Sports Medicine
https://doi.org/10.1007/s40279-018-1001-6

SYSTEMATIC REVIEW

Effects of Resistance Training on Arterial Stiffness in Persons at Risk for Cardiovascular Disease: A Meta-analysis

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Abstract

Background Arterial stiffness (AS) is a key measure in predicting risk for cardiovascular disease (CVD) and related events, independent of other risk factors. Resistance training (RT) has been shown to increase AS in young healthy subjects. However, the effects of RT on AS in persons with or at risk for CVD remain unclear; this uncertainty is a barrier to RT prescription in this population. Considering RT may be as effective as or superior to aerobic exercise prescription in treating some co-morbidities associated with CVD, it would be helpful to clarify whether RT does lead to clinically meaningful increases (detrimental) in AS in those with CVD or CVD risk factors.

Objectives The aim of this study was to (1) assess the effects of RT on measures of AS in at-risk populations, and (2) discuss the implications of the findings for clinical exercise physiologists.

Data Sources The electronic databases PubMed, Web of Science, SPORTDiscus, and Google Scholar were searched from inception to February 2018. The reference lists of eligible articles and reviews were also checked.

Study Selection Inclusion criteria were: (1) the trial was a randomized controlled trial; (2) exercise prescription of RT or a combination of resistance and aerobic exercise for at least 8 weeks; (3) control group characteristics allowed for comparison of the main effects of the exercise prescription; (4) subjects had known CVD or a risk factor associated with CVD according to the American College of Sports Medicine (ACSM) guidelines; (5) article measured at least carotid to femoral pulse wave velocity (PWV) or augmentation index (AIx).

Appraisal and Synthesis Methods Initially, 1427 articles were identified. After evaluation of study characteristics, quality and validity data from 12 articles and 13 cohorts involving 651 participants (223 women, 338 men, 90 unknown) were extracted for the meta-analysis. To enable comparisons between assessments, and to infer clinical significance, standardized mean differences (SMD) were calculated. When data were not available, values were estimated according to Cochrane guidelines.

Results According to the JADAD scale, the mean quality of studies was 3 out of 5. The duration of the included studies ranged from 8 weeks to 24 months. RT trended towards decreasing (improving) PWV (SMD = − 0.168, 95% CI − 0.854 to 0.152, $p = 0.057$). There were no significant differences in AIx (SMD = − 0.286), diastolic blood pressure (SMD = − 0.147), systolic blood pressure (SMD = − 0.126), or central systolic blood pressure (SMD = − 0.405).

Conclusion The available evidence suggests that RT does not increase (worsen) AS in patients who have or are at risk for CVD. Considering RT may be as effective as or superior to aerobic exercise prescription in treating some co-morbidities associated with CVD, these findings suggest that RT is a suitable exercise prescription in primary and secondary prevention settings.

Key Points

Resistance training (RT) does not appear to increase arterial stiffness (AS) in those with or at risk for cardiovascular disease (CVD).

RT is suitable for clinical exercise prescription in primary and secondary prevention of CVD.

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Published online: 24 October 2018

1 Introduction

Exercise is widely accepted as an important behavioral strategy for the primary and secondary prevention of cardiovascular diseases (CVD) [1, 2]. However, while aerobic exercise (AE) has been widely promoted for primary and secondary prevention of CVD [1], resistance training (RT) is not as widely advocated. This is despite evidence suggesting that RT may be as effective as or superior to AE in treating some co-morbidities associated with CVD, such as sarcopenia and impaired glucose handling and lipid metabolism, and can be an effective strategy for improving the ability to perform activities of daily living [3–7]. RT is less commonly prescribed because the safety of RT in moderate- to high-risk patients remains largely in question [8]. In support of these concerns, RT can place an acute burden on the heart, and, at least in young healthy people, can lead to chronically increased arterial stiffness (AS) [9, 10].

