PEDRO AUGUSTO BIANCHI DA FONSECA

COMPARISON OF TRADITIONAL AND ADVANCED RESISTANCE-TRAINING PARADIGMS ON MUSCLE HYPERTROPHY IN TRAINED INDIVIDUALS: A SYSTEMATIC REVIEW, META-ANALYSIS, AND CRITICAL EVALUATION OF THE LITERATURE

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Dissertation presented to the Graduate Program in Physical Education, concentration area: "Physical Education, Sport and Health" (Line of Research: "Psychobiological Aspects of Physical Exercise Related to Health and Performance", Federal University of Triangulo Mineiro, as a partial requirement for obtaining the master's degree

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UBERABA

2023

I dedicate this to everyone who was willing to be part of my life before and during the execution of this work, the result of the smallest to the greatest contribution of each one of you.

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"The term *limit* here does not imply that there are no other limits..."

Simon Gandevia (GANDEVIA, 2001)

RESUMO

Indivíduos treinados podem exigir maiores variações nos estímulos de treinamento e uso de sistemas avançados de treinamento de força (ADV) para aumentar a hipertrofia muscular. No entanto, nenhuma meta-análise examinou como os ADV e as abordagens tradicionais (TRAD) podem afetar diferencialmente os resultados hipertróficos em indivíduos treinados. O objetivo desta revisão foi determinar se as respostas de hipertrofia muscular esquelética induzidas por TRAD diferem de ADV em indivíduos treinados em força, analisando os estudos a respeito do controle dietético, nível de treinamento dos participantes e quantificação das cargas de treinamento. Foram incluídos estudos revisados por pares, ensaios clínicos randomizados, publicados em inglês, conduzidos com adultos saudáveis, indivíduos treinados em força realizando um período de TRAD e ADV com medidas pré e pós de hipertrofia muscular. As bases de dados Pubmed, Web of Science, SPORTdiscus e MEDLINE foram pesquisadas até outubro de 2022. A meta-análise foi realizada no *software* Revman5 e o risco de viés foi avaliado pela escala RoB2. Dez estudos preencheram os critérios de inclusão. A meta-análise não mostrou diferença entre ADV e TRAD em qualquer avaliação de hipertrofia muscular: espessura muscular (SMD = 0.05, IC 95%:-0.20 0.29, [p = 0.70]), massa magra (SMD = - 0.01, IC 95%: -0.26 0.23, [p = 0.92]), área de seção transversal do músculo (SMD = -0.07, IC 95%: [-0.36 0.22], [p = 0.64]) ou todas as medidas analisadas juntas (SMD = -0.00, IC95%: [-0.15 0.14], [p = 0.95]). O uso de ADV em curto prazo não induziu respostas de hipertrofia muscular esquelética superiores quando comparado ao TRAD em indivíduos treinados. Independentemente do uso de sistemas ADV ou TRAD, a realização de cargas de volume semelhantes parece induzir respostas hipertróficas semelhantes. Portanto, atletas e treinadores devem considerar o monitoramento dessa métrica durante a elaboração de um programa de treinamento.

Palavras-chave: sobrecarga excêntrica; séries descendentes; volume germânico; pré-exaustão; treino em pirâmide.

ABSTRACT

Trained individuals may require higher variations in training stimuli and advanced resistance training paradigms (ADV) to increase muscle hypertrophy. However, no meta-analysis has examined how ADV, and traditional (TRAD) approaches may differentially affect hypertrophic outcomes in trained populations. The aim of this review was to determine whether the skeletal muscle hypertrophy responses induced by TRAD differ from ADV in resistance-trained individuals, and analyzing the studies regarding the dietary control, participants' training status, and quantification of training loads. Search for peer-reviewed studies randomized controlled trials, published in English, conducted with healthy adults, resistance-trained individuals performing a period of TRAD and ADV with Pre-to-Post measurement of muscle hypertrophy. Pubmed, Web of Science, SPORTdiscus, and MEDLINE databases were searched up to October 2022. Meta-analysis was conduct in Revman5 and risk of bias was assessed by RoB2. Ten studies met the inclusion criteria. Meta-analysis showed no difference between ADV and TRAD in any muscle hypertrophy assessment: muscle thickness (SMD = 0.05, 95%CI:-0.20 0.29, [p = 0.70]), lean mass (SMD = - 0.01, 95%CI:-0.26 0.23, [p = 0.92]), muscle cross-sectional area (SMD = -0.07, 95%CI:[-0.36 0.22] , [p = 0.64]), or all measurements analyzed together (SMD = -0.00, 95%CI:[-0.15 0.14], [p = 0.95]). Short-term ADV does not induce superior skeletal muscle hypertrophy responses when compared with TRAD in trained individuals. Independently of the use of ADV or TRAD systems, performing similar volume loads appears to induce similar hypertrophic responses. Therefore, coaches and athletes programing a period of resistance training should consider monitoring this metric.

Keywords: accentuated-eccentric; drop-sets; german-volume; pre-exhaustion; pyramid-training; rest-pause.

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SUMMARY

1 INTRODUCTION

The ability of the skeletal muscle to generate strength and power is primarily dictated by neural drive (i.e., motor unit recruitment and firing rate) and the quantity of muscle contractile and structural proteins (AAGAARD, 2003; CORMIE; MCGUIGAN; NEWTON, 2011). Under the appropriate nutrient provision, resistance training (RT) optimizes the accretion of contractile and structural proteins and promotes skeletal muscle hypertrophy (PHILLIPS, 2014; RUSSELL; MOTLAGH; ASHLEY, 2000; SPIERING; KRAEMER; ANDERSON; ARMSTRONG *et al.*, 2008). Despite recent investigations challenging the hypothesis that RT-induced increases in muscle size meaningfully contribute to increases in muscle strength (DANKEL; BUCKNER; JESSEE; GRANT MOUSER *et al.*, 2018; LOENNEKE; DANKEL; BELL; BUCKNER *et al.*, 2019), athletes often seek to maximize a hypertrophic response to training with the general acceptance that this translates into performance gains (PHILLIPS, 2014).

The American College of Sports Medicine suggests that moderate loading (70-85% of one-repetition maximum [1RM]) with 8-12 repetitions per set, for 1-3 sets per exercise, is effective for facilitating muscle hypertrophy in novice (untrained individuals with no RT experience, or who have not trained for several years) and intermediate trainees (AMERICAN COLLEGE OF SPORTS, 2009). However, for individuals that possess an advanced training status, a loading range of 70-100% of 1RM with 1-12 repetitions per set, for 3-6 sets per exercise in a periodized manner is recommended such that the majority of training is devoted to 6-12RM training, and less training devoted to 1-6RM loading (AMERICAN COLLEGE OF SPORTS, 2009).

The above recommendations are related to the fact that, while untrained individuals can develop strength using any reasonable RT program (STONE; PLISK; STONE; SCHILLING *et al.*, 1998), the potential for further functional and morphological improvements diminishes as an individual becomes more well-trained. In this regard, a "window of adaptation" in trained individuals may exist (CORMIE; MCGUIGAN; NEWTON, 2011; FLECK, 1999), resulting in slower rates of strength and hypertrophy increases than in untrained individuals (FLECK, 1999; STONE; PLISK; STONE; SCHILLING *et al.*, 1998). To avoid a ‘plateau’ in skeletal muscle adaptation during the training process, reputable strength and conditioning guidelines advise that trained individuals may require higher variations in training stimuli, more sophisticated planning strategies, and longer training periods to achieve changes in strength and hypertrophy (FLECK; KRAEMER, 2014; KRAEMER; RATAMESS, 2004).

These and associated recommendations for novice and advanced training statuses are often denoted as traditional RT approaches (TRAD) (ANGLERI; UGRINOWITSCH; LIBARDI, 2017). Conversely, advanced RT paradigms (ADV), or specialized training techniques advocated to optimize muscle growth, include the utilization of drop-sets, forced repetitions, rest-pause repetitions, super slow repetitions, pyramid sets, pre-exhaustive sets, supersets, accentuated eccentric overload, and German volume training (ANGLERI; UGRINOWITSCH; LIBARDI, 2019; ANGLERI; UGRINOWITSCH; LIBARDI, 2017; SCHOENFELD, 2011a). Some ADV have been investigated and compared to TRAD regarding the potentiation of muscle hypertrophy in resistance-trained individuals (ANGLERI; UGRINOWITSCH; LIBARDI, 2019; ANGLERI; UGRINOWITSCH; LIBARDI, 2017). However, a recent narrative review (ANGLERI; UGRINOWITSCH; LIBARDI, 2019) concluded that the currently available evidence could not determine whether ADV variations can optimize muscle strength and mass gains compared to TRAD.

