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HYPERTROPHIC RESPONSE OF LOWER EXTREMITY MUSCLES TO DIFFERENT RESISTANCE TRAINING INTENSITIES: A META-ANALYSIS AND META-REGRESSION

HIPERTROFIČNI ODGOVOR MIŠIC SPODNJIH OKONČIN NA RAZLIČNE INTENZITETE TRENINGA ZA MOČ: META-ANALIZA IN META-REGRESIJA

ABSTRACT

This study evaluates the effectiveness of different resistance training intensities (high, moderate, and low) on quadriceps femoris muscle hypertrophy in healthy adults. A literature search was conducted in January 2023 using multiple databases, including Web of Science, SPORTDiscus, Embase, and PubMed. The methodological quality of the studies was assessed using the TESTEX scale. A total of 22 studies with 519 participants were included in this meta-analysis. Statistical analysis, performed using ReviewManager 5.2, showed that all resistance training intensities led to hypertrophy in the quadriceps femoris muscle compared to control or pre-test values. High-intensity training resulted in a muscle thickness increase of 2.3 mm (95% CI: 2.21-2.38), moderate-intensity training led to an increase of 1.88 mm (95% CI: 1.74-2.02), and low-intensity training showed an increase of 10.92 mm (95% CI: 10.77-11.08), all with $p < .001$. Meta-regression analysis revealed a significant relationship between training intensity and hypertrophy in the vastus intermedius ($\beta = 0.01$, $p = 0.05$, $R^2 = 0.56$) and vastus lateralis ($\beta = 0.01$, $p = 0.007$, $R^2 = 0.34$). However, no significant effect was found for the rectus femoris ($\beta = 0.03$, $p = 0.417$, $R^2 = 0.04$) or vastus medialis ($\beta = 0.003$, $p = 0.895$, $R^2 = 0.002$). In conclusion, resistance training at different intensities promotes hypertrophy across all quadriceps muscles, with variations depending on the specific muscle group. Meta-regression suggests that every 10% increase in training intensity corresponds to a 0.1 mm increase in vastus intermedius hypertrophy. No significant effect of training intensity was observed for the vastus lateralis, vastus medialis, or rectus femoris muscles.

Keywords: Muscle hypertrophy, quadriceps femoris, knee extensors, muscle thickness

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IZVLEČEK

Ta študija ocenjuje učinkovitost različnih intenzitet vadbe za moč (visoka, zmerna in nizka) na hipertrofijo mišične skupine kvadriceos femoris pri zdravih odraslih. Iskanje literature je bilo izvedeno januarja 2023 z uporabo več podatkovnih baz, vključno z Web of Science, SPORTDiscus, Embase in PubMed. Metodološka kakovost študij je bila ocenjena s pomočjo lestvice TESTEX. V to metaanalizo je bilo vključenih skupno 22 študij s 519 udeleženci. Statistična analiza, izvedena z uporabo programa ReviewManager 5.2, je pokazala, da so vse intenzitete vadbe za moč povzročile hipertrofijo mišice kvadriceps femoris v primerjavi s kontrolnimi ali predtestnimi vrednostmi. Visoko-intenzivni trening je povzročil povečanje debeline mišice za 2,3 mm (95% CI: 2,21–2,38), zmerno-intenzivni trening je privedel do povečanja za 1,88 mm (95% CI: 1,74–2,02), nizko-intenzivni trening pa je pokazal povečanje za 10,92 mm (95% CI: 10,77–11,08), vse z $p < .001$. Meta-regresijska analiza je pokazala pomembno povezavo med intenziteto treninga in hipertrofijo mišice vastus intermedius ($\beta = 0,01$, $p = 0,05$, $R^2 = 0,56$) ter vastus lateralis ($\beta = 0,01$, $p = 0,007$, $R^2 = 0,34$). Vendar pa ni bilo ugotovljenega pomembnega vpliva na mišici rectus femoris ($\beta = 0,03$, $p = 0,417$, $R^2 = 0,04$) in vastus medialis ($\beta = 0,003$, $p = 0,895$, $R^2 = 0,002$). Zaključno lahko rečemo da vadba za moč pri različnih intenzitetah spodbuja hipertrofijo vseh mišic kvadriceps, pri čemer obstajajo razlike glede na posamezno mišično skupino. Meta-regresijska analiza nakazuje da vsakih 10 % povečanja intenzitete vadbe ustreza 0,1 mm povečanju hipertrofije mišice vastus intermedius. Vendar pa ni bilo ugotovljenega pomembnega vpliva intenzitete vadbe na mišice vastus lateralis, vastus medialis in rectus femoris.

Ključne besede: Mišična hipertrofija, kvadriceps femoris, iztegovalke kolena, debelina mišice

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INTRODUCTION

Resistance training is a suggested form of exercise since it can enhance the ability to accomplish everyday tasks improve overall health and well-being indicators, including physical independence and decreased risk of all-cause death, and also increase sportive performance in the athletic population. Muscle hypertrophy is one of the primary responses seen with resistance training with chronic exposure (Brad Schoenfeld & Grgic, 2018). As a result of muscle hypertrophy and an increase in myofibrils, the principal alteration entails a rise in the cross-sectional area of the total muscle and specific muscle fibers. Early in the resistance exercise process, satellite cells become activated; their growth and fusion with preexisting fibers are crucial for the hypertrophic response. Additional potential architectural modifications in quadriceps muscles involve hyperplasia, modifications to muscle design, myofilament thickness, connective tissue composition, and tendon and connective tissue structure (Folland & Williams, 2007).

In addition, many internal and external factors are also influential in muscle hypertrophy. Exercise characteristics like frequency, intensity, time/duration, and type are examples of various external factors, called the FITT principle (Campbell et al., 2019). However, there are multiple studies on the effect of resistance training intensity (Borde, 2015; Fry, 2004; Brad Schoenfeld, Grgic, Ogborn, & Krieger, 2017), frequency (Borde, 2015; Polito, Papst, & Farinatti, 2021; Brad Schoenfeld, Grgic, & Krieger, 2019), number of sets (Borde, 2015; Krieger, 2009), repetition (Hackett, Ghayomzadeh, Farrell, Davies, & Sabag, 2022; Nicholson, Ispoglou, & Bissas, 2016; Brad Schoenfeld, Peterson, Ogborn, Contreras, & Sonmez, 2015), and type (Henselmans & Schoenfeld, 2014; Roig et al., 2009; Brad Schoenfeld, Ogborn, Vigotsky, Franchi, & Krieger, 2017) on muscle hypertrophy. One of the most crucial variables is exercise intensity since high-intensity exercises, particularly in elderly and very young individuals, may lead to adverse outcomes like higher injury risk and psychological burden and lower training motivation. Therefore, if lowering exercise intensity will not reduce hypertrophic responses, which some studies suggest, engaging in low-intensity resistance training can be preferable.