The gold standard approach for measuring AS is pulse-wave velocity (PWV), particularly at the level of the aorta [11]. The elastic aorta is directly proximal to the heart and is responsible for dampening the speed and amplitude of retrograde pressure waves that increase the heart's workload during systole [12]. Aortic PWV has clinical relevance to cardiovascular-related prognosis, with a 1 m/s increase in aortic PWV corresponding to a 14% and 15% increase in total CV events and CV mortality, respectively, independent of traditional risk factors [13]. Of relevance to RT prescription, a previous meta-analysis reported that RT increased aortic PWV by 0.72 m/s [9]. While the clinical relevance of this increase in aortic PWV is uncertain, the increase is a concern to practitioners working in primary and secondary CVD-prevention programs [9]. However, this analysis was conducted in young, healthy adults. Findings in older adults, including those with CVD or CVD risk factors, have been inconclusive [9, 14]. Considering these findings and that RT may confer important health benefits above and beyond AE, there is a clear need to determine whether RT does lead to clinically meaningful increases in aortic PWV in those with CVD or CVD risk factors.

1.1 Objectives

The current review aimed to identify and quantitatively assess randomized controlled trials (RCTs) assessing RT intervention, with or without AE, on aortic PWV in subjects with CVD or CVD risk factors according to the American College of Sports Medicine (ACSM). Our findings are then discussed in terms of their relevance to exercise guidelines in persons with CVD or CVD risk factors.

2 Methods

The review adopted the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [15].

2.1 Data Sources and Search Strategy

Two investigators (QW and WE) searched the electronic databases (PubMed, Web of Science, SPORTDiscus, Google Scholar) using population, intervention, control, and outcome (PICO) search terms: (resistance training OR strength training OR weight training OR aerobic OR aerobic Training OR combination OR resistance exercise) AND (arterial stiffness OR augmentation index OR pulse wave velocity). The reference lists of the identified trials and reviews were also examined. The search was limited to English-language articles published between database inception and February 2018.

2.2 Article Selection and Inclusion Criteria

For the purpose of this meta-analysis, the term 'article' is used synonymously with 'study', and 'trial' is the unit included in the meta-analysis. A given article may have resulted in more than one eligible 'trial' if the article included more than one intervention group. Initially, article titles and abstracts were screened for relevance. The full-text versions of potentially eligible articles were obtained to review eligibility for inclusion. The following criteria were used to select trials for inclusion in the review: (1) randomized controlled trial; (2) exercise prescription of RT or a combination of resistance and aerobic exercise (AE+RT) for at least 8 weeks; (3) control group characteristics allowed for comparison of the main effects of the exercise prescription; (4) subjects had known CVD or a risk factor associated with CVD according to the ACSM guidelines; (5) at least one item from carotid to femoral PWV or augmentation index (AIx) was reported. Articles were not excluded based on exercise intensity, modality, frequency, or progression protocol. Repeated publications for the same trial were excluded. In trials with multiple treatment arms and a single control group, the sample size of the control group was divided by the number of treatment groups to avoid over-inflation of the sample size [16]. Two researchers (WE, QW) completed the study selection independently, with consultation from a third researcher (LS) in the case of discrepancies.

2.3 Data Extraction and Quality Assessment

Data extracted for each eligible trial included bibliography information (author, publication year), collected measures (PWV, AIx, etc.), disease state/risk factor(s), sample characteristics (age, sex, body weight, etc.), details of intervention, and results of reported outcomes. If these data were

not included in the article, the investigators contacted the authors for further information. In two situations when the author did not respond, these data were estimated from graphs including the data. Data represented in tables were estimated to the nearest whole number. Study quality was assessed through a modified JADAD scale (0–5), which includes items related to randomization, blinding, and description of dropout/withdrawals [17]. Because blinding of subjects to exercise interventions is not feasible, blinding of the operator was considered as a quality criterion. Data extraction, quality assessment, and scrutiny of the exercise interventions were independently completed by two researchers (WE, QW), with consultation from a third researcher (LS) in the case of discrepancies.

2.4 Data Synthesis

For each outcome of interest, the pre- and post-intervention values (mean and standard deviation) as well as mean differences and associated standard deviations were entered into a spreadsheet. When mean differences and associated standard deviations were not published, they were estimated from the pre- and post-intervention values based on methods from the Cochrane Handbook for Systematic Reviews of Interventions [16]. For studies reporting multiple time points, only the final time point was used in analyses. Aggregation and calculation of final results was conducted by three authors (QE, QW, LS).

