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REVIEW

Does resistance training modulate cardiac autonomic control? A systematic review and meta-analysis

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Abstract

Purpose To systematically evaluate the literature on the effects of resistance training (RT) on cardiac autonomic control in healthy and diseased individuals.

Methods Electronic databases Pubmed, PEDro, and Scopus were systematically searched from their inception up to June 2018. Randomized controlled trials, quasi-experimental trials, and cross-over controlled trials investigating the effect of RT (of at least 4 weeks duration) on cardiac autonomic control assessed either by linear or non-linear measures of heart rate variability (HRV), baroreflex sensitivity, or post-exercise heart rate recovery were included. Of the studies retrieved, 28 were included in the systematic review. Meta-analysis was performed on 21 studies of the total 28 studies.

Results Quality and characteristic assessment revealed fair quality evidence. The majority of literature on healthy humans suggested no change in cardiac autonomic control following RT. Standardized mean differences (SMD) showed a significant effect of RT on root mean square of successive differences between adjacent inter-beat (R-R) intervals (RMSSD) [SMD 0.96, 95% confidence interval (CI) 0.20–1.73; $p=0.01$], ratio of low- to high-frequency power of HRV (LF/HF ratio; SMD −0.72, 95% CI −1.03 to −0.42; $p<0.00001$), standard deviation of the instantaneous beat-to-beat variability (SD1; SMD 1.78, 95% CI 1.07–2.49, $p<0.00001$), and sample entropy (SMD 1.17, 95% CI 0.36–1.97, $p=0.005$) in diseased individuals.

Conclusion This rigorous systematic analysis revealed that RT has no or minimal effects on cardiac autonomic control of healthy individuals, but RT leads to improvement in cardiac autonomic control of diseased individuals.

Keywords Heart rate variability · Exercise · Autonomic control of heart · Strength training

Introduction

Resistance training (RT) has been described as a safe form of exercise for athletes, healthy individuals, and diseased individuals [1, 2]. An increase in muscle strength and force production [3], enhanced balance [4], metabolic adaptations in skeletal muscle [5], improved glucose tolerance [6], and insulin sensitivity [7] are amongst the well-established physiological adaptations in response to RT. However, it is still difficult to reach a conclusion on the impact of RT on enhancing cardiovascular health and reducing cardiovascular mortality. Cardiac autonomic control [i.e., control of heart function by sympathetic and parasympathetic branches of the autonomic nervous system (ANS)] is an important indicator of cardiovascular health [8]. Prospective longitudinal cohort studies have shown that impaired cardiac autonomic control is a strong predictor of all-cause and cardiovascular disease mortality [9] and can be diagnosed clinically by assessing linear and non-linear indices of heart rate

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variability (HRV), baroreflex sensitivity (BRS), and post-exercise heart rate recovery (HRR) [10, 11].

Physical exercise may profoundly modulate the autonomic control of the heart. Aerobic training (AT) has a beneficial role in modulating cardiac autonomic control by improving HRV, HRR, and BRS [12–15]. Position statements published by the American College of Sports Medicine (ACSM) and American Heart Association (AHA) support using RT as a core component of exercise rehabilitation programs [1]. Although several studies have examined the effects of RT on cardiac autonomic control in human participants, they have failed to reach any consensus, which underscores the urgent need to critically evaluate the existing literature to better elucidate limitations and also to reach a definitive conclusion. A previous review [16] conducted to examine the effects of RT on cardiac autonomic control overlooked many relevant studies and only included studies up to 2013. A plethora of evidence has arisen after its publication, strongly warranting an update. Therefore, the objective of the present review was to comprehensively and systematically evaluate clinical trials (in terms of characteristics, quality, and treatment outcomes) to investigate the effects of RT on cardiac autonomic control in healthy and diseased individuals.

Methods

We conducted a systematic literature review investigating the effects of RT on cardiac autonomic control in healthy and diseased individuals in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for reporting systematic reviews [17].

Data sources and search strategy

Electronic databases such as Pubmed, PEDro (Physiotherapy Evidence Database), and Scopus (Elsevier) were searched from the date of inception to June 2018. We identified articles using main search terms, which were a combination of key words for intervention type (resistance training, resistance exercise, exercise, strength training, weight exercise) and outcome measures (cardiac autonomic control, HRV, baroreflex sensitivity, arterial baroreflex function, HRR, autonomic function). These search terms were combined with Boolean operators OR and AND to broaden or to narrow the search results in Pubmed and Scopus databases and were combined with truncation for searching in the PEDro database. Besides the electronic database search, references of the relevant articles were also screened. The complete search strategy for Pubmed database was ("weight exercise" OR "strength training" OR "exercise" OR "resistance exercise" OR "resistance training") AND ("autonomic function" OR "heart rate recovery" OR "baroreflex sensitivity" OR "heart rate variability" OR "cardiac autonomic control").

Inclusion and exclusion criteria

The inclusion criteria for relevant studies in the review were: (1) clinical trials administering RT for at least 4 weeks; (2) randomized controlled trials (RCTs), quasi-experimental trials, and cross-over controlled trials on both healthy as well as diseased individuals ("diseased" was defined as the presence of any physical illness pertaining to the human body); and (3) clinical trials assessing cardiac autonomic control using one of the following outcome measures: linear and non-linear indices of HRV, BRS, and HRR.

The exclusion criteria consisted of: (1) studies comprising other forms of exercise training (AT, high-intensity interval training, yoga, tai chi, qi qong, breathing exercises) other than RT; (2) review articles, case reports, theses, or dissertations; or (3) epidemiological studies (cross-sectional and cohort).

Data collection and analysis

Selection of studies

The search was applied to each database and all the retrieved articles were transferred to the Endnote reference manager (EndNote™ Online version, Clarivate Analytics) where the results were combined and duplicates were removed. Two authors (P.B. and J.M.) applied inclusion criteria to the titles and thereafter selected articles to be screened by their abstracts. After screening of the abstracts, the full text of each relevant article was obtained, and the same authors independently reapplied the inclusion and exclusion criteria blinded to the author and publication data. Finally, the references of the full-text articles selected for inclusion in the review were screened by the author P.B. to retrieve a final set of articles to be included in the review. Disagreements at any stage were resolved by consensus with a third reviewer (E.H.).

Data extraction

After designing the data extraction forms, data regarding the characteristics of the trial (year conducted, study design, duration), the participants (sample size, age, sex), intervention (type, intensity, number of sessions, frequency, duration, progression), control treatment, main outcome measures (HRV, BRS, HRR), and the main findings were extracted by two authors independently (P.B. and J.M.). If the reported data were incomplete or unclear, authors of that study were contacted. For meta-analysis, descriptive data, i.e. mean and standard deviation (SD) of the relevant outcome measures, were recorded and if the data were not presented descriptively, they were extracted from figures of the articles. Any conflicts between the reviewers were resolved by consensus or in consultation with a third reviewer (E.H.).

Quality assessment

Methodological quality of studies was examined using an 11-point PEDro scale. In the PEDro scale, ten criteria were rated as either "Yes" (score = 1) or "No" (score = 0) for each included study, as the first criteria did not receive any score. The total methodological quality score for each study was calculated by adding all the criterion scores (maximum score = 10). Studies were classified as poor (score of < 4), fair (score of 4–5), good (score of 6–8), or excellent (score of > 8) quality [18].

Data synthesis and analysis

Meta-analysis was performed for only those studies providing sufficient information on either of the pre-established outcome measures. The standardized mean difference (SMD) $\left[\text{SMD} = \frac{\text{MD}}{\text{SDpooled}}\right]$, where MD is difference in means of the intervention and control groups and SD is the standard deviation, was used to define the effect estimates for HRV. Three time domain indices, namely, SD of normal to normal (N–N) intervals (SDNN), mean of N–N intervals (mean NN), root mean square of successive differences between adjacent inter-beat (R-R) intervals (RMSSD) that measure ANS-mediated overall HRV and vagal activity, respectively, along with three frequency domain indices, namely normalized low-frequency (LFnu) power, normalized high-frequency (HFnu) power, and the LF/HF ratio measuring sympathetic activity, vagal activity, and sympatho-vagal balance, respectively [19], were used as outcome variables for the meta-analysis. Non-linear HRV measures such as SD of the instantaneous beat-to-beat variability (SD1), an indicator of parasympathetic activity [19], and sample entropy, a measure used to quantify irregularity in R–R interval time series which is an indicator of complexity in heart period and is associated with better cardiac autonomic health [20], were also extracted from the included studies. The meta-analysis was performed separately for studies on healthy and diseased human participants using Cochrane Collaboration's Review Manager 5.3 software. Cohen's d criteria were used to determine magnitude of effect size (small, < 0.2; moderate, 0.2–0.5; or large > 0.5) [21]. Statistical significance was set at 5% (0.05). Cochrane's Q test of heterogeneity was determined. Heterogeneity between the studies was quantified using the I^2 test, which measures the percentage of the observed variability between effect estimates beyond chance. A value of $I^2 < 25\%$ indicates low heterogeneity, 25–75% indicates moderate heterogeneity, and > 75% indicates high heterogeneity [22].

Results

Search results

The initial search yielded a total of 3422 records, and after removal of duplicates, 3160 records were screened by their titles and 145 articles were selected. Abstracts of the selected records were then screened and 44 potential studies were included in the full-text analyses. Sixteen studies were excluded due to lack of a control group (not engaged in any structured exercise program) [23–35], lack of follow-up of a control group during the study period (post-study autonomic function assessment was not performed) [36], cross-sectional study design [37], and outcome measure of autonomic function not included in the present review [38]. Twenty-eight studies [39–66] were included in the quality and characteristic assessment. Studies judged to be of poor quality [44, 56, 60] based on the PEDro-based quality assessment and those providing insufficient data and/or data in an unsuitable form [47, 62, 63, 66] were excluded. The remaining 21 studies were included in meta-analysis [39–43, 45, 46, 48–55, 57–59, 61, 64, 65]. The selection of the studies is illustrated in the PRISMA 2009 flow diagram (Fig. 1).