High-intensity resistance training ($\geq 70\%$ of 1 repetition maximum (RM)) has been promoted for many years as the primary method for promoting improvements in muscular hypertrophy. Recent findings, however, have questioned this concept in terms of hypertrophy, with multiple studies revealing equivalent increases in muscle hypertrophy across low ($\leq 50\%$ of 1RM) and

high ($\geq 75\%$ of 1RM) resistance training loads (Brad Schoenfeld et al., 2015). In contrast, the optimal resistance intensity regarding the quadriceps muscle group hypertrophic adaptations remains uncertain. Though in healthy people, high (Brigatto et al., 2022; Csapo & Alegre, 2016; Brad Schoenfeld, Contreras, et al., 2019) and low (Correa et al., 2012; Brad Schoenfeld et al., 2015) intensity resistance exercises were demonstrated to improve muscle mass for quadriceps femoris, and other studies highlighted no intensity-based differences (Amirthalingam et al., 2017; Carvalho et al., 2022; Correa et al., 2012; Mitchell et al., 2012; Brad Schoenfeld, Grgic, et al., 2017). Therefore, this study searches for the answer to the question, “what is the net range of intensity of resistance training one provides to increase quadriceps femoris muscle hypertrophy?”. It has not been directly examined in the literature separately for each muscle in the quadriceps femoris muscle in healthy adults.

METHODS

Registration

The study was registered before the literature search in Open Science Framework (OSF) (<https://doi.org/10.17605/OSF.IO/UWYSA>), and it adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards (Liberati, Tetzlaff, & Altman, 2009).

Sources of Data And Search Strategy

Seven electronic databases (Web of Science, SPORTDiscus, Embase, PubMed, Google Scholar), ClinicalTrials website (<https://clinicaltrials.gov/>), and grey literature database (<https://opengrey.eu/>) were scanned with (“Resistance training” OR “Strength training”) AND (“Muscle hypertrophy” OR “Muscle thickness”) keywords till January 2023. All randomized or non-randomized experimental studies are included. During the literature search, hand searching was performed by going to the reference’s reference and looking for relevant systematic reviews simultaneously.

Inclusion and Exclusion Criteria

The inclusion criteria were; (i) studies examining the effect of resistance training on muscle hypertrophy, (ii) studies in lower extremity muscle thickness is measured by ultrasonography, (iii) studies in which the measurements of muscle hypertrophy are clearly stated, (iv) studies with healthy individuals without chronic disease or disability, (v) had a minimum duration of 4

weeks, (vi) carried out training to muscle failure, (vii) open access and randomized or non-randomized human trials were included. The exclusion criteria were; (i) studies that do not include resistance or strength exercises, (ii) studies in which measurements such as muscle volume and circumference (not taken by ultrasonography; since ultrasonography is accepted as the gold standard in determining muscle thickness (hypertrophy) in various studies (Amirthalingam et al., 2017; Brad Schoenfeld, Contreras, et al., 2019; Brad Schoenfeld et al., 2015). For this reason, studies conducted with this method have been preferred.), (iii) studies that include measurements other than the muscles in the lower extremity, (iv) studies that include individuals with chronic diseases or rats and not open access were excluded.

Data Extraction

From each trial, two authors independently retrieved descriptive and result data. These obtained data were as follows: author and year of studies, design, samples, resistance exercise protocols (intensity (% 1RM) and total sets (number of sets * repetitions) of exercises), duration of the study, hypertrophy area, and results. In addition, the raw mean and standard deviation of post-training muscular hypertrophy measurements and the number of participants were extracted. If data is given graphically, WebPlotDigitizer (<https://automeris.io/WebPlotDigitizer/>) was used to interpret data that could only be presented visually. The data was then imported into the meta-analysis tool from the excel file.

Evaluation Of Methodological Quality

A new proven method for evaluating the quality of the study and report in exercise training research, the “*Tool for the assessment of Study quality and reporting in EXercise*” (TESTEX) Scale, is used to determine the risk of bias in this study. This scale considers eligibility and allocation concealment and includes 12 criterion evaluations with a maximum score of 15. In exercise training research, subsequent blinding of participants and researchers is rarely possible and only affects quality assessment (Smart et al., 2015). Answers to every item on the TESTEX scale are "yes" or "no," with "yes" being connected with a point and "no" being related to a score if criteria are not satisfied. Studies are categorized as having "excellent quality" (12–15 points), "good quality" (9–11 points), "fair quality" (6–8 points), or "poor quality" (6 points) based on the summary scores (Nunes et al., 2021). Additionally, two researchers (C.D.E and Y.B) will independently assess the methodological quality.

Statistical Analysis

For continuous data, meta-analyses were done using the post-intervention lower extremity muscle thickness measurements' raw mean value and standard deviation measurements for effect size calculation. The effect sizes were evaluated as “small” (≤ 0.2), “moderate” (0.21-0.5), “large” (0.51-0.8), and “very large” (> 0.8) (Cohen, 1992). A random effect model was used for all analyses. Meta-analysis was conducted for each result with RevMan 5.2 tool for lower extremity (Vastus Lateralis, Medialis, Intermedius, and Rectus Femoris) muscles. The I^2 test was used to determine the degree of heterogeneity (Sutton & Higgins, 2008). TESTEX scale was used to detect the quality of the studies (Smart et al., 2015). Additionally, the relationship between resistance training intensity and change in quadriceps femoris muscle thickness was explored by conducting a meta-regression analysis with MedCalc (MedCalc software, version 16.1; MedCalc, Ostend, Belgium) program. For that, muscle thickness (mm) was the primary moderator as a continuous variable for meta-regression analysis. Ninety-five percent confidence intervals were employed, and the significance level was 5%.

RESULTS

Selection of Studies

All of the studies that were considered reported comparing the effects of various resistance exercise intensities (low, moderate, high) on the development of muscular hypertrophy in the lower extremity in healthy adults. As a result of the literature review, a total of 607 studies were reached via various databases. Following the elimination of duplicate studies, 81 were kept for screening. Twenty-two of them were evaluated for eligibility, while 59 were eliminated. In total, 22 studies were evaluated (Figure 1).

Characteristics of The Included Studies

The total number of articles found was based on the type of analyzed variables: Eighteen articles for the RF, 20 for the VL, 9 for the VM, and 7 for the VI muscles. Twenty-two trials included 519 healthy participants in the existing meta-analysis. Every study had between 15 (Gonzalez et al., 2017; Ikezoe, Kobayashi, Nakamura, & Ichihashi, 2020) and 58 individuals (Correa et al., 2012). The duration of resistance training varies between 5 and 16 weeks, and the most common application period is eight weeks. Additionally, there are eight studies for high-intensity ($\geq 80\%$ of 1 RM) resistance training, 11 for moderate-intensity (60-79% of 1 RM)

resistance training, and 6 for low-intensity (30-59 % of 1 RM) resistance training. The most commonly studied resistance training intensity is moderate (60-79%) (Carvalho et al., 2022).

