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REVIEW ARTICLE

The effectiveness of vigorous training on cardiorespiratory fitness in persons with spinal cord injury: a systematic review and meta-analysis

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DESIGN: Systematic review and meta-analysis.
BACKGROUND AND PURPOSE: Traditional forms of upper-body moderate intensity exercise consistently provide little cardiovascular benefits for persons with spinal cord injury (PwSCI). Explorations of new training methods are vital to improve cardiovascular fitness among PwSCI. This study sought to evaluate the effectiveness of vigorous training on cardiorespiratory fitness in PwSCI.
METHODS: Database search through PubMed, Web of Science, Scopus, SportDiscus, and Cumulative Index of Nursing and Allied Health Literature (CINAHL) was conducted from the databases' inception to November 2020 to identify relevant exercise studies with PwSCI. Two independent reviewers screened articles for inclusion. Data were extracted from included studies and methodological quality evaluated.
RESULTS: Sixteen trials (eight pre-post trials and eight controlled trials [CTs]) with a total of 145 participants were analyzed. Results from pre-post studies revealed significant improvements in cardiorespiratory fitness following high-intensity interval training (HIIT) (Peak Oxygen Uptake [VO_{2peak}], standardized mean difference [SMD] = 0.81; 95% CI 0.23–1.39; $P < 0.01$ and Peak Power Output [PPO], SMD = 0.91; 95% CI 0.32–1.5; $P < 0.01$) and circuit resistance training (CRT) (VO_{2peak}, MD = 0.38; 95% CI 0.19–0.57; $P < 0.01$ and PPO, MD = 20.17; 95% CI 8.26–32.08; $P < 0.01$). Meta-analysis of CTs did not demonstrate significant improvements in cardiorespiratory fitness following vigorous training interventions in comparison to lower intensity training interventions.
CONCLUSION: Evidence from HIIT and CRT interventions suggest benefits for cardiovascular functions; however, vigorous training was not more beneficial than other forms of endurance training. More CTs are needed to better understand the effectiveness of vigorous training on cardiorespiratory fitness in PwSCI.

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INTRODUCTION

As nearly 18,000 new traumatic spinal cord injury (SCI) cases occur each year in the United States in predominantly young adults, the overall population of persons with chronic SCI (PwSCI) continues to grow and currently exceeds 300,000 [1]. Unfortunately, as the prevalence of SCI grows, so do rates of cardiovascular disease (CVD) [2]. Complications related to CVD (i.e., heart attack, stroke, and heart failure) has recently emerged as the focal cause of premature death in PwSCI [2], becoming a worldwide epidemic and health concern. Even with the development and revision of physical activity guidelines for PwSCI (PAG-SCI) to combat the grim cardiopulmonary outcomes related to SCI [2], guidelines have not appeared to sufficiently improve this population's cardiovascular heath [3].

Several reasons could explain the dismal improvements associated with the PAG-SCI [3]. First, the PAG-SCI recommend a minimum of 30 min of moderate intensity aerobic exercise three times per week (90 min/week), roughly 66% lower than recommendations by the American College of Sport Medicine (ACSM) for the general population [4]. ACSM recommendations are also built around lower body exercises (i.e., running, swimming, and biking), while PAG-SCI targets the upper body. As the legs elicit a greater cardiovascular response than the arms during exercise [5], it seems unlikely that the PAG-SCI—which recommend reduced volumes for less efficient exercises—would elicit positive outcomes. Many PwSCI are also limited in overall cardiac output capacity [6], making prolonged exercise unsustainable and central cardiovascular adaptations unlikely. As the PAG-SCI prescribes an extensive amount of prolonged exercise, it makes sense that minimal cardiovascular improvements accompany these guidelines [3]. Attention must be shifted to exercise modes calibrated to the unique physiology of persons with SCI to maximize health benefits [5, 6].

Specifically, we must adjust upper limb-based exercise to efficiently stimulate the cardiovascular system without increasing upper limb injury risk. As vigorous exercise typically requires less time and incorporates more periods of recovery than traditional forms of aerobic training, this exercise method may offer a

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solution. Rest/recovery periods built within several vigorous protocols may also reduce injury risk by allowing active soft tissue to recover in between periods of physical exertion [7, 8], enabling individuals to reach higher workloads compared to those of prolonged, continuous movement.