Several studies (ANGLERI; UGRINOWITSCH; LIBARDI, 2017; BRANDENBURG; DOCHERTY, 2002; ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021) have examined RT adaptations in well-trained participants following RT interventions. However, no meta-analysis has examined how different RT paradigms (e.g., TRAD vs. ADV) may affect hypertrophic outcomes in previously trained individuals. Therefore, this systematic review and meta-analysis sought to determine whether the skeletal muscle hypertrophy responses induced by TRAD differ from ADV in resistance-trained individuals. Based on previous literature (ANGLERI; UGRINOWITSCH; LIBARDI, 2019; ANGLERI; UGRINOWITSCH; LIBARDI, 2017; BRANDENBURG; DOCHERTY, 2002; ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021), we hypothesized that ADV and TRAD would elicit similar effects regarding muscle hypertrophy responses. We also hypothesized that dietary factors, RT experience, and the training loads employed may influence the observed effects. A secondary objective was to analyze the studies regarding dietary control, the training status, and the quantification of training loads.

2 METHODS

2.1 SEARCH STRATEGY

This review is in line with the current Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) checklist (PAGE; MCKENZIE; BOSSUYT; BOUTRON *et al.*, 2021). Population, Intervention, Comparator, Outcome and Time PICOT strategy was adopted (P: trained individuals, I: ADV, C: TRAD, O: Hypertrophy, T: Intervention time described at least on number of sessions or weeks). The search was conducted in Pubmed, Web of Science, SPORTdiscus with full text, and MEDLINE complete databases using the following combinations of words and operators: ("resistance train*" OR "strength train*" OR "weight train*") AND ("accentuated eccentric" OR "drop-set" OR "super-slow" OR "pyramid*" OR "pre-exhaustion" OR "eccentric overload" OR "rest-pause" OR "German volume training" OR "forced repetition*" OR superset OR "bi-set" OR "tri-set") AND (hypertrophy OR "muscle mass" OR "fiber cross-sectional area" OR "muscle thickness" OR "muscle volume") AND (session* OR week*). The initial search was conducted in January 2022. A final search was conducted on October 17, 2022.

2.2 STUDY SELECTION

Inclusion criteria for studies were as follows: i) peer-reviewed, published in English, and available as a full-text manuscript; ii) randomized controlled trials conducted with healthy resistance-trained adults performing a period of TRAD and ADV; iii) measurement of skeletal muscle hypertrophy pre-to-post training change scores at the macroscopic and microscopic level with the following techniques: B-mode, panoramic, extended field of view or three-dimensional ultrasonography, dual-energy x-ray absorptiometry (DEXA), computed tomography, peripheral quantitative computed tomography, magnetic resonance imaging, muscle biopsies, and/or measurement of lean body mass change by plethysmography; iv) RT program presented as ADV must match the description provided by previous literature (see Advanced paradigms section); v) data presented as mean and standard deviation provided in the text, Table(s), or Figure(s). Studies observing responses to low-load blood flow restriction, non-isoinertial RT (e.g., flywheel, isokinetic and pneumatic devices), creatine, protein or other supplements, anti-inflammatory drugs, or the influence of training frequency, or studding elderly or unhealth individuals were not included. The studies were imported into the software Rayyan online for systematic reviews (OUZZANI; HAMMADY; FEDOROWICZ; ELMAGARMID, 2016) to find duplicates and two authors performed the blind study selection according to the aforementioned inclusion criteria. Section 2.3 describes each ADV identified and used for classifying and including the studies reviewed.

2.3 ADVANCED RESISTANCE TRAINING PARADIGMS DESCRIPTION

Advanced paradigms consist of pre-defined RT protocols based on the configuration of RT variables (i.e., load, number of repetitions and sets, movement velocity, rest intervals between sets, exercises or repetitions, or exercise order, among others).

2.3.1 Accentuated eccentric

Accentuated eccentric or eccentric overload aims to provide a greater load in the eccentric phase of the movement (ANGLERI; UGRINOWITSCH; LIBARDI, 2019; BRANDENBURG; DOCHERTY, 2002). The concentric phase is performed with a regular load (e.g., 70% of 1RM) whereby the load is adjusted for the eccentric phase (usually above the concentric 1RM, e.g., 110-120% of 1RM), which requires external assistance (BRANDENBURG; DOCHERTY, 2002).

2.3.2 Drop-sets

Drop-sets involve reducing the load (e.g., 20%) to perform additional repetitions after achieving failure in a set (BENTES; SIMÃO; BUNKER; RHEA *et al.*, 2012; SCHOENFELD, 2011b). The process can be repeated on the same set, and a minimal rest interval is allowed between load reductions (BENTES; SIMÃO; BUNKER; RHEA *et al.*, 2012; SCHOENFELD, 2011b).

2.3.3 Forced repetitions

After achieving concentric failure during a set, proper assistance (i.e., by the coach or partner) is provided to the lifter to perform additional repetitions (SCHOENFELD, 2011b).

2.3.4 German volume training

German volume training is characterized by the performance of 10 sets of 10 repetitions in no more than two exercises with a load of approximately 60% of 1RM (AMIRTHALINGAM; MAVROS; WILSON; CLARKE *et al.*, 2017; ANGLERI; UGRINOWITSCH; LIBARDI, 2019).

2.3.5 Paired sets

Paired sets, supersets, or bi-sets are described as the combination of two exercises executed in sequence without rest (SCHOENFELD, 2011a). Supersets are a specific agonistantagonist combination of exercises (SCHOENFELD, 2011a), and a variation of a bi-set with three exercises is also known as tri-set (ANGLERI; UGRINOWITSCH; LIBARDI, 2019).

2.3.6 Pre-exhaustion

A single-joint exercise set is performed until failure immediately before a set of a multi-joint exercise of the same muscular group to induce more fatigue in a specific muscle (ANGLERI; UGRINOWITSCH; LIBARDI, 2019; GENTIL; OLIVEIRA; JÚNIOR; DO CARMO *et al.*, 2007).

2.3.7 Pyramid

The pyramid system consists of a configuration of sets leading to a progressive increase (i.e., crescent pyramid) or decrease (i.e., decrescent pyramid) in the load for each set performed (ANGLERI; UGRINOWITSCH; LIBARDI, 2019; ANGLERI; UGRINOWITSCH; LIBARDI, 2017). The number of repetitions performed follows an inverse relationship pattern for each configuration (ANGLERI; UGRINOWITSCH; LIBARDI, 2019; ANGLERI; UGRINOWITSCH; LIBARDI, 2017).

2.3.8 Rest pause

An overestimated number of repetitions is fixed to a given load. When failure is reached, a short rest interval (e.g., 20 seconds) is taken before subsequent repetitions are performed until failure is achieved again (ANGLERI; UGRINOWITSCH; LIBARDI, 2019; MARSHALL; ROBBINS; WRIGHTSON; SIEGLER, 2012).

2.3.9 Super slow

Super slow training is characterized by using a very slow movement velocity for each repetition (e.g., 10 seconds to concentric and 4 seconds to eccentric) (ANGLERI; UGRINOWITSCH; LIBARDI, 2019; SCHUENKE; HERMAN; GLIDERS; HAGERMAN *et al.*, 2012).

2.4 DATA EXTRACTION

One author (PF) extracted data from the included studies, and a second author (BI) double-checked the data. Disagreements were resolved through personal communication between the authors. In addition to measurements of skeletal muscle hypertrophy, the following additional data were extracted from the included studies: i) participants' characteristics (i.e., sex and RT experience); ii) quantification of training loads; iii) the dietary control(s) employed. When reported, mid-time analysis of included studies was not considered.

The RT status reported in the studies was compared to the scale provided by Rhea (RHEA, 2004) proposed to interpret effect sizes. According to Rhea (RHEA, 2004), untrained individuals were considered those who had not been consistently training for one year, recreationally trained performed consistent RT for one to five years, and highly trained were considered as those who trained consistently for at least five years.

The quantification and monitoring of training loads were extracted as reported (e.g., exercises performed, number of sets, number of repetitions, relative intensity, etc.). Volume load quantification was considered as sets × repetitions × mass (HAFF, 2010; SCOTT; DUTHIE; THORNTON; DASCOMBE, 2016). In addition, the RT programs performed by the participants before their engagement in the studies were also analyzed. Dietary control was considered when the study provided a nutritional intake record, a proper nutritional plan to the participants, or any post-training standardized supplementation to enhance the targeted adaptations.

2.5 RISK OF BIAS ASSESSMENT

Following recommendations for randomized controlled trials, the risk of bias was assessed by the scale Risk of Bias-2 scale of Cochrane (HIGGINS, 2011; HIGGINS; ALTMAN; GØTZSCHE; JÜNI *et al.*, 2011) by two reviewers (PF and BI). The domains assessed were the randomization process (A), deviations from the intended interventions (B), missing outcome data (C), measurement of the outcome (D), and selection of the reported result (E). The overall risk of bias was determined according to each study's higher risk domain (F) presented. The assessment was done by answering the pre-specified questions about the adequacy of each study. The analysis was conducted according to recommendations using software provided by Cochrane. According to the pre-specified questions, the studies were classified in each domain as low, unclear, and high risk of bias. The overall risk of bias was determined by the higher risk attributed to any domain. If necessary, discrepancies were resolved by consensus with a third reviewer (GM).