Study characteristics

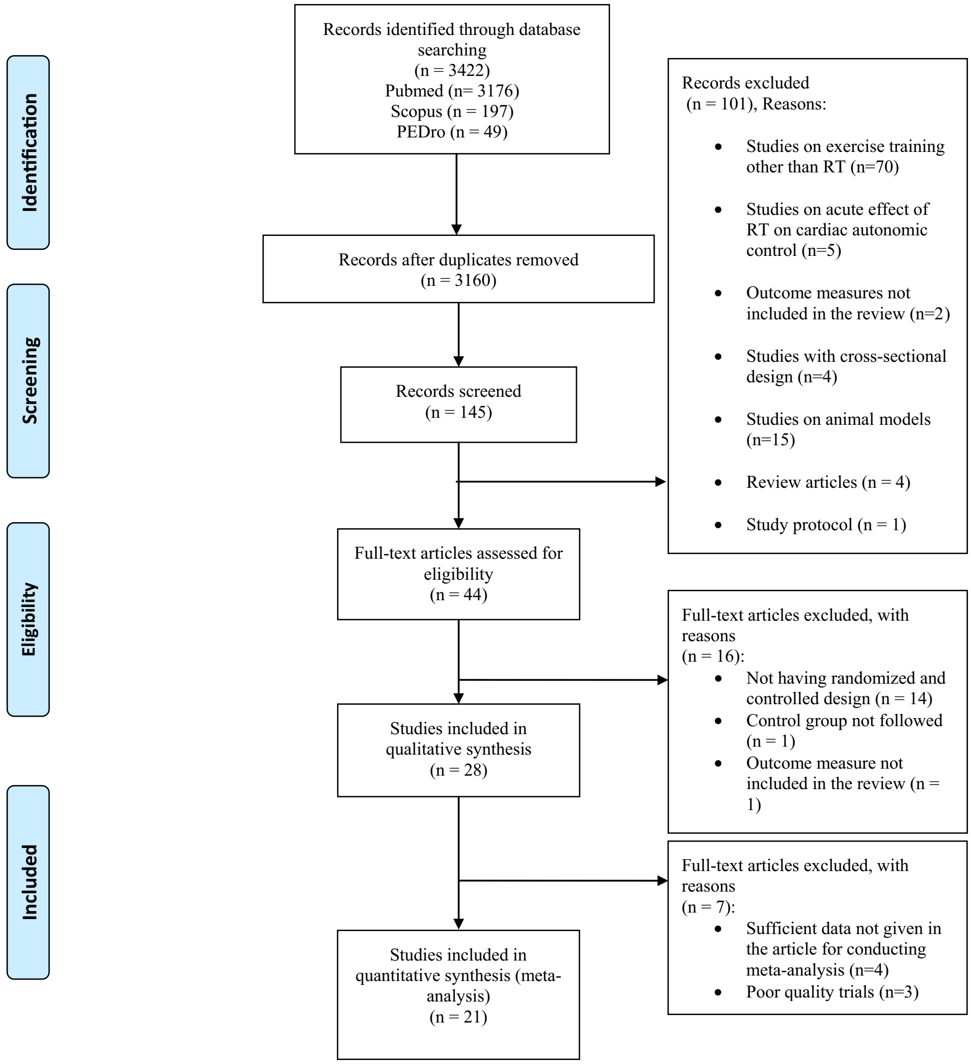
Study design

Of the 28 studies identified, 13 were randomized parallel-group control trials [39, 40, 42, 45, 46, 50, 52, 53, 55–57, 59, 64], 4 studies were randomized parallel-group active controlled trials [48, 51, 54, 65], and 4 were randomized parallel-group multiple-arm comparative controlled trials [49, 61–63]. Four studies were non-randomized parallel-group controlled trials [41, 44, 47, 58], two were cross-over controlled trials [43, 60], while one study was a partially randomized parallel-group multiple-arm comparative controlled trial [66]. The control group was either given usual care or some other form of exercise training apart from RT or was not given any form of intervention. Details regarding the study design and the control group are shown in Table 1.

Participants

Twenty-eight of the included studies comprised a total of 1025 participants, with sample sizes ranging from 14 to 93 and the average age of the participants ranging from 22 to 72 years. Ten trials included only men [41, 43, 45, 46, 51, 54, 59–61, 63], nine trials included only women [42,

Fig. 1 Flow chart of search strategy and retrieval of articles. *RT* resistance training



44, 47, 48, 53, 56, 57, 62, 65], while nine trials included both sexes [39, 40, 49, 50, 52, 55, 58, 64, 66]. The majority of the trials (15) assessed older adults (age ≥ 60 years) [39, 40, 42, 45, 48, 49, 51–55, 58, 61, 62, 64], whereas four trials assessed young adults (age 18–26 years) [35, 37, 60, 63] and 8 trials assessed middle-aged adults (age 27–59 years) [44, 46, 47, 50, 56, 57, 65, 66]. One trial did not provide information regarding ages of the participants [59]. Thirteen studies examined the healthy population [41–43, 45, 46, 48, 52, 53, 59–63] and 15 studies assessed the diseased population [39, 40, 44, 47, 49–51, 54–58, 64–66]. Pathologies addressed by the studies in this review were hypertension, chronic heart failure (CHF), coronary artery disease (CAD), fibromyalgia (FM), non-alcoholic fatty liver disease (NAFLD), Parkinson's disease, polycystic ovary syndrome (PCOS), metabolic syndrome, and combinations of hypertension, hyperlipidemia, and diabetes. Previous studies have clearly indicated that cardiac autonomic dysfunction is certainly a common loop in the patho-physiology of these diseases [67–73] (Table 1).

Intervention

At least one of the groups in each study used RT as an intervention. The majority of the studies utilized dynamic RT except three studies that used isometric RT [39, 58, 64], and one used eccentric RT [45]. Weight machines and free weights were used for RT in the majority of the studies, while one study used an isokinetic dynamometer [45] and three used a hand-grip dynamometer [39, 58, 64]. Exercise intensity ranged from low to high and was based on either repetition maximum (RM), maximum voluntary contraction (MVC), or peak torque. Lengths of the exercise sessions per day ranged from 30 to 60 min, 2–5 times/week and the duration of RT ranged between 6 weeks and 8 months (Table 1).

Table 1 Characteristics of the studies included in review

Trial	Participants	Study design	Intervention	Control group	Outcome measures	Main findings
Turri-Silva et al. [66]	50 patients with metabolic syndrome Age: 51.6 ± 6.37 years M/W: 13:19	Partially randomized parallel-group multiple-arm comparative controlled trial	Conventional RT versus FRT for 12 weeks Leg Ex. were the same for both the training groups: leg press, leg curl machine, and extension machine All Ex. were performed at 30–100% of 1 RM using 2–3 sets over 30 sessions Upper extremity Ex.: FRT: Ex. in dorsal (back and pectoral Ex.) and ventral positions (for biceps and triceps Ex.) on a 45^0 inclined cross-over machine Conventional RT: classical executions were adopted for the same muscular groups in specific machines (biceps, triceps, and back) Session supervision: supervised Session length: unclear (not reported)	Control group remained sedentary and did not practice any Ex. training during the study period	Chaotic forward parameters of non-linear HRV at rest	Significant improvement in chaotic behavior of HR dynamics after both types of RT
De Sousa Fortes et al. [63]	31 healthy young men Age: 21.8 ± 1.74 years	Randomized parallel-group multiple-arm comparative controlled trial	Clustering versus multi-sets RT Clustering RT: 3 sets of (2 × 4 reps) with 20-s rest between reps at 75% of 1 RM for 8 weeks (3/week) Multi-sets RT: 3 sets of 8 reps at 75% of 1 RM for 8 weeks (3/week) Ex.: Bench press and 45^0 leg press Progression: progression was not done Session supervision: supervised	Participants in control group remained physically inactive during the 8-week study period	Resting HRV: RMSSD	Significant ↑ in RMSSD after both types of RT with no significant difference between the groups

Table 1 (continued)

Trial	Participants	Study design	Intervention	Control group	Outcome measures	Main findings
Glasgow et al. [57]	26 women with FM with 9 healthy controls Age: 50.5 ± 10.5 years	Randomized parallel-group controlled trial	RT for 8 weeks (2/week), 3 sets of 8–12 reps at 50–60% of 1 RM Ex.: chest press, leg extension, leg curl, seated row Progression: resistance was increased by 2–10% when participants were able to complete 12 reps on all 3 sets over 2 consecutive training days Session length: 30 min Session supervision: supervised	Participants in this group maintained their normal diet and usual activities of daily living throughout 8 weeks	Resting HRV: LF power, HF power, LF/HF ratio Resting HRC: sample entropy	No change in HRV or HRC after RT
Caruso et al. [54]	20 coronary artery disease patients (all men) Age: 61.1 ± 4.7 years	Randomized parallel-group active controlled trial	RT on 45^0 leg press for 8 weeks (2/week) at 30% of 1 RM, 3 sets of 10 reps along with AT Session length: 40 min Session supervision: unclear (not reported)	AT: 20–30 min of treadmill running or cycling at 50–70% of MHR for 8 weeks	HRV during Ex.: RMSSD, SDNN, LF power, SD1	↑ RMSSD & SDNN, SD1 in the RT group ↓ RMSSD in the control group
Kanegusuku et al. [55]	30 patients with Parkinson's disease Age: 65 ± 8 years M/W: 22/5	Randomized parallel-group controlled trial	RT for 12 weeks (2/week) Ex.: horizontal leg press, squat, rotary calf, lateral pull down, chest press Progression: 1–2 weeks: 2 sets of 12–10 RM 3–4 weeks: 3 sets of 12–10 RM 5–6 weeks: 3 sets of 10–8 RM 7–10 weeks: 4 sets of 8–6 RM 11–12 week: 4 sets of 8–6 RM Session length: unclear (not reported) Session supervision: supervised	Patients in the control group maintained their usual lifestyle without engaging themselves in any Ex. program	Resting HRV: LF power, HF power, LF/HF ratio	↑ HF, ↓ LF & LF/HF ratio in the RT group

Table 1 (continued)