Exercise at a vigorous intensity can be defined as activity which elicits a training response >70% Peak Heart Rate (HR_{peak}), 60% Heart Rate Reserve, 64% Peak Oxygen Uptake (VO_{2peak}), or 14 Rate of Perceived Exertion (RPE) [4, 9]. In the general population, vigorous training has exhibited comparable benefits to moderate intensity exercise in just half the time [9, 10]. Vigorous intensity exercise provokes peripheral mitochondrial adaptations, which may compensate for the central cardiovascular inefficiencies of upper extremity exercise in PwSCI [5, 6]. Recently, several researchers have examined various types of vigorous training protocols like circuit resistance training (CRT) [11]—resistance training broken up with low intensity arm ergometry—and high-intensity interval training (HIIT)—explosive anaerobic bursts broken up with low intensity exercise [12]—exhibiting superior cardiovascular benefits to moderate intensity exercise [11, 12].

Vigorous intensity exercise presents a potentially promising alternative to traditional forms of endurance exercise in PwSCI. Systematic reviews in the able-bodied population show superior cardioprotective benefits following vigorous intensity exercise versus moderate intensity exercise [13, 14]. However, in PwSCI, recent systematic reviews have grouped moderate and vigorous intensity exercise together to explore PAG-SCI efficacies [2, 15]. Therefore, this will be the first systematic review evaluating the effectiveness of vigorous intensity training compared to moderate intensity training in PwSCI. We predict that vigorous intensity protocols such as HIIT will lead to the greatest improvements in VO_{2peak} and peak power output (PPO) as the incorporation of recovery periods will enable PwSCI to maximize exercise bursts within training sessions.

METHODS

Protocol and registration

The Cochrane Handbook [16] was followed to conduct the systematic review and meta-analysis and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis [17] checklist was used to guide the reporting. The study protocol was registered with the International Prospective Registry of Systematic Reviews (PROSPERO): CRD 42020171181.

Data sources and search strategy

The databases search on PubMed, Web of Science, Scopus, SportDiscus and Cumulative Index to Nursing and Allied Health Literature (CINAHL) was conducted from their inception to April 2020 and updated in November 2020 to identify relevant exercise studies in PwSCI. In the PubMed database, we used MeSH terms combined with keywords including spinal cord injuries, paraplegia, tetraplegia, cardiorespiratory fitness, CVDs, cardiovascular, physical capacity and oxygen consumption, HIIT, circuit training, training intensity, high-intensity hybrid training, high-intensity virtual reality, physical education, and training. Search strategies were adjusted for each database. Filters were implemented to exclude animal studies and reviews. See Supplementary Appendix I for full search strategies.

Two review authors (KD and JP) independently screened relevant titles and abstracts to tag potential articles in which PwSCI were engaged in vigorous intensity interventions and cardiovascular fitness markers such as VO_2, heart rate, and power output were measured. If articles fulfilled these initial criteria, the full text of the article was obtained. Then, two review authors (AA and JP) independently screened articles using the preestablished eligibility criteria to identify the trials analyzed in this review. Ancestor and descendant searching were utilized to find other relevant studies which qualified for inclusion. Any discordance was resolved through discussion with a third author (LA).

Eligibility criteria

Inclusion and exclusion criteria were based on the Participants, Interventions, Comparators, Outcomes, and Study designs framework.

Participants. We included studies involving adults (≥18 years old) with SCI, regardless of time since injury, level, and completeness of injury. We excluded studies involving individuals with other neurological or cardiometabolic disease.

Interventions. We included studies examining various forms of vigorous, aerobic and resistance training. This included training modes such as HIIT, sprint interval training (SIT), CRT, respiratory muscular endurance training (RMET) and vigorous continuous training (VICT). HIIT protocols consisted of explosive anaerobic bursts broken up with periods of low intensity exercise. SIT consisted of maximal exercise broken up with rest. CRT consisted of resistance training broken up with low intensity arm ergometry. RMET consisted of a 30 min continuous bout of exercise to exhaustion. VICT consisted of a continuous bout of high-intensity exercise. We excluded studies which only examined the effects of moderate and light forms of exercise, defined by ACSM as 30–59% Heart Rate Reserve, 37–63% VO_{2peak}, 57–76% HR_{max}, and 9–13 RPE [4].

Comparators. We included studies comparing:

Vigorous intensity training modes versus control (light-to-moderate intensity training or routine training patterns).

Pre-post vigorous intensity training modes with no control group.

We considered conventional moderate intensity continuous training (MICT) to be continuous exercise in accordance with ACSM and American Heart Association guidelines [4, 9], which describes moderate intensity as exercise within 40–59% Heart Rate Reserve, 64–70% HR_{max}, 46–63% VO_{2max}, or RPE 12–13.