2.5 Data Analysis

All extracted data were entered into software designed specifically for the meta-analyses (Open Meta-Analyst, http://www.cebm.brown.edu/open_meta). Random effects modelling, with the DerSimonian–Laird method, was used because it accounts for both within- and between-study variability when estimating effects [18]. The software calculated the effect size as the mean difference, as well as the standardized mean difference (SMD). The SMD was used to determine the magnitude of the effect, where <0.2 was defined as trivial, 0.2–0.3 as small, 0.4–0.8 as moderate, and >0.8 as large [18, 19]. We chose a SMD of 0.2 as the smallest worthwhile change for all clinically-associated mechanistic parameters. The statistical heterogeneity across different trials in the meta-analysis was assessed by the I^2 statistic [20], where $<25\%$ indicates a low risk of heterogeneity, 25–75% indicates a moderate risk of heterogeneity, and $>75\%$ indicates a considerable risk of heterogeneity [20, 21]. Publication bias was evaluated by visual inspection of the Begg's funnel plot Egger's test for asymmetry when (1) at least ten trials were included in the meta-analysis, and (2) there was substantial variation in sample size for the included trials [22]. Sensitivity analyses were carried out by excluding one trial at a time to test the robustness of the pooled results. One author (LS) conducted the data analysis.

3 Results

3.1 Synthesis of Results

Our initial search of the PubMed database returned 1427 articles. Following initial screening of abstracts and titles, 1411 articles were excluded. Our findings are summarized in Fig. 1. Of the 22 randomized controlled trials remaining, ten RCTs were excluded because they did not meet the criteria for the following reasons: acute exercise ($n=1$), no RT group ($n=2$), use of non-traditional RT (blood flow restriction, neuromuscular stimulation, robot assistance) ($n=3$), no known CVD or CVD risk factors ($n=2$), or unable to compare the main effect of RT ($n=2$).

3.2 Characteristics of Included Studies

The trials were conducted in the USA ($n=9$) [23–31], South Korea ($n=1$) [32], Australia ($n=1$) [33], and Finland ($n=1$) [34]. The intervention settings included fitness centers ($n=1$) [33], laboratories ($n=5$) [23, 25–27, 34], hospitals ($n=1$) [28], at home ($n=1$) [33], or supervised but otherwise not reported ($n=4$) [24, 29–31]. The number of participants included in each trial ranged from 21 to 114 with an average sample size of 56. All but two of the studies included participants whose mean age ranged from 52 to 69 years. For the other two studies, participants' mean ages were 15 and 21 years [29, 30], though both were populations at risk for CVD because of obesity and prehypertension, respectively. Only two studies reported ethnicity, of which one recruited African American and mixed ethnicities, and one recruited African American, Caucasian, and Asian ethnicities [28, 30].

3.3 Quality Assessment

The results of JADAD assessment are summarized in Table 1. The quality of results ranged from 1 to 4, with a median quality score of 3. All of the articles were randomized, but only seven articles reported the method used for randomization [23–25, 28, 31–33]. For blinding, six articles blinded the observer during outcome assessment, but specific blinding methods were not available [24–26, 28, 30, 32]. Lastly, drop outs were listed and described in the majority of articles ($n=7$) [23, 27–29, 31–33].

