Pinto et al. (2012) [11]	FULL ROM group (n=15): Performed elbow flexon exercises between 0º and 130º degrees of ROM	A dumbell	10 wk, 2 sessions pw, 8-20 reps of 2-4 sets	Elbow flexors	2D B-mode ultrasound, 60% distance between the lateral epicondyle of the acromion	MT	Not mentioned	Not mentioned	ANOVA	0.05	-There were significant main effects for time points for both exercise groups (p<0.05, FULL: 9.52%, PARTI

	PARTIAL ROM group (n=15): Performed elbow flexion exercises between 50º and 100º degrees of ROM Control group (n=10): Did not train										AL: 7.37%), but not for the control group (p=0.36).
Radaelli et al. (2015) [12]	1 SET group (n=12): Performed 1 set of the weight training program 3 SETS group (n=13): Performed 3 sets of the weight training program 5 SETS group (n=13)	Weight training machines	6 months, 3 sessions pw, totally 73 sessions, 5-12 reps of 1 RM to concentric failure, after 12 RM a 5-10% increment, leg extension, bench press, shoulder press, leg press, front lat pull-down, triceps extensio	Elbow flexors (biceps brachii + brachialis) and elbow extensors (long+ medial head of the triceps brachii)	2D B-mode ultrasound, 60% distance from the acromial process of the scapula to the lateral epicondyle of the humerus	MT	Not mentioned	Not mentioned	2-way ANOVA, Tukey post hoc test, effect size (ES) magnitude	0.05	-In the 1 SET group, the MT of elbow flexors and extensors did not significantly change between pre- and post-test -In the 3-SETS and 5-SETS group MT of elbow flexors significantly increased in compa

	: Performed 5 sets of the weight training program CG (n=10): Did not involve the weight training program. However, performed a traditional military callisthenics program of bodyweight exercises		n, leg curl, abdominal crunch lying on the floor, biceps curl								rison with the CG and 1 SET group ($p \leq 0.05$). Additionally, the change of MT of elbow flexors in the 5 SETS group was significantly greater than the difference in the 3 SETS group ($p \leq 0.05$). -For the changes of MT of elbow flexors, the ES was 1.10 for the 5 SETS group, 0.73 for the 3 SETS group and 0.10 for the 1 SET group -The only signifi

											cant increment of the MT of elbow extensors was observed for the 5 SETS group comparing the CG, 1 SET group and 3 SETS group ($p \leq 0.05$). - The ESs for MT increments of elbow extensor 2.33 for the 5 SETS group, 0.05 for the 3 SETS group and 0.05 for the 1 SET group
Simão et al. (2012) [13]	NLP group (n=11): Nonlinear periodized resistance training	A barbell, a front lat-pull down machine, a triceps extension machi	12 wk, 2 sessions pw NLP: Phase 1 (1-6 wk): Local muscular endurance (1-2 wk, 2	Biceps brachii and triceps brachii	2D B-mode US, 60% of the arm length	MT(mm)	NLP: Elbow extensors: 38.4± 5.8, Elbow flexors:	NLP: Elbow extensors: 41.9 ± 3.4, Elbow flexors:	2-way ANOVA and the effect size (ES) magnitude	0.05	NLP group showed significantly higher MT increment in comparison with