Outcomes. We chose to evaluate training adaptations to VO_{2peak}, PPO, and peak minute ventilation (VE_{peak}). These outcome measures are common measurements of maximal exercise capacity and can be used to predict an individual's CVD risk [4]. VO_{2peak} is the peak oxygen uptake response during a graded exercise test upon volitional fatigue and test termination. PPO is the maximum workload sustained during the graded exercise test when VO_{2peak} occurs. VE_{peak} is the maximum volume of air expired during the VO_{2peak} assessment. Studies were included if they clearly stated that VO_{2peak}, PPO, or VE_{peak} were measured during a maximal exercise test.

Study designs. Both randomized and nonrandomized (i.e., pre-post trials) clinical trials were included in this review. We excluded case study reports and preliminary reports.

All studies were required to be published in English, French, Spanish, or Portuguese. JP and KD identified if studies' participants, interventions, comparators, and study designs met these criteria, with discordances resolved by LA. JP and AS identified the relevant outcomes, with discordances resolved by LA.

Data extraction

Data extracted independently by two reviewers (KD and JP) were consolidated into an Excel spreadsheet table, tailored for this review. Discrepancies were resolved through discussion with a third author (LA). Data extraction included: study ID, study design, intervention comparison (i.e., experimental vs. control conditions), dosage (duration and frequency), participant characteristics (sample size, age, gender, AIS score, injury level), outcome measures related to cardiorespiratory fitness and a summary of the study's main findings related to cardiovascular fitness.

Quality assessment

The Cochrane Risk of Bias Tool was used to assess the selection bias, performance bias, detection bias, attrition bias, reporting bias, and other biases of the included controlled trials (CT). Each study was rated as "high", "low", or "unclear" risk of bias [16]. The Quality Assessment Tool for Before-After (pre-post) Studies with no Control Group was used to assess the pre-post trials [18]. This tool rates the quality of 12 items related to the: (1) study question, (2) eligibility criteria and study population, (3) population of interest representation, (4) eligibility of participants, (5) sample size, (6) intervention clarity, (7) outcome measure clarity, (8) blinding of researchers, (9) follow-up rates, (10) statistical analysis, (11) repeating of outcome measurements, and (12) group-level interventions and individual-level outcome efforts. All 12 items were scored as "yes", "no", "cannot determine" (CD), "not applicable" (NA), or "not reported" (NR). Overall scientific quality of the pre-post trials was further assessed as good, fair, or poor. AA and JP independently assessed all included studies, with consensus reached through discussion with LA.

Statistical analysis

Meta-analysis was performed to pool studies with similar comparisons while also accounting for study differences in training design, dosage, and participant characteristics. All data analysis was conducted using Review Manager version 5.3.5 (Cochrane, London, UK). Changes in mean scores and standard deviation (SD) were extracted from all CTs to estimate the mean effect and 95% CI. In case SD was not reported, it was estimated according to the Cochrane handbook [16]. I^2 was used to determine statistical heterogeneity between studies [16]. Because of low heterogeneity ($I^2 = 0\%$), the fixed effect model (FEM) was used for meta-analysis of CT. When less optimal outcomes were reflected in higher scores, the data were transformed to have a consistent direction indicating optimal clinical outcomes. For pre-post studies included in the meta-analysis, baseline data was compared to post-intervention data. Because of low heterogeneity ($I^2 = 0\%$), FEM analysis was conducted [16]. Mean difference (MD) was used to estimate the effect size when only one outcome measure (e.g., VO_{2peak}) was pooled in a meta-analysis and standardized mean difference (SMD) was used when different outcome measures (e.g., VO_{2peak} and PPO) were pooled together in the same meta-analysis [16].

RESULTS

Search process

The search retrieved 225 articles. One article was found through ancestor and descendant searching. Following the removal of duplicates and screening of titles and abstracts, 23 articles were assessed for eligibility. After further analysis, 16 studies were deemed fully eligible for systematic review inclusion with 13 of these articles included in the meta-analysis. Three CTs by McLeod et al., Fischer et al., and Kressler et al. were not included in the meta-analysis due to incomplete data, unique outcome measures, or study design differences [19–21]. Figure 1 illustrates the stages of study selection.