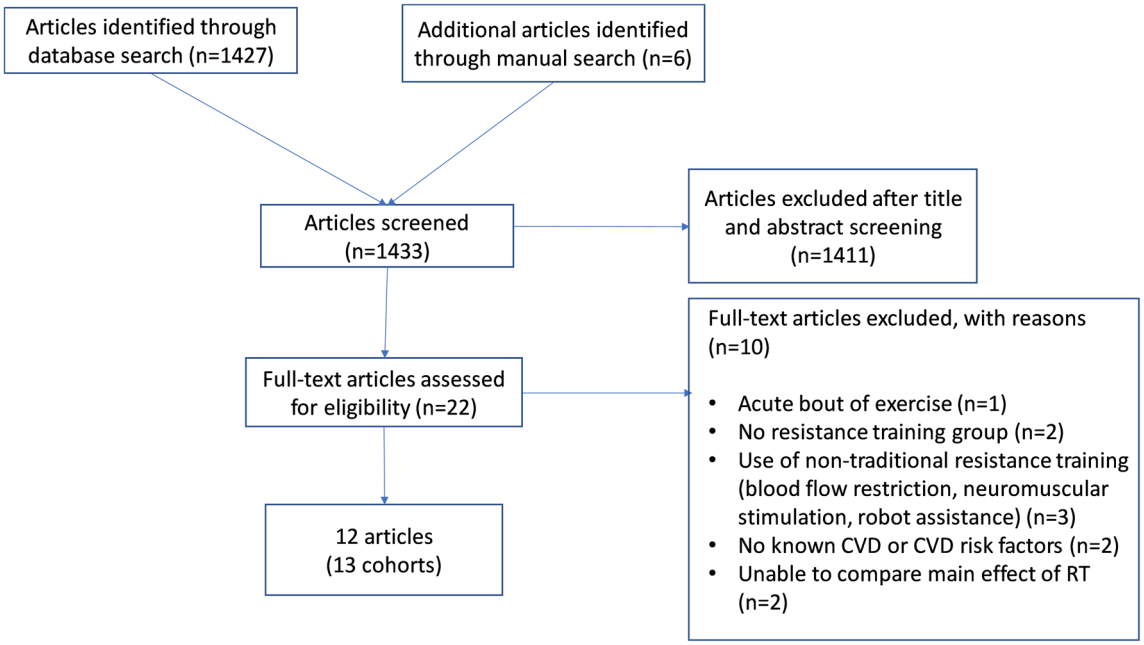

Fig. 1 Flow chart of search strategy and explanation for inclusion or exclusion of studies. *CVD* cardiovascular disease, *RT* resistance training

3.4 Interventions

The effects of RT or RT + AE on the five outcomes are summarized in Table 2. Numerical values are presented as the mean difference (95% confidence interval (CI)) unless otherwise reported.

3.5 Arterial Stiffness

There was a trivial, non-significant decrease in PWV following exercise intervention (Fig. 2). Sensitivity analysis indicated that the removal of one trial [28] resulted in a greater mean difference (MD) of − 0.5 (95% CI − 0.9 to 0.0, $p = 0.051$) and a small effect size (SMD − 0.2). With respect to AIx, there was a small, non-significant decrease in AIx.

3.5.1 PWV Subgroup Analysis: Exercise Type

Following RT there was a small, non-significant decrease (MD: − 0.4, 95% CI − 0.9 to 0.2, $p = 0.167$), and following RT + AE there was a trivial, non-significant decrease (MD − 0.3, 95% CI − 1.4 to 0.9, $p = 0.666$). Removal of Greenwood et al. [28] resulted in a greater MD for RT + AE (− 0.719, 95% CI − 1.7 to 0.3, $p = 0.172$) and a small effect size (SMD − 0.3).

3.6 Systolic Blood Pressure

There was a trivial, non-significant decrease in systolic blood pressure (SBP) following exercise intervention. Sensitivity analysis indicated that none of the trials unduly influenced the outcome. With respect to central systolic blood pressure (cSBP), there was a moderate, non-significant decrease.

3.6.1 SBP Subgroup Analysis: Exercise Type

Following RT there was a small, non-significant decrease in SBP (MD − 2.9, 95% CI − 6.4 to 0.5, $p = 0.095$), and following RT + AE there was a trivial, non-significant decrease in SBP (MD − 0.9, 95% CI − 3.2 to 1.5, $p = 0.470$).

3.7 Diastolic Blood Pressure

There was a trivial, non-significant decrease in diastolic blood pressure (DBP) following exercise intervention. Sensitivity analysis indicated that the removal of one trial [24] resulted in a greater MD (1.5, 95% CI − 3.0 to 0.0, $p = 0.044$) and a trivial effect size (SMD − 0.2).