2.6 STATISTICAL ANALYSIS

The level of between-study heterogeneity was assessed using the chi-square (χ^2) test and I-square (I^2) statistic (LIBERATI; ALTMAN; TETZLAFF; MULROW *et al.*, 2009). I^2 outcomes of 25, 50, and 75% correspond to low, moderate, and high heterogeneity (HIGGINS;

THOMPSON; DEEKS; ALTMAN, 2003), with a value of 0% indicating no heterogeneity, and above 75% were rated as heterogeneous. In addition, a fixed-effects model of meta-analysis with a standardized mean difference (SMD) was used, and the degree(s) of freedom (*df*) and the 95% confidence interval (CI) were reported. Differences at the level of $p < 0.05$ were considered statistically significant. The Review Manager software Version 5.4 (The Cochrane Collaboration, 2020) was used for data entry and statistical analysis (HIGGINS, 2011).

3 RESULTS

A total of 262 records were found from Web of Science (n = 75), Scopus (n = 58), Pubmed (n = 47), MEDLINE complete (EBSCO, n = 42), and SPORTdiscus with full text (EBSCO, n = 40). After removing duplicates, 103 records remained. According to inclusion criteria, 20 studies were considered possibly eligible. After full-text assessments, 12 studies were excluded. In addition to the eight studies, two additional studies were included after consulting the articles' reference list. This led to 10 studies being included in the final analysis. Figure 1 shows the flowchart diagram of the study screening process.

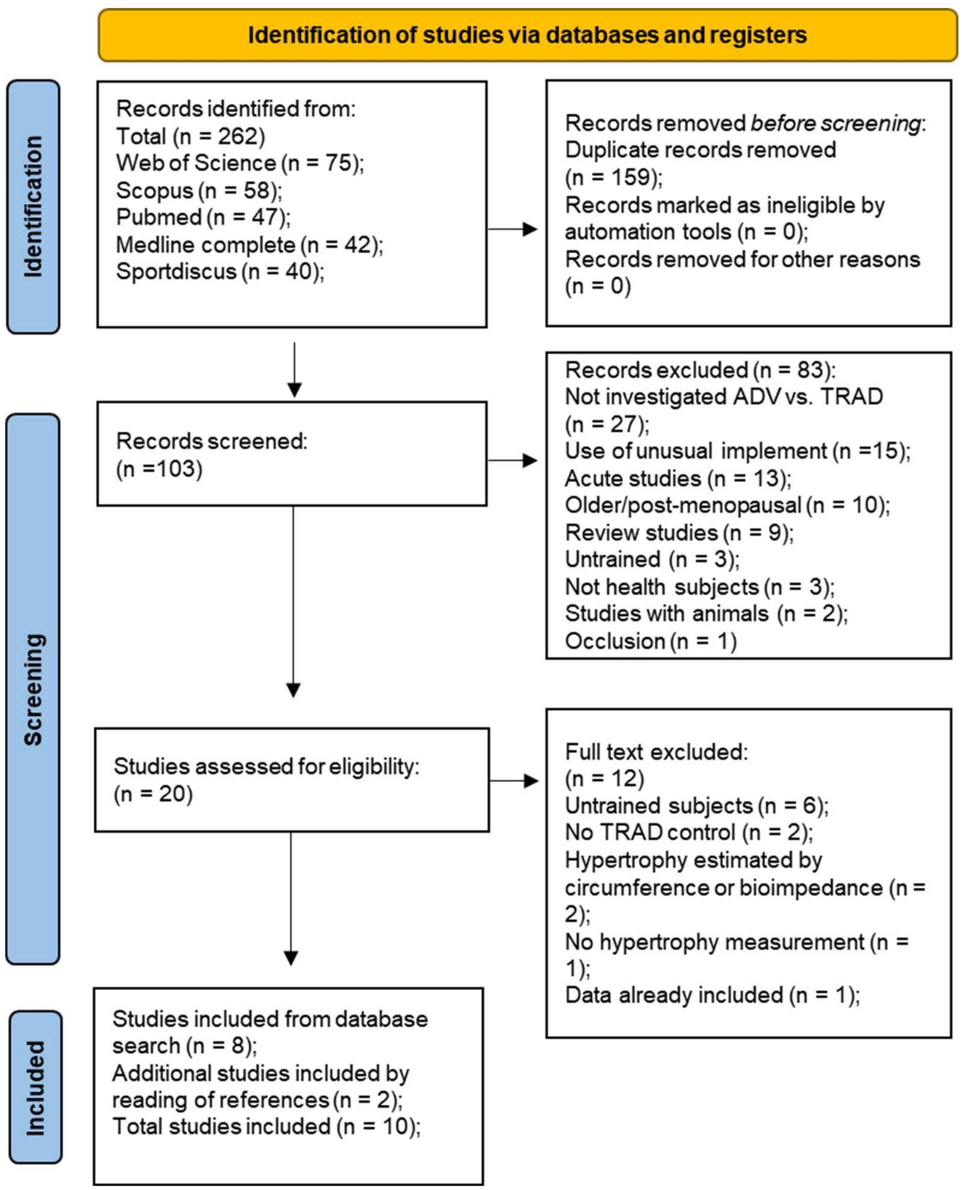

Figure 1-Flowchart illustrating the distinct phases of the search and selection strategy.

3.1 RISK OF BIAS ANALYSIS

Analysis of the risk of bias revealed that only two studies (BRANDENBURG; DOCHERTY, 2002; WALKER; BLAZEVICH; HAFF; TUFANO *et al.*, 2016) presented a high risk of bias due to unequal dropouts of the ADV group (domain C of Risk of Bias-2 scale). Both studies investigated eccentric overload. All studies presented a lack of information in domain A (which does not inform if the allocation was concealed), resulting in an unclear risk (F) for the remaining eight studies. However, most studies presented a low risk in domains B-E. A summary of the risk of bias analysis is illustrated in Figure 2.

3.2 GENERAL DESCRIPTION OF THE STUDIES

The description of studies regarding the RT programs that investigated muscle hypertrophy outcomes is presented in Table 1.

Table 1-General description of the studies. Resistance training programs investigated, muscle hypertrophy assessments, and main results. Continue.

Study	Participants	Duration and frequency of the program	Muscle hypertrophy assessment	Main results for TRAD	Main results for ADV	Differences between protocols
Amirthalingam 2017	19 men TRAD (n = 9) or GVT (n = 10)	6 weeks 3 $d.wk.^{-1}$	LM and MT	↑3.1, ↑4.2, and ↑7.8% in total, trunk, and arm LM. No significant changes in MT	↑1.9, ↑1.0, and ↑3.5% in total, trunk, and arm LM. No significant changes in MT	-
Angleri 2017	32 men (16 legs in CP, 16 in DS and 32 in TRAD)	10 weeks 2 $d.wk.^{-1}$	ACSA	↑7.6% in ACSA	CP: ↑7.5% in ACSA DS: ↑7.8% in ACSA.	-
Branderburg 2002	18 men TRAD (n = 10); EO (n = 8)	11 weeks 2-3$d.wk.^{-1}$	ACSA	-	-	-
Enes 2021	28 men TRAD (n = 9); DS (n = 9); RP (n = 10)	8 weeks 2 $d.wk.^{-1}$	MT	↑14.2 and ↑6.5% in the proximal thigh and middle thigh MT.	DS: ↑11.6 and ↑7.7% in the proximal and middle thigh MT. RP: ↑8.8 and ↑5.1% in the proximal and middle thigh MT.	-

Table 2-General description of the studies. Resistance training programs investigated, muscle hypertrophy assessments, and main results. Conclusion.

Study	Participants	Duration and frequency of the program	Muscle hypertrophy assessment	Main results for TRAD	Main results for ADV	Differences between protocols
Fisher 2014	41 participants Control* (n = 3 men and 5 women); TRAD (n = 4 men and 13 women); PE (n = 2 men and 12 women)	12 weeks 2 d.wk.$^{-1}$	LM	-	-	-
Fisher 2016 A	59 participants TRAD (n = 10 men/9 women); EO: (n = 10 men/10 women); SS: (n = 10 men/10 women)	10 weeks 2 d.wk.$^{-1}$	LM	-	-	-
Fisher 2016 B	41 participants TRAD (n = 6 men and 5 women). DS (n = 3 men and 8 women). HDS (n = 2 men and 12 women).	12 weeks 2 d.wk.$^{-1}$	LM	-	-	-
Hackett 2018	12 men TRAD (n = 6) and GVT (n = 6)	12 weeks 3 d.wk.$^{-1}$	LM	-	-	-
Prestes 2019	18 participants (14 men and 4 women). TRAD (n = 9) and RP (n = 9)	6 weeks 4 d.wk.$^{-1}$	MT	-	↑11% in thigh MT	↑ in thigh MT was greater for RP
Walker 2016	28 men TRAD (n = 10), EO (n = 10) and Control* (n = 8)	10 weeks 2 d.wk.$^{-1}$	MT and LM	↑11 and ↑16% in vastus lateralis and medialis MT. No significant changes in LM*	↑13 and ↑11% in vastus lateralis and medialis MT, respectively. No significant changes in LM*	-

TRAD: Traditional resistance training; GVT: German volume training; LM: Lean mass; MT: Muscle Thickness; ↑ = increase; - : no significant differences or changes; CP: Crescent pyramid; DS: Drop set; ACSA: Anatomical cross-sectional area; EO: Eccentric overload; RP: Rest pause; PE: Pre-exhaustion; SS: Super slow; HDS: heavy DS; * = Data not used in calculation of standardized mean difference due incomplete report.