	(concentric) LP group (n=10): Linear periodized resistance training (concentric) Control group (n=9): Kept daily routine	ne, a straight bar	sets of 12-15 RM), hypertrophy (3-4 week, 3 sets of 8-10 RM), strength (wk 5-6, 4 sets of 3-5 RM) Phase 2 (7-12 wk): Day 1: local muscular endurance (2 sets of 12-15 RM), Day 2: Hypertrophy (3 sets of 8-10 RM), day 3: strength (4 sets of 3-5 RM) LP: Local muscular endurance (1-4 wk, 2 sets of 12-15 RM), hypertrophy (5-8 wk, 3 sets of 8-10 RM), strength (9-12 wk, 4 sets of 3-5 RM)				39.8± 4.9 LP: Elbow extensors: 39.2± 4.4, Elbow flexors: 36.6± 6 CG: Elbow extensors: 32.5± 4.8, Elbow flexors: 36.6± 4.6	41.5 ± 4.9 LP: Elbow extensors: 39.5 ± 7.6, Elbow flexors: 38.7 ± 3.9 CG: Elbow extensors: 32± 3.9, Elbow flexors: 36.5 ± 3.7			CG (for elbow extensors: p= 0.046, for elbow flexors: p= 0.014), no significant differences observed between pre-test and post-test values of MT for any group. NLP ES magnitude for elbow flexors MT: 0.61, for elbow extensors MT: 0.36 LP ES magnitude for elbow flexors MT: 0.35, for elbow extensors MT: 0.05 CG ES magnitude for elbow

											flexors MT: -0.03, for elbow extensors MT: 0.00
Spineti et al. (2010) [14]	LG-SM group: Nonlinear periodised resistance training, began training for large muscle groups and progressed to small muscle groups (n=11) SM-LG Group: Nonlinear periodised resistance training, beginning, began training for small muscle groups and progressed to large muscle groups (n=10)	A Barbell, a front lat-pull down machine, a triceps extention machine, a straight bar	12 wk, 2 sessions pw, The exercise order of LG-SM: Barbell bench press, machine front lat pull down, machine triceps extension, free weight standing biceps curl Exercise order of SM-LG: Was opposite to the LG-SM The first session: 4 sets of light intensity 12-15 reps, The second session: 3 sets of moderate-intensity 8-10 reps The final session: 2 sets of high	Biceps brachii and triceps brachii	2D B-mode US, 60% of the arm length and MV	MV (cm^3)	LG-SM group: Triceps MV: 398.4 ± 105.6 Biceps MV: 416.6 ± 103.1 SM-LG group: Triceps MV: 408.6 ± 69.3 Biceps MV: 368.7 ± 41.8 CG: Triceps MV: 347.1 ± 63.7 Biceps MV: 299.3 ± 59.2	LG-SM group: Triceps MV: 457.7± 78.1 Biceps MV: 457.4± 10.8.7 SM-LG group: Triceps MV: 459.3± 78.3 Biceps MV: 416.2± 59.0 CG: Triceps MV: 339.1± 54.1 Biceps MV: 283.0± 61.3	ANOVA	0.05	Both training groups showed significant increments of biceps brachii and triceps brachii MV in comparison with the control group. LG-SM ES magnitude for triceps brachii MV: 0.4, for biceps brachii MV: 0.56 SM-LG ES magnitude for triceps brachii MV: 1.08, for biceps brachii MV: 0.69

	Control group (n=9): Kept daily routine		intensity 2-5 reps								CG ES magnitude for triceps brachii MV: -0.13, for biceps brachii MV: -0.28
Spineti et al. (2014) [15]	LG-OP (n=11): Performed resistance training starting from large muscle groups to small in ondulatory periodisation. SM-OP (n=10): Performed resistance training starting from small muscle groups to large in ondulatory	Not mentioned	12 wk, 2 sessions pw, local muscular endurance, hypertrophy and strength training. 2-4 sets, 3-15 reps	Biceps brachii and triceps brachii	2D B-mode US, 60% of the arm length	MT (cm)	Not mentioned	Not mentioned	Factorial ANOVA	0.05	-For biceps brachii, LP-OP and SM-OP groups showed significant increments compared to control group -For triceps brachii, all the training groups showed significant increases compared to control group

	periodisation. LG-LP (n=10): Performed resistance training starting from large muscle groups to small in linear periodisation. SM-LP (n=13): Performed resistance training starting from small muscle groups to large in linear periodisation. Control group (n=9): Kept daily routine										
Yasuda et al. (2011a) [16]	HI-RT Group (n=10): Performed high-	A barbell, an elastic cuff	6 wk, 3 sessions pw, free-weight flat bench press	Triceps brachii, pectoralis major	MRI, 3 contiguous muscle CSA slices (10 mm	CSA (in cm^2)	HI-RT: Triceps Brachii:	Not mentioned	2-way repeated-measures ANOVA,	0.05	- There were significant increases for the