3.7.1 Subgroup Analysis: Exercise Type

Following both RT (MD − 1.0, 95% CI − 4.0 to 2.0, $p = 0.534$) and RT + AE (MD − 1.4, 95% CI − 3.1 to 0.4, $p = 0.120$) there were trivial but non-significant decreases in DBP. Removal of Croymans et al. [24] increased the MD

Table 1 Characteristics of included studies

References	Quality[a]	Country	Disease/condition	Supervised	Adverse events reported	Setting	Sample size	Female (*n*)	Age, years (SD or range)	Intervention	Control group	Duration (wks)
Beck et al. [22]	3	USA	Young prehypertensive subjects	Yes	0	Laboratories	30	9	21 (0.6)	4 multi-joint and 3 single-joint exercises on machines	Maintained lifestyle	3 d/wk; 8 wks
Croymans et al. [23]	3	USA	Obese young men	Yes	0	N/A	36	0	22	12 different exercises between two sessions	Maintained lifestyle	3 d/wk; 12 wks
DeVallance et al. [24]	3	USA	Metabolic Syndrome	Yes	0	Laboratories	57	40	49 (11.5)	6 multi-joint exercises machines and free weight	Maintained lifestyle	3 d/wk; 8 wks
Dobrosielski et al. [26]	2	USA	Type 2 diabetics	Yes	0	Laboratories	114	37	57 (6)	7 exercises	Usual care	3 d/wk; 26 wks
Figeuroa et al. [27]	1	USA	Postmenopausal women	Yes	Not reported	Laboratories	24	24	54 (2)	9 exercises of 12 reps for 20 min followed by 20 min of treadmill at 60% of heart rate max	Maintained lifestyle	3 d/wk; 12 wks
Greenwood et al. [28]	4	USA	Overweight kidney transplant recipients	Yes	0	Hospital	46	19	52 (10.6)	3 multi-joint and 5 single joint exercises machines and free weight	Usual care	2 d/wk; 12 wks
Heffernan et al. [29]	2	USA	Prehypertensive and hypertensive older adults	Yes	0	N/A	21	15%	60 (2)	4 upper body, 3 lower body, and 2 core exercises	Maintained lifestyle	3 d/wk; 12 wks

Table 1 (continued)

References	Quality[a]	Country	Disease/condition	Supervised	Adverse events reported	Setting	Sample size	Female (*n*)	Age, years (SD or range)	Intervention	Control group	Duration (wks)
Ho et al. [33]	3	Australia	Overweight and obese adults	60% of sessions	0	Fitness center and home	64	N/A	53 (40-64)	3 multi-joint and 2 single-joint exercises on machines at center. 1 multi-joint and 4 single-joint exercises at home	Maintained lifestyle	5 d/wk; 12 wks
Horner et al. [30]	2	USA	Obese adolescents	Yes	Not reported	N/A	81	40	15 (1.8)	10 whole body exercises	Maintained lifestyle	3 d/wk; 12 wks
Lee et al. [32]	4	South Korea	Patients with chronic poststroke hemiparesis	Yes	0	Community center	26	N/A	64 (6.5)	4 multi-joint and 10 single joint exercises with bands and 10 min walk	Maintained lifestyle	3 d/wk; 16 wks
Loimaala et al. [34]	2	Finland	Type 2 diabetics	Yes	0	Laboratories	48	0	54 (5)	Aerobic training and resistance training	Usual care	2 d/wk of aerobic exercise + 2d/wk of resistance exercise; 2 yrs
Stewart et al. [31]	3	USA	Older persons	Yes	0	N/A	104	51	63	4 upper body and 3 lower body exercises	Maintained lifestyle	3 days/wk; 26 wks

N/A not available, *reps* repetitions, *max* maximum, *min* minute, *wk* week, *d* days, *yrs* years, *SD* standard deviation, *max* maximum

[a]Study quality was assessed through a modified JADAD scale (0–5), which includes items related to randomization, blinding and description of dropout/withdrawals [17]. Because blinding of subjects to exercise interventions is not feasible, blinding of the operator was considered as a quality criterion

Table 2 The effect of resistance training, with and without aerobic training, on arterial stiffness

