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Review

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The effect of progressive resistance training on aerobic fitness and strength in adults with coronary heart disease: A systematic review and meta-analysis of randomised controlled trials

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Abstract

Design: We aimed to evaluate the effect of progressive resistance training on cardiorespiratory fitness and muscular strength in coronary heart disease, when compared to control or aerobic training, and when combined with aerobic training. Secondary aims were to evaluate the safety and efficacy of progressive resistance training on other physiological and clinical outcomes.

Methods and results: Electronic databases were searched from inception until July 2016. Designs included progressive resistance training vs control, progressive resistance training vs aerobic training, and combined training vs aerobic training. From 268,778 titles, 34 studies were included (1940 participants; 71.9% male; age 60 ± 7 years). Progressive resistance training was more effective than control for lower (standardized mean difference 0.57, 95% confidence interval (0.17–0.96)) and upper (1.43 (0.73–2.13)) body strength. Aerobic fitness improved similarly after progressive resistance training (16.9%) or aerobic training (21.0%); (standardized mean difference –0.13, 95% confidence interval (–0.35–0.08)). Combined training was more effective than aerobic training for aerobic fitness (0.21 (0.09–0.34), lower (0.62 (0.32–0.92)) and upper (0.51 (0.27–0.74)) body strength. Twenty studies reported adverse event information, with five reporting 64 cardiovascular complications, 63 during aerobic training.

Conclusion: Isolated progressive resistance training resulted in an increase in lower and upper body strength, and improved aerobic fitness to a similar degree as aerobic training in coronary heart disease cohorts. Importantly, when progressive resistance training was added to aerobic training, effects on both fitness and strength were enhanced compared to aerobic training alone. Reporting of adverse events was poor, and clinical gaps were identified for women, older adults, high intensity progressive resistance training and long-term outcomes, warranting future trials to confirm safety and effectiveness.

Keywords
Cardiac rehabilitation, exercise, weightlifting

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Introduction

Cardiovascular disease (CVD) has the highest global mortality of any diagnosis, with coronary heart disease (CHD) accounting for almost half of CVD-related deaths.[1] In the last 30 years, age-standardized and overall CHD mortality rates in developed countries have significantly decreased,[1,2] attributable in part to medical and surgical care. Although mortality rates

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are dropping, the actual burden of CHD is growing due to an increased prevalence with age[3] and the aging population of developed countries.[4,5] Thus, with both higher prevalence and survival rates, there is a need to improve secondary and tertiary prevention programs to limit recurrent events, improve the quality of life (QOL) for survivors and reduce global burden.

Cardiac rehabilitation (CR) is a multi-faceted, multi-disciplinary intervention targeting underlying risk factors, functional capacity, recovery and psychological well-being.[6] It is a cost-effective method of reducing cardiovascular (CV) mortality, secondary events and hospital re-admissions across the globe,[7] while also improving QOL and overall prognosis.[8–11] However, only 10% of eligible patients typically enroll in the program,[12] suggesting that conventional models could be improved.[13] In CR, the efficacy of moderate intensity, continuous aerobic training (AT) has been extensively studied,[14–17] based on the association between higher cardiorespiratory fitness (CRF) and lower all-cause[18] and cardiac-related mortality.[19–21] Thus, AT forms the basis of most international guidelines for physical activity and clinical programs.[9]

However, growing evidence suggests that progressive resistance training (PRT) is also a safe and effective exercise modality for patients with CHD.[22–24] In older adults, PRT has been shown to increase CRF similarly to AT,[25] and increase muscular strength more than AT in both older adults and cardiac patients.[25,26] Notably, higher muscle strength is associated with improved prognosis, survival, and functional performance,[27–33] promoting independent living and a return to work following a cardiac event.[34] Additionally, PRT can improve co-morbidities commonly associated with CHD such as sarcopenia, frailty, falls, arthritis, diabetes, depression, cognitive impairment, peripheral vascular disease, and renal failure, among others.[35,36] Despite this evidence, detailed recommendations for PRT are not routinely included in CR guidelines,[9] which may explain its limited clinical uptake.

Four meta-analyses to date have investigated PRT efficacy within CR,[26,37–39] finding that the combination of aerobic and resistance training produced greater improvements in peak work capacity and strength compared to AT alone in CHD patients. However, only one of these reviews has directly compared PRT to control and AT, as well as in combination with AT.[38] In addition, limitations in previous meta-analyses include inadequate search sensitivity,[26,37–39] poor or improper definitions of intervention and control groups[38], unclear statistical methods,[26,37–39] and incomplete reporting of adverse events.[37,38]

A comprehensive review of this literature that addresses these limitations is needed to determine the true efficacy of PRT in CR, in order to guide and improve policy and practice. Thus, the purpose of this review was to evaluate the effect of isolated PRT on CRF and muscular strength in CHD, when compared to control or AT, as well as when combined with AT vs AT alone.

Methods

Criteria for study inclusion

Studies were included if they met the following criteria: (a) full length article published in a peer-reviewed journal, (b) randomized controlled trial (RCT) study design, (c) human participants with CHD, a recent cardiac event such as myocardial infarction (MI), or coronary artery surgical intervention (i.e. coronary artery bypass graft (CABG), angioplasty, or stent), (d) the intervention included some form of PRT. Progressive resistance training was defined as a movement that causes the muscles to contract against an external resistance with the expectation of increases in strength, tone, mass and/or endurance,[40] and may include isokinetic or isotonic contractions for both upper and lower body. Isometric contractions, where the joint angle and muscle length remain unchanged during contraction, were also included.

Studies were excluded if: (a) all participants had a documented heart failure diagnosis regardless of ejection fraction (studies with CHD participants and reduced ejection fractions were not excluded), (b) participants had undergone valvular or heart transplant surgery, (c) the comparison group activities did not permit the isolation of PRT effects (e.g. PRT was in both study arms), (d) the intervention lasted less than three weeks.

Search strategy

The following electronic databases were searched from earliest possible date to July 2016, with updates till February 2017: AMED, CINAHL, Embase, MEDLINE, PEDro, PreMEDLINE and SPORTSDiscus. Reference lists of all eligible trials and relevant review articles were manually searched for further eligible studies. The search strategy included a combination of 'condition' and 'intervention' terms (Figure 1) and did not include 'comparison intervention' or 'outcome' terms in order to maximize search sensitivity. No language or date restrictions were applied to the search strategy.

Study selection and data extraction

One reviewer (MH) conducted the search and following the removal of duplicates, screened papers by title and