	intensity resistance training (at 75% of 1RM) LI-BFR Group (n=10): Performed low-intensity resistance training with blood flow restriction (at 30% of 1RM) CB-RT Group (n=10): Performed 2 sessions of the low-intensity resistance training with blood-flow restriction and 1 session of high-intensity resista		HI-RT group: 3 sets of 10 reps LI-BFR group: 30 reps= 3 sets of 15 reps		thickness) for muscle belly averaged		21.5± 3.8 Pectoralis Major: 28.4± 6.3 LI-BFR: Triceps Brachii: 20.5± 5.7 Pectoralis Major: 31.8± 5.2 CB-RT: Triceps Brachii: 21.6± 3 Pectoralis Major: 29.7± 2.4 CG: Triceps Brachii: 20.7± 2.8 Pectoralis Major: 30.3± 4.7		Tukey post hoc test (% changes)		triceps brachii and pectoralis major muscle CSA in training groups ($p<0.01$). But there was no significant increment for the CG. - In the HI-RT group, the % change of triceps brachii CSA (8.6%) was significantly greater ($p<0.01$) than LI-BFR (4.9%) group and the CG (-1.1%). Similarly, the % change of pectoralis major muscle CSA in HI-RT group (17.6%) was significantly

	nce training weekly. CG (n=10): Kept daily routine										greater ($p<0.01$) than the LI-BFR group (8.3%), the CG (0%) and the CB-RT group (10.5%, $p<0.05$).
Yasuda et al. (2011) [17]	HIT group (n=10): Performed high intensity resistance training LI-BFR group (n=10): Performed low intensity blood-flow restricted training Control group (n=10): Kept daily routine	Elastic cuffs	6 wk, 3 sessions pw, bench press exercises, HIT: 10 reps x 3 sets at 75% of 1RM, LI-BFR: 30 x 1, 15 x 3 sets at 30% of 1-RM	Triceps brachii and pectoralis major	MRI, 3 contiguous transverse muscle CSA images (10 mm thickness)	CSA (cm^2)	Triceps brachii: HIT: 21.5± 3.8, LI-BFR: 21.2± 4.3, Control group: 20.7± 2.8 Pectoralis major: HIT: 28.4± 6.3, LI-BFR: 31.8± 5.2, Control group: 30.3± 4.7	Triceps brachii: HIT: 23.3 ± 4.1, LI-BFR: 22.2 ± 4.2, Control group: 20.5 ± 2.9 Pectoralis major: HIT: 33.4 ± 7.5, LI-BFR: 34.5 ± 6.3, Control group: 30.2 ± 4.7	2-way repeated measures ANOVA	0.05	-There were significant increases in triceps bacchii and pectoralis major muscles in both training groups. -Relative increases for triceps brachii and pectoralis major CSAs in the HIT group were significantly higher than the LI-BFR and Contro

											l groups.

Abbreviations: ANCOVA, Analysis of covariance; ANOVA, Analysis of variance; BFR, Blood-flow restriction; CB-RT, Combined resistance training; Con-vBFR, concentric venous blood flow restriction; CG, Control group; CSA, cross-sectional area; Ecc-vBFR, Eccentric venous blood-flow restriction; ES, Effect size; HIT, high-intensity resistance training, HI-RT, High-intensity blood-flow restriction; LG-LP, large-linear; LG-SM, Large group-small group; LG-OP, large- undulatory; LI-BFR, Low-intensity blood-flow restriction; LP, Linear periodised; LTG, Left training group; LP, Linear periodised; MT, Muscle thickness; MV, Muscle Volume; NLP, Nonlinear periodised; pw: Per week; RM, Repetition maximum; reps: Repetitions; RTG, Right training group; RT, Resistance training; SM-LG, Small group-large group; SM-LP, small-linear; SM-OP, small- undulatory; TG, Training group wk: Week; 2D, Two-dimensional.