Categorization of Research

Two researchers (C.D.E and Y.B) independently focused on studies. They recorded data relating to the following variables into a worksheet: year of study, author, design, participant group, the protocol of resistance exercises (determined as regions of maximal repetitions or by a percentage of the 1RM test), muscle area, TESTEX scores of studies and results. Resistance exercise loads are classified into three categories according to the latest meta-analysis (Carvalho et al., 2022): low (30-59 % of 1 RM or 16-35 RM), moderate (60-79% of 1 RM or 8-12 RM), and high (≥ 80 % of 1 RM or ≤ 7 RM). The table containing the studies accessed and categorized as a result of the literature review is as follows (Table 1).

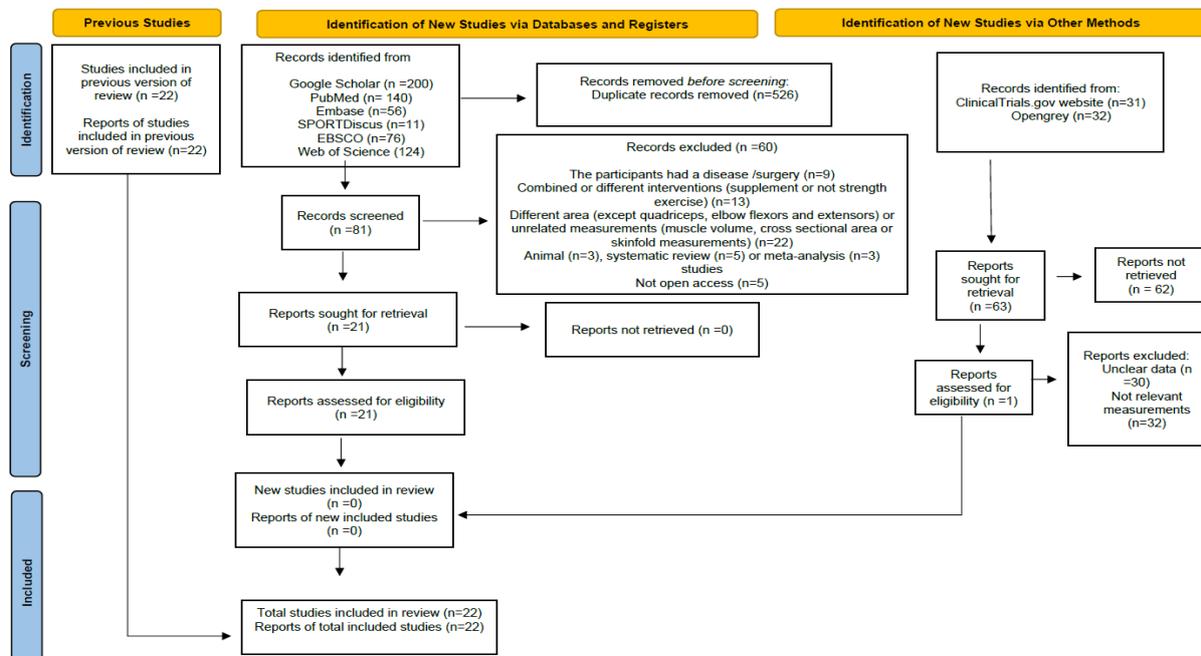


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flow Chart of Study Selection Process (Page et al., 2021).

Table 1. All Included Papers' Methodological Features and Outcomes

Author, year	Design	Sample	Resistance exercise protocol	Duration	Muscle area	Results
**Carvalho et al. (2020) TESTEX: 10	Randomized parallel group Repeated measures	26 resistance-trained men	3-week 4 sets *1-3 RM with 3 min rest and 5-week 4 sets * 8-12 RM back squat and leg press training	8 weeks (2d/w)	VL	Resistance exercise protocol induced more significant muscle growth in VL ($p < 0.05$) in 3 weeks.
Alkan (2019) TESTEX: 10	Pre-post	20 young individuals Experiment-1: 20 Experiment-2: 20	3-4 sets*10 repetitions (80-100 % 1RM) Experiment-1: Resisted leg raise and knee extension Experiment-2: Resisted knee flexion	8 weeks (3d/w)	VI RF	After an 8-week training period, both groups had increased muscle thickness ($p < 0.05$).
Santos, Valamatos, Mil-Homens, and Armada-da-Silva (2018) TESTEX: 11	RCT	28 young male adults Experiment-1: 9 (Focused on eccentric exercise) Experiment-2: 11 (Focused on concentric exercise) Control: 8 (no exercise)	Experiment: First 3 weeks 5 sets * 6 repetitions with 60°s^{-1} angular velocity. The number of contraction sets conducted at 60°s^{-1} reduced to only 2 during the next 12 weeks, but extra sets were performed at 90°s^{-1} (weeks 4-6), 120°s^{-1} (weeks 7-9), 150°s^{-1} (weeks 10-12), and 180°s^{-1} (weeks 13-15). isokinetic knee flexion and extension training	15 weeks (3d/w)	VL VI VM RF	All QF muscle thickness increased with strength exercise ($p < 0.05$) except VL muscle.
Ikezoe et al. (2020) TESTEX: 10	Pre-post	15 healthy men Experiment-1: 7 Experiment-2: 8	Experiment-1: 12 sets * 8 repetitions (30% 1RM) with 90 s rest Experiment-2: 3 sets * 8 repetitions (80% 1RM) with 90 s rest concentric and eccentric contractions in biodex dynamometer	8 weeks (3d/w)	RF	The 8-week resistance training increased by 11.3% and 20.4% RF muscle thickness for both training conditions ($p < 0.01$).
Müller et al. (2020) TESTEX: 10	Pre-post	35 older men Experiment-1: 18 Experiment-2: 17	Experiment-1: 2-4 sets * 6-15 repetitions (65-80% 1RM) Experiment-2: 3-4 sets * 6-8 repetitions (40-60 %1 RM) bilateral leg press and bilateral knee extension exercises-	16 weeks (2d/w)	VL VM RF	Significant increases ($p < 0.05$) were observed in QF muscle thickness in both groups with no differences between groups.

Table 1. Continued

Boone, Stout, Beyer, Fukuda, and Hoffman (2015) TESTEX: 10	RCT	18 untrained young men Experiment: 9 Control: 9 (no exercise)	3 sets * 8-10 repetitions (80% 1RM) leg press and leg extension training	4 weeks (3d/w)	RF VL	Resistance training resulted in significant increases in RF ($p < 0.001$) and VL ($p < 0.001$) muscle thickness.
*Cadore et al. (2014) TESTEX: 11	Pre-post	22 healthy individual (F: 14 M:8) Experiment-1: 11 Focused on eccentric exercise Experiment-2: 11 Focused on concentric exercise	2-5 sets * 8-12 repetitions- isokinetic exercise with 60°s ⁻¹ angular velocity.	6 weeks (2d/w)	VL	Both groups exhibited increased VL muscle thickness ($p < 0.05$).
*Yoshiko and Watanabe (2021) TESTEX: 11	Pre-post	16 healthy older (F:13 M:3) Experiment-1: 8 Experiment-2: 8	Experiment-1: 4 sets * 35 RM weight-bearing deep squat exercise Experiment-2: 4 sets * 35 RM weight-bearing shallow squat exercise	12 weeks (3d/w)	VL VI RF	No significant change was observed for QF muscle thickness in both groups.
*Zaras et al. (2020) TESTEX: 10	Pre-post	16 healthy male Experiment-1: 8 Experiment-2: 8	Experiment-1: 4 sets * 6 repetitions (85 % 1RM) leg press exercise with 3 min rest Experiment-2: 4 sets * 6 repetitions (85 % 1RM) leg press exercise with 3 min rest +20 s inter-repetition rest period between single repetitions.	7 weeks (2d/w)	VL VI	Following resistance training, the thickness of the VL muscle increased dramatically over time ($p = 0.043$).
*Nakamura et al. (2021) TESTEX: 10	Pre-post	16 healthy young men Experiment-1: 8 Experiment-2: 8	Experiment-1: 3 sets * 10 RM parallel squat exercise with 3 min rest Experiment-2: Static stretching exercises	5 weeks (2d/w)	VL VI VM RF	QF muscle thickness increased in both groups, but no significant difference was observed.