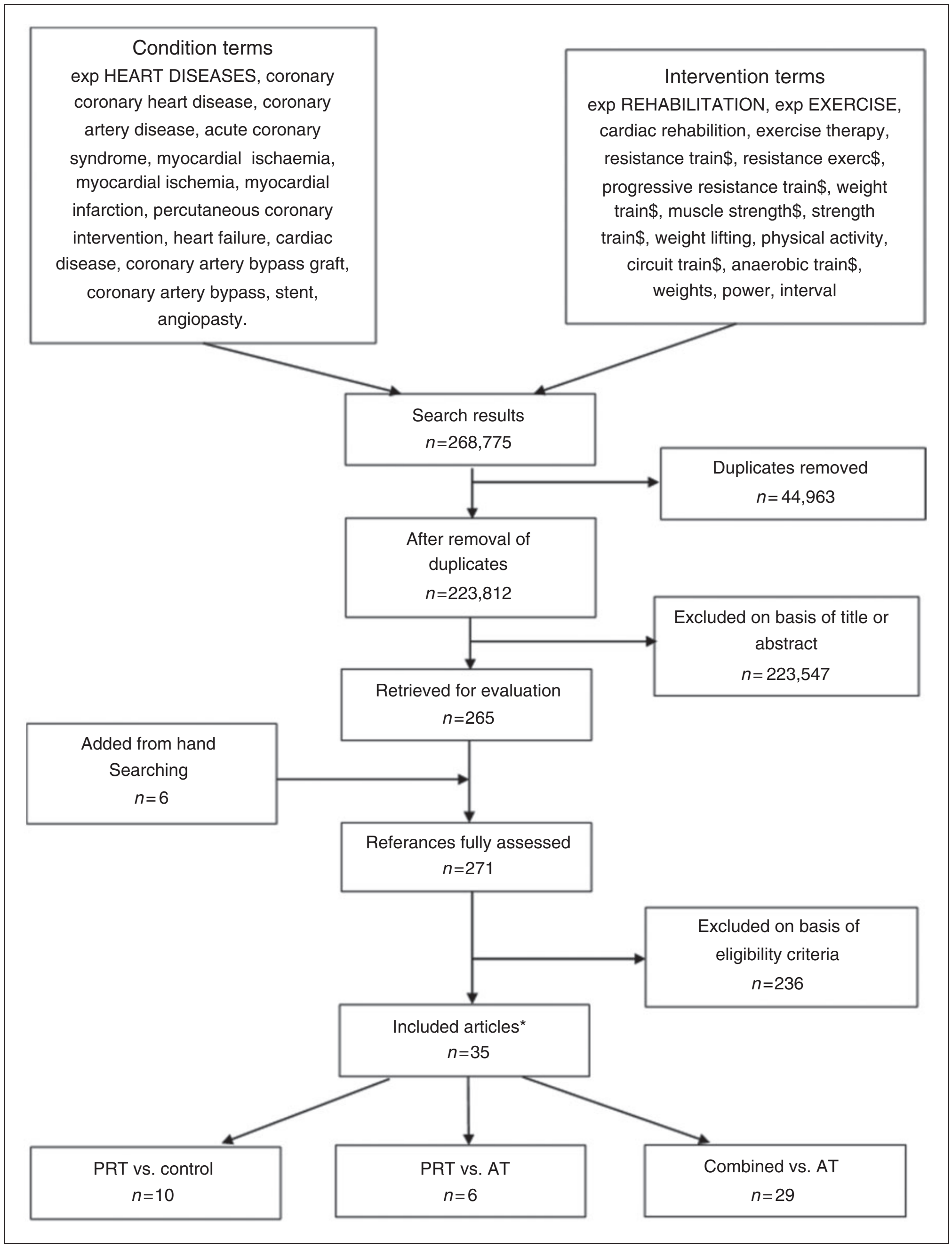

Figure 1. Flow of papers through search, screening and identification process.
AT: aerobic training; *n*: number of studies; PRT: progressive resistance training.*Seven studies had multiple comparison groups.

abstract based on the eligibility criteria. Studies to be fully assessed were appraised by two reviewers (MH and JF). MH extracted data into pre-designed, piloted tables. Disagreements were resolved by consensus or by a third reviewer if required (MFS).

Quality assessment

Two reviewers (MH and JF) assessed the quality of eligible trials using a modified version of the Physiotherapy Evidence Database (PEDro) scale,[41] which appraises trial quality based on external validity (criteria 1), internal validity (criteria 2–9) and quality of statistical reporting (criteria 10–11).

Three additional criteria relating to exercise prescription and monitoring were included. Criterion 1 required at least one training session per week to be supervised by a qualified health or medical professional. Criterion 2 required each of the following elements of PRT dose to be reported; program duration, session frequency, number of exercises, volume, intensity and type of resistance used. Criterion 3 required program adherence to be reported using specific attendance rates, not just minimum requirements for inclusion. These additional elements contributed to the overall quality rating of trials, but were not included in the final PEDro score so as to allow comparison to previous literature.

Data synthesis and analysis

Studies were split into three groups; (a) PRT vs control, (b) PRT vs AT, (c) combined training (CT) vs AT. Aerobic training, defined as rhythmical contraction and relaxation of large muscle groups over a prolonged period of time with the aim of improving CV fitness,[40] required two or more of the following prescriptive parameters to be classified as exercise and not unstructured physical activity: frequency, intensity, time. CT included both PRT and AT within the intervention group. The control group was an intervention that did not match any of the above definitions. Typically, this included non-exercising, usual care groups instructed to maintain habitual levels of physical activity.

Primary outcome measures for this review were muscular strength and CRF. Muscular strength could be measured using isotonic (one repetition maximum (1RM)), isometric (maximal voluntary contraction (MVC)) or isokinetic measures (peak torque (N/m)). Cardiorespiratory fitness included peak oxygen uptake (VO_{2peak}) or peak workload achieved on a cycle ergometer or treadmill. All reported adverse events and other clinical/physiological variables were extracted as secondary outcomes.

Detailed statistical methods are available in Supplementary Material, Methods. Data were at the aggregate level for each trial. This included method of assessment, mean ± standard deviation (SD) or frequency of event at all time-points, or other summary statistic as appropriate. A meta-analysis was performed for all measures of peak muscular strength and CRF using Review Manager (RevMan, Version 5.3; The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark).[42] For measures of peak strength, the most common exercises reported for upper (bench press) and lower body (knee extension) strength were used. Relative measures of aerobic capacity (ml/kg/min) were preferentially extracted as VO_{2peak}. Where this was not reported, absolute VO_{2peak} (l/min) was instead extracted, for the purpose of capturing the most data points for analysis. Due to heterogeneity in units of measurement, data were calculated and presented as a standardized mean difference (SMD) effect size (ES). The ES was calculated by subtracting the mean change in the comparison condition from the mean change in the intervention condition, and dividing by the pooled SD at baseline, then adjusted for small sample bias (Hedges' g ES).[43] Data with a high level of heterogeneity ($I^2 \geq 75\%$) were considered unsuitable for pooled analysis and only trial-level ESs were reported. ESs were categorized according to Cohen's interpretation of 'trivial' (<0.20), 'small' (≥0.20 to <0.50), 'moderate' (≥0.50 to <0.80) and 'large' (≥0.80).[44]

Univariate meta-regression analyses were used to assess the influence of key cohort and prescriptive variables on heterogeneity. Variables assessed included mean age, program duration, number of exercises, intensity, sets, repetitions, weekly volume, and total volume. Meta-regression analyses employed a random intercept, fixed slopes model using "Wilson's SPSS macro to compute meta-regression"[45] and SPSS for Windows, version 22.0 (IBM Corp. Armonk, New York, USA).

Results

Study selection

The initial keyword search returned 268,775 titles. Following title and abstract exclusions, 271 full-text articles were evaluated in detail (Figure 1). A further 237 were excluded on the basis of the eligibility criteria; no full-length publication ($n = 16$), no RCT study design ($n = 25$), explicit heart failure diagnosis ($n = 30$), valvular or heart transplant surgery ($n = 5$), no CHD diagnosis ($n = 2$), no PRT intervention ($n = 61$), no isolation of PRT effects ($n = 97$) and insufficient intervention duration ($n = 1$). The remaining 34 articles were included.

Study characteristics

Study design. Across the 34 included studies, there were 44 different comparisons across three distinct study designs; PRT vs control, PRT vs AT and CT vs AT. This included four studies with multiple comparison groups[46–49] and three studies examining different PRT dose prescriptions during CT interventions.[50–52] The characteristics of included studies are presented in Supplementary Material, Table 1.

Quality. Overall quality of the included studies was moderate, with a mean PEDro score of 5 ± 1 (range: 3–8/10) (see Supplementary Material, Figures 1 and 2 for details). Only seven studies (21%) were considered to be of high quality (≥6/10).[47,48,51–55] Common limitations were lack of allocation concealment, subject, therapist and assessor blinding, intention-to-treat