Seven different types of ADV were identified including German volume training in two studies (AMIRTHALINGAM; MAVROS; WILSON; CLARKE *et al.*, 2017; HACKETT;

AMIRTHALINGAM; MITCHELL; MAVROS *et al.*, 2018), crescent pyramid in one study (ANGLERI; UGRINOWITSCH; LIBARDI, 2017), drop-sets and heavy drop-sets in three studies (ANGLERI; UGRINOWITSCH; LIBARDI, 2017; ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021; FISHER, JAMES P; CARLSON, LUKE; STEELE, JAMES, 2016), eccentric overload/accentuated eccentric in three studies (BRANDENBURG; DOCHERTY, 2002; FISHER, JAMES PETER; CARLSON, LUKE; STEELE, JAMES, 2016; WALKER; BLAZEVICH; HAFF; TUFANO *et al.*, 2016), pre-exhaustion in one study (FISHER; CARLSON; STEELE; SMITH, 2014), super-slow in one study (FISHER, JAMES PETER; CARLSON, LUKE; STEELE, JAMES, 2016), and rest-pause in two studies (ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021; PRESTES; TIBANA; DE ARAUJO SOUSA; DA CUNHA NASCIMENTO *et al.*, 2019).

Different types of hypertrophy assessments were identified, including B-mode ultrasonography MT with 14 comparisons, lean body mass via DEXA, or air displacement plethysmography with 12 comparisons (WALKER; BLAZEVICH; HAFF; TUFANO *et al.*, 2016) also performed lean body mass analysis. However, data were incomplete and were not included in the calculation of SMD), and anatomical cross-sectional area (ACSA) via B-mode ultrasonography or magnetic resonance imaging with seven comparisons. Five studies (AMIRTHALINGAM; MAVROS; WILSON; CLARKE *et al.*, 2017; ANGLERI; UGRINOWITSCH; LIBARDI, 2017; ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021; PRESTES; TIBANA; DE ARAUJO SOUSA; DA CUNHA NASCIMENTO *et al.*, 2019; WALKER; BLAZEVICH; HAFF; TUFANO *et al.*, 2016) reported significant hypertrophy changes after interventions, and two studies (AMIRTHALINGAM; MAVROS; WILSON; CLARKE *et al.*, 2017; WALKER; BLAZEVICH; HAFF; TUFANO *et al.*, 2016) reported significant changes in MT but not in lean mass for both TRAD and ADV.

3.3 COMPARISON OF TRADITIONAL AND ADVANCED PARADIGMS ON MUSCLE HYPERTROPHY

Some studies contained multiple groups (i.e., more than one ADV group, resulting in 24 groups) or multiple hypertrophy analyses (i.e., lean body mass, ACSA, and muscle thickness [MT] in different locations). Therefore, 33 comparations were considered for the meta-analysis (see Figure 2). Control groups that have trained with their own previous RT routines (i.e., outside the laboratory) were not considered. One study (FISHER; CARLSON; STEELE; SMITH, 2014) compared two protocols with pre-exhaustion (called TRAD and control - see

Table 4). Only TRAD was included in the analysis as the control group altered the sequence in the study (FISHER; CARLSON; STEELE; SMITH, 2014). The forest and funnel plots of all included comparisons are presented in Figures 2 and 3.

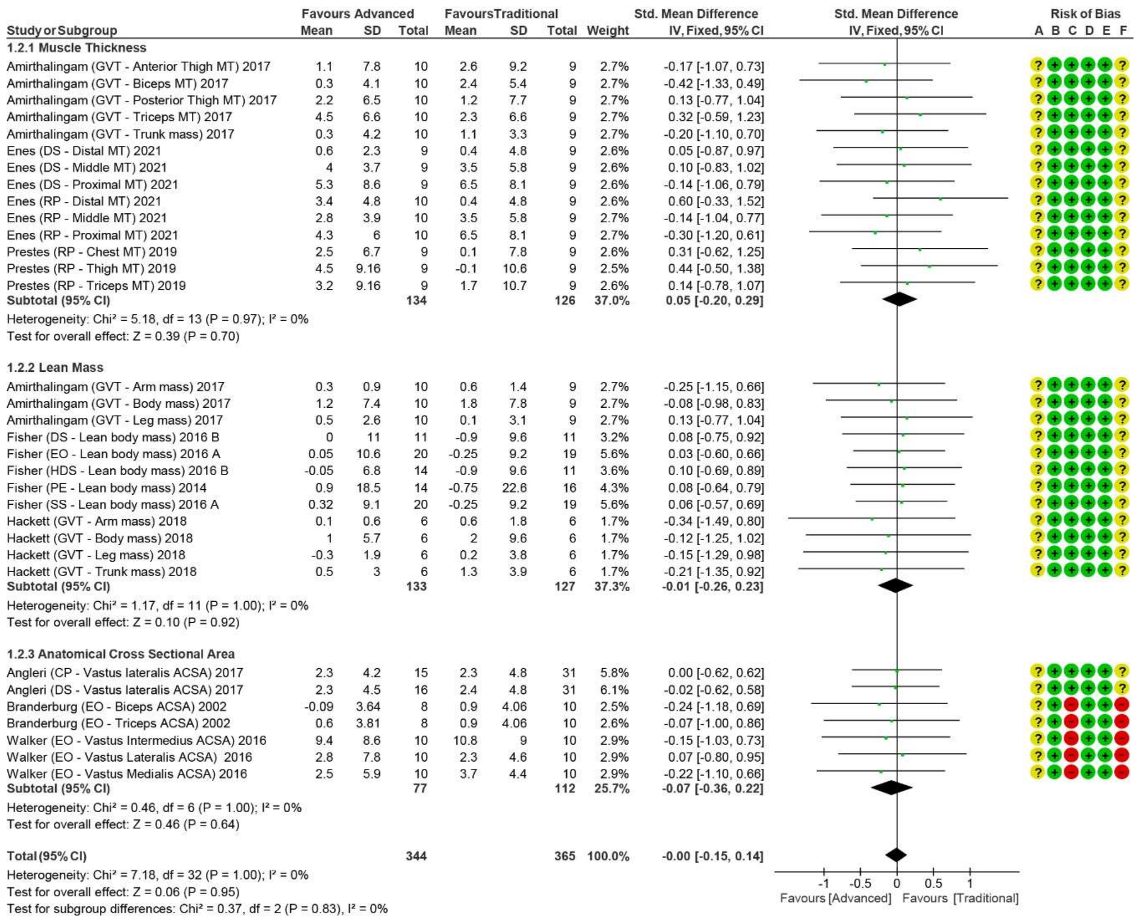

Figure 2-Forest plot of the analyses and risk of bias. SD: Standardized deviation; GTV: German volume training; MT: muscle thickness; DS: drop-set; RP: rest-pause; EO: eccentric overload; HDS: heavy DS; PE: pre-exhaustion; SS: super slow; ACSA: anatomical cross-sectional area; CP: crescent pyramid; Risk of Bias Legend – A: randomization process; B: deviations from the intended interventions; C: missing outcome data; D: measurement of the outcome; E: selection of the reported result; F: overall risk of bias

Visual inspection of the funnel plot reveals that the results were unlikely to be influenced by publication risk bias (MARTYN-ST JAMES; CARROLL, 2006).