Outcome	Trials (*n*)	Reference no.	Sample (*n*)	Mean difference				SMD[a]			Heterogeneity	
				Pooled difference				Pooled difference			I^2 (%)	*p* value
				MD	LCI	UCI	*p* value	SMD	LCI	UCI		
PWV	9	23–26, 28, 30, 31, 33, 35	458	−0.351	−0.854	0.152	0.171	−0.168	−0.431	0.095	47	0.57
SBP	13	23–34	594	−1.567	−3.453	0.319	0.103	−0.126	−0.294	0.041	0	0.704
DBP	12	23–33	520	−1.274	−2.897	0.349	0.124	−0.147	−0.338	0.043	19	0.254
AIx	4	23, 25, 29, 32	105	−3.000	−7.086	1.087	0.150	−0.286	−0.675	0.102	9	0.349
cSBP	4	23–25, 29	116	−3.583	−8.174	1.008	0.126	−0.405	−0.869	0.058	44	0.150

SMD standardized mean difference, *PWV* pulse-wave velocity, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *AIx* augmentation index, *cSBP* central systolic blood pressure, *SMD* standardized mean difference, *MD* mean difference, *LCI* lower confidence interval, *UCI* upper confidence interval

[a]SMD qualified effect size, where < 0.2 was defined as trivial, 0.2–0.3 as small, 0.4–0.8 as moderate, and > 0.8 as large

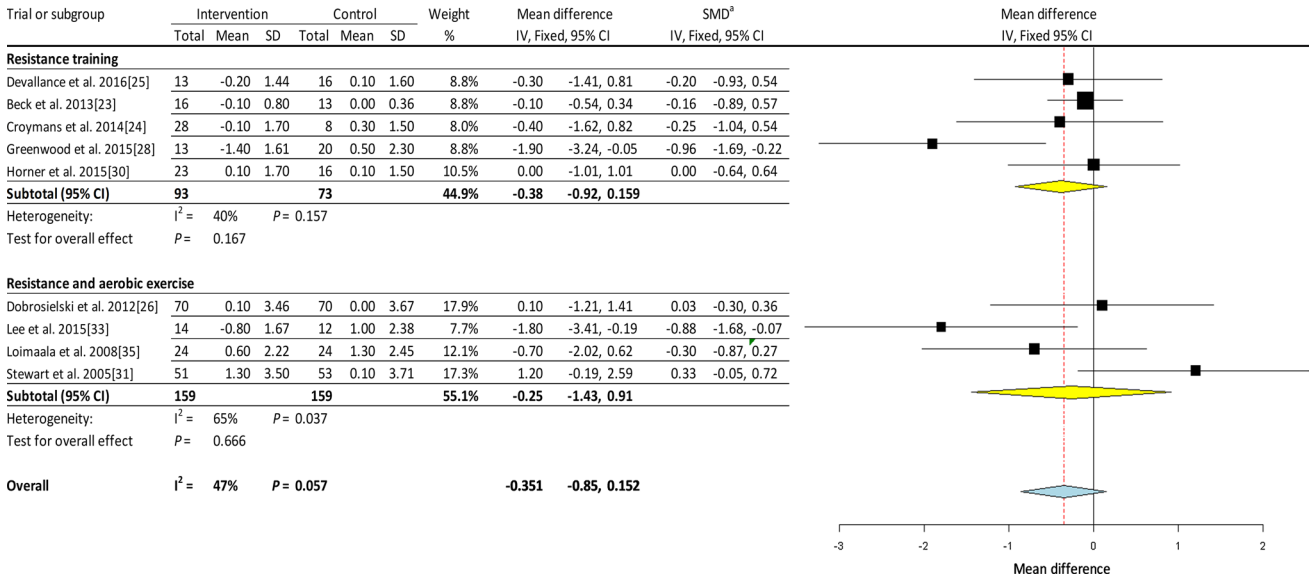

Fig. 2 Meta-analysis of studies comparing resistance training only, and resistance training plus aerobic training on pulse-wave velocity (m/s). The dashed vertical line indicates the mean difference (effect size). *CI* confidence interval, *IV* inverse-variance method, *SD* standard deviation, *SMD* standardized mean difference. [a]SMD qualified effect size, where < 0.2 was defined as trivial, 0.2–0.3 as small, 0.4–0.8 as moderate, and > 0.8 as large

in DBP for RT to −1.8 (95% CI −4.8 to 1.2, $p = 0.242$), a trivial effect size (SMD −0.2).