Table 1. Continued

Karsten, Fu, Larumbe-Zabala, Seijo, and Naclerio (2021) TESTEX: 11	Pre-post	18 resistance-trained men	Chest and bench press, deadlift, lateral pull down, dumbbell fly, barbell lying arm extension, barbell shoulder press, reverse grip bent-over row exercises	6 weeks (2d/w)	VM	The VM muscle thickness increased (+3.28 ±2.32 mm) only significantly ($p < 0.05$) in the experiment-1 group.
		Experiment-1: 9 Experiment-2: 9	Experiment-1: 4 sets * 10 repetitions (75 % 1RM) with 2 min rest Experiment-2: 8 sets * 5 repetitions (75 % 1RM) with 1 min rest			
Korkmaz (2018) TESTEX: 11	Pre-post-randomised	23 footballer	Experiment-1: 4 sets * 8-12 repetition (80% 1RM) knee extension exercise with 2 min rest Experiment-2: 4 sets * 8-12 repetition (80% 1RM) knee extension exercise with 2 min rest and blood flow restriction	6 weeks (2d/w)	VL	Blood flow restricted training provides better benefits than traditional strength training to improve muscular hypertrophy.
		Experiment-1: 12			RF	
		Experiment-2: 11				
Pinto et al. (2014) TESTEX: 10	RCT	36 sedentary elderly women	2-3 sets * 12-15 RM knee flexion, leg press and knee extension exercises	6 weeks (2d/w)	VL	All measurements of the QF muscle thickness (vastus lateralis, medialis, intermedius, and rectus femoris) showed a significant increase only in the experiment group ($p \leq 0.05$).
		Experiment: 19 Control: 17 (no exercise)			VI	
					VM	
					RF	
**Correa et al. (2012) TESTEX: 10	RCT	58 healthy older woman	First period (6 weeks) 2-3 sets * 12-20 RM Second period (6 weeks) 3-4 sets * 8-12 RM leg press, knee extension and flexion exercises with 2 min rest	12 weeks (2d/w)	VL	After 6 weeks of resistance training, a significant increase occurred in QF muscle thickness ($p < 0.05$).
		Experiment: 41 Control: 17 (no exercise)	VM			
			RF			
Usui, Maceo, Tayashiki, Nakatani, and Kanehisa (2015) TESTEX: 11	Pre-post	16 healthy young men	Experiment-1: 3 sets * 10 repetitions (50% 1RM) parallel squat training 3 s lowering and 3 s lifting without a pause phase Experiment-2: 3 sets * 10 repetitions (50% 1RM) parallel squat training 1 s lowering and 1 s lifting with 1 s pause phase	8 weeks (3d/w)	VL	In experiment-1 group, RF muscle thickness increased at +10% ($p=0.026$). No changes were observed experiment -2 group.
		Experiment-1: 9	VI			
		Experiment-2: 7	VM			
			RF			

Table 1. Continued

Brad Schoenfeld and Grgic (2018) TESTEX: 10	Pre-post	30 male volunteers	4 sets * 8-12 RM standing barbell curl and the machine leg extension with 2 min rest.	8 weeks (3d/w)	VL	RF and VL muscle thickness showed small and insignificant effect sizes favoring experiment 1 and 2 groups ($p=0.418$ and $p=0.999$, respectively).
		Experiment-1: 15 Experiment-2: 15	Experiment-1: focused on contracting the target muscle during training Experiment-2: focused on the outcome of the lift		RF	
Gonzalez et al. (2017) TESTEX: 11	Pre-post RCT	15 resistance trained men	4 sets * 10 RM bench press, barbell back squat and deadlift training with 2 min rest	8 weeks (3d/w)	VL RF	Significant improvements occurred with resistance training for all muscle thickness measurements ($p < 0.05$)
Zaroni et al. (2018) TESTEX: 10	Pre-post RCT	18 healthy men Experiment-1: 9 (training a muscle group 5 days per week) Experiment-2: 9 (training a muscle group 1 day per week)	Experiment: 3 sets * 10-12 RM bench press, hack squat, deadlift, machine lat pull down, biceps curl, nosebreaker, dumbbell hammer curl, leg press, parallel back squat, cable triceps	8 weeks (TOTAL routine training a muscle group 5 days per week)	VL	Total routine strength training significantly increases in VL muscle ($p < 0.05$).
*Nogueira et al. (2009) TESTEX: 11	Pre-post	20 healthy older men Experiment-1: 9 Experiment-2: 11	Experiment-1: 3 sets * 8 repetitions (40-60 % 1RM) knee and elbow flexion/extension, leg and chess press exercise with 90 s rest interval Experiment-2: Power exercises	10 weeks (2d/w)	RF	RF muscle thickness increased solely in power training ($p < 0.05$).
*Evangelista et al. (2019) TESTEX: 12	Pre-post	29 sedentary healthy adults Experiment-1: 17 Experiment-2: 12	Experiment-1: 4 sets * 8-12 RM bench press, knee flexion and extension, arm curl, seated row exercises with 90 s rest interval Experiment-2: 4 sets * 8-12 RM bench press, knee flexion and extension, arm curl, seated row exercises with 90 s rest interval + stretching exercises	8 weeks (2d/w)	RF VL	RF muscle thickness increased ($p \leq 0.0001$) in both groups.