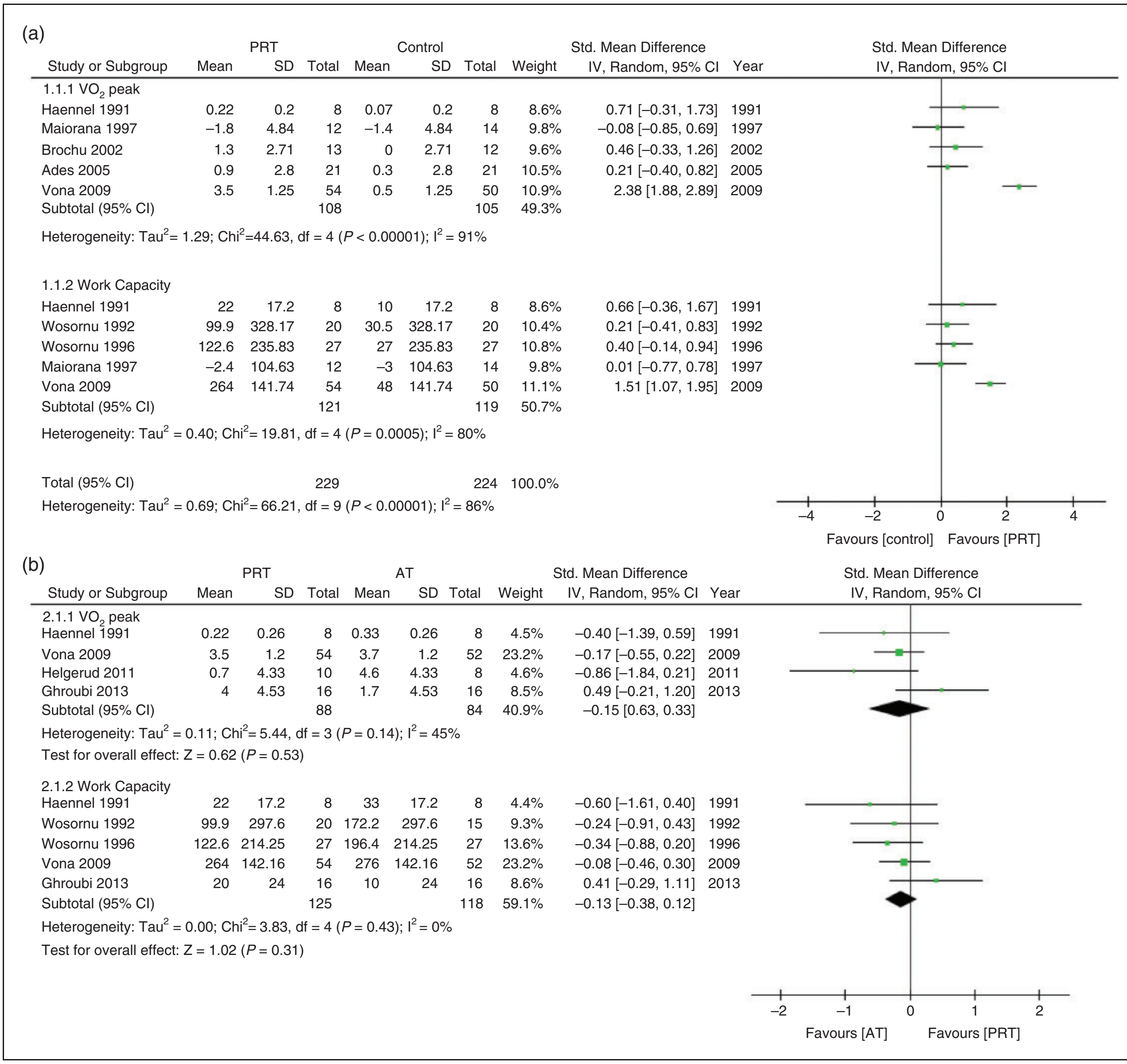

Figure 2. Effect of progressive resistance training (PRT) on aerobic fitness: (a) PRT vs control; (b) PRT vs aerobic training (AT); (c) combined training vs AT. CI: confidence interval; SD: standard deviation; VO_{2peak}: peak oxygen uptake. Some analyses were not pooled due to excessive heterogeneity ($I^2 > 75\%$).

analysis, and reporting of key outcome measures for more than 85% of randomised subjects. It is acknowledged that blinding of therapists and subjects is not possible in these study designs, thus potentially limiting the achievable maximal score to eight rather than 10. Reported lack of allocation concealment, assessor blinding, and intention-to-treat analysis, however, are serious threats to study validity and were deficient in most studies.

On average, 2 ± 1 (range: 0–3/3) of the additional quality criteria were met. While adherence reporting was poor (10; 29%), PRT dose (30; 88%) and exercise supervision (22; 65%) were more commonly reported.

Participants. A total of 1940 participants (71.9% men) were included. Fourteen studies (41.2%) included only men, six only women (17.6%), 13 (38.2%) included a combination of both, and one (2.9%) did not specify sex.[56] Mean reported age was 60 ± 7 years, ranging from 49–79 years. Nineteen studies (55.9%) reported baseline weight (81.8 ± 6.0 kg), 16 (47.0%) reported body mass index (BMI), which was in the overweight range on average ($27.7 \pm 3.5\,kg/m^2$) and nine (26.4%) reported body fat ($31.8 \pm 5.1\%$). Smoking status was reported in 10 studies (29.4%) and the majority of these participants had some history of smoking at the time of randomization. Eleven studies (32.3%) included

(c)

Study or Subgroup	Combined Mean	Combined SD	Combined Total	AT Mean	AT SD	AT Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
3.1.1 VO_2 peak									
Wilke 1991	3.33	3.33	12	2.05	3.33	12	2.2%	0.37 [–0.44, 1.18]	1991
Yamasaki 1995	4.1	4.59	22	3.5	4.59	19	3.7%	0.13 [–0.49, 0.74]	1995
Daub 1996 (20% 1RM)	3.7	4.13	5	2.9	4.13	5	0.9%	0.17 [–1.07, 1.42]	1996a
Daub 1996 (40% 1RM)	2	3.19	4	2.9	3.19	5	0.8%	–0.25 [–1.57, 1.07]	1996b
Daub 1996 (60% 1RM)	1.2	2.79	5	2.9	2.79	5	0.9%	–0.55 [–1.83, 0.73]	1996c
Stewart 1998	3.1	5.11	12	1.6	5.11	11	2.1%	0.28 [–0.54, 1.11]	1998
Pierson 2001	2.4	4.61	10	2.7	4.61	10	1.9%	–0.06 [–0.94, 0.81]	2001
Izawa 2006	0.6	7.3	10	–1.5	7.3	8	1.6%	0.27 [–0.66, 1.21]	2006
Arthur 2007	0.14	0.24	37	0.26	0.24	35	6.2%	–0.49 [–0.96, –0.03]	2007
Schmid 2008	2.5	5.29	17	2.2	5.29	21	3.4%	0.06 [–0.58, –0.70]	2008
Marzolini 2008 (1 set)	0.21	0.4	9	0.17	0.4	7	1.5%	0.09 [–0.89, –1.08]	2008a
Marzolini 2008 (3 sets)	0.25	0.43	9	0.17	0.43	7	1.5%	0.18 [–0.81, 1.17]	2008b
Vona 2009	4.5	1.36	53	3.7	1.36	52	8.7%	0.58 [0.19, 0.97]	2009
Gayda 2009	7.5	7.96	8	3	7.96	8	1.4%	0.53 [–0.47, 1.54]	2009
Hansen 2011	0.32	0.44	22	0.25	0.44	25	4.2%	0.16 [–0.42, 0.73]	2011
Busch 2012	0.16	0.2	61	0.13	0.2	65	10.6%	0.15 [–0.20, 0.50]	2012
Subtotal (95% CI)			296			295	51.7%	0.14 [–0.02, 0.31]	
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 14.82$, df = 15 ($P < 0.46$); $I^2 = 0\%$									
Test for overall effect: $Z = 1.73$ ($P = 0.08$)									
3.1.2 Work capacity									
Kelemen 1986	75	113.09	20	11	113.09	20	3.5%	0.55 [–0.08, 1.19]	1986
Ewart 1986	75	104.14	20	12	104.14	20	3.5%	0.59 [–0.04, 1.23]	1986
McCartney 1991	151.16	61.95	9	24.09	61.95	9	1.1%	1.95 [0.78, 3.13]	1991
Butler 1992	101	84.38	9	114	84.38	10	1.8%	–0.15 [–1.05, 0.75]	1992
Yamasaki 1995	132	106.57	22	84	106.57	19	3.6%	0.44 [–0.18, 1.06]	1995
Daub 1996 (20% 1RM)	199	114.89	5	164	114.89	5	0.9%	0.28 [–0.97, 1.52]	1996a
Daub 1996 (40% 1RM)	151	114.65	4	164	114.65	5	0.8%	–0.10 [–1.42, 1.22]	1996b
Daub 1996 (60% 1RM)	111	107.53	5	164	107.53	5	0.9%	–0.45 [–1.71, 0.82]	1996c
Beniamini 1999	138	181.15	18	72	181.15	16	3.1%	0.36 [–0.32, 1.04]	1999
Schmid 2008	21.52	47.89	17	16.46	47.89	21	3.4%	0.10 [–0.54, 0.74]	2008
Gayda 2009	54	42.76	8	26	42.76	8	1.4%	0.62 [–0.39, 1.63]	2009
Vona 2009	324	162	53	276	162	52	8.9%	0.29 [–0.09, 0.68]	2009
Hansen 2011	32	35.17	22	27	35.17	25	4.2%	0.14 [–0.43, 0.71]	2011
Busch 2012	12	13	64	10	13	69	11.1%	0.15 [–0.19, 0.49]	2012
Subtotal (95% CI)			276			284	48.3%	0.30 [0.12, 0.48]	
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 13.70$, df = 13 ($P < 0.40$); $I^2 = 5\%$									
Test for overall effect: $Z = 3.33$ ($P = 0.0009$)									