Trial	Participants	Study design	Intervention	Control group	Outcome measures	Main findings
Ribeiro et al. [56]	27 women with PCOS and 26 healthy controls Age: 30 ± 1.05 years	Non-randomized parallel-group controlled trial	Periodized RT for 4 months at 70% of 1 RM Ex.: bench press, leg extension, front lateral pull down, leg curl, lateral raise, leg press, triceps pulley, calf leg press, arm curl, abdominal Progression: In the first 3 weeks of each mesocycle, Ex. were performed 3/week and the intensity was ↑ by 5% per week. In the 4th week, Ex. were performed 2/week and intensity was ↓ by 5% Session length: unclear (not reported) Session supervision: unclear (not reported)	Participants in the control group did not engage in any Ex. training during the study period of 4 months	HRV at rest and during the tilt test: mean NN, variance, LF power, HF power, LF/HF ratio	No change in HRV measures at rest and during the tilt test after RT
Gambassi et al. [53]	26 healthy elderly women Age: 65 ± 3.0 years	Randomized parallel-group controlled trial	RT for 12 weeks (2/week) Ex.: leg press, seated row, leg curl, bench press, abduction machine push down, adduction machine, bicep curl Progression: first 2 weeks: load at which 3 sets of 15 reps can be performed Next 10 weeks: load at which 8 reps can be performed Session length: unclear (not reported) Session supervision: unclear (not reported)	Not engaged in any physical Ex. program for 12 weeks	Resting HRV: SDNN, mean NN, RMSSD, LF power, HF power, LF/HF ratio	↑ HRV indices in the RT group

Table 1 (continued)

Trial	Participants	Study design	Intervention	Control group	Outcome measures	Main findings
Caruso et al. [51]	20 coronary artery disease patients (all men) Age: 61.15 ± 4.8 years	Randomized parallel-group active controlled trial	RT on 45^0 leg press for 8 weeks (2/week) at 30% of 1 RM, 3 sets of 20 reps along with AT Session length: 60 min Session supervision: unclear (not reported)	AT: 20–30 min of treadmill running or cycling at 70% of MHR, 2/week for 8 weeks	HRV: RMSSD, SD1, SD2, ApEn	↑ RMSSD, SD1, and ApEn in the RT group after 8 weeks
Kanegusuku et al. [55]	25 healthy older adults Age: 63.5 ± 4 years M/W: 7/18	Randomized parallel-group controlled trial	High-intensity progressive RT for 16 weeks (2/week) Ex.: horizontal leg press, bilateral knee flexion, unilateral hip extension, plantar flexion in horizontal leg press, chest press, lateral pull down, upright row Session length: unclear (not reported) Session supervision: supervised	Not engaged in any physical Ex. program for 16 weeks	HRV: TP, LF power, HF power, LF/HF ratio	No change in HRV in the RT training group
Gavi et al. [65]	66 women with FM Age: 46.4 ± 7.77 years	Randomized parallel-group active controlled trial	RT for 16 weeks (2/week) at 45% of 1 RM Ex.: leg press, leg extension, hip flexion, pectoral fly, triceps extension, shoulder flexion, leg curl, calf pull down, shoulder abduction, bicep flexion, and shoulder extension	Flexibility Ex. for 16 weeks	Resting HRV: TP, pNN50, RMSSD, LF power, HF power, LF/HF ratio	No change in HRV after RT

Table 1 (continued)

Trial	Participants	Study design	Intervention	Control group	Outcome measures	Main findings
Karavirta et al. [62]	19 healthy women Age: 51.5 ± 7.25 years	Randomized parallel-group multiple-arm controlled trial	RT versus ET versus combined RT and ET RT: leg press, knee extension, leg curl, seated calf raise, hip abduction or adduction, bench press, bicep curl, triceps pull down, lateral pull down, abdominal crunch, seated back extension for 21 weeks (2/week) Progression: week 1–7: 40–60% of 1 RM, 3 sets of 12–20 reps Week 8–14: 60–80% of 1 RM, 3 sets of 5–12 reps Week 15–21: 70–85% of 1 RM, 2–4 sets of 8–5 reps Session length: unclear (not reported) Session supervision: supervised ET: training on cycle ergometer for 21 weeks (2/week) Combined RT and ET: both ET and RT (4/week for 21 weeks)	These participants did not perform any kind of Ex. training for the 21-week study period	HRV at rest and during aerobic Ex.: SDNN, LF power, HF power, LF/HF ratio HRC at rest and during aerobic Ex.: complexity index of multiscale entropy analysis	There was no change in HRV or HRC after RT ↑ HRC after ET alone

Table 1 (continued)

Trial	Participants	Study design	Intervention	Control group	Outcome measures	Main findings
Wanderley et al. [49]	50 older adults with various pathologies Age: 68 ± 5.5 years M/W: 11/39	Randomized parallel-group multiple-arm comparative controlled trial	AT versus RT AT: walking at 50–80% of $HR_{reserve}$ progressed over 8 months, 2/week, 8 months RT: starting at 50–60% of 1 RM and progressed to 80% of 1 RM, 1–2 sets of 12–15 reps Ex.: leg press, chest press, leg extension, seated row, seated leg curl, abdominal flexion, bicep curl, low back extension, triceps extension Progression: progressive RT (details of progression not reported) Session length: 50 min for AT and RT Session supervision: supervised	Maintained their usual lifestyle and were not engaged in any physical Ex. program for 8 months	Resting HRV: SDNN, HF power	No significant change in HRV after RT
Jakovljevic et al. [50]	17 non-alcoholic fatty liver disease patients Age: 55.5 ± 10 years M/W: 12/5	Randomized parallel-group controlled trial	RT for 8 weeks (3/week) Ex.: bicep curl, calf raise, triceps press, chest press, seated hamstring curl, shoulder press, leg extension, lateral pull down Progression: initially 2 circuits at 50% of 1 RM, later, 3 circuits at 70% of 1 RM were performed Session length: 45–60 min Session supervision: partially supervised	Received usual care	HRV at rest and after sub-maximal Ex.: mean NN, LF power, HF power, LF/HF ratio (at rest and after sub-maximal ex.) BRS and BPV	No significant change in HRV after RT

Table 1 (continued)

Trial	Participants	Study design	Intervention	Control group	Outcome measures	Main findings
Gerage et al. [48]	31 healthy older women Age: 65.9 ± 4.6 years	Randomized parallel-group active controlled trial	RT for 12 weeks (3/week) Ex.: bench press, leg extension, lateral pull down, leg curl, bicep curl, seated calf raise, triceps push down, abdominal crunches 2 sets of 15 reps for each Ex., weight was increased by 2–5% for upper limb ex. and 5–10% for lower limb Ex.. when 15 reps were completed successfully Session length: unclear (not reported) Session supervision: supervised	Stretching program for 12 weeks (2/week)	Resting HRV: LF power, HF power, LF/HF ratio, SDNN, RMSSD, SD1, SD2	No change in HRV indices after RT, but ↓ HRV in the control group
Millar et al. [58]	23 older hypertensive patients Age: 66 ± 6.0 years M/W: 18/5	Non-randomized parallel-group controlled trial	Isometric RT for 8 weeks (3/week) at 30% of MVC, four sets of 2-min isometric contraction performed by hand grip dynamometer Session length: unclear (not reported) Session supervision: partially supervised	Patients in the control group did not received any Ex. training during the 8-week study period	Resting HRV: SDNN, RMSSD, pNN50, LF power, HF power, LF/HF ratio HRC at rest: sample entropy, short-term scaling exponent	Significant ↑ in sample entropy after isometric RT but no change in linear HRV indices
Stiller-Moldovan et al. [64]	20 older hypertensive patients Age: 61.3 ± 7.3 years M/W: 10/10	Randomized parallel-group controlled trial	Isometric RT for 8 weeks (2/week) at 30% of MVC, four sets of 2-min isometric contractions using hand grip dynamometer Session length: unclear (nor reported) Session supervision (partially supervised)	Patients in the control group were asked to visit the laboratory twice/week for BP check-ups and were instructed to record Ex., nutrition, and medication status	Resting HRV: LF power, HF power, LF/HF ratio, TP, VLF	No change in HRV measures after 8 weeks of isometric RT

Table 1 (continued)

Trial	Participants	Study design	Intervention	Control group	Outcome measures	Main findings
Kingsley et al. [47]	9 women with FM with 15 healthy controls (total = 29) Age: 43.5 ± 5 years	Non-randomized parallel-group controlled trial	RT for 12 weeks (2/week) Ex.: chest press, seated row, leg extension, leg press, leg curl Progressed from 50–60% to 75–85% of 1 RM, 3 sets of 12 reps Session length: 30 min Session supervision: supervised	Not engaged in any physical Ex. program for 12 weeks	HRV at rest and after acute resist ex. bout: TP, LF power, HF power, LF/HF ratio	No change in HRV indices at rest and after resistance ex. bout in the RT group
Karavirta et al. [61]	93 healthy older men Age: 55.6 ± 7.4 years	Randomized parallel-group multiple-arm controlled trial	RT versus ET versus Combined RT and ET RT: 7–10 Ex. which activated main muscle groups for 21 weeks (2/week) Progression: weeks 1–7: 40–60% of 1 RM, 3 sets of 12-20 reps Weeks 8–14: 60–80% of 1 RM, 3 sets of 5-12 reps Weeks 15–21: 70–85% of 1 RM, 2–4 sets of 8–5 reps Session length: unclear (not reported) Supervision: supervised ET: training on cycle ergometer for 21 weeks (2/week) Combined RT and ET: ET and RT for 4/week for 21 weeks	Participants in this group did not engage in any kind of Ex. training for the 21-week study period	Resting HRV: LF power, HF power, LF/HF ratio Short-term scaling exponent at rest	No change in HRV after RT
Hu et al. [46]	74 healthy men Age: 31.6 ± 7.35 years	Randomized parallel-group controlled trial	RT for 10 weeks (2–3/week) Ex.: dose (intensity and volume) not reported Session length: unclear (not reported) Session supervision: supervised	Not engaged in any physical Ex. program for 10 weeks	Non-linear HRV during sub-maximal Ex.: SD1, SD1n	↑ in SD1 and SD1n in the RT group

Table 1 (continued)

Trial	Participants	Study design	Intervention	Control group	Outcome measures	Main findings
Takahashi et al. [45]	17 healthy older men Age: 63 ± 3 years	Randomized parallel-group controlled trial	RT for 12 weeks (2/week) Ex.: bilateral knee eccentric flexion and extension on isokinetic dynamometer 2–4 sets of 8–12 reps at 70–80% of peak torque Session length: unclear (not reported) Session supervision: unclear (not reported)	Not engaged in any physical Ex. program for 12 weeks	RMSSD index during isometric Ex.	No change in RMSSD index in the RT group
Heffernan et al. [60]	34 healthy young men Age: 23 ± 1 years	Cross-over controlled trial	RT for 6 weeks (3/week) Ex.: two-way body part split training in which legs, back, and biceps were exercised on one day; chest, shoulder, and triceps were exercised on second day with five Ex. in each session Progression: first 2 weeks: weight was selected to ensure fatigue between 12 and 15 reps Final 4 weeks: weight that could induce fatigue between 8 and 12 reps Session length: 60 min Session supervision: unclear (not reported)	Participants did not participate in any structured Ex. training during the control period of 4 weeks before RT	HRC at rest: short-term scaling exponent	No significant change in HRC after RT