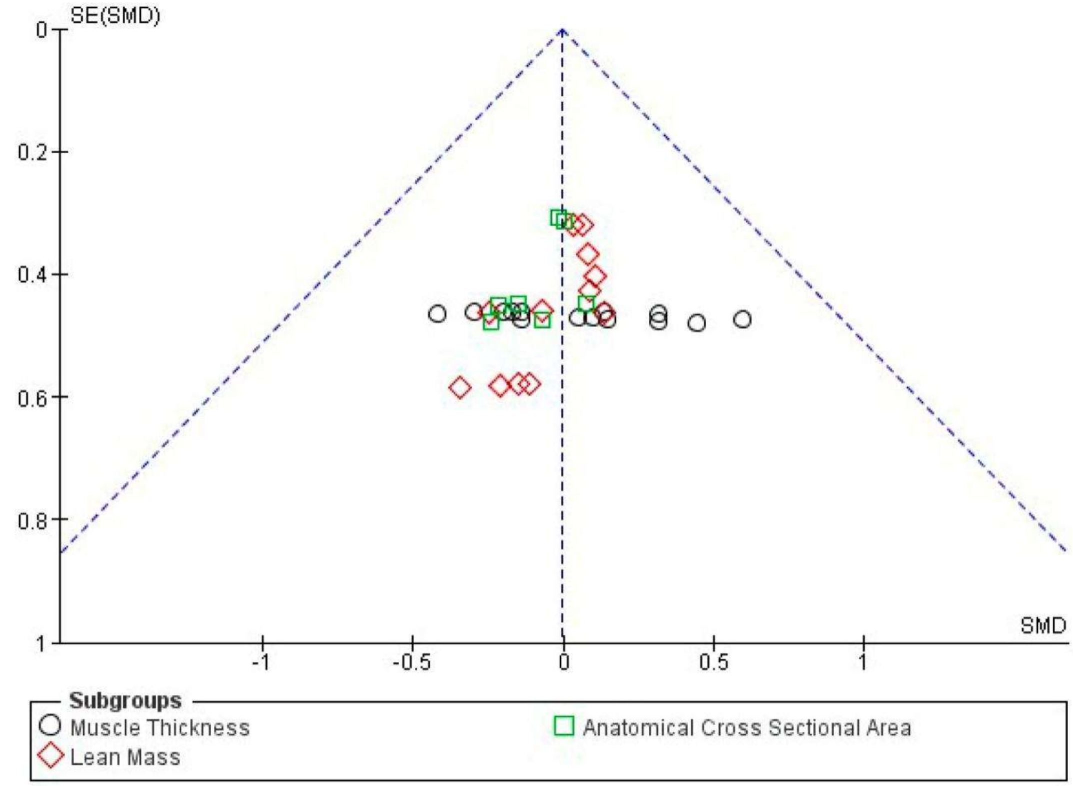

Figure 3-Funnel plot of included studies. SE: standardized error for SMD; SMD: standardized mean difference.

3.3.1 Muscle Thickness Changes

Separate analysis of MT indicated no heterogeneity between studies (χ^2 = 5.18, *df* = 13 (p = 0.97), I^2 = 0%). Considering a fixed effect model, the analysis of SMD showed no difference between ADV and TRAD when MT was used as hypertrophy assessment (Test for overall effect: Z = 0.39 [p = 0.70], SMD = 0.05 CI: [-0.20 0.29]).

3.3.2 Lean Body Mass Changes

Separate analysis of lean body mass changes indicated no heterogeneity between studies (χ^2 = 1.17, *df* = 11 (p = 1.00), I^2 = 0%). Considering a fixed effect model, the analysis of SMD showed no difference between ADV and TRAD when lean body mass was used as hypertrophy assessment (Test for overall effect: Z = 0.10 [p = 0.92], SMD = -0.01 CI: [-0.26 0.23]).

3.3.3 Anatomical Cross-Sectional Area Changes

Separate analysis of ACSA indicated no heterogeneity between studies (χ^2 = 0.46, *df* = 6 (p = 1.00), I^2 = 0%). Considering a fixed effect model, the analysis of SMD showed no difference between ADV and TRAD when CSA was used as hypertrophy assessment (Test for overall effect: Z = 0.46 [p = 0.64], SMD = -0.07 CI: [-0.36 0.22]).

3.3.4 All Muscle Hypertrophy Assessments

Analysis of all hypertrophy measurements together indicated no heterogeneity between studies (χ^2 = 7.18, degree of freedom *df* = 32 (p = 1.00), I^2 = 0%). Considering a fixed effect model, the analysis of SMD showed no difference between ADV and TRAD (Test for overall effect: Z = 0.06 [p = 0.95], SMD = -0.00 CI: [-0.15 0.14]).

3.4 DIETARY CONTROL

Table 2 shows a summary of the dietary control reported in each study.

Table 3-Dietary control employed in the studies. Continue.

Study	Nutritional intake record	Nutritional plan	Post-training standardized supplementation
Amirthalingam 2017	The dietary intake was obtained via a 3-day food diary before and after the experimental training period	Participants were encouraged to increase their caloric intake by 1000-2000 kJ above their estimated daily energy requirements	Whey protein (30.9 g of protein, 0.2 g of fat, and 0.9 g of carbohydrate) 30 min post each training session
Angleri 2017	-	Participants were advised to have a light meal 2 h before each testing session and to maintain their eating habits	30 g of whey protein post each training session
Branderburg 2002	-	-	-
Enes 2021	Participants completed a 3-day nonconsecutive dietary intake record before the intervention, at the mid-point, and conclusion of the study period. No difference in dietary intake was founded between the groups	Participants were instructed to have a meal two hours before each training session and to maintain their habitual dietary intake.	-
Fisher 2014	-	-	-
Fisher 2016 A	-	-	-
Fisher 2016 B	-	-	-
Hackett 2018	-	Participants were encouraged to increase their caloric intake	Whey protein (30.8 g of protein, 0.2 g of fat, and 0.9 g of carbohydrate) 30 min post each training session

Table 4-Dietary control employed in the studies. Conclusion.

Study	Nutritional intake record	Nutritional plan	Post-training standardized supplementation
Prestes 2019	No difference in dietary intake was founded between groups but data was not available	-	-
Walker 2016	-	-	A standardized recovery drink containing 23 g of whey protein (8.5 g leucine and 5.1 g isoleucine per 100 g), 3 g of carbohydrate, and 1.6 g of fat immediately post each training session

-: Not prescribed or performed.

Only six studies presented some type of dietary control (AMIRTHALINGAM; MAVROS; WILSON; CLARKE *et al.*, 2017; ANGLERI; UGRINOWITSCH; LIBARDI, 2017; ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021; HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS *et al.*, 2018; PRESTES; TIBANA; DE ARAUJO SOUSA; DA CUNHA NASCIMENTO *et al.*, 2019; WALKER; BLAZEVICH; HAFF; TUFANO *et al.*, 2016). Four studies instructed their participants how to proceed with their nutritional intake habits during the period of the study (AMIRTHALINGAM; MAVROS; WILSON; CLARKE et al., 2017; ANGLERI; UGRINOWITSCH; LIBARDI, 2017; ENES; ALVES; SCHOENFELD; ONEDA et al., 2021; HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS et al., 2018), four studies provided a standardized protein supplementation post-exercise (AMIRTHALINGAM; MAVROS; WILSON; CLARKE et al., 2017; ANGLERI; UGRINOWITSCH; LIBARDI, 2017; HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS et al., 2018; WALKER; BLAZEVICH; HAFF; TUFANO et al., 2016), and two studies calculated nutritional intakes from dietary records (ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021; PRESTES; TIBANA; DE ARAUJO SOUSA; DA CUNHA NASCIMENTO *et al.*, 2019). One of these studies (PRESTES; TIBANA; DE ARAUJO SOUSA; DA CUNHA NASCIMENTO *et al.*, 2019) did not report these data.

3.5 PARTICIPANTS' TRAINING STATUS

Table 3 shows participants' RT experience, training status reported in the study and training status according to the scale suggested by Rhea (RHEA, 2004).

Table 5-Participants' training status, and strength level.

Study	RT experience	Initial strength level	Training status reported in the study	Training status according to Rhea (2004)
Amirthalingam 2017	TRAD: 4.8 ± 4.8 years. GVT: 3.5 ± 1.0 years. More than 1 year, 3 months consistently	Not reported, but according to data the RS on the bench press was ~1.0	Healthy men	Untrained to highly trained
Angleri 2017	6.4 ± 2.0 years	Squat RS > 1.3	Well-trained young men	Recreationally to highly trained
Branderburg 2002	At least 1 year	Bench press RS > 1.0	Trained individuals	Recreationally trained
Enes 2021	TRAD: 4.4 ± 0.7 years. DS: 5.6 ± 1.5 years. RP: 5.2 ± 2.2 years. At least 2 years	RS on the squat: TRAD = 1.6 ± 0.2; DS = 1.7 ± 0.2; RP = 1.7 ± 0.2.	Resistance-trained males	Recreationally trained
Fisher 2014	At least 6 months	-	Trained participants	Untrained
Fisher 2016 A	At least 6 months	-	Trained participants	Untrained
Fisher 2016 B	At least 6 months	-	Trained males and females	Untrained
Hackett 2018	More than 1 year, 3 months consistently	Not reported. but according to data the RS on the bench press was ~1.0	Healthy males	Untrained to recreationally trained
Prestes 2019	More than 1 year	Not reported. but according to data the RS on the bench press was ~1.1	Trained subjects	Recreationally trained
Walker 2016	0.5–6 years 2.6 ± 2.2 years	-	Strength-trained men	Untrained to highly trained

TRAD: traditional resistance training; GVT: German volume training; RS: relative strength; DS: drop set; RP: rest-pause; -: Not reported.