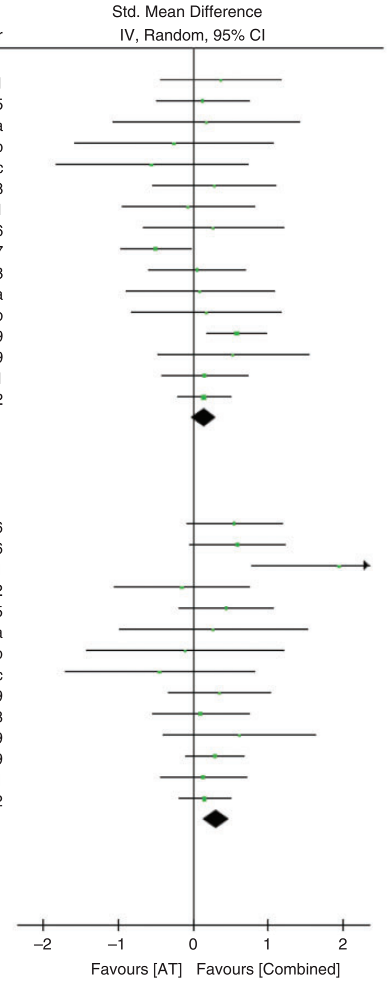

Figure 2. Continued.

post-myocardial infarction (MI) participants exclusively, three (8.8%) were post-CABG exclusively and the remaining 21 (61.8%) included a combination of both diagnoses. Mean time post-event/surgery to the start of the intervention was 27.9 ± 10.3 weeks (range: 1.9–176.8), as reported by 13 studies (38.2%). Twenty-four studies (70.6%) reported current medication usage. The most commonly reported medications were beta-blockers (17 studies) and angiotensin-converting enzyme (ACE) inhibitors (11 studies), with average prevalence of 58.3% and 43.6%, respectively. Comorbidities were reported in 10 studies, and the most prevalent were dyslipidemia (70.4%), hypertension (58.6%), and diabetes (24.3%).

Interventions. Appendix 1 presents individual study intervention characteristics. Intervention programs were 3–26 weeks in duration (12 ± 7) with 2–5 exercise sessions per week (3 ± 1). PRT interventions were mainly machine-based, isotonic, whole-body, multi-joint movements. Intensity was highly variable (20–90% 1RM). Most studies ($n = 24$; 71%) prescribed PRT at light-to-moderate intensity (30–69% 1RM), 11 studies used vigorous intensity (70–84% 1RM) and only one used maximal intensity (≥85% 1RM) according to ACSM classifications.[40] Prescribed volume varied widely from 1–12 different exercises, with 1–10 sets of 2–30 repetitions performed, giving a total volume of 16–600 repetitions per session and 48–1800 repetitions per week. In general, intensity was inversely related to volume prescribed. For example, individual prescriptions ranged from 4×4 repetitions at 90% 1RM on one exercise[57] to 10 × 30 repetitions at 30% 1RM on two exercises.[58] Rest time between sets varied from 10–

300 s. Supervision of exercise was provided in 22 studies, with 14 defining supervisor qualifications: exercise specialist (seven studies), physical therapist (five studies), cardiac nurse (three studies) and non-defined rehabilitation staff (two studies).

Most control groups were prescribed no structured exercise, but recommended participants maintain habitual physical activity levels. Three studies had control groups participate in stretching or light yoga on three days/week for 30-40 min, however no aerobic exercise was specified for these groups.[59–61]

Aerobic exercise comparisons were primarily continuous and moderate intensity, with only one study examining the use of high intensity interval training.[57] Exercise sessions ranged from 60–95% HR_{max} and 18–90 min in duration. The most common modes were stationary cycling, walking, and jogging. For PRT vs AT comparison studies ($n = 6$), intensity was rarely equalized between training groups; three studies did not specify intensity,[46,48,49] one study compared vigorous AT to light PRT[58] and only two studies attempted to prescribe equal intensity.[47,57] The total session number was equal for all but one study in which the AT group completed six more sessions than PRT group over an eight-week period.[57] Some CT vs AT studies ($n = 11$; 38%) attempted to equalize overall exercise dose either by replacing AT sessions with PRT sessions,[47,51,62,63] reducing AT duration in the CT group,[53,64] or adding additional stretching or recreational activities to the AT-alone group.[65–69]

Outcomes

Cardiorespiratory fitness

PRT vs control. Overall CRF was reported for 453 participants, with median change of 11.9% (range: –7.2–33.3%) in PRT and 3.1% (–5.8–10.0%) in control. Significant heterogeneity meant it was not suitable to pool overall ($I^2 = 86\%$) (Figure 2(a)).

PRT vs AT. Overall CRF improved robustly in both groups; median change 15.6% (range: 2.4–33.3%) in PRT and 20.1% (8.3–34.3%) in AT. Sub-analyses of VO_{2peak} and work capacity showed no difference between PRT or AT comparison groups ((VO_{2peak}: $n = 172$; SMD: –0.15; 95% confidence interval (CI): –0.63–0.33; $I^2 = 45\%$); work capacity: $n = 243$; SMD: –0.13; 95% CI: –0.38–0.12; $I^2 = 0\%$)) (Figure 2(b)).

CT vs AT. There was a clinically meaningful improvement in overall CRF in both CT (median 18.4%; range: 2.0–41.9%) and AT (median 15.4%; –5.5–34.3%). However, CT resulted in a significantly greater improvement in peak work capacity compared to AT ($n = 560$; SMD: 0.30; 95% CI: 0.12–0.48; $I^2 = 5\%$), with no difference in VO_{2peak} ($n = 567$; SMD: 0.14; 95% CI: –0.02–0.31; $I^2 = 0\%$) (Figure 2(c)).

Muscular strength

PRT vs control. Median lower body strength increase by 24.7% (range: 12.5–57.5%) in PRT vs 2.6% (2.5–12.4%) in control groups. The benefit of PRT for lower body strength was significantly greater than control with a moderate ES in pooled analysis ($n = 133$; SMD: 0.57; 95% CI: 0.17–0.96; $I^2 = 20\%$) (Figure 3(a)). Similarly, median upper body strength change was a robust 45.6% (range: 18.3–47.3%) in PRT vs 10.2% (–3.5–10.5%) in control groups. The pooled ES of PRT on upper body strength was large and significant compared to control ($n = 93$; SMD: 1.43; 95% CI: 0.73–2.13; $I^2 = 53\%$) (Figure 4(a)). There were insufficient data for sub-analyses based on contraction type.

PRT vs AT. Only two studies comparing PRT to AT reported muscular strength, meaning insufficient data were available to warrant pooling (Figure 3(b)). Haenell et al.[46] reported similar strength increases of 24.7% and 31.1% for PRT and AT respectively, while Ghroubi et al.[58] reported higher strength increases in PRT compared to AT (46.7% and 7.6% respectively).

CT vs AT. Median change in lower body strength was 19.9% (range: 1.9–92.1%) in CT vs 6.3% (–15.8–22.0%) in AT. This preferential benefit of CT was significant, with a moderate ES compared to AT in the pooled analysis of 675 participants (SMD: 0.60; 95% CI: 0.32–0.89; $I^2 = 65\%$) (Figure 3(c)). In sub-analyses, CT also had a large, significant effect on isotonic strength ($n = 300$; SMD: 1.00; 95% CI: 0.53–1.47; $I^2 = 70\%$) however, there was no difference on isokinetic ($n = 151$; SMD: 0.35; 95% CI: –0.04–0.73; $I^2 = 23\%$) or isometric strength ($n = 224$; SMD: 0.06; 95% CI: –0.20–0.32; $I^2 = 0\%$) (Figure 3(c)). Upper body strength improved by 20.8% (range: 6.5–58.6%) in CT compared to only 1.3% (–2.5–55.9%) in AT. This benefit of CT over AT was moderate and significant in pooled analyses ($n = 320$; SMD: 0.52; 95% CI: 0.30–0.75; $I^2 = 0\%$) (Figure 4(b)). Insufficient data were available for sub-analyses based on contraction type.