Table 1 (continued)

Trial	Participants	Study design	Intervention	Control group	Outcome measures	Main findings
Figueroa et al. [44]	10 women with FM and 9 healthy controls (total = 19) Age: 49.5 ± 9 years	Non-randomized parallel-group controlled trial	RT for 16 weeks (2/week) Ex.: chest press, leg extension, leg curl, leg press, arm curl, seated dip, overhead press, seated row, abdominal crunch 1 set of 8–12 reps at 50–80% of 1 RM Session length: 30 min Session supervision: unclear (not reported)	Not engaged in any physical Ex. program for 16 weeks	Resting HRV: TP, LF power, HF power, LF/HF ratio, RMSSD BRS	↑ RMSSD, TP and HF power in the RT group
Heffernan et al. [43]	14 healthy young men Age: 25 ± 1.1 years	Cross-over controlled trial	RT for 6 weeks (3/week) Ex.: 2-way body part split Ex. Each session consisted of five Ex. First session: primary muscles of leg (quadriceps and hamstring), back (latisimus dorsi), upper, middle and lower trapezius, erector spinae & rhomboids, and biceps Next session: chest (pectoralis major/minor), shoulder (deltoid), triceps Progression: first 2 weeks: load at which 12–15 reps can be performed Next 4 weeks: load at which 8–12 reps can be performed Session length: 60 min Session supervision: supervised	During the control period, participants were not engaged in any physical Ex.	Resting HRV: mean NN, SDNN, LF power, HF power, LF/HF ratio, sample entropy, LZEn HRR,	SampEn, LZEn ↑, HRR improved & HRV linear variables remained unchanged after RT

Table 1 (continued)

Trial	Participants	Study design	Intervention	Control group	Outcome measures	Main findings
Madden et al. [42]	45 healthy elderly women Age: 70.5 ± 1.76 years	Randomized parallel-group multiple-arm comparative controlled trial	RT versus ET for 6 months (5/week) RT Ex.: upper and lower body strength training (Ex. not specified) and goal was to progress to 85% of 1RM at the end of 6 months, 3 sets of 8–12 reps Session length: unclear (not reported) Session supervision: supervised ET Cycling at 60% MHR initially for 2 months, later progressed to 80–85% MHR	Not engaged in any Ex. program for 6 months	Resting HRV: SDNN, RMSSD, pNN50, TP, LF power, HF power, LF/HF ratio	No change in HRV indices in the RT group ↑ SDNN, LF power, HF power, TP in the ET group
Cooke & Carter [41]	22 healthy young men Age: 22 ± 0.8 years	Non- randomized parallel-group controlled trial	RT for 8 weeks (3/week) Ex.: leg press, leg curl, chest press, latissimus pulldown, shoulder press, biceps curl, triceps press 3 sets (10 reps in first 2 sets and as many reps in 3rd set) at 75–80% of 1 RM Session length: unclear (not reported) Session supervision: supervised	Maintained normal daily recreational activities without engaging in any Ex. program for 8 weeks	Resting HRV: mean NN, SDNN, LF power, HF power, LF/HF ratio BRS	No change in HRV indices & BRS in the RT group

Table 1 (continued)

Trial	Participants	Study design	Intervention	Control group	Outcome measures	Main findings
Selig et al. [40]	39 chronic heart failure patients Age: 65 ± 11 years M/W: 33/6	Randomized parallel-group controlled trial	RT for 12 weeks (3/week) Ex.: elbow extension/flexion, stair climbing, knee extension/flexion, shoulder press/pull, alternating between upper and lower body cycling Moderate-intensity RT (intensity not specified) progressed by ↑ intensity or reps Session length: unclear (not reported) Session supervision: unclear (not reported)	Received usual care	Resting HRV: mean NN, SDNN, RMSSD, LF, HF, LF/HF ratio	↓ LF & LF/HF ratio, ↑ HF & SDNN & no change in RMSSD in the RT group
Taylor et al. [39]	17 older adults with hypertension Age: 66.7 ± 5.75 years M/W: 10/7	Randomized parallel-group controlled trial	Isometric RT for 10 weeks (3/week) at 30% of MVC, Four 2-min isometric contractions performed by hand grip dynamometer using alternating hands Session length: unclear (not reported) Session supervision: unclear (not reported)	Received usual care	Resting HRV: LF power, HF power, LF/HF ratio	↓ LF, LF/HF ratio, ↑HF in the RT group after 10 weeks

Table 1 (continued)

Trial	Participants	Study design	Intervention	Control group	Outcome measures	Main findings
Van Hoof et al. [59]	30 sedentary men Age: unclear (not reported)	Randomized parallel-group controlled trial	RT for 16 weeks (3/week) Ex.: leg press, bench press, leg curl, shoulder press, leg extension at 70% of 1 RM followed by 70% of maximum numbers of sit-ups performed in 1 min Progression: Initial 4 weeks: 3 sets of 12 reps of above mentioned 6 Ex. Remaining 12 weeks: 3 sets of 10 reps at 70% of 1 RM of bench press and leg press each time followed by 4 reps at 90% of 1 RM of the same Ex. at each training session Session length: unclear (not reported) Session supervision: supervised	Participants in the control group were asked not to change their sedentary lifestyle during the study	HRV: variance, LF power, HF power, LF/HF ratio	RT did not lead to any change in HRV measures

RT resistance training, *reps* repetitions, *RM* repetition maximum, *FRT* functional resistance training, *HR* heart rate, *AT* aerobic training, *ET* endurance training, *MHR* maximum heart rate, *HR reserve* heart rate reserve, *min* minutes, *PCOS* polycystic ovary syndrome, *FM* fibromyalgia, *MVC* maximum voluntary contraction, *Ex.* exercise, *M* men, *W* women, *BPV* blood pressure variability, *HRC* heart rate complexity, *BP* blood pressure, *BRS* baroreflex sensitivity, *HRR* heart rate recovery, *HRV* heart rate variability, *SDNN* standard deviation of N–N intervals, *RMSSD* root mean square of successive differences between adjacent R–R intervals, *pNN50* percentage of interval differences of adjacent RR intervals greater than 50 ms, *TP* total power; *VLF* very low frequency power, *LF* low frequency, *HF* high frequency, *ApEn* approximate entropy, *LzEn* Lz entropy, *SD1* standard deviation of instantaneous beat to beat variability, *SD1n* normalized value of SD1, age of the participants is reported as mean ± SD, main findings are based on the results the of RT group after completion of training

Outcome measures

All studies examined and reported HRV as a measure of cardiac autonomic control. One study assessed BRS [50] and another assessed post-exercise HRR [43] in addition to HRV. Almost all studies reported linear HRV indices, while nine studies also reported non-linear indices [43, 46, 48, 51, 54, 57, 58, 61, 62]. Two studies explicitly assessed non-linear HRV [60, 66] without investigating linear HRV measures. For most trials, HRV was assessed in resting conditions, while two trials also investigated HRV after exercise [47, 50] and five studies assessed HRV during exercise [45, 46, 54, 61, 62] (Table 1).

Quality of the trials

The average PEDro score for all studies was 4.8/10 (fair quality). The scoring of each study for each criterion of the quality assessment scale is detailed in Table 2. Based on quality scoring, 8 studies were of good quality [40, 50, 51, 54, 55, 62, 63], 17 were of fair quality [39, 41–43, 45–49, 52, 53, 57–59, 61, 64, 66], and 3 studies were of poor quality [44, 56, 60]. Good-quality studies shared potential methodological strengths as all provided information on priori sample size calculation, performed randomization, and concealed allocation of participants. However, despite these strengths, two studies [51, 54] lacked a non-exercise control group. All the fair-quality trials had common procedural weakness, none concealed allocation of participants into groups except for two studies [47, 64], and the outcome assessor was not blinded. One study [49] enrolled very heterogeneous samples, which was an important methodological risk. Some studies provided information on power calculation [40, 41, 48, 52, 57, 66], which added some strength to the methodology used. All poor-quality studies [44, 56, 60] lacked transparency since they did not provide information on drop-outs, were not randomized, or did not guarantee concealed allocation of participants into groups.

Effect of RT on cardiac autonomic control

Twelve studies reported positive adaptations in cardiac autonomic control after RT [39, 40, 43, 44, 46, 51, 53–55, 58, 63, 66], of which 9 involved diseased individuals, while 14 studies showed no change in cardiac autonomic control after RT [41, 42, 45, 47, 48, 52, 56, 57, 59–62, 64, 65]. Two studies demonstrated statistically insignificant positive changes in HRV measures after completion of RT, while the autonomic function of participants in the control group in these studies deteriorated with time [49, 50] (Table 1).

Magnitude of effect: results of meta-analysis The meta-analysis showed that no statistically significant changes were observed in cardiac autonomic control after RT in healthy human participants (Figs. 2, 3, and 4). In diseased humans, time domain indices of HRV, namely the mean NN, was reported in two studies, while SDNN and RMSSD were reported in the required form in four studies. The pooled analysis revealed statistically non-significant moderate and large increases in mean NN (SMD 0.23, 95% CI −0.33 to 0.79, $p=0.43$) or SDNN (SMD 0.67, 95% CI −0.12 to 1.46, $p=0.10$), whereas a statistically significant increase was observed in RMSSD (SMD 0.96, 95% CI 0.20–1.73, $p=0.01$) after RT (Fig. 5). Frequency domain variables such as LFnu power were reported by seven studies, HFnu power and LF/HF ratio were reported by six studies in the required form. The meta-analysis performed on these studies suggested that RT was able to cause a significant improvement in HFnu power (SMD 0.62, 95% CI 0.03–1.20, $p=0.04$) and in LF/HF ratio (SMD −0.72, 95% CI −1.03 to −0.42, $p<0.00001$) of diseased human participants post-RT. There was an insignificant large reduction in LFnu power (SMD −0.66, 95% CI −1.36 to 0.05, $p=0.07$) after RT (Fig. 6). Non-linear HRV indices, namely SD1 (SMD 1.78, 95% CI 1.07–2.49, $p<0.00001$) and sample entropy (SMD 1.17, 95% CI 0.36–1.97, $p=0.005$), also demonstrated significant improvement after RT in diseased individuals (Fig. 7).