Table 1. Continued

Brad Schoenfeld et al. (2016) TESTEX: 10	Pre-post	23 young resistance-trained men	Experiment-1: 3 sets * 8-12 RM flat barbell press, plate-loaded leg press, plate-loaded seated cable row, barbell back squat exercise with 1 min rest	8 weeks (3 times per day)	VL	Long interval resting group significantly increased QF muscle thickness from baseline to post by 5.4% and 7% ($p < 0.01$).
		Experiment-1: 12 Experiment-2: 11	Experiment-2: 3 sets * 8-12 RM flat barbell press, plate-loaded leg press, plate-loaded seated cable row, barbell back squat exercise with 3 min rest			
Bartolomei et al. (2021) TESTEX: 12	Pre-post	21 resistance-trained men	5 sets* 6 RM deep squat, leg curl and extension, lunges, triceps extension, bench press, front raises exercises with 2 min rest.	10 weeks (4d/w)	VL	In experiment-2 group, changes in VL muscle thickness were substantially larger ($p=0.037$) than in experiment-1 group.
		Experiment-1: 10 Experiment-2: 11	Experiment-1: Focusing on all muscle group Experiment-2: Focusing on one muscle group			

Abbreviations: d/ w: days a week, QF: Quadriceps femoris, RCT: Randomised Controlled Trial, RDB: Randomise Double Blind, RF: Rectus Femoris, RM: Repetition Maximum, VI: Vastus Intermedius, VL: Vastus Lateralis, VM: Vastus Medialis
 *: Only the results of resistance exercises from two different exercises or practices were evaluated. **: Only the measurements of the relevant weeks were evaluated.

Evaluation of Quality

The average score on the TESTEX scale was 10,6. Three studies (Bartolomei et al., 2021; Evangelista et al., 2019; Pinto et al., 2014) were classified as excellent, and 19 studies (Alkan, 2019; Boone et al., 2015; Cadore et al., 2014; Carvalho et al., 2020; Correa et al., 2012; Gonzalez et al., 2017; Ikezoe et al., 2020; Karsten et al., 2021; Korkmaz, 2018; Müller et al., 2020; Nakamura et al., 2021; Nogueira et al., 2009; Santos et al., 2018; Brad Schoenfeld & Grgic, 2018; Brad Schoenfeld et al., 2016; Usui et al., 2015; Yoshiko & Watanabe, 2021; Zaras et al., 2020; Zaroni et al., 2018) had good quality. None of the evaluated studies were assessed for their fair or poor methodological quality. The findings of the quality evaluation are shown (Table 2).

Table 2. TESTEX Scala (Overall TESTEX score out of 15 points)

Study	Eligibility criteria specified	Randomly allocated participants	Allocation concealed	Groups similar at baseline	Assessors blinded	Outcome measure assessed more than %85 of participants*	Intention to treat analysis	Reporting of between group statistical comparison	Point measures and measures variability reported #	Activity monitoring in control group	Relative exercise intensity review	Exercise volume and energy expenditure	Overall TESTEX score
Alkan, 2019	YES	YES	YES	YES	NO	2	NO	YES	2	YES	NO	YES	10
Karsten et al., 2021	YES	YES	YES	YES	NO	2	NO	YES	2	NO	YES	YES	11
Pinto et al., 2014	YES	YES	YES	YES	NO	2	NO	YES	2	YES	YES	YES	12
Schoenfeld et al., 2018	YES	YES	NO	YES	NO	2	NO	YES	2	YES	NO	YES	10
Correa et al., 2012	YES	YES	NO	YES	NO	2	NO	YES	2	NO	YES	YES	10
Evangelista et al., 2019	YES	YES	YES	YES	NO	2	NO	YES	2	YES	YES	YES	12
Bartolomei et al., 2021	YES	YES	YES	YES	NO	2	NO	YES	2	YES	YES	YES	12
Zaras et al., 2020	YES	NO	NO	YES	NO	2	NO	YES	2	YES	YES	YES	10
Cadore et al., 2014	YES	YES	NO	YES	NO	2	NO	YES	2	YES	YES	YES	11
Usui et al., 2015	YES	YES	NO	YES	NO	2	NO	YES	2	YES	YES	YES	11
Nogueira et al., 2009	YES	YES	NO	YES	NO	2	NO	YES	2	YES	YES	YES	11
Santos et al., 2018	YES	YES	NO	YES	NO	2	NO	YES	2	YES	YES	YES	11
Gonzalez et al., 2017	YES	YES	NO	YES	NO	2	NO	YES	2	YES	YES	YES	11
Zaroni et al., 2018	YES	YES	NO	YES	NO	2	NO	YES	2	NO	YES	YES	10
Schoenfeld et al., 2016	YES	YES	NO	YES	NO	2	NO	YES	2	NO	YES	YES	10
Carvalho et al., 2020	YES	YES	NO	YES	NO	2	NO	YES	2	NO	YES	YES	10
Ikezoe et al., 2020	YES	YES	NO	YES	NO	2	NO	YES	2	NO	YES	YES	10
Müller et al., 2020	YES	YES	NO	YES	NO	2	NO	YES	2	NO	YES	YES	10
Nakamura et al., 2021	YES	YES	NO	YES	NO	2	NO	YES	2	NO	YES	YES	10
Boone et al., 2015	YES	YES	NO	YES	NO	2	NO	YES	2	NO	YES	YES	10
Korkmaz, 2018	YES	YES	NO	YES	NO	2	NO	YES	2	YES	YES	YES	11
Yoshiko & Watanabe, 2021	YES	YES	NO	YES	NO	2	NO	YES	2	YES	YES	YES	11
Mean Score													10.59

Notes. *: Three points possible - 1 point if adherence is greater than 85%, 1 point if adverse events are reported, 1 point if exercise attendance is reported. #: Two points possible - 1 point if primary outcome is reported, 1 point if all other results are reported.

Resistance Training's Impact on Muscular Hypertrophy

Based on the random effects model, high, moderate, and low-intensity resistance training significantly increased quadriceps muscle hypertrophy compared to the control or pre-test group (Table 3).

Table 3. The effect of resistance exercise intensities on muscle hypertrophy (meta-analyses results).

Subgroups	ES (%95 CI)	p-value	Heterogeneity (I ²)	Weight
High Intensity Resistance Training				
VL	2.45 [2.26, 2.64]	<i>p</i> < .001	96%	20.3%
VM	0.70 [0.27, 1.13]	<i>p</i> = .001	Not applicable	4.1%
VI	0.62 [0.46, 0.78]	<i>p</i> < .001	99%	30.0%
RF	3.48 [3.35, 3.60]	<i>p</i> < .001	99%	45.6%
Total	2.30 [2.21, 2.38]	<i>p</i> < .001	99%	100%
Moderate Intensity Resistance Training				
VL	2.45 [2.27, 2.63]	<i>p</i> < .001	85%	60.0%
VM	2.01 [0.84, 3.19]	<i>p</i> = .0008	0%	1.4%
VI	0.57 [-1.01, 2.14]	<i>p</i> = .0048	85%	0.8%
RF	0.99 [0.76, 1.22]	<i>p</i> < .001	55%	37.8%
Total	1.88 [1.74, 2.02]	<i>p</i> < .001	87%	100%
Low Intensity Resistance Training				
VL	14.21 [13.87, 14.56]	<i>p</i> < .001	99%	20.3%
VM	2.46 [0.66, 4.26]	<i>p</i> = .007	0%	0.8%
VI	15.59 [15.25, 15.93]	<i>p</i> < .001	72%	21.0%
RF	8.19 [7.98, 8.39]	<i>p</i> < .001	100%	57.9%
Total	10.92 [10.77, 11.08]	<i>p</i> < .001	100%	100.0%

Data demonstrated are presented as a standardized ES estimate (signifying the raw mean difference between experiment and pre or control groups) with 95% CI and p-value. Positive ES values favor resistance training performed in experiment groups.