Other clinically relevant outcome measures. A number of additional outcome measures were identified, however there were insufficient data to warrant further analysis. Details of the data collected are available in

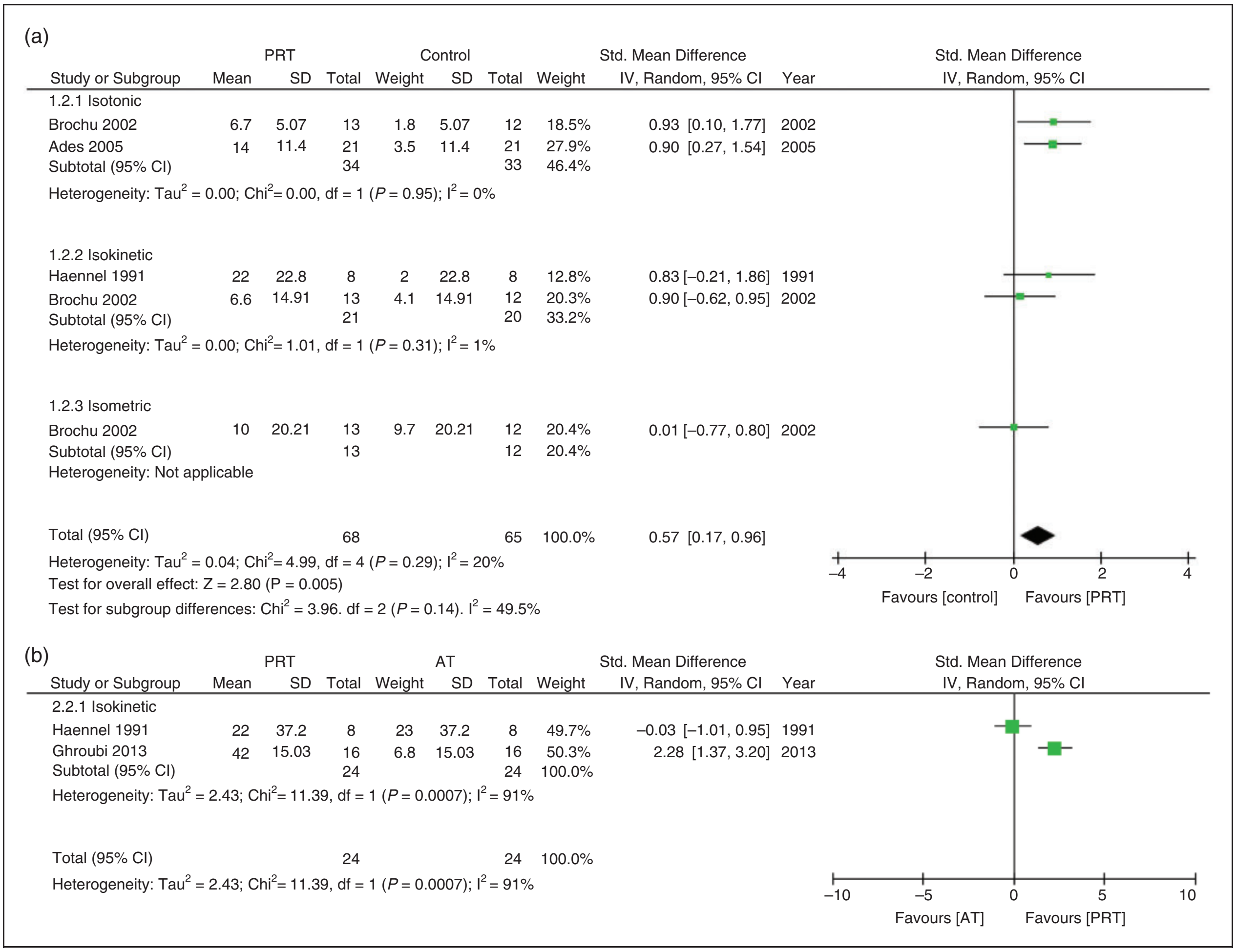

Figure 3. Effect of progressive resistance training (PRT) on lower body muscular strength: (a) PRT vs control; (b) PRT vs aerobic training (AT); (c) combined training vs AT. Some analyses were not pooled due to excessive heterogeneity ($I^2 > 75\%$).
CI: confidence interval; SD: standard deviation.

Supplementary Material, Table 2. Only one study reported re-infarction and mortality rates over a 42-month period,[56] all other studies were short-term, and cardiac events or deaths were rarely reported.

Adverse events. Details of adverse events are available in Appendix1. Twelve studies (35.2%) did not explicitly report adverse event information and 11 studies (32.4%) reported no adverse events. Six studies (17.6%) reported 63 non-fatal CV complications during testing or training, with all but one of these occurring during aerobic exercise. No CV adverse events led to study termination, alteration of intervention, extended hospitalization, or death.

Additionally, eight studies (22.9%) reported 23 musculoskeletal complaints or complications, 20 during PRT testing or training. In most cases, this was exacerbation of pre-existing conditions (e.g. knee arthritis), which was alleviated by reducing intensity or changing body position. Five musculoskeletal complaints led to termination of the intervention.[48,62,63]

Meta-regression analyses. In PRT vs control trials, sets and weekly volume were directly associated with VO_2 improvements ($r = 0.94$ and 0.98 respectively, $p < 0.001$). Sets were also directly associated with increased workload ($r = 0.97$, $p < 0.001$), while total volume showed an inverse association ($r = -0.87$, $p < 0.01$). In PRT vs AT studies, sets, repetitions, weekly volume and total volume were positively associated with increased VO_2 ($r = 0.84$, 0.93, 0.99, 0.93 respectively; $p < 0.05$) however, no variables explained heterogeneity in workload. Caution should be taken in interpretation of above results due to the limited number of data points ($n = 3$–5). In CT vs AT trials ($n = 10$–19), no variables explained heterogeneity in

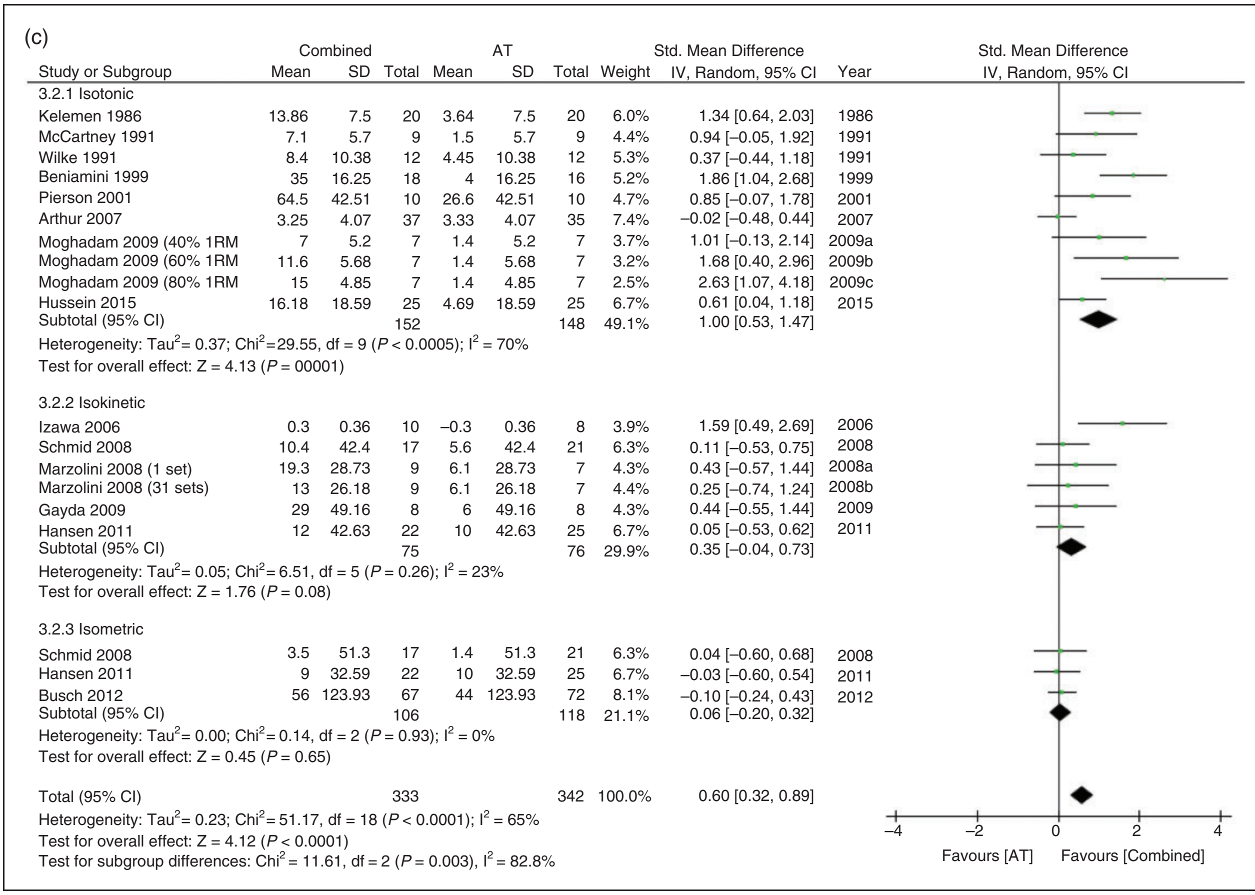

Figure 3. Continued.