Discussion

Purpose and main findings

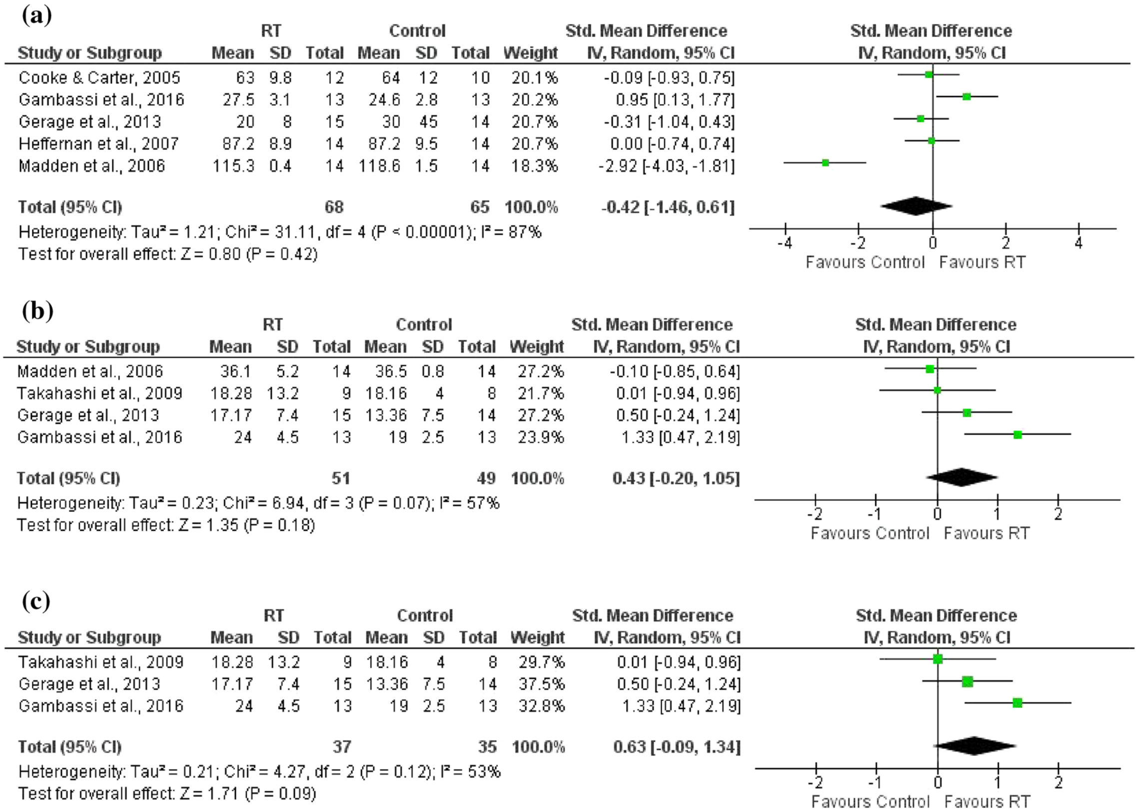
This systematic review was conducted to summarize and evaluate the existing literature on the effect of RT on cardiac autonomic control in both healthy and diseased individuals. Most studies on the clinical population revealed positive adaptations in cardiac autonomic control after RT; however, the results of the studies on healthy individuals were inconclusive with most showing no change post-RT. The meta-analysis suggested a significant improvement in linear HRV indices in terms of vagal control (RMSSD and HFnu power) and sympatho-vagal balance (LF/HF ratio) along with significant improvement in non-linear measures of HRV (SD1 and sample entropy) after RT in diseased individuals.

Healthy individuals

Overall, 13 clinical trials assessed healthy adults. Of the five studies on young and middle-aged healthy adults, three [43, 46, 63] showed a positive change in cardiac autonomic control after RT. A cross-over controlled trial [43] suggested that a 6-week RT was able to modulate the resting cardiac autonomic function through non-linear HRV indices and HRR, although the linear HRV indices remained unchanged. Although the participants enrolled and training were very

Table 2 Quality scoring of the studies based on PEDro scale

Trial	Random allocation	Concealed allocation	Group Similarity at baseline	Participant blinding	Therapist blinding	Assessor blinding	Description of drop-outs	Intention-to-treat analysis	Between-group differences reported	Point estimates and variability reported	Total score	Quality
Turri-Silva et al. [66]	No	No	Yes	No	No	No	Yes	Yes	Yes	No	4/10	Fair
De Sousa Fortes et al. [63]	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	6/10	Good
Glasgow et al. [57]	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10	Fair
Caruso et al. [54]	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7/10	Good
Kanegusuku et al. [55]	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	6/10	Good
Ribeiro et al. [56]	No	No	No	No	No	No	No	No	Yes	Yes	2/10	Poor
Gambassi et al. [53]	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4/10	Fair
Caruso et al. [51]	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7/10	Good
Kanegusuku et al. [55]	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10	Fair
Gavi et al. [65]	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	6/10	Good
Karavirta et al. [62]	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6/10	Good
Wanderley et al. [49]	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10	Fair
Jakovljevic et al. [50]	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6/10	Good
Gerage et al. [48]	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10	Fair
Millar et al. [58]	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	5/10	Fair
Stiller-Moldovan et al. [64]	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	5/10	Fair
Kingsley et al. [47]	No	Yes	Yes	No	No	No	Yes	No	Yes	Yes	5/10	Fair
Karavirta et al. [61]	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4/10	Fair
Hu et al. [46]	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10	Fair
Takahashi et al. [45]	No	No	Yes	No	No	No	Yes	No	Yes	Yes	4/10	Fair
Heffernan et al. [60]	No	No	Yes	No	No	No	No	No	Yes	Yes	3/10	Poor
Figueroa et al. [44]	No	No	No	No	No	No	Yes	No	Yes	Yes	3/10	Poor
Heffernan et al. [43]	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	5/10	Fair
Madden et al. [42]	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4/10	Fair
Cooke & Carter [41]	No	No	Yes	No	No	No	Yes	No	Yes	Yes	4/10	Fair
Selig et al. [40]	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	6/10	Fair
Taylor et al. [39]	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4/10	Fair
Van-Hoof et al. [59]	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10	Fair



(a)

Study or Subgroup	RT Mean	RT SD	RT Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Cooke & Carter, 2005	63	9.8	12	64	12	10	20.1%	-0.09 [-0.93, 0.75]
Gambassi et al., 2016	27.5	3.1	13	24.6	2.8	13	20.2%	0.95 [0.13, 1.77]
Gerage et al., 2013	20	8	15	30	45	14	20.7%	-0.31 [-1.04, 0.43]
Heffernan et al., 2007	87.2	8.9	14	87.2	9.5	14	20.7%	0.00 [-0.74, 0.74]
Madden et al., 2006	115.3	0.4	14	118.6	1.5	14	18.3%	-2.92 [-4.03, -1.81]
Total (95% CI)			**68**			**65**	**100.0%**	**-0.42 [-1.46, 0.61]**

Heterogeneity: Tau² = 1.21; Chi² = 31.11, df = 4 (P < 0.00001); I² = 87%
Test for overall effect: Z = 0.80 (P = 0.42)

(b)

Study or Subgroup	RT Mean	RT SD	RT Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Madden et al., 2006	36.1	5.2	14	36.5	0.8	14	27.2%	-0.10 [-0.85, 0.64]
Takahashi et al., 2009	18.28	13.2	9	18.16	4	8	21.7%	0.01 [-0.94, 0.96]
Gerage et al., 2013	17.17	7.4	15	13.36	7.5	14	27.2%	0.50 [-0.24, 1.24]
Gambassi et al., 2016	24	4.5	13	19	2.5	13	23.9%	1.33 [0.47, 2.19]
Total (95% CI)			**51**			**49**	**100.0%**	**0.43 [-0.20, 1.05]**

Heterogeneity: Tau² = 0.23; Chi² = 6.94, df = 3 (P = 0.07); I² = 57%
Test for overall effect: Z = 1.35 (P = 0.18)

(c)

Study or Subgroup	RT Mean	RT SD	RT Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Takahashi et al., 2009	18.28	13.2	9	18.16	4	8	29.7%	0.01 [-0.94, 0.96]
Gerage et al., 2013	17.17	7.4	15	13.36	7.5	14	37.5%	0.50 [-0.24, 1.24]
Gambassi et al., 2016	24	4.5	13	19	2.5	13	32.8%	1.33 [0.47, 2.19]
Total (95% CI)			**37**			**35**	**100.0%**	**0.63 [-0.09, 1.34]**

Heterogeneity: Tau² = 0.21; Chi² = 4.27, df = 2 (P = 0.12); I² = 53%
Test for overall effect: Z = 1.71 (P = 0.09)

Fig. 2 Results of the meta-analysis and forest plots for time domain HRV indices in healthy individuals. **a** mean NN, **b** SDNN, **c** RMSSD. *SD* standard deviation; *CI* confidence interval; *RT* resistance training; *HRV* heart rate variability; *mean NN* mean of N–N intervals; *SDNN* standard deviation of N–N intervals; *RMSSD* root mean square of successive differences between adjacent R-R intervals

similar, an analogous trial [60] by these authors showed no changes in fractal components of HRV. Different non-linear HRV indices were used by the former studies, indicating that not all non-linear HRV measures are equally sensitive to trace exercise-induced changes in ANS. Another RCT on healthy middle-aged adults [46] also showed enhanced vagal cardiac control during sub-maximal exercise post-RT. These findings were associated with reduced blood lactate concentrations during sub-maximal exercise bouts, suggesting a role of lactate in training-induced changes in cardiac vagal tone. One study [41] evaluating healthy young men indicated that an 8-week high-intensity RT was unable to produce significant changes on resting vagal cardiac control or cardio-vagal BRS. Overall, these investigations on young and middle-aged individuals indicated that RT might lead to significant positive changes in cardiac autonomic control, which may be tracked by specific non-linear HRV measures. Moreover, the non-significant findings in some of these studies [41, 60] may also be attributable to the healthy young population not presenting any autonomic dysfunction at baseline, which thus may have less scope for improvement or produce only small changes if tracked by conventional linear measures of HRV; however, improvements may be identified by specific non-linear HRV measures. Surprisingly, a very recent RCT comparing two different modes of RT (clustering versus multi-sets) illustrated positive changes in linear measures (increase in RMSSD) of cardiac autonomic control at rest after 8 weeks of RT in healthy young adults. These findings may have been a result of the inclusion of resistance-trained individuals, which indicates that prior exposure to RT may make healthy individuals more responsive to training.