According to Table 3, high-intensity resistance training had a significantly increasing effect (*p* < .001) on quadriceps femoris muscle hypertrophy [Raw mean difference (RMD) = 2.30; confidence interval (CI) 95%: [2.21, 2.38]] with 99 % heterogeneity ratio compared to control/pre-test group. Moderate-intensity resistance training had a significantly increasing effect (*p* < .001) on quadriceps muscles hypertrophy [Raw Mean difference (RMD) = 1.88; confidence interval (CI) 95%: [1.74 – 2.02]] with 87% heterogeneity ratio compared to control or pre-test group. Low-intensity resistance training had a significantly increasing effect (*p* < .001) on quadriceps muscles hypertrophy [Raw mean difference (RMD) = 10.92; confidence interval (CI) 95%: [10.77 – 11.08]] with 100% heterogeneity ratio compared to control or pre-test group. Shortly, resistance training is effective on the quadriceps muscles hypertrophy.

Meta-Regression Analysis

Meta-regressions to examine the relationship between muscle thickness and resistance training intensity were carried out to recognize the sources of heterogeneity because they were statistically significant ($p < .001$) and had a large amount of unexplained heterogeneity. The dose-response relationship between resistance training intensity (% of 1RM) and change in quadriceps femoris muscle thickness (mm) is shown with scatter plots. The 95% confidence intervals are represented by dotted lines (Figures 2. and 3.). According to meta regression, it was determined that there was a non-significant direct relationship between resistance training intensity (% of 1RM) and change in RF ($\beta = 0.03$; $p = 0.417$; $R^2 = 0.04$) and VM muscle thickness ($\beta = 0.003$; $p = 0.895$; $R^2 = 0.002$). It was also determined that there was a significant direct relationship between resistance training intensity and change in VI ($\beta = 0.01$; $p = 0.05$; $R^2 = 0.56$) and VL muscle thickness ($\beta = 0.01$; $p = 0.007$; $R^2 = 0.34$).