VO_2, workload or strength. See Supplementary Material, Tables 3, 4, and 5 for detailed models.

Discussion

Our review and meta-analyses demonstrate that PRT provides improvements in CRF that are comparable to AT in adults with CHD. The addition of PRT to AT programs further improves both fitness and strength significantly more compared to AT alone, while PRT was shown to improve strength more than non-exercising controls. Given that muscle strength and CRF are independent risk factors for mortality,[20,70] these results support the use of PRT for adults with CHD, both in isolation and combined with AT. Women and older adults are notably under-represented in this literature however, so results should be applied cautiously to these cohorts.

Our review substantially advances the literature over the previous four reviews,[26,37–39] as we conducted a significantly broader search, included more trials and all study designs, catalogued all reported adverse events and are the first to include meta-regression analyses. A detailed comparison of previous meta-analyses is available in Supplementary Material, Table 6.

Enhanced CRF from CT compared to AT alone was observed for work capacity rather than VO_{2peak}, consistent with previous meta-analyses.[26,38] However, the current investigation shows a smaller benefit of CT over AT for this outcome than both previous reviews, which we attribute to differences in number of studies, definition of study design and statistical analysis methods. Specifically, previous analyses used the standardized mean response, an atypical ES measure which uses pooled SDs of the change scores rather than baseline SDs, resulting in much larger effect sizes.[71] The SMD used in the current study is more standard, using pooled baseline SD as required in the calculation of Cohen's *d* ES.[44] The SMD effect size was chosen for VO_{2peak} so some studies were not unnecessarily excluded from analyses, as all previous meta-analyses have when using relative VO_2 and the weighted mean difference (WMD) ES.

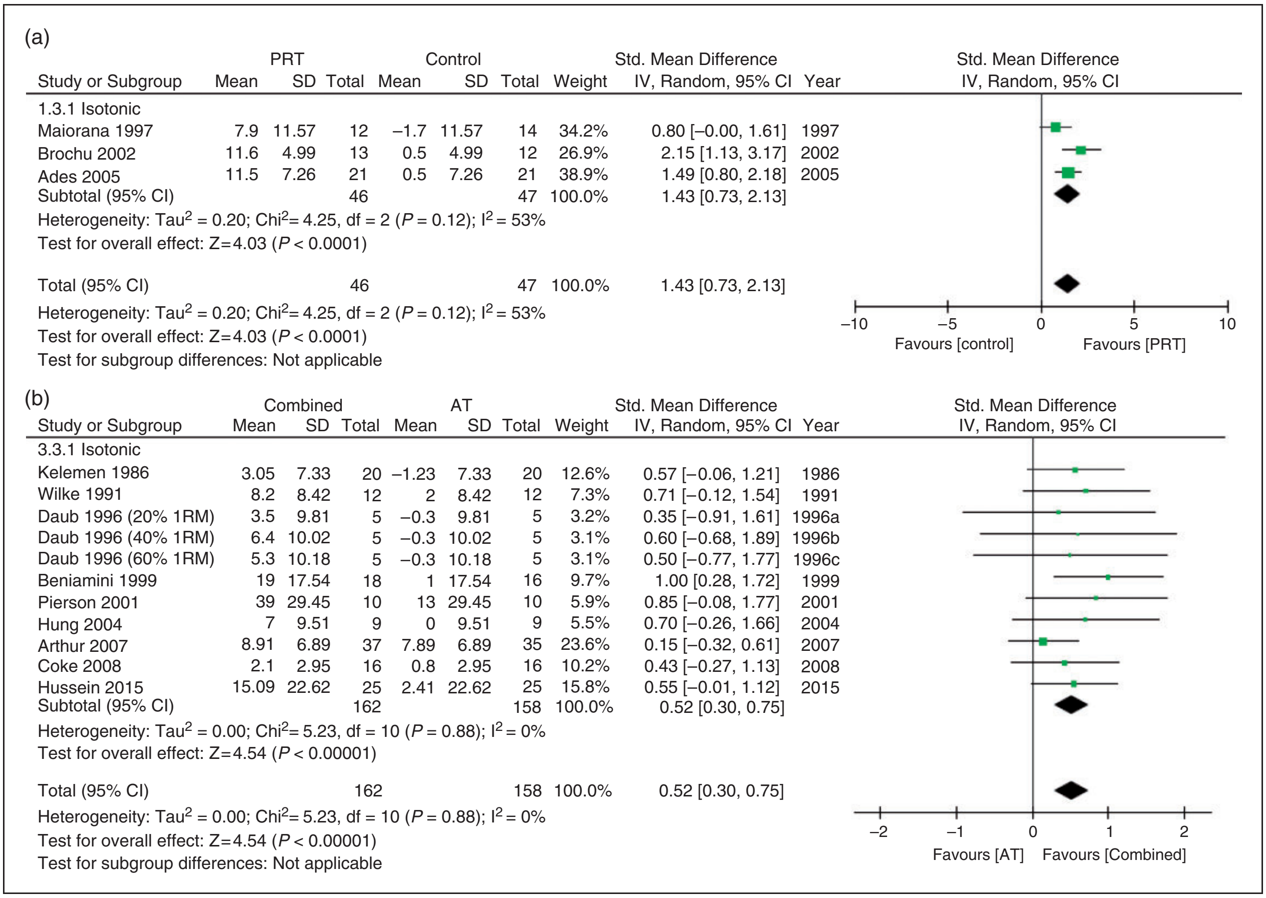

Figure 4. Effect of progressive resistance training (PRT) on upper body muscular strength: (a) PRT vs control; (b) combined training vs aerobic training (AT).
CI: confidence interval; SD: standard deviation.

Importantly, when isolated exercise modalities were compared, fitness improvements were similar for PRT and AT, consistent with what is seen in older adults,[25] a fact not widely appreciated clinically. CRF has an independent protective effect for both CVD and all-cause mortality,[72] with some evidence suggesting that a single metabolic equivalent (MET) increase in fitness corresponds with a 12% reduction in mortality.[18] Our analyses suggest that exercise programs for adults with CHD should include a combination of aerobic and resistance training for optimal aerobic fitness outcomes. However, in situations where aerobic exercise may not be viable, accessible or appropriate, PRT can provide CRF improvements that are equivalent in magnitude to AT, which may contribute to a reduced mortality risk. For example, the Health Professionals Follow-Up study reported a 23% reduction in the risk of fatal and non-fatal MI in men who reported 30 min or more per week of PRT,[73] comparable to the 18% reduction for men who reported 3.5 h per week of walking. More recently, a 19% reduction in all-cause mortality in fully-adjusted models was observed in older adults reporting participation in at least two days per week of PRT.[74] Notably, these epidemiological studies do not identify the mechanism of this PRT benefit, as both CRF and muscle strength are linked to reduced mortality,[18,28] and PRT improves both aspects of fitness.

While PRT vs AT showed similar CRF improvements, only two studies compared strength changes between these two modalities. Although there is insufficient data to conclude efficacy in CHD cohorts, evidence in older adults without CHD suggests a moderate effect in favor of PRT.[25] Furthermore, our meta-analyses demonstrate that the addition of PRT to AT programs has a large, significant effect on peak isotonic strength compared to AT alone. Similar results are noted in recent meta-analyses,[26,38,39] however a direct comparison of ESs is not appropriate due to previously outlined differences in statistical methods and unclear definitions of strength outcomes, such as which muscle groups[38,39] or contraction-types[26] were included in the final analyses. Our review shows that the modality of testing influenced the outcome, with smaller ESs observed during isokinetic tests of muscle strength, suggesting that specificity of testing should be a consideration for future trials and in clinical practice. Muscle strength has a strong association with mortality independent of muscle mass, suggesting that it is muscle function and not quantity that is important in aging.[70] With an increasing number of older adults living with CHD diagnoses, strength serves an important role for activities of daily living,[34] increasing gait speed[75] and reducing the recurrence of falls.[32] As PRT is the most potent exercise modality for strength improvements, this further highlights the importance of its inclusion in exercise programs and guidelines for older adults with CHD.