Most studies on healthy participants involved older adults. The earliest clinical trial was by Madden et al. [42], which investigated the effect of endurance and RT on resting HRV in healthy elderly women. Endurance training was able to increase both time and frequency domains of HRV, which are indicative of vagal activity (RMSSD, HF power), while RT produced no change in HRV variables after 6 months. However, in this study, RT was given at high intensity (85% 1 RM, 5 days/week) and it is important to note that previously high-intensity exercise could not positively influence HRV [41]. The post-RT increase in arterial stiffness might have resulted in decreased BRS, which would have contributed to non-significant changes in HRV parameters in the RT group, as

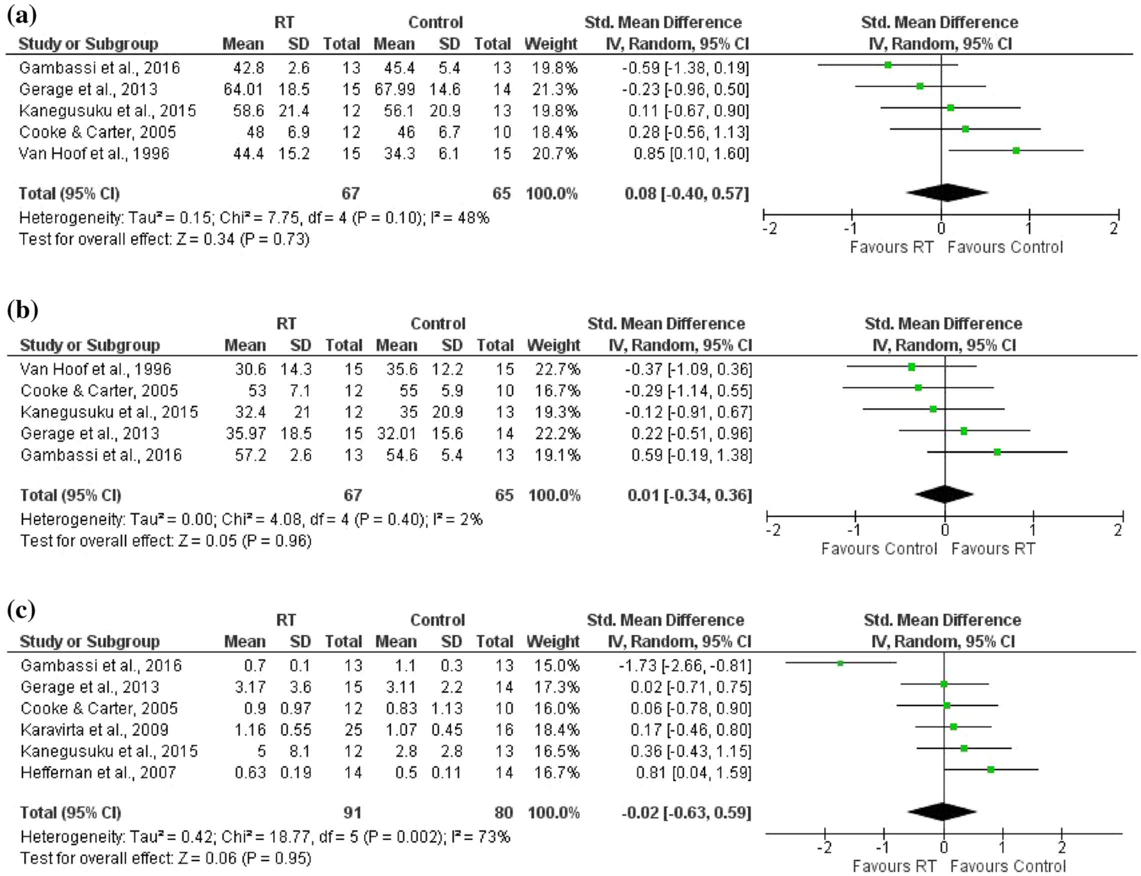


Fig. 3 Results of the meta-analysis and forest plots for frequency domain indices of HRV in healthy individuals. **a** LFnu power, **b** HFnu power, and **c** LF/HF ratio. *SD* standard deviation; *CI* confidence interval; *RT* resistance training; *HRV* heart rate variability; *LF* low frequency; *HF* high frequency; *LF/HF ratio* ratio of low- and high-frequency power; *nu* normalized units

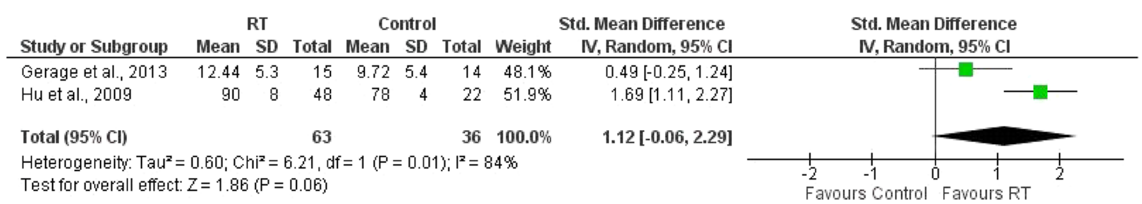


Fig. 4 Results of the meta-analysis and forest plot for non-linear HRV measure, SD1 in healthy individuals. *SD* standard deviation; *CI* confidence interval; *RT* resistance training; *HRV* heart rate variability; *SD1* standard deviation of instantaneous beat-to-beat N–N interval variability

it has been previously shown that high-intensity RT leads to increased arterial stiffness [74]. However, it must be underlined that RT showed no significant positive changes in HRV variables compared to controls, which conversely showed deterioration in HRV measures. Similarly, another study [48] showed no effect of 12 weeks of moderate to high-intensity RT on resting cardiac autonomic control of healthy elderly post-menopausal women despite reduction in systolic blood pressure (BP). The reasons behind unaltered resting cardiac autonomic control after RT were speculated to be lower exercise volume used in this study since adaptations in ANS are exercise volume-dependent [75]. Furthermore, studies investigating the effect of RT (progressed up to 85% of 1 RM over 21 weeks) separately on elderly men [61] and women [62] demonstrated no effect of RT on cardiac autonomic control at rest and during exercise. Furthermore, Takahashi et al. [45] evaluated the effect of 12 weeks of eccentric strength training (EST) of knee flexors and extensors on HRV during submaximal isometric exercise in healthy elderly men and found no significant changes in the RMSSD index after 12 weeks. Although there were no changes in the RMSSD

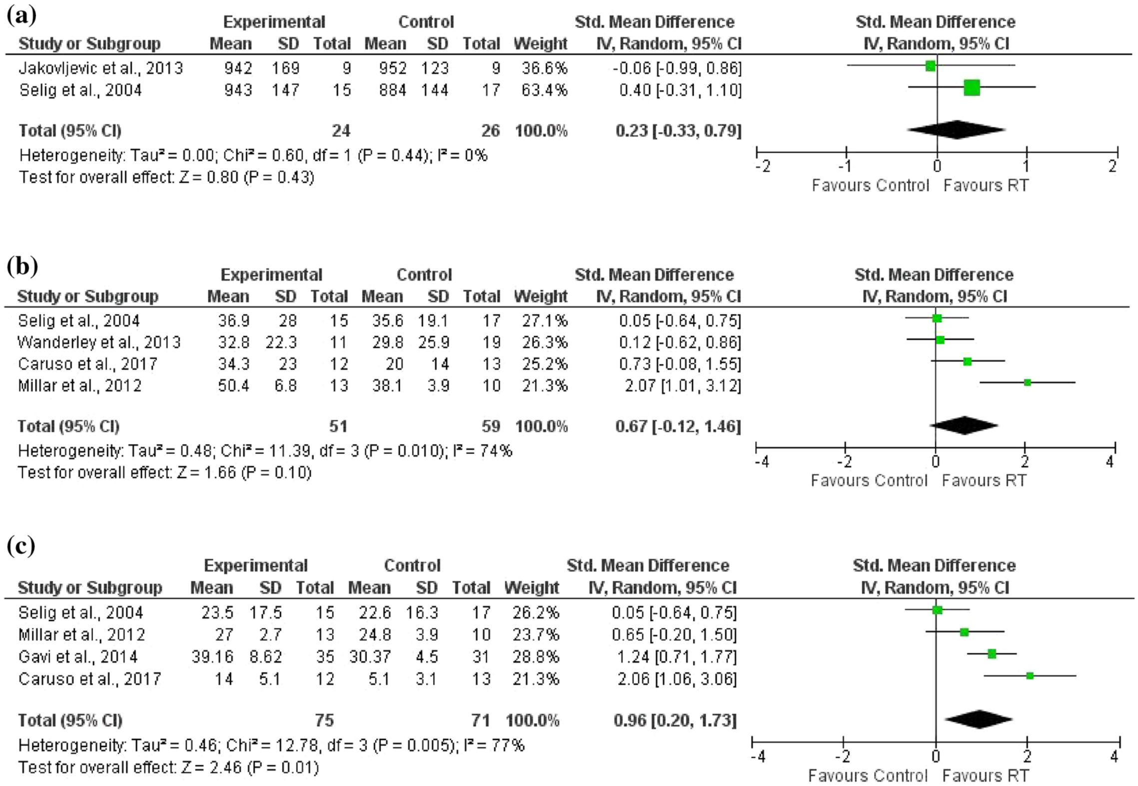


Fig. 5 Results of meta-analysis and forest plots for time domain HRV indices in diseased individuals. **a** Mean NN, **b** SDNN, and **c** RMSSD. *SD* standard deviation; *CI* confidence interval; *RT* resistance training; *HRV* heart rate variability; *mean NN* mean of N–N intervals; *SDNN* standard deviation of N–N intervals; *RMSSD* root mean square of successive differences between adjacent R-R

index post-EST, the study was performed on a small sample ($n = 17$) and did not provide any information on resting HRV measures, which exemplify resting cardiac autonomic control [45]. None of the measures of sympathetic nervous system (SNS) activity were considered. Training might have led to changes in SNS markers and sympathetic withdrawal might have occurred, which is also indicative of cardiovascular health, but no definitive conclusions can be drawn as no such variable was studied. Furthermore, another study examining healthy older adults [52] and an earlier investigation [59] on sedentary men of unknown age also demonstrated insignificant findings in response to high-intensity RT (70–90% of 1 RM). The findings on healthy elderly individuals were quite consistent and led to speculation that the ANS of older individuals was less responsive to change than younger adults for the same training stimulus [76], which indicates that deterioration of physiological regulatory mechanisms due to aging may impair the ability of the cardiovascular regulatory system to adapt to different physiological stimuli, such as exercise [77, 78]. Surprisingly, recent evidence on healthy elderly post-menopausal women [53] suggests a positive effect of moderate-intensity RT on resting HRV after 12 weeks accompanied by a reduction in body fat content. Thus, RT-induced positive adaptation in HRV may be dependent on changes in body composition [79, 80]. Furthermore, the positive findings in this study indicate that previous studies failed to demonstrate any positive change in cardiac autonomic control likely because they utilized high-intensity RT protocols, which may not be sufficiently effective to modulate the deteriorated ANS of these individuals and that moderate-intensity RT may be more suitable. However, these inferences require evidence from further studies investigating the effects of moderate-intensity RT on cardiac autonomic control in older individuals.