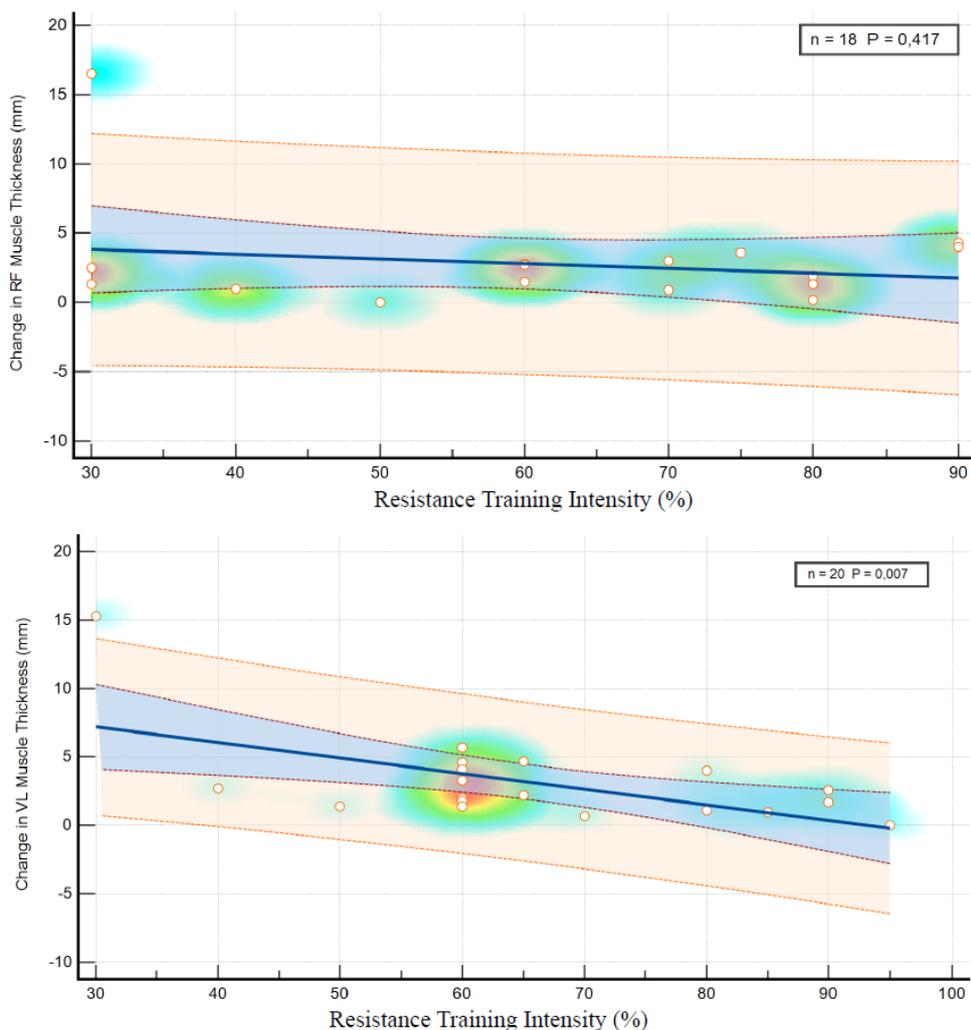


Figure 2. Scatter Plots of RF and VL Muscles

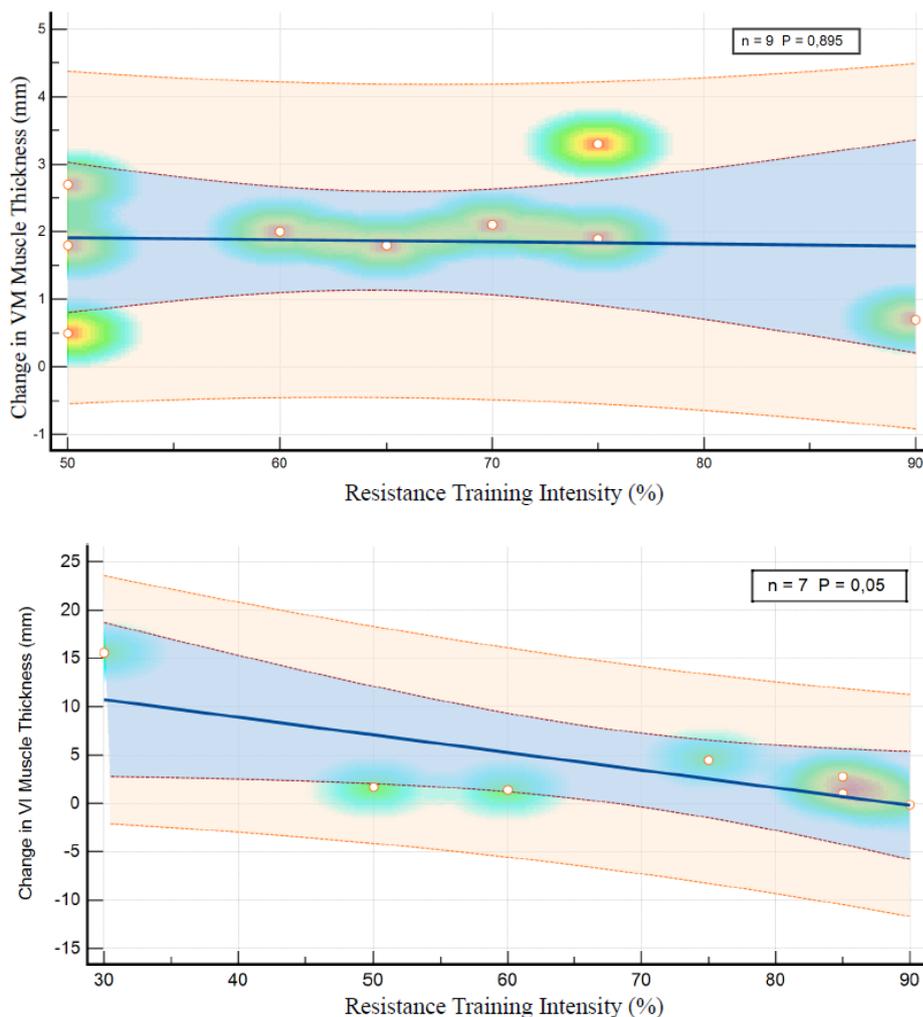


Figure 3. Scatter Plots of VM and VI Muscles

Based on the scatter plots, when resistance exercise intensity increases by 10%, RF muscle thickness increases by 0.3 mm, and VM muscle thickness increases by 0.03 mm. When resistance exercise intensity increases by 10%, VI and VL muscle thickness increases by 0.1 mm. While the increase in RF and VM muscle thicknesses is not statistically significant, the rise in VI and VL is statistically significant ($p = 0.417$, $p = 0.89$, $p = 0.05$, $p = 0.007$, respectively).

Additionally, R^2 values indicate that the relationship between resistance training intensity and changes in RF, VM, and VL muscle thickness is insufficient except for the change in VI muscle thickness ($R^2 = 56\%$).

DISCUSSION

This study searches for the answer to the question, “What is the net range of intensity of resistance training one provides to increase quadriceps muscle hypertrophy?”. To the best of the authors’ knowledge, there is no study in which the hypertrophic effects of resistance exercises are evaluated separately for each muscle in the quadriceps femoris. The main finding of this study is that resistance exercises, at all intensities (high-moderate-low), significantly enhance quadriceps femoris muscle size. Further, a significant direct relationship between resistance training intensity and change in VI and VL in which as intensity increases by 10%, muscle thickness increases by 0.1 mm.

Given that it has been proven that resistance training’s acute and chronic effects diminish with time, it is necessary to manipulate resistance training components, including “intensity,” for consistent strength and morphological changes (Borde et al., 2015). Based on the results of this meta-analysis, athletes and coaches can maintain resistance exercise intensity in any range from low (30% of 1RM) to high (80% of 1RM) for various purposes at different periods of the training period without affecting the hypertrophic adaptation magnitude of quadriceps femoris. Parallel to this, in the meta-analysis by Carvalho et al. (2022), even when volume load is equalized across conditions, muscle hypertrophy is identical regardless of the level of resistance intensity from 30% to 80% of 1RM. Another meta-analysis, which examined the effects of high and low-intensity resistance exercises on muscle hypertrophy, determined no difference between the intensities (Brad Schoenfeld, Grgic, et al., 2017). Furthermore, according to these conclusions from three meta-analyses, one can perform resistance training with lower intensities (30-59% of 1RM), in turn, enlarge the training volume loads (Morton et al., 2019). The evidence suggests a dose-response relationship between training volume load and hypertrophic adaptations, therefore this might affect on changes in muscle size (Lasevicius et al., 2022). In other meta-analysis studies, dose response analysis was not evaluated. However, in this study, dose response connection was applied to investigate how resistance training intensity change would affect the hypertrophic response. Determining at what intensity there is significant hypertrophy may be useful to inform practitioners. On the other hand, it was proposed by three studies that higher training intensities induce greater increases in muscle fiber cross sectional area of vastus lateralis in “*untrained*” individuals (Campos et al., 2002; Holm et al., 2008; Schuenke et al., 2012). Supporting our and the other two meta-analyses abovementioned, Brad Schoenfeld et al. (2015) demonstrated that both low and high resistance intensities, even when training load volume equated, induce a similar increase in muscle size

after 8 weeks of resistance training in “*resistance trained*” men. It can be speculated that the resistance training experience may determine the size of hypertrophic adaptation depending on the intensity of resistance training, at least in the first few months. Even though low-volume, high-intensity resistance training is demonstrably beneficial to promoting muscle growth, the high intensities (80% 1RM) employed may be challenging for untrained individuals or remote training programs with limited access to equipment. In individuals with less resistance exercise experience, relatively greater volumes of lower intensity resistance training may be a more viable choice (Fyfe, Hamilton, & Daly, 2021). It could be the most effective approach to keep an elevated resistance intensity for the first several months and gradually reduce it. Lastly, it should be remembered that the “repetition to failure” regimen has been demonstrated as a key component for low intensity resistance training to be as effective as high loads for muscle growth (Lasevicius et al., 2022; Lim et al., 2019).

The consensus is that an intensity of more than $\geq 60\%$ of 1 RM is required to produce meaningful improvements in muscle size using conventional resistance training techniques. Nevertheless, there is mounting evidence that low-intensity resistance exercise, also using various techniques, can significantly improve muscle hypertrophy, often comparable to typical high-intensity exercise (B. J. Schoenfeld, 2013). In response to resistance training, three central components have been postulated to drive hypertrophic alterations: muscle damage, mechanical tension, and metabolic stress (B. J. Schoenfeld, 2010). Resistance training-related mechanical tension compromises the skeletal muscle's stability by prompting myofibers and satellite cells to respond mechanically and chemically (Toigo & Boutellier, 2006). Motor unit activation frequency, which determines both the intensity and length of excitation coupling, is thought to transmit signals for a variety of downstream pathways, including CaMKII (upregulates muscle atrophy) and CAMKIV (promotes mitochondrial biogenesis) (Chin, 2005). Conversely, it has been demonstrated that higher-intensity resistance training can regulate the acute secretion of growth hormone, particularly in routines meant to increase metabolic stress (Hoffman et al., 2003). Similarly, it has been suggested that glycolytic activity may elevate the acidic environment, accelerate muscle damage, and further stimulate sympathetic nerve function, resulting in a higher adaptation for muscle hypertrophy (Buresh, Berg, & French, 2009). On the other hand, it has also been hypothesized that the mechanisms of exercise-induced muscle growth are entirely intrinsic and unaffected by temporary changes in circulating hormones (West, Burd, Staples, & Phillips, 2010).