As 35.2% of studies did not explicitly report adverse event information, it is difficult to draw any conclusion on the safety of PRT in this cohort. Within the five studies that reported CV-related complications, 63 occurred during aerobic exercise and testing, one during PRT training, with no CV-complications during PRT testing. While reporting of adverse events was poor within the available literature, the limited data suggest that PRT has a lower rate of adverse CV events than AT. A hemodynamic comparison of maximal aerobic and muscular strength tests in adults with CHD reported 42% of participants experienced ischemic changes during a maximal treadmill test, whereas no changes were noted during maximal strength testing.[76] In addition, heart rate and double-product values were significantly lower during maximal strength tests compared to maximal aerobic tests, and diastolic pressures were higher during strength testing. The relative protection from ischemic symptoms during resistive exercise may be attributed in part to this higher diastolic pressure compared to aerobic exercise. During systole, myocardial extravascular compression causes coronary flow and thus perfusion of the myocardium to be near zero, yet it is relatively high during diastole (opposite of all other vascular beds in the body).[77] Thus, particularly in those with CHD, the risk differential would favor PRT over AT for ischemic risk on physiological grounds. The perception that PRT should be avoided in CHD due to its excessive CV risk compared to AT does not appear to be evidence-based.

Resistance training benefits for strength,[78–80] functional outcomes,[25] osteoporosis,[81] depression,[82] and other outcomes are greatest with high intensity training in older adults. In the current investigation however, only 8/34 studies prescribed PRT at high intensity (above 80% 1RM) and only one study above 85% 1RM. Although no dose-response studies were identified, there is evidence that high-intensity PRT produces a lower hemodynamic response than low-intensity PRT in adults with CHD,[83] suggesting that more evidence is needed to properly discern the safety and efficacy high-intensity PRT in adults with CHD. Further research directly comparing a wider range of intensities and volumes is required to properly discern whether CHD guidelines should be altered from the current recommendations for low-to-moderate intensity PRT.[9]

Limitations

Due to lack of resources, only one author was responsible for initial study selection and data extraction, although consensus was obtained for all studies. Furthermore, unpublished data were neither searched for nor included.

Conclusion

This review showed that PRT improved cardiorespiratory fitness to a similar degree as AT in adults with CHD. When PRT is added to AT programs, the effect on both fitness and strength is enhanced. Thus, CR programs are suboptimal with respect to improvements in fitness, strength, and associated health and functional benefits if they include only an AT component. In addition, literature from other cohorts supports potential advantages for high intensity PRT, rather than the low-to-moderate intensity PRT paradigms currently recommended in CHD, which indicate the need for dose-response trials in this cohort specifically. Advancements in the field require high quality, robust trials which enroll women and older adults. They should also aim to report all adverse events, blind assessors, measure other key clinical outcomes in addition to fitness and strength such as function, psychological health, metabolic health, and QOL, and better describe cohort and intervention characteristics.

Author contribution

MH, JF and MFS contributed to the conception of the work. All authors contributed to the acquisition, analysis, or interpretation of data. MH drafted the manuscript and all authors critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Appendix 1

Summary of intervention characteristics

Study	n (male/female)	Mean age ± SD	Diagnosis	Study design	Program duration (weeks)	Number of PRT exercise/mode	Freq (d/wk)	Sets × Reps	Intensity (%1RM)	Progression	Comparison	Freq (d/wk)	Intensity	Time (min)	Type	Adverse events
Carson et al., 1982[56]	303/0	51.6 ± 0.7[a]	MI	PRT vs control	12	NR/circuit training	2				Control					Not reported
Ewart et al., 1986[67,b]	43/0	55.0 ± 8.5	MI, AP, CABG	CT vs AT	10	10/Machine weights	3	2 × 12–15	40%	1RM reassessed at week 5	Aerobic exercise (+volleyball)	3	70–85% HR_{max}	40	Walk/jog, modified volleyball	Not reported
Kelemen et al., 1986[68,b]	43/0	55.0 ± 8.5	MI, AP, CABG	CT vs AT	10	10/Machine weights + body weight	3	2 × 10–15	40%	1RM reassessed after week 5	Aerobic exercise (+volleyball)	3	85% HR_{max}	40	Walk, jog, volleyball	Angina during AT testing (CT: $n = 1$, AT: $n = 1$)
Haennel et al., 1991[46]	24/0	53.2 ± 2.7[a]	MI, CABG	PRT vs control, PRT vs AT	8	3/Hydraulic resistance device	3	3 × 8–16		Cylinder intensity ↑ every 2 wk to stay in rep range	Control				Did not wish to participate in exercise, non-exercising controls	No adverse events
											Aerobic exercise	3	70% HRR	24	Cycle ergometer	
McCartney et al., 1991[69,b]	24/0	52.0 ± 2.0	MI, AP, CABG	CT vs AT	10	4/Free + machine weights	2	2–3 × 10–15	40–80%	1RM reassessed every 2 weeks	Aerobic exercise (+recreational games)	2	60–85% HR_{max}	35	Arm and leg cycle ergometry, walking, jogging, volleyball, badminton	No adverse events
Wilke et al., 1991[63]	40/0	61.0 ± 7.0	MI	CT vs AT	12	7/Free + machine weights	3	3 × 9.5	70%	1RM reassessed every 4 weeks	Aerobic exercise	3	70–85% HR_{max}	40	Arm and leg cycle ergometry	Aggravation of pre-existing shoulder injury (CT: $n = 2$)
Butler et al., 1992[84]	25/0	52.5 ± 8.5	MI, CABG, PCI	CT vs AT	6	8/Pneumatic resistance machines	3	2 × 10	40%	↑ to maintain 40% 1RM	Aerobic exercise	3	70–85% HR_{max}, 65–80% HRR	30	75% stationary bike, 25% treadmill	Chest pain, upon exam had re-stenosis following CABG (CT: n = 1)
Wosornu et al., 1992[48]	55/0	57.7 ± 7.2[a]	MI, CABG	PRT vs control, PRT vs AT	26	10/Machine weights	3			gradually increased depending on individual's progress and symptoms	Control				No formal exercise training	Dropped out due to complications with scar (PRT: $n = 2$)
											Aerobic exercise	3	NS	12–40	calisthenics (Canadian air force XBX physical fitness program)	
Yamasaki et al., 1995[85]	45/14	62.8 ± 8.8[a]	MI	CT vs AT	8	1/Machine weights	3	4–6 × 5	60%		Aerobic exercise	3		30–40	Treadmill	Not reported
Daub et al., 1996[50]	57/0	49.3 ± 7.1	MI	CT vs AT	10	6/Machine weights	3	2 × 20 2 × 10 2 × 7	20% 40% 60%		Aerobic exercise	3	70–85% HR_{max}	40	Walking, cycling	During AT, 45 CV complications including ST depression, angina, arrhythmias ($n = 30$). During PRT, 1 asymptomatic arrhythmia ($n = 1$)

(continued)

Continued

Study	n (male/female)	Mean age ± SD	Diagnosis	Study design	Program duration (weeks)	Number of PRT exercise/mode	Freq (d/wk)	Sets × Reps	Intensity (%1RM)	Progression	Comparison	Freq (d/wk)	Intensity	Time (min)	Type	Adverse events
Wosornu et al., 1996[49]	81/0	57.4 ± 7.6	MI, CABG	PRT vs control, PRT vs AT	26	10/Machine weights	3	3 × 10		gradually increased depending on individual's progress and symptoms	Control				No formal exercise training	No adverse events
											Aerobic exercise	3	NS	12–40	Calisthenics (Canadian air force XBX physical fitness program)	
Beniamini et al., 1997[66,b]	29/9	58.5 ± 12.0[a]	MI, AP, CABG	CT vs AT	12	4/Machine weights	2	3 × 8,8, 8–12	50–80%		Aerobic exercise (+flexibility)	2	65–80% HR_{max}; 3 × 30 s hold, 1 min rest	18	Overhead towel stretch, triceps flexion, chair seated hip flexion, floor seated hamstring stretch	Knee osteoarthritis pain exacerbated (AT: $n = 1$)
Maiorana et al., 1997[86]	26/0	60.0 ± 8.5 [a]	MI, CABG	PRT vs control	10	12/Free + machine weights		1–3 × 10–15	60%		Control				Instructed to maintain usual activities	No adverse events
Stewart et al., 1998[64,c]	23/0	54.6 ± 9.7[a]	MI	CT vs AT	10	7/NR	3	2 × 10–15	40%	↑ 5–10lbs if 15 reps within 30 s	Aerobic exercise	3	70–80% HR_{max}	20–25 (8 for CT)	Dual action cycle (arms and legs concurrent)	No adverse events
Beniamini et al., 1999[65,b]	29/9	58.5 ± 12.0[a]	MI, AP, CABG, Ang	CT vs AT	12	4/Machine weights	2	3 × 8,8, 8–12	50–80%		Aerobic exercise (+flexibility)	2	65–80% HR_{max}; 3 × 30 s hold, 1 min rest	20–25	Overhead towel stretch, triceps flexion, chair seated hip flexion, floor seated hamstring stretch	Knee osteoarthritis pain exacerbated (AT: $n = 1$)
Pierson et al., 2001[87]	13/7	59.9 ± 8.2[a]	MI, CABG	CT vs AT	24	7/Machine weights	3	2 × 12–15	40%	↑ to next increment after 6 consecutive sets of 15 reps	Aerobic exercise	3	65–80% HR_{max}	30	Treadmill, stationary cycle, recumbent cycle, rower, stair stepper	Discomfort during PRT that required decrease in load (PRT: $n = 6$)
Brochu et al., 2002[61]	0/25	70.6 ± 4.7[a]	MI, AP	PRT vs control	24–26	8/Free weights + elastic tubing	3	1–2 × 10	50–80%	1RM reassessed monthly	Control (normal rehabilitation)	3		30–40	Stretching, calisthenics, deep-breathing progressive relaxation exercises, light yoga	Symptomatic angina during AT testing ($n = 6$). Knee osteoarthritis pain exacerbated during PRT ($n = 2$)
Ades et al., 2003[5,9]	0/42	72.3 ± 5.6	MI, AP, CABG, PCI	PRT vs control	24	8/Free + machine weights	3	1–2 × 10	50–80%	1RM reassessed monthly	Control (normal rehabilitation)	3		30–40	Stretching, calisthenics, deep-breathing progressive relaxation exercises, light yoga	Symptomatic angina during AT testing ($n = 8$)