Four studies (AMIRTHALINGAM; MAVROS; WILSON; CLARKE et al., 2017; ANGLERI; UGRINOWITSCH; LIBARDI, 2017; ENES; ALVES; SCHOENFELD; ONEDA et al., 2021; WALKER; BLAZEVICH; HAFF; TUFANO et al., 2016) reported time of experience in RT of participants, and the other six reported the minimum of time experience required for a participant to be eligible for the study (BRANDENBURG; DOCHERTY, 2002; FISHER, JAMES P; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER, JAMES PETER; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER; CARLSON; STEELE; SMITH, 2014; HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS et al., 2018; PRESTES; TIBANA; DE ARAUJO SOUSA; DA CUNHA NASCIMENTO et al., 2019). According to Rhea's classification (RHEA, 2004) of training level, six studies (AMIRTHALINGAM; MAVROS;

WILSON; CLARKE et al., 2017; FISHER, JAMES P; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER, JAMES PETER; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER; CARLSON; STEELE; SMITH, 2014; HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS et al., 2018; WALKER; BLAZEVICH; HAFF; TUFANO et al., 2016) included untrained subjects, four studies (ANGLERI; UGRINOWITSCH; LIBARDI, 2017; BRANDENBURG; DOCHERTY, 2002; ENES; ALVES; SCHOENFELD; ONEDA et al., 2021; PRESTES; TIBANA; DE ARAUJO SOUSA; DA CUNHA NASCIMENTO et al., 2019) included recreationally trained subjects, and no study included only highly trained individuals. However, one study reported individuals that varied between untrained to recreationally trained (HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS et al., 2018), two studies from untrained to highly trained (AMIRTHALINGAM; MAVROS; WILSON; CLARKE et al., 2017; WALKER; BLAZEVICH; HAFF; TUFANO et al., 2016), and one study from recreationally trained to highly trained (ANGLERI; UGRINOWITSCH; LIBARDI, 2017).

3.6 QUANTIFICATION OF TRAINING LOADS

Training variables on traditional and advanced interventions are summarized on Table 4. Participants' previous training experience, progression and quantification of training loads are presented in Table 5.

Table 6-Training variables on traditional and advanced interventions. Continue.

Study	TRAD intervention	ADV intervention
Amirthalingam 2017	5 sets of 10 rep with 60-80%1RM and 60-90s of rest interval (only in 6 exercises of 15)	GVT. 10 sets of 10 rep with 60-80%1RM and 60-90s rest interval (Only in 6 exercises of 15)
Angleri 2017	3-5 sets of 6-12 rep with 75%1RM and 120s of rest. Training occurred according to pre-established VL	VL of DS and CP were equalized with TRAD. DS: sets were performed until failure, with a drop load of ~20% on each failure until reached the prescribed VL. CP: 3-5 of 6-15 rep. with 65-85%1RM and 120s rest interval
Branderburg 2002	4 sets of ~10 rep with 75%1RM	EO. 3 sets of ~10 rep with 75%1RM on concentric and 110-120%1RM on the eccentric phase
Enes 2021	4 sets of 12 rep with 70%1RM and 120s of rest interval	DS. 3 sets of 10 with 70%1RM and 3 additional sets of 6 rep with 55%1RM with 120s of rest between sets and no rest before additional sets (only 3 of 5 exercises) RP. 3 sets of 10 with 75%1RM and 3 additional sets of 6 rep with 75%1RM with 120s of rest between sets and 20s before additional sets (only 3 of 5 exercises)
Fisher 2014	TRAD: one set of ~12RM and 60s of rest Control*: one set of ~12RM and 60s of rest	PE: one set of ~12RM and 60s of rest between sets and 5s between isolated and compound exercises

Table 7. Training variables on traditional and advanced interventions. Conclusion.

Study	TRAD intervention	ADV intervention
Fisher 2016 A	One set of 8-12 reps with 75%1RM with 120s of rest interval between exercises and cadence of 6s per rep	EO: one set of 8 reps with 105%1RM with 60s of rest interval between exercises and cadence of 10s per rep (only one session, the other was realized identical to TRAD) SS: one set of 6 reps with 75%1RM with 60s of rest interval between exercises and cadence of 12s per rep
Fisher 2016 B	One set of 8-12RM	DS: one set of 8-12RM with additional set with reduction of ~30% on load (only 3 exercises, 12 exercises of 15 was realized identical to TRAD). HDS: one set of ~4RM with an additional set with two reductions of ~20% on load (only 3 exercises of 15 exercises)
Hackett 2018	5 sets of 10 reps with 60-80%1RM and 60-the 90s of rest interval (only in 6 of 10 exercises)	GVT: 10 sets of 10 reps with 60-80%1RM and 60-90s of rest interval (only in 6 of 10 exercises)
Prestes 2019	3 sets of 6 rep with 80%1RM and 120-180s of rest interval	RP: one set of 18 rep with 80%1RM (performed with intra-set rests of 20s) and 120s of rest between exercises
Walker 2016	3 sets of 6RM or 10RM with 120-180s of rest interval	EO: 3 sets of 6RM or 10RM with +40% of the load in eccentric phase and 120-180s of rest interval

Rep: repetitions; 1RM: one-repetition maximum test; GVT: German volume training; VL: volume-load; DS: drop set; CP: crescent pyramid; TRAD: traditional resistance training; EO: eccentric overload; RP: rest-pause; RM: repetition maximum (performed until failure); PE: pre-exhaustion; SS: super slow; HDS: heavy DS; *: group was not considered in the calculation of standardized mean difference.

Table 8-Resistance training programs performed by the participants before the engagement in the study, progression, and quantification of training loads during interventions. Continue.

Study	RT program performed before the engagement in the study	Progression of training loads	Quantification of training load
Amirthalingam 2017	-	Loads were adjusted by 5-10% once the participants were able to complete 10 repetitions on the final set of each exercise	Only the initial and final VL for 3 exercises
Angleri 2017	Participants reported training lower limbs at least 2 $d.wk.^{-1}$ and performing leg press 45° and leg extension	Initial VL was defined as 120% of the VL that each participant performed in the 2 weeks before the study. The number of sets and repetitions were adjusted every time that the VL was increased (~7% every 3 weeks)	Total VL reported for the whole RT program
Branderburg 2002	-	The load was adjusted when the average number of repetitions performed per set in a training session became greater than 10	Programmed volume load (calculated as sets x repetitions x percentage of 1RM) was reported to be equal between protocols
Enes 2021	-	The load was adjusted by 5% in the fifth week.	Total VL reported for the whole RT program

Table 9. Resistance training programs performed by the participants before the engagement in the study, progression, and quantification of training loads during interventions. Conclusion.

Study	RT program performed before the engagement in the study	Progression of training loads	Quantification of training load
Fisher 2014	Previous experience with PE system	Once participants were able to perform more than 12 repetitions before achieving failure, the load was adjusted by 5%.	-
Fisher 2016 A	Participants reported having done single-set training until failure for multiple exercises including most major muscle groups 2 d.wk.$^{-1}$	Once participants were able to perform more than desired repetitions, the load was adjusted by 5%.	-
Fisher 2016 B	Participants reported having done single-set training until failure for multiple exercises including most major muscle groups 2 d.wk.$^{-1}$	Once participants were able to perform more than 12 repetitions before achieving failure, the load was increased by 5% (only reported for TRAD)	-
Hackett 2018	Participants reported training at least 3 d.wk.$^{-1}$	When participants were able to complete >10 repetitions on the final set the load was increased by approximately 5–10%	Average VL for only 2 exercises (a total of 15 exercises were utilized)
Prestes 2019	The subjects were accustomed to training 3-5 days per week with split-body training routines and 3-4 sets of 8-12RM per exercise with the objective of muscle hypertrophy	No progression or adjustments were reported	-
Walker 2016	-	The load was adjusted to provide muscle failure in at least one of three sets	-

-: Not reported; VL: volume-load; RT: resistance training; 1RM: one repetition maximum; PE: pre-exhaustion; TRAD: traditional resistance training.

None of the studies reported complete data about the quantification of training loads. Two studies (ANGLERI; UGRINOWITSCH; LIBARDI, 2017; ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021) reported the total volume load. Angleri et al. (ANGLERI; UGRINOWITSCH; LIBARDI, 2017) reported a total of ~150 tons executed in TRAD, drop-set, and crescent pyramid, while Enes et al. (ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021) reported 412263 ± 50764 kg for drop-set, 440363 ± 45953 kg for rest-pause, 405428 ± 45748 kg for TRAD. One study (HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS *et al.*, 2018) reported the average volume load of the sessions, but for less than a fifth of the exercises performed.