4 Discussion

This meta-analysis suggests that RT exercise prescription does not negatively affect PWV or other measures of AS in those with CVD or CVD risk factors. While these findings should be interpreted with caution, given the small sample size and low general quality of the studies, they do suggest RT does not chronically increase the burden placed on the heart in subjects with or at risk for CVD. Considering RT prescription may confer important health benefits above and beyond AE prescription, these findings are important for clinicians prescribing exercise in primary and secondary prevention programs.

4.1 Arterial Stiffness

Our analysis revealed that RT exercise prescription resulted in a favorable decrease in aortic PWV, which approached significance ($p = 0.057$). However, the trivial decrease of 0.351 m/s is below the 1.0 m/s that would be deemed clinically meaningful [13]. Our results are limited by the small number of trials (nine, and $n = 484$) and low general quality (mean = 2.6), but to our knowledge, this is the first

meta-analysis to assess the effects of RT on aortic PWV in those with CVD or CVD risk factors.

Our findings are contrary to a meta-analysis in younger healthy populations that reported an increase of 0.72 m/s following RT. In explaining these findings, Miyachi et al., propose that RT may increase stiffness in young populations with low levels of baseline stiffness, but not in old populations because of a stiffness threshold [9]. This threshold is likely surpassed at baseline in elderly populations, in effect nullifying increased stiffness during RT. Nonetheless, studies assessing elderly populations with low baseline stiffness values are required to test this hypothesis.

Of note, PWV is confounded by blood pressure, and it has been recommended by the American Heart Association (AHA) that PWV be adjusted for blood pressure [35]. As such, this was a consideration for the current work. Twelve cohorts reported DBP. Thirteen cohorts reported SBP. For both SBP and DBP, the SMD was trivial. Therefore, it is unlikely that blood pressure would have influenced our interpretation of the findings. To confirm this, we conducted a meta-regression for changes in DBP, and there was no association between change in DBP and change in PWV (slope: −0.023, 95% CI −0.098 to 0.051, $p=0.535$).

Augmentation index, an index of augmented central systolic pressure and an indication of left ventricular work load, has been shown to be a better predictor of reductions in left ventricular mass than traditional blood pressure [36]. The current meta-analysis showed that RT resulted in a non-significant decrease of 3%, which does not meet the clinically significant change of 10% [37]. To our knowledge, this is the first meta-analysis assessing the effects of RT on AIx. These findings are comparable with the changes in PWV. However, only four trials were available and the quality of the trials was mixed. Further, we did include one trial in which AIx was normalized to heart rate as this was the only reported measure [32]; we opted to specify AIx non-normalized to heart rate when possible, as normalizing to a heart rate is questionable [32, 38]. Though these analyses are preliminary, AIx is an established predictor of cardiovascular events [37], and the current findings support the PWV outcome.

4.2 Blood Pressure

Elevated brachial blood pressure is a traditional risk factor for CVD, and AS is a primary cause of increasing SBP with age [39]. Our analysis, which included 12 trials, 12 of the 13 total cohorts and a total sample of 594 participants with 306 and 288 in the intervention and control groups, respectively, indicates that RT results in a non-significant and trivial 1.6 mmHg decrease in SBP, and a 1.3 mmHg decrease in DBP. These findings are contrary to a previous meta-analysis in healthy adults, which included 28 RCTs and 1028 participants, and which reported that dynamic RT significantly decreased SBP and DBP by 2.8 mmHg and 2.7 mmHg, respectively [40]. A meta-analysis by Ashor et al. does support our work, and found that RT did not significantly affect blood pressure, but included both healthy and unhealthy populations; the reason for these differential findings is unclear [14].