(continued)

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Study	*n* (male/female)	Mean age ± SD	Diagnosis	Study design	Program duration (weeks)	Number of PRT exercise/mode	Freq (d/wk)	Sets × Reps	Intensity (%1RM)	Progression	Comparison	Freq (d/wk)	Intensity	Time (min)	Type	Adverse events
Hung et al., 2004[88]	0/18	70.5 ± 6.5[a]	MI	CT vs AT	8	8/Free + machine weights	3	1–2 × 8–10	55%	↑ 2.5% per week	Aerobic exercise	3	70–85% HR_{max}	30	Treadmill, cycle	Not reported
Ades et al., 2005[60]	0/51	72.2 ± 5.5[a]	MI, AP, CABG, PCI	PRT vs control	24	8/Free + machine weights	3	1–2 × 10	50–80%	1RM reassessed monthly	Control (normal rehabilitation)	3		30–40	Stretching, calisthenics, deep-breathing progressive relaxation exercises, light yoga	Not reported
Izawa et al., 2006[89]	16/2	65.9 ± 9.8[a]	MI	CT vs AT	24	2/Bodyweight	2	4 × 5	11–13 Borg RPE		Aerobic exercise	2	11–13 Borg RPE	60	Walking	Not reported
Arthur et al., 2007[53,c]	0/92	Post-menopausal	MI, CABG, PCI	CT vs AT	16	NR	2	2 × 8–12	30–70%		Aerobic exercise	2	40–70% functional capacity	40 (20–25 for CT)	Stationary cycles, treadmills, arm ergometers, stair climbers	No adverse events
Coke et al., 2008[90]	0/32	64.5 ± 10.5[a]	MI, AP, CABG, PCI	CT vs AT	12	5/Free weights	2	1 × 12	40–60%	↑ to maintain 13 (RPE) and new intensities (not reassessed)	Aerobic exercise	3				No adverse events
Marzolini et al., 2008[51,d]	65/7	60.6 ± 2.5[a]	MI, CABG, PCI	CT vs AT	24	10/Free weights, bodyweight & resistance bands	1	1 × 10–15 3 × 10–15	60–75% 60–75%		Aerobic exercise	5 (4 in CT)	60% VO_{2peak}	30–60	Walking and/or jogging	No adverse events
Schmid et al., 2008[62,d]	32/6	56.0 ± 9.5[a]	MI	CT vs AT	12	6/Machine weights + bodyweight	2	2 × 10	40–60%	↑ 10% 1RM every 4 weeks	Aerobic exercise	6 (4 in CT)	70–85% HR_{max}			Discontinued due to knee osteoarthritis pain (PRT: *n* = 1)
Gayda et al., 2009[91]	16/0	55.0 ± 8.0	MI, CABG, Ang	CT vs AT	7	2/Machine weights	3	3 × 10	40%		Aerobic exercise	3	Ventilatory threshold power output	60–120	30 min calisthenics, stretching and respiratory exercises, 30 min cycle ergometer, advised to take a 60 min walk outside	Not reported
Moghadam et al., 2009[52]	60/28	52.3 ± 5.9	CABG	CT vs AT	5	5/NR	2	2 × 12 2 × 12 2 × 12	40% 2RM 60% 2RM 80% 2RM	↑ 10% when 2x12 successfully completed	Aerobic exercise	5	60–80% HR_{max}	30	Treadmill walking, stationary cycling, arm crank ergometer	No adverse events

(continued)

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Study	n (male/female)	Mean age ± SD	Diagnosis	Study design	Program duration (weeks)	Number of PRT exercise/mode	Freq (d/wk)	Sets × Reps	Intensity (%1RM)	Progression	Comparison	Freq (d/wk)	Intensity	Time (min)	Type	Adverse events
Vona et al., 2009[47,d]	155/54	56.4 ± 7.6[a]	MI, CABG, PCI	PRT vs control, PRT vs AT	4	10/Free weights + resistance bands	4	4 × 10–12	60%	yes, not specified how	Control				Avoided regular physical activity	No adverse events
											Aerobic exercise	4	75% HR_{max}	40	Stationary cycling	
				CT vs AT	4	10/Free weights + resistance bands	2	4 × 10–12	60%	yes, not specified how	Aerobic exercise	4 (2 in CT)	75% HR_{max}	40	Stationary cycling	
Hansen et al., 2011[92]	44/3	59.6 ± 8.0[a]	MI, AP, CABG, PCI	CT vs AT	6	2/Machine weights	3	2 × 12–20	65%	based on subject RPE	Aerobic exercise	18sess/49 days	65% VO_{2peak}	40	Cycling, walking, arm cranking	Not reported
Helgerud et al., 2011[5,7]	16/2	63.7 ± 4.6[a]	MI, AP	PRT vs AT	8	1/Machine weights	3	4 × 4	85–90%	↑ 2.5 kg when all sets and reps were completed	Aerobic interval training	3–5	85–95% HR_{max}/60–70% HR_{max} active recovery	28 (4 × 4 min interval, 3 min rest)	Treadmill walking	Not reported
Busch et al., 2012[54]	54/119	78.5 ± 3.2	CABG	CT vs AT	3	4/Free + machine weights	5	1 × 8–12	60%		Normal CR (aerobic)	3		90	Walking, calisthenics, cycle ergometer	Not reported
Ghroubi et al., 2013[58]	32/0	59.1 ± 4.3[a]	CABG	PRT vs AT	8	2/Isokinetic dynamometer	3	10 × 20–40	20–30%	↑ reps to maintain 70% HRR	Aerobic exercise	3	70% HRR	20	Cycle ergometer	Exercise-induced ST depression with no angina during AT (AT: $n = 2$). Complaints of knee pain (AT: $n = 5$, PRT: $n = 3$)
Caruso et al., 2015[55]	20/0	61.2 ± 4.8[a]	MI	CT vs AT	8	1/Machine weights	2	3 × 20	30%		Aerobic (CR program)	2	70% HR_{max}	20–30	Cycle ergometer, treadmill	Not reported
Hussein et al., 2015[93]	24/26	60.5 ± 13.3[a]	MI, AP, CABG, Ang	CT vs AT	6	3/Machine weights	3	2 × 8–12	60%	1RM reassessed every 2 weeks	Aerobic exercise	3	40–60% HRR	20	Cycling, treadmill, stepper, rower	No adverse events

%1RM: percentage of one repetition maximum; Ang: angioplasty; AP: angina pectoris; AT: aerobic training; CABG: coronary artery bypass graft; CT: combined training; freq (d/wk): frequency (days/week); HR_{max}: maximum heart rate; HRR: heart rate reserve; MI: myocardial infarction; *n*: number; NR: not reported; PCI: percutaneous coronary intervention; PRT: progressive resistance training; reps: repetitions; RPE: rate of perceived exertion; SD: standard deviation; VO_{2peak}: peak oxygen uptake.

[a]Mean age ± SD not reported in paper and manually calculated; [b]CT studies adding additional activities into AT group; [c]studies reducing AT time in the CT group; [d]studies replacing AT with PRT sessions in the CT group.