The mean volume load of sessions for German volume training was 4879 ± 773 kg, and 24491 ± 4180 kg for the bench press and leg press, respectively (HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS *et al.*, 2018). The mean volume load of sessions for TRAD was 2407 ± 483 kg and 13498 ± 2712 kg for the bench press and leg press, respectively (HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS *et al.*, 2018). Additionally, one study (AMIRTHALINGAM; MAVROS; WILSON; CLARKE *et al.*, 2017) reported the volume load for two sessions only (initial and final) and three exercises (bench press, cable pull-down, and leg press) only. Volume load of these three exercises on the initial session were 4583 ± 852 kg, 3962 ± 712 kg, and 20901 ± 9942 kg for GTV, and 1845 ± 700 kg, 1596 ± 408 kg, and 10117 ± 2636 kg for TRAD, respectively for bench press, cable pull-down, and leg press. Volume load of these three exercises on the final session were 5078 ± 775 kg, 3862 ± 689 kg, and 24883 ± 3424 kg for German volume training, and 2329 ± 766 kg, 1826 ± 444 kg, and 12941 ± 3051 kg for TRAD, respectively for bench press, cable pull-down, and leg press.

None of the studies reported the RT program performed by the participants before their engagement in the study. Only one study (ANGLERI; UGRINOWITSCH; LIBARDI, 2017) estimated the previous volume load realized by the participants two weeks before engagement in the study; however, the data was unavailable. One study reported the usual ranges of sets and repetitions performed by the participants (PRESTES; TIBANA; DE ARAUJO SOUSA; DA CUNHA NASCIMENTO *et al.*, 2019). One study (ANGLERI; UGRINOWITSCH; LIBARDI, 2017) reported previous experience with exercises used in the intervention.

4 DISCUSSION

The primary aim of this meta-analysis was to determine whether the muscular hypertrophic responses induced by TRAD are different from ADV in resistance-trained individuals. Our results indicate that, regardless of skeletal muscle hypertrophy assessment (i.e., MT, lean mass, or ACSA), no significant advantage was provided by ADV versus TRAD (see Fig. 2). This finding corroborates with our hypothesis and previous literature (ANGLERI; UGRINOWITSCH; LIBARDI, 2019; ANGLERI; UGRINOWITSCH; LIBARDI, 2017).

4.1 COMPARISON OF TRADITIONAL AND ADVANCED PARADIGMS ON MUSCLE HYPERTROPHY

Most of the included studies did not report differences in outcomes between ADV and TRAD (see Table 1). These data suggest that skeletal muscle hypertrophy may not be enhanced through 6-12-week of ADV in previously trained individuals. However, one study (PRESTES; TIBANA; DE ARAUJO SOUSA; DA CUNHA NASCIMENTO *et al.*, 2019) reported significant increases in thigh MT differences after six weeks of the rest-pause system compared to TRAD (11% increase for rest-pause, and no increases for TRAD - see Table 1). Analysis of MT may be accurate to estimate muscle size (i.e., muscle volume assessed by magnet resonance image) when considering a single time point assessment (FRANCHI; LONGO; MALLINSON; QUINLAN *et al.*, 2018). However, when assessing chronic muscle hypertrophy changes, MT has some limitations (FRANCHI; LONGO; MALLINSON; QUINLAN *et al.*, 2018) associated with muscle physiology (i.e., heterogeneous distribution of hypertrophy (DINIZ; TOURINO; LACERDA; MARTINS-COSTA *et al.*, 2020; FRANCHI; ATHERTON; REEVES; FLÜCK *et al.*, 2014)) and the geometric nature of the measure that is limited to a specific site of the muscle (FRANCHI; LONGO; MALLINSON; QUINLAN *et al.*, 2018). Moreover, despite this study presenting differences in thigh MT, no differences in the chest and arm MT were found (PRESTES; TIBANA; DE ARAUJO SOUSA; DA CUNHA NASCIMENTO *et al.*, 2019).

Curiously, five of ten studies included in this review failed to observe hypertrophy in both groups (i.e., ADV and TRAD - (BRANDENBURG; DOCHERTY, 2002; FISHER, JAMES P; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER, JAMES PETER; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER; CARLSON; STEELE; SMITH, 2014; HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS *et al.*, 2018)). Since these studies aimed to compare hypertrophy changes induced by TRAD and ADV, failure to achieve skeletal muscle hypertrophy in both groups is a limitation. The small sample size, inducing insufficient statistical power (HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS *et al.*, 2018), lack of dietary control (AMIRTHALINGAM; MAVROS; WILSON; CLARKE *et al.*, 2017; FISHER, JAMES P; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER, JAMES PETER; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER; CARLSON; STEELE; SMITH, 2014), and lower sensibility of some measurements tools in detecting small hypertrophy changes (e.g., plethysmography - (FISHER, JAMES P; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER, JAMES PETER; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER; CARLSON; STEELE; SMITH, 2014)), and inconsistencies in training load monitoring (BRANDENBURG; DOCHERTY, 2002; FISHER, JAMES P; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER, JAMES PETER; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER; CARLSON; STEELE; SMITH, 2014; HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS *et al.*, 2018; PRESTES; TIBANA; DE ARAUJO SOUSA; DA CUNHA NASCIMENTO *et al.*, 2019) may be among the possible candidates to explain these results.

The studies included in this review compared muscle hypertrophy outcomes using different measurement tools (e.g., MT, lean mass, or ACSA - see Table 1). This is important to note, given that it has been reported that disagreements among muscle imaging techniques exist (HAUN; VANN; ROBERTS; VIGOTSKY *et al.*, 2019; RUPLE; MESQUITA; GODWIN; SEXTON *et al.*, 2022; RUPLE; SMITH; OSBURN; SEXTON *et al.*, 2022). Thus, this remains a limitation of the current meta-analysis. Notwithstanding, our sub-group analysis of MT, lean mass, and ACSA did not reveal any differences between TRAD and ADV paradigms (SMD = 0.05 [-0.20 0.29], -0.01 [-0.26 0.23], -0.07 [-0.26 0.23], respectively - see Figure 2); lending further support that 6-12 weeks of ADV do not confer additional hypertrophic benefits in previously trained individuals.

4.2 DIETARY CONTROL

As one of our secondary aims, we sought to determine if dietary factors were associated with hypertrophic outcomes in the analyzed studies. Three types of dietary controls were identified in the studies: a) consuming a protein supplementation dose (e.g., ~30 g of whey protein) after RT sessions (AMIRTHALINGAM; MAVROS; WILSON; CLARKE *et al.*, 2017; ANGLERI; UGRINOWITSCH; LIBARDI, 2017; HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS *et al.*, 2018; WALKER; BLAZEVICH; HAFF; TUFANO *et al.*, 2016); b) general instructions to: increase caloric intake (AMIRTHALINGAM; MAVROS;

WILSON; CLARKE *et al.*, 2017; HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS *et al.*, 2018), maintenance of dietary habits (ANGLERI; UGRINOWITSCH; LIBARDI, 2017; ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021), having a light meal two hours before the RT sessions (ANGLERI; UGRINOWITSCH; LIBARDI, 2017; ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021); c) two studies recorded the dietary intake from individuals (AMIRTHALINGAM; MAVROS; WILSON; CLARKE *et al.*, 2017; ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021), one reported that caloric intake was equal between groups, but the data were not available (PRESTES; TIBANA; DE ARAUJO SOUSA; DA CUNHA NASCIMENTO *et al.*, 2019). Four studies did not perform any type of dietary control ((BRANDENBURG; DOCHERTY, 2002; FISHER, JAMES P; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER, JAMES PETER; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER; CARLSON; STEELE; SMITH, 2014) - for details see Table 2).

Therefore, several positions statements highlight the importance of a proper nutritional intake for the athletic performance and the development of skeletal muscle hypertrophy (DELDICQUE, 2020; JOANISSE; LIM; MCKENDRY; MCLEOD *et al.*, 2020; MORTON; MCGLORY; PHILLIPS, 2015). Some increments on strength have been reported after RT programs performed with low macronutrient intake (e.g., low-carbohydrate diets), however none increase of lean mass was observed (PAOLI; CENCI; POMPEI; SAHIN *et al.*, 2021). Thus, not controlling the participant’s nutritional intake maybe considered as a substantial limitation of all studies investigating skeletal muscle hypertrophy responses.

Four studies provided protein-based supplement to the participants after each RT session (AMIRTHALINGAM; MAVROS; WILSON; CLARKE *et al.*, 2017; ANGLERI; UGRINOWITSCH; LIBARDI, 2017; HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS *et al.*, 2018; WALKER; BLAZEVICH; HAFF; TUFANO *et al.*, 2016). This is in accordance with reported dose-response relationship of dietary protein intake and supplementation for promoting hypertrophy (MORTON; MURPHY; MCKELLAR; SCHOENFELD *et al.*, 2018; STOKES; HECTOR; MORTON; MCGLORY *et al.*, 2018). This strategy, combined with a recorded dietary intake could guarantee the appropriate daily ingestion of protein to maximize hypertrophy (i.e., 1.6g/kg of body mass - (MORTON; MURPHY; MCKELLAR; SCHOENFELD *et al.*, 2018)). Despite this strategy diminishing a risk of bias of different protein intake between individuals, it is important to mention that there may be differences induced by training status and age in protein intake influencing hypertrophy outcomes (MORTON; MURPHY; MCKELLAR; SCHOENFELD *et al.*, 2018). High dosage of protein intake does not guarantee that all individuals present the same responses but may mitigate the possible bias created by different protein consumption.