Our analysis also included cSBP, which is more closely associated with CVD risk than peripheral BP [41–43]. The four trials ($n=116$) that included this measure indicated a nonsignificant 3.6 mmHg decrease following RT. Clear clinical cut points are still being assessed for cSBP, but findings from two independent prospective cohorts suggest that a cSBP of 130 mmHg increases cardiovascular mortality risk (hazard ratio: 3.08, 95% CI 1.05–9.05) [44]. Our study did not have sufficient data to determine whether RT is beneficial in terms of reaching these cut points. Considering that cSBP more closely reflects left ventricular and cerebrovascular load than brachial pressure [41, 45], the use of cSBP in subsequent trials is recommended.

4.3 Subgroup Analyses

Our subgroup analysis did not show any differences between AE + RT versus RT alone on PWV or brachial blood pressure. This was likely a result of the low volume and intensity of AE prescribed (i.e., 150 min of moderate intensity exercise per week) [31]. Our primary focus was on the effects of RT, but if a combination of RT and AE are to be used, it should be acknowledged that the total volume of exercise may be important. For example, a previous study in older adults with type 2 diabetes, hypertension, and hypercholesterolemia showed a 20% and 13% reduction in radial and femoral PWV, respectively, following AE alone [46]. This study prescribed AE for 40-min sessions three times per week at 60–75% of maximum heart rate (HRmax) using the Karvonen formula. However, other studies using a similar prescription at or below this volume have reported no significant changes in AS [47, 48]. In the current meta-analysis, only one trial prescribed what may be deemed a sufficient volume of AE (3 days per week for 26 weeks for 45 min at 60–90% of HR_{max}) [26]. Future investigation is required to determine the optimal volume of AE when combined with RT.

4.4 Implications

Our findings lend support to prescription of RT in at-risk populations. Though this analysis focused on AS, it is of equal importance to address how RT could be used in light of the broad health outcomes in populations at risk for CVD. When implementing RT in clinical populations, RT should not replace AE if reducing AS is the primary outcome.

4.4.1 Benefit-to-Risk Ratio

When considering RT as an exercise prescription, the benefit-to-risk ratio must be taken into account. We show here that RT is likely not detrimental to AS and may even mitigate CVD risk. According to a recent statement from the AHA, there are two major limitations to clinical prescription of RT: (1) the inability to measure central hemodynamic load during RT; and (2) the potential for negative structural changes to the myocardium [8]. Regarding the first limitation, Fryer et al. recently determined that oscillometric pulse-wave analysis can be reliably used to monitor central hemodynamic load during RT [49]. With respect to the second limitation, the current analysis indicates that RT likely does not result in chronic increases in AS and there were no adverse events reported in any of the included trials (Table 1). As such, we suggest RT performed at moderate intensity in patients with CVD or CVD risk factors is safe and does not appear to compromise arterial health.

4.4.2 Limitations

There are several limitations when considering these findings. First, a small ($n = 12$) number of trials were available, and only nine trials reported PWV. Secondly, the small number of trials limits the conclusions from the subgroup analyses. Third, this study did not compare the effects of AE alone on AS relative to RT and RT + AE, so the possibility that RT limits the benefits of AE cannot be ruled out in these populations. Fourth, the quality of the included trials was generally low and there was a lack of information on blinding and method of randomization. Lastly, there was considerable variation in the volume and intensity of exercise prescriptions, which could limit practitioners' ability to optimize exercise prescription in clinical populations.

5 Conclusion

The evidence presented in this review suggests that RT does not increase AS in patients who have or are at risk for CVD. Because RT may confer additional benefits to those of AE on cardiometabolic outcomes, these findings suggest that RT is a suitable exercise prescription in primary and secondary prevention settings. Practically, these findings help clinicians and clinical exercise physiologists comfortably prescribe RT as an alternative or additional form of physical activity to motivate patients in clinical settings, improve cardiometabolic health, and improve quality of life.

Author contributions LS is the guarantor. WE, LS, and QW drafted the manuscript. QW, LS, and WE contributed to the selection criteria and data extraction. LS provided statistical expertise and data analysis. LS and EH contributed substantially to the interpretation and revisions of the article. All authors read, responded with feedback, and agreed on the final manuscript.

Compliance with Ethical Standards

Funding No sources of funding were used to assist in the preparation of this article.

Conflict of interest William Evans, Quentin Willey, Erik Hanson, and Lee Stoner declare that they have no conflicts of interest relevant to the content of this review.

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