Another main finding is that as the intensity of resistance exercise increases, there is no significant increase in RF and VM muscle thicknesses; in contrast, a significant increase is observed in VI and VL muscle thicknesses. Since there is no meta-analysis where the hypertrophic response of four muscle heads (VL, RF, VM, and VI) to resistance training is investigated, it is impossible to make a direct comparison. More recently, the literature has offered contradictory findings about resistance training “intensity” and increases in VL-VI muscle size. Several researchers have seen larger gains in muscle growth with increasing intensity (Campos et al., 2002; Holm et al., 2008; Schuenke et al., 2012), whereas others revealed no statistically significant difference between low and high intensity (Tanimoto et al., 2008). A potential limitation in most of this research is that training volume differed between groups. When volume equated, all intensities (40%, 60% and 80% of 1RM) were found to enhance VL cross-sectional area similarly (Lasevicius et al., 2018; Brad Schoenfeld et al., 2015). For this reason, the result of this meta-analysis is that the muscle thickness in VL and VI increases in an intensity-dependent manner, which may be caused by the “volume” of resistance training. Moreover, the fact that almost all studies in this meta-analysis employed "closed chain" exercises, which predominantly leads to hypertrophy of vastus muscles (Ema, Sakaguchi, Akagi, & Kawakami, 2016), may have contributed to the failure of RF to respond even when "intensity" rises.

VL, RF, VM, and VI are the four muscle heads that make up the quadriceps femoris. The surface head VL is located outside the thigh. RF is positioned in the center of the anterior side of the thigh, while VM is on the side. VI is positioned at the interior of the thigh because it is above the femur and beneath the three surface heads (Pasta, Nanni, Molini, & Bianchi, 2010). Physiological cross-sectional area (PCSA), the biggest cross-sectional area point of a pennate muscle perpendicular to its muscle fibers, volume, muscle length, fascicle length, and fascicle pennation angle are all distinctive architectural characteristics of each head (Lieber, 2002). Because of its location, the VL head of the quadriceps is the most investigated. It has been used as a substitute for the entire quadriceps muscle to assess muscle size, electromyographic activity, metabolic characteristics, and muscle fiber composition, whether for clinical or sports purposes (Coratella et al., 2020; El-Ansary et al., 2021; Methenitis et al., 2016). According to a recent current experimental study, the best substitutes for the entire resistance training-induced hypertrophy of the quadriceps appear to be VL and VI (Spiliopoulou et al., 2022). VL and VI could offer accurate data on whole quadriceps muscle hypertrophic response lower-body resistance training when ultrasonography is employed. In the current study, the best

hypertrophic result against the increase in density was seen in VL and VI, which is attributed to the broader presence of PCSA. In addition, when the types of exercises performed based on the studies included in the analysis are examined, it is observed that the resistance exercises performed on the lower extremities are primarily aimed at the VL and VI muscles. The lack of training of the RF and VM muscles in exercise applications and the smaller PCSA will make it difficult to observe a hypertrophic effect on these muscles. Especially in recent years, the increase in the risk of lower extremity injuries in sportive activities and competitions has increased the number of studies on this subject. It has been suggested that the most critical issue that increases this risk is due to the power imbalance in the hamstring/quadriceps ratios (Cheung, Smith, & Wong, 2012; Padasala, Joksimovic, Bruno, Melino, & Manzi, 2020; Yoo, 2016). To minimize the risk of injury, the focus should be on hypertrophy of all quadriceps muscles. Based on the current results of the meta-analysis, special programs should be applied mainly for RF and VM muscles in lower extremity resistance exercise applications with lower intensities ($\leq 80\%$ of 1RM).

CONCLUSION

This meta-analysis indicated that resistance training had a significantly increasing effect on quadriceps femoris muscle hypertrophy. Meta-regression analysis identified a substantial relationship between resistance training intensity and change in VI and VL muscle thickness and a non-significant direct link between resistance training intensity and change in RF and VM muscle thickness.

It can be said that the increase in VI muscle hypertrophy is dependent on the resistance training intensity based on its R^2 value. Conversely, resistance training intensity is less likely to explain VL, VM, and RF muscle hypertrophy. By this perspective, analyses using multiple covariates such as frequency, type, time or total protein intake status, and type of sets (interset/drop set) in line with the FITT principle can be done in future studies. In addition, it was determined that the number of studies on VI and VM muscle hypertrophy was low. Therefore, future studies can focus on filling this gap in the literature. These results point to a potential advantage of including a wide range of loading values in a hypertrophy-focused exercise for quadriceps femoris muscles.

Consequently, the meta-analysis results determined that the resistance training intensity gave similar results in the hypertrophy of the quadriceps femoris muscle. However, since the

percentage of muscle hypertrophy explained by exercise intensity is high ($R^2=56\%$), every 10% increase in resistance exercise provides a hypertrophic response of 0.1 mm in the VI muscle.

This study is vital in performing muscle-specific strengthening exercises and detecting the intensity of a significant hypertrophy point. In addition, there will be benefits such as providing information to practitioners on this subject and indicating to researchers at what point there needs to be more literature.

LIMITATIONS

This meta-analysis has several limitations. Hypertrophic adaptations to resistance training are influenced by multiple variables beyond training intensity, including movement tempo, exercise execution tempo, repetition cadence, and eccentric-concentric loading patterns. However, due to the heterogeneity of training protocols across the included studies and incomplete reporting of these parameters, their independent effects on muscle hypertrophy could not be systematically analyzed.

Moreover, factors such as total training volume, rest intervals, training experience of participants, and neuromuscular adaptations may have contributed to variability in hypertrophic responses. The lack of uniformity in measurement techniques (e.g., ultrasound vs. MRI) and differences in anatomical sites used for assessing muscle thickness could also introduce methodological inconsistencies. Additionally, variations in participant characteristics such as age, sex, baseline strength levels, and genetic predispositions may have influenced the results, limiting the generalizability of the findings.

Future research should aim to standardize resistance training protocols, ensuring consistent reporting of movement tempo, contraction phases, and repetition cadences. Additionally, studies employing advanced imaging techniques with strict methodological controls are needed to isolate the effects of specific training variables on quadriceps hypertrophy.

PRACTICAL APPLICATIONS

- This study searches for the answer to the question, “What is the net range of intensity of resistance training one provides to increase quadriceps muscle hypertrophy?”.
- Starting from here, this study aims to detect the effectiveness of different resistance training intensities (high, moderate, and low) for quadriceps femoris muscle group hypertrophic response in healthy adults.

- The meta-analysis results detected that the different resistance training intensities gave similar results in the hypertrophy of the quadriceps femoris muscle.
- The meta-regression analysis showed that for every 10% greater difference in resistance exercise intensity, the hypertrophic response in the VI muscle was determined to be 0.1 mm greater significantly. However, no significant hypertrophic response was observed for VL, VM, and RF muscles.
- This study may be helpful in performing muscle-specific strengthening exercises and detecting the intensity of a significant hypertrophy point for practitioners on this subject and athletes who want to track muscle hypertrophy.

Declaration of Conflicting Interests

The authors report no conflicts of interest and no source of funding.

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