Given the literature on the effects of RT on cardiac autonomic control in healthy individuals and the majority of studies showing lack of positive change in cardiac autonomic control post-RT, there may be less impairment in the cardiac autonomic control of healthy participants and, thus, there was less scope for improvement, and specifically for the elderly, a reduced “trainability” of their ANS [45], which makes it less sensitive to RT. Nonetheless, four studies [43, 46, 53, 63] were still able to prove the effectiveness of RT on cardiac autonomic function. However, the meta-analysis did not reveal significant positive changes in any of the HRV indices post-RT in healthy individuals (Figs. 2, 3, 4).

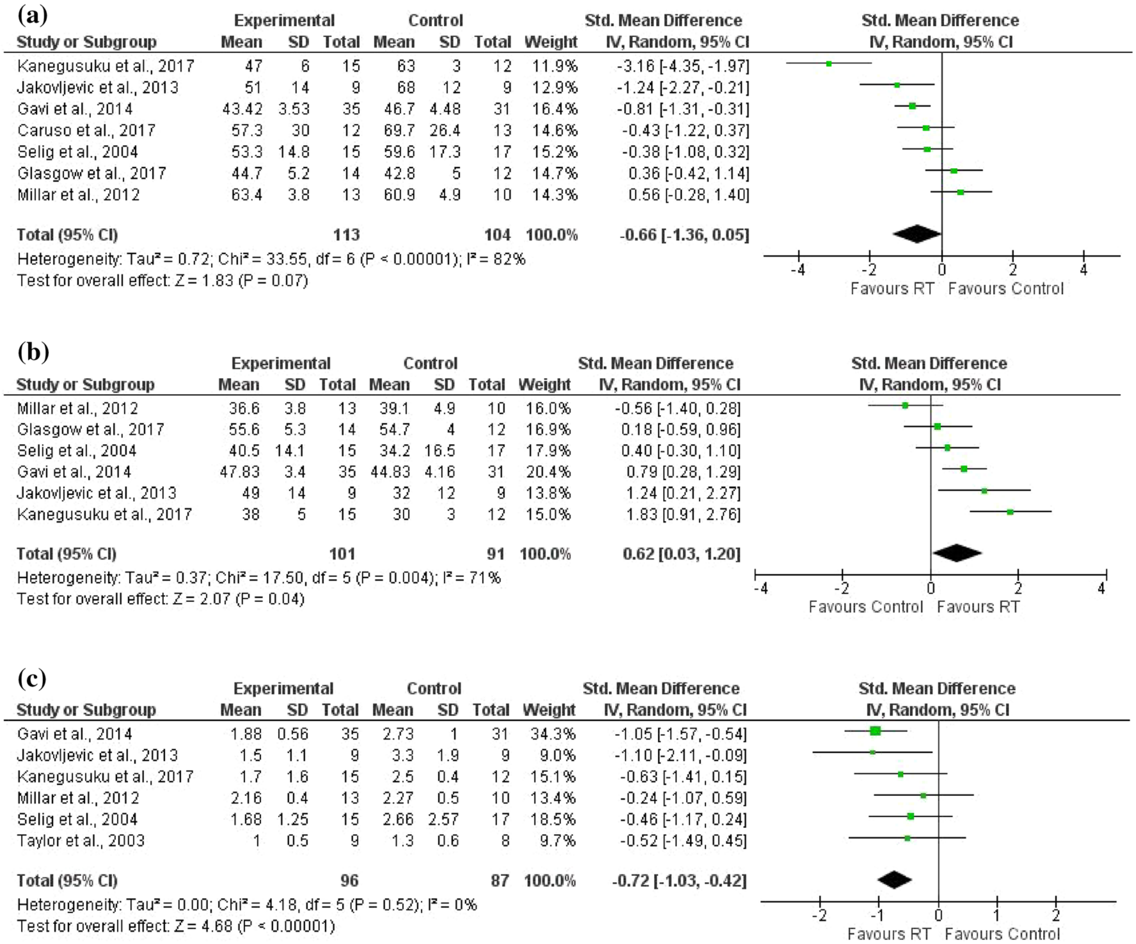


Fig. 6 Results of meta-analysis and forest plots for frequency domain indices of HRV in diseased individuals. **a** LFnu power, **b** HFnu power, and **c** LF/HF ratio. *SD* standard deviation; *CI* confidence interval; *RT* resistance training; *HRV* heart rate variability; *LF* low frequency; *HF* high frequency; *LF/HF ratio* ratio of low- and high-frequency power; *nu* normalized units

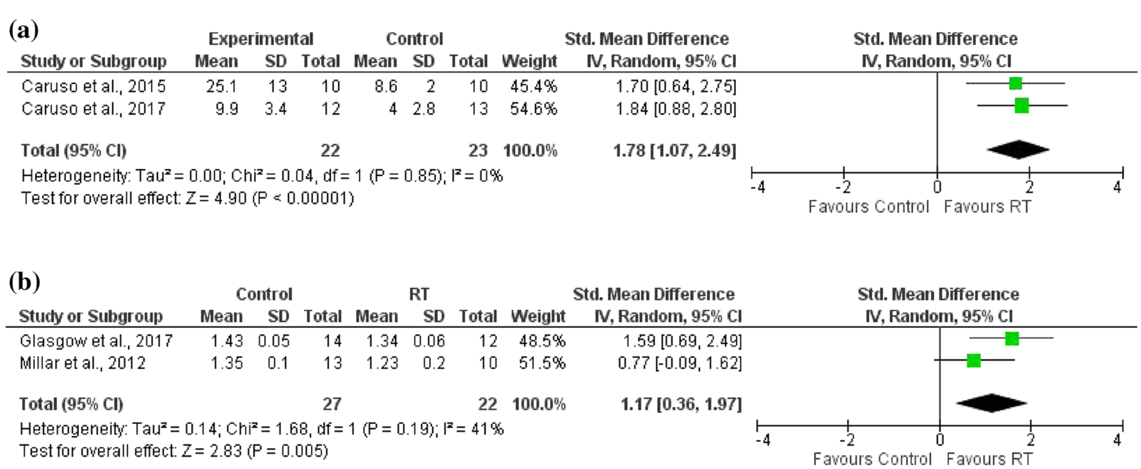


Fig. 7 Results of meta-analysis and forest plot for non-linear HRV indices. **a** SD1 and **b** sample entropy in diseased individuals. *SD* standard deviation; *CI* confidence interval; *RT* resistance training; *HRV* heart rate variability; *SD1* standard deviation of instantaneous beat-to-beat N–N interval variability

Diseased individuals

Low-intensity (30% of MVC) isometric RT on resting HRV in hypertensive older adults showed an improvement in sympatho-vagal balance and a reduction in arterial BP after 10 weeks [39]. Isometric exercise may have induced an increase in forearm blood flow leading to reduced peripheral resistance. Together with baroreflex resetting after isometric RT, these might represent the physiological mechanism underlying the observed improvement in BP and HRV. Nevertheless, this is merely speculative based on previous studies [81]. Other studies examining isometric RT at 8 weeks have shown insignificant changes in linear HRV measures in hypertensive patients on pharmacotherapy [58, 64], which may be explained by the absence of autonomic dysfunction in these individuals due to drug-controlled BP and is contrasted against newly diagnosed, treatment-free hypertensive's who undoubtedly had more scope for improvement in cardiac autonomic function [39]. Moreover, since Taylor et al. [39] executed the intervention program for 10 weeks in comparison to other studies [58, 64] that implemented isometric RT for 8 weeks, it is possible that the duration of training (8 versus 10 weeks) plays a role in inducing autonomic adaptations in patients with hypertension. Nevertheless, other studies [58] have reported significant improvement in non-linear measures of HRV, which again shows that these complexity measures are more sensitive for detecting training-induced cardiac autonomic adaptations. A subsequent study [40] also showed similar positive changes in CHF patients followed by 12 weeks of whole-body RT. These adaptations in autonomic cardiac control were accompanied by enhanced forearm blood flow, which supports the hypothesis stated by Taylor et al. [39] that vascular function may have a role in modulating ANS. Furthermore, a clinical trial on FM women [47] observed no changes in autonomic modulation at rest or after acute leg resistance exercises following 12 weeks of RT. Despite the absence of positive change in HRV post-RT, a few considerations should be made before drawing any inferences. First, this study constituted a non-randomized design using a healthy control group. Second, the FM women in this study had similar autonomic function at baseline as the participants in healthy control group, which suggests that these FM women were relatively fit and had less scope for improvement. However, previously, the same authors [44] showed positive changes in HRV after a 16-week RT. However, the women in this study had some degree of autonomic dysfunction at baseline in contrast to the FM sample in the Kingsley et al. [47] study, which suggests that the status of cardiac autonomic function before training may influence responses to RT. Moreover, in accordance with Kingsley et al. [47], two studies [57, 65] have also shown no changes in cardiac autonomic control post-RT despite the presence of autonomic dysfunction before training, which warrants further research on this patient population.