Moreover, four of five studies that did not realize any type of dietary control, failed in inducing muscle hypertrophy in both groups (BRANDENBURG; DOCHERTY, 2002; FISHER, JAMES P; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER, JAMES PETER; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER; CARLSON; STEELE; SMITH, 2014). Meanwhile, only one study that provided a proper dietary control, fail in observing increases in lean mass, despite a small effect size observed (HACKETT; AMIRTHALINGAM; MITCHELL; MAVROS *et al.*, 2018). However, this study included 12 subjects only (i.e., six per group), authors suggested that a larger sample size is required to achieve sufficient power. These findings highlight the undoubted importance of dietary control when assessing skeletal muscle hypertrophy changes. Since adequate nutrition seems to be mandatory to hypertrophy, studies comparing different strategies of RT to maximize hypertrophy must implement dietary control to improve internal and external validly of results.

In summary, most of the included studies in this review failed in providing a proper dietary control to the participants. Considering the high impact of nutritional apport in optimizing skeletal muscle hypertrophy, we consider this aspect as a substantial limitation in drawing conclusions when comparing TRAD and ADV systems. Future studies aiming to observe and compare muscle hypertrophy changes induced by different RT systems should strongly consider adopting a rigorous dietary control in the experimental designs.

4.3 PARTICIPANTS' TRAINING STATUS

The utilization of ADV is chiefly intended to promote further training adaptations in trained individuals (ANGLERI; UGRINOWITSCH; LIBARDI, 2019; KRZYSZTOFIK; WILK; WOJDAŁA; GOŁAŚ, 2019). This theory is based on training progression recommendations for trained individuals that often require more variations in RT stimulus (KRAEMER; RATAMESS, 2004). In addition, RT experience may be inversely associated with hypertrophic responses (BENITO; CUPEIRO; RAMOS-CAMPO; ALCARAZ *et al.*, 2020), with highly trained individuals (i.e., bodybuilders) presenting non-significant changes in ACSA following 24 weeks of RT (ALWAY; GRUMBT; STRAY-GUNDERSEN; GONYEA, 1992). Conversely, it is common to observe hypertrophy in shorter-term studies ranging from 6-12 weeks with untrained individuals (CAMPOS; LUECKE; WENDELN;

TOMA *et al.*, 2002; FINK; KIKUCHI; NAKAZATO, 2018; HOLM; REITELSEDER; PEDERSEN; DOESSING *et al.*, 2008; JENKINS; MIRAMONTI; HILL; SMITH *et al.*, 2017; LASEVICIUS; SCHOENFELD; SILVA-BATISTA; BARROS *et al.*, 2022; LASEVICIUS; UGRINOWITSCH; SCHOENFELD; ROSCHEL *et al.*, 2018; LIM; KIM; MORTON; HARRIS *et al.*, 2019; MITCHELL; CHURCHWARD-VENNE; WEST; BURD *et al.*, 2012; NÓBREGA; UGRINOWITSCH; PINTANEL; BARCELOS *et al.*, 2018; POPOV; SWIRKUN; NETREBA; TARASOVA *et al.*, 2006; TANIMOTO; ISHII, 2006). However, hypertrophy outcomes are typically modest (i.e., less than 15%) compared to strength increases (i.e., up to 61%), indicating that early initial increase in strength is more influenced by neural rather than morphological adaptations (CARROLL, 2002; ENOKA, 1988; FOLLAND; WILLIAMS, 2007). In addition, local edema may influence hypertrophy outcomes (DEFREITAS; BECK; STOCK; DILLON *et al.*, 2011; MOQUIN; WETMORE; CARROLL; FRY *et al.*, 2021), which may be another reason why untrained subjects experience more robust hypertrophy responses with shorter-term training interventions (e.g., 3-6 weeks).

Despite most studies included in this review reporting studying *resistance-trained* individuals, this training status did appreciably differ between studies (see Table 3). The training status classification proposed by Rhea (RHEA, 2004) was chosen because it is widely used in the literature (AMDI; CLEATHER; TALLENT, 2021; HERTZOG; RUMPF; HADER, 2020; MONTANO; TOROSSIAN; MARTINEZ; LHANIE *et al.*, 2021; SCHMIDT; FERRAUTI; KELLMANN; BEAUDOUIN *et al.*, 2021; TIMÓN; OLCINA; GONZÁLEZ-CUSTODIO; CAMACHO-CARDENOSA *et al.*, 2021).

Participants of the included studies varied from untrained (i.e., less than a year) to highly trained (i.e., more than five years - see Table 3). Four studies that reported analyzing trained individuals (FISHER, JAMES P; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER, JAMES PETER; CARLSON, LUKE; STEELE, JAMES, 2016; FISHER; CARLSON; STEELE; SMITH, 2014; WALKER; BLAZEVICH; HAFF; TUFANO *et al.*, 2016) may have studied untrained individuals, and two studies investigated individuals whose training status varied from untrained to highly trained (AMIRTHALINGAM; MAVROS; WILSON; CLARKE *et al.*, 2017; WALKER; BLAZEVICH; HAFF; TUFANO *et al.*, 2016). However, regardless of this divergent training status classification, the studies reported similar hypertrophy outcomes between TRAD and ADV (see Tables 1 and 3). Moreover, five studies (AMIRTHALINGAM; MAVROS; WILSON; CLARKE *et al.*, 2017; ANGLERI; UGRINOWITSCH; LIBARDI, 2017; ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021;

PRESTES; TIBANA; DE ARAUJO SOUSA; DA CUNHA NASCIMENTO *et al.*, 2019; WALKER; BLAZEVICH; HAFF; TUFANO *et al.*, 2016) observed pre-to-post differences in hypertrophy measures. Still, only two of these included untrained individuals (AMIRTHALINGAM; MAVROS; WILSON; CLARKE *et al.*, 2017; WALKER; BLAZEVICH; HAFF; TUFANO *et al.*, 2016), indicating that factors other than training status affected reported outcomes (e.g., dietary control, training monitoring, and use of different hypertrophy measurements).

4.4 QUANTIFICATION OF TRAINING LOADS

All studies reviewed failed to report complete data about the quantification of training loads, especially regarding the volume load. Considering the appreciable influence of volume load in inducing skeletal muscle hypertrophy (HEASELGRAVE; BLACKER; SMEUNINX; MCKENDRY *et al.*, 2019; LONGO; SILVA-BATISTA; PEDROSO; DE SALLES PAINELLI *et al.*, 2022; RADAELLI; FLECK; LEITE; LEITE *et al.*, 2015; SCHOENFELD; CONTRERAS; KRIEGER; GRGIC *et al.*, 2019; SCHOENFELD; OGBORN; KRIEGER, 2017; VANN; SEXTON; OSBURN; SMITH *et al.*, 2022), we did not anticipate differences in hypertrophy outcomes with equalized volume load approaches. Nevertheless, despite the apparent importance and simplicity of the volume load calculus, only two studies reviewed reported the metric properly (ANGLERI; UGRINOWITSCH; LIBARDI, 2017; ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021). The progressive overload strategy employed by Angleri et al. (ANGLERI; UGRINOWITSCH; LIBARDI, 2017) was based on the previous volume load performed by the participants (i.e., 120% of the previous weekly volume load - see Table 5), with increases of ~7% every three weeks. The authors reported that similar changes in ACSA occurred between training paradigms (7.6%, 7.5%, and 7.8% to TRAD, crescent pyramid, and drop-set, respectively), and these outcomes coincided with a similar total volume load of protocols (~150 tons). Corroborating these results are the data published by Enes et al. (ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021), indicating that similar volume loads produced similar hypertrophy outcomes across multiple training paradigms (i.e., TRAD, drop-set, and rest-pause (ENES; ALVES; SCHOENFELD; ONEDA *et al.*, 2021)). Additionally, the results of this meta-analysis suggest that ADV appears to be secondary when assessing hypertrophy, as other factors such as dietary control and volume load performed may have a greater impact on results.

4.5 LIMITATIONS

This meta-analysis is not without limitations. First, there was heterogeneity in the included studies regarding dietary control and volume load monitoring. A universal definition to depict training status does not exist, which likely impacted some of our conclusions regarding the influence of training status on associated outcomes. We may also have overlooked studies that failed to report participants as trained subjects.

5 CONCLUSION

The use of ADV is usually recommended for RT trained individuals to maximize hypertrophic responses. However, the results of this meta-analysis revealed that short-term ADV does not induce superior skeletal muscle hypertrophy responses when compared with TRAD in trained individuals. Independently of the use of ADV or TRAD systems, performing similar volume loads appears to induce similar hypertrophic responses. Therefore, coaches and athletes programing a period of RT should consider monitoring this metric (i.e., volume load).

Considering that training status classification and dietary strategies were divergent among studies reviewed, we recommend considering that our results may apply to recreationally trained individuals (e.g., more than one year of RT experience), and that dietary strategies adopted may have a great impact on hypertrophic responses.

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