Eight weeks of moderate-intensity RT (50–70% of 1 RM) induced improvement in sympatho-vagal balance of NAFLD patients [50]. Although, there were no group differences for HRV and BRS at rest after RT, non-significant positive changes were observed only in the RT group, suggesting that prolonged training might have elicited a significant difference. Changes observed in HRV and BRS measures were accompanied by a reduction in the resting HR post-RT, suggesting that vagal modulation was likely responsible. Interestingly, a clinical trial [49] investigated the effects of 8 months of moderate-intensity AT and RT on cardiac autonomic function of community-dwelling elderly patients with various co-morbidities (hypertension, hyperlipidemia, diabetes). Again, statistically insignificant increase was observed for HF power of HRV in both groups along with a reduction in systemic inflammation, indicating the involvement of immunomodulatory activity of the vagus nerve, whereby the activation of the vagal efferent arm results in regulation of cytokine production (cholinergic anti-inflammatory pathway) [82]. Significant changes in HRV indices were absent after either type of training, likely due to the heterogeneous population or because only two HRV measures (SDNN and HF power) were examined that might not adequately present a clear picture of cardiac autonomic status. A recent study [56] involving PCOS has claimed that a 4-month RT was ineffective in inducing significant positive changes in cardiac autonomic control.

Recently, three good-quality RCTs [51, 54, 55] were conducted to elucidate the effects of RT on cardiac autonomic control. Two of these trials were performed by the same authors on CAD patients [51, 54]. The authors investigated the effects of an 8-week low-intensity (30% of 1 RM) high-repetition leg press RT on autonomic control of the heart. Both studies reported positive results with a significant increase in HRV indices indicative of vagal modulation during constant load resistance exercise [54] and at rest [51]. These changes in autonomic function were accompanied by a reduction in resting heart rate (HR) and blood lactate levels during sub-maximal exercise [54], which again suggests RT-induced vagal modulation. Mechanisms reported to cause RT-induced autonomic adaptations included changes in baroreflex [83, 84] and modifications in cardiopulmonary reflexes [83]. However, the results of these clinical trials should be considered in light of their limitations. Both studies consisted of an active control group undergoing AT, although the participants in the RT group also underwent regular aerobic cardiac rehabilitation similar to patients in the control group. Furthermore, the intensity, duration, or frequency of aerobic exercise for any of the patients in the control and RT groups was not controlled, introducing a potential variability in the training program, although it was present for both the groups and thus it may be ignored [51]. A non-exercise control group would have strengthened these findings; however, adaptations seems to be mediated by RT only since in the control group, reduction in vagal modulation (decreased RMSSSD) was seen. Another good-quality study conducted on patients with Parkinson's disease [55] demonstrated positive changes in almost all measures of HRV after 12 weeks of moderate-intensity RT. In addition to the beneficial changes in HRV, favorable changes were also observed in cardiovascular autonomic reflex tests. Reduction in oxidative stress due to RT or increases in brain-derived neurotrophic factor levels [85] in areas of cardiovascular control were the probable mechanisms proposed by this study. The most recent trial [66] conducted on patients with metabolic syndrome has also demonstrated significant improvement in non-linear measures of autonomic modulation after both conventional and functional RT.

In summary, the majority of studies on clinical populations demonstrated significant positive changes in cardiac autonomic control after RT except for seven studies [47, 49, 50, 56, 57, 64] which had the methodological limitations discussed above. Systemic analysis revealed a significant positive effect of RT on linear measures of HRV such as RMSSD, HFnu power, and the LF/HF ratio (Fig. 5, 6, 7). Standardized mean differences showed significant effects of RT on non-linear HRV indices such as SD1 (SMD 1.78, 95% CI 1.07, 2.49, $p < 0.00001$) and sample entropy (SMD 1.17, 95% CI 0.36–1.97; $p = 0.005$) in diseased individuals (Fig. 6). RT may cause enhanced vagal activity (increase in RMSSD and SD1) along with improved sympatho-vagal balance (reduction in the LF/HF ratio) in the clinical population. Moreover, it may lead to enhanced complexity in HR dynamics (increase in sample entropy), which means cardiovascular risk is reduced to a great extent in diseased participants with impaired autonomic function.

Effect of age and sex on RT-induced cardiac autonomic adaptations

Due to the variable number of studies on different age groups and sex, definite conclusions on the differential effect of RT with aging would be difficult; however, some inferences can still be drawn. Fifty percent (2 of 4) of studies on young adults showed a significant positive autonomic response to RT; conversely, only 42.8% studies (3/7) on middle-aged adults were able to demonstrate significant autonomic improvements post-RT. Findings of studies on older adults were moderately more complex, since when analyzed in combination (healthy and diseased), only 14.2% of studies showed significant positive changes in cardiac autonomic control after RT. When stratified by the presence or absence of pathology, results differed greatly with 75% of the studies involving diseased older adults demonstrating significant improvement in cardiac autonomic control after RT. Older adults may be responsive to RT when in the presence of an existing pathology; however, the underlying mechanism is unknown. The implementation of high-intensity RT in studies involving healthy older adults was probably unable to modulate cardiac autonomic control in these subjects, in contrast to the utilization of low- or moderate-intensity RT in studies on a clinical older population. Although these findings are inconclusive, these may nonetheless provide some indication regarding the importance of dose of RT in modulating autonomic control that should be considered in future studies. Furthermore, when studies on all three age groups (young, middle-aged, and older) were examined in combination (healthy and diseased together), young adults were found to be more responsive to RT, which indicates that physiological responsiveness to exercise training declines with age [77, 78]. With regard to sex differences, half (5/10) of the studies involving men showed significant positive changes in cardiac autonomic control after RT; however, 22.2% of the total studies on women (2/9) showed improvement in the autonomic control of the heart with RT, which indicates that men were more responsive to RT. Women may thus have better cardiac autonomic health than their male counterparts [86], which certainly creates less scope for improvement in these subjects. This differential responsiveness of men and women to RT is based on simplistic observation of the present review and thus should be verified by further sex-based studies to identify appropriate exercise interventions for both sexes.

Possible physiological mechanisms behind cardiac autonomic adaptations by RT

After reviewing different clinical trials on human participants, some physiological mechanisms may be speculated to cause adaptations in cardiac autonomic control. Firstly, enhanced responsiveness of the baroreflex and improved baroreflex homeostasis after RT have been suggested by literature on human [40] and on animal models [87–90] as mechanisms for improving cardiac autonomic control. Second, vascular adjustments caused by the RT such as increased forearm blood flow [40] and increased nitric oxide (NO) bioavailability [89] may potentially contribute to enhanced autonomic control. Particularly important is the baroreflex-NO axis, which works with a positive feedback mechanism decreasing cardiac and vascular sympathetic modulation [89]. Some studies in this review also suggested that changes in autonomic function may be partly mediated by changes in body composition (reduction of body fat content) [53] and enhanced lactate tolerance [46] post-RT.

Strengths and limitations

The present review has some limitations. First, along with the RCTs, the authors included cross-over controlled and quasi-experimental studies to better represent the existing literature; however, since randomization is an extremely important component of clinical trials, their inclusion might have confounded the results of the review. Second, due to inadequate data reporting [descriptive data were either reported in logarithmic form or were in different (ms^2) units], three studies [47, 62, 63] were excluded from the meta-analysis despite being of fair quality, Third, because of the heterogeneity in reporting of data, not all 21 studies included in the meta-analysis provided information on each HRV variable; therefore, the authors included measures of autonomic function that were frequently reported (at least twice) in multiple studies (SDNN, RMSSD, mean NN, LFnu power, HFnu power, LF/HF ratio, SD1, sample entropy) for the meta-analysis. If, for example, values of spectral measures were not reported as normalized units, the authors did not convert data accordingly, but such data were excluded from the meta-analysis. Considering these limitations, the findings of this meta-analysis should be interpreted with caution. Despite these limitations, the present review has some potential strengths. First, this was a large review rigorously evaluating 28 clinical trials on the effect of RT on cardiovascular autonomic control in healthy and diseased human participants providing extensive insight from a large body of evidence in a single document. Second, the findings of this review might help researchers and clinicians to formulate RT regimens for both healthy and patient populations. Last, this review precisely outlines limitations in the existing literature and proposes extensive opportunities for future research on RT and cardiac autonomic control.

Recommendations for future research

Well-controlled adequately sampled high-quality RCTs should be conducted on clinical populations, which present autonomic dysfunction, such as diabetes mellitus, metabolic syndrome, and myocardial infarction (MI) [91–93]. Furthermore, the present review was unable to formulate an optimal dose of RT that might lead to positive adaptations in cardiac autonomic control. Therefore, future studies should focus on the effects of different resistance exercise doses to better formulate exercise standards for RT-mediated autonomic adaptation. Moreover, there is strong need to study the mechanisms behind RT-mediated changes in cardiac autonomic control in humans, and future research should consider this gap in the currently available literature. Indications regarding the mechanisms underlying adaptations may be taken from similar studies published on animal models [87–90] and outcomes assessing baroreflex mechanisms, NO mechanisms, and vascular function should be incorporated in human studies to support their findings. Moreover, very few studies have examined autonomic control by non-linear HRV, BRS, and post-exercise HRR and studies in the future should counter these limitations, as these data will provide a holistic interpretation of autonomic function. More specifically, including non-linear HRV measures to trace cardiovascular autonomic control post-RT would be beneficial as this review indicated that these complex non-linear measures are more sensitive than conventional linear measures to identify RT-mediated adaptations in cardiac autonomic control.

Conclusions

The present review demonstrated that RT has minimal effects on conventional linear measures of HRV in healthy individuals. However, in patient populations, RT (at moderate and low intensities) modulates the autonomic control of the heart as observed by both linear and non-linear measures of cardiac autonomic control. Although deriving a definite conclusion would be difficult at this stage due to the heterogeneity in the available data, this rigorous systematic analysis of existing evidence allows one to conclude that RT is a form of exercise which likely has minimal effects on cardiac autonomic control of healthy individuals, but it does result in positive adaptations in the cardiovascular autonomic control of diseased individuals. However, in the future, there is a strong need for high-quality studies in both healthy and clinical populations focusing exclusively on RT to precisely elucidate its effect on cardiac autonomic control.

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Compliance with ethical standards

Conflicts of interest The authors declare they have no conflicts of interest.

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