Characteristics of included studies

Data from the 16 eligible studies are included in Table 1. Eight studies were pre-post trials and the other eight studies were CTs [11, 12, 22–27]. A total of 145 participants with lesion levels from C2-L5 and American Spinal Injury Association Impairment Scale (AIS) A, B, C, and D were studied. Participants were mostly males (83%). Eight studies utilized HIIT [12, 22–24, 27–30], four utilized CRT [11, 21, 25, 26], two VICT [31, 32], one SIT [19], and one RMET

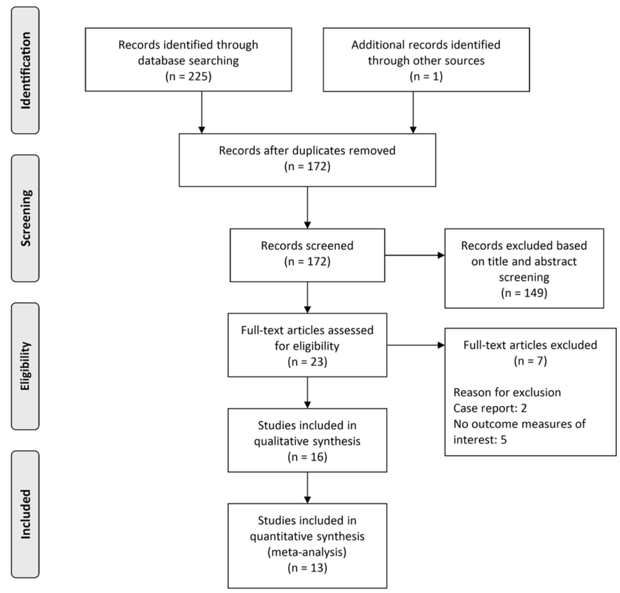

Fig. 1 PRISMA study selection flowchart.

[20]. Two HIIT-based studies incorporated the use of functional electric stimulation of the lower extremities with one of these studies also incorporating virtual reality into the training protocol [23, 24]. The main outcome measures analyzing cardiorespiratory fitness were derived from incremental exercise tests to exhaustion. The cardiorespiratory measures of VO_{2peak}, VE_{peak}, and PPO were analyzed in the meta-analysis.

Quality of studies

Results for the risk of bias assessment for CTs can be found in Table 2. Four of the eight CTs presented with a low risk of bias [19, 20, 31, 32]. Of these studies, two were included in the meta-analysis [31, 32]. McLeod et al.'s and Fischer et al.'s studies were excluded from meta-analysis due to design differences [19, 20]. The most common biases in the CTs were selective reporting bias and "other biases". Results of the quality assessment for the pre-post studies with no control group can be found in Table 3. Overall, three of the eight pre-post studies were rated as having good quality [11, 25, 26], while the other five were rated as having fair quality [12, 22–24, 27].

Effect of vigorous intensity exercise interventions

High-intensity interval training. Figure 2a includes five pre-post design studies examining the effect of HIIT interventions on cardiorespiratory fitness [12, 22–24, 27]. The five studies were rated as having fair overall methodological quality. They were pooled in three meta-analyses (FEM) analyzing VO_{2peak}, VE_{peak}, PPO, and with results expressed as SMD and MD. The analysis of VO_{2peak} revealed a significant difference before and after HIIT (SMD = 0.81; 95% CI 0.23–1.39; $P < 0.01$). Similarly, the analysis of PPO revealed a significant difference before and after HIIT (SMD = 0.91; 95% CI 0.32–1.5; $P < 0.01$). In contrast, VE_{peak} did not show a significant difference. However, the combination of these three meta-analyses showed a statistically significant pre- and post-training difference (SMD = 0.69; 95% CI 0.35–1.04; $P < 0.01$).

Figure 2b includes three CTs that examined the effect of a HIIT intervention compared to MICT or low intensity interval training [28–30]. All three studies presented with a unclear risk of bias. The three were pooled in two meta-analyses analyzing VO_{2peak} and PPO with the results expressed as SMD. The meta-analysis did not show a significant between-group difference for VO_{2peak} (SMD = 0.14; 95% CI −0.73–1.01; $P > 0.05$) or PPO (SMD = 0.09; 95% CI −0.94–1.12; $P > 0.05$).

Table 1. Details of the included studies.

Study, Ref.	Study design	Comparison	Dosage	Participants	Measure of performance/fitness	Main findings
Bougenot et al. [22]	Pre-post study	Exp: HIIT Comp: none	6 weeks 3×/week 45 min	7 individuals, 7 M: 0 F Mean age: 35 ± 13 y (range 21–55 y) AIS A T6–L5	VO_{2peak} VE_{peak} PPO	HIIT significantly increased VO_{2peak} (16%) HIIT did not increase VE_{peak} HIIT (20%) significantly increased PPO
Brurok et al. [23]	Pre-post study	Exp: HIIT Comp: none	7 weeks regular activity (control), followed 8 weeks intervention 3×/week Duration: NR	6 subjects, 6 M: 0 F Mean age: 40 ± 11 y (range 22–53 y) AIS A C7–T9	VO_{2peak} VE_{peak} PPO	HIIT significantly increased VO_{2peak} (25%) HIIT significantly increased VE_{peak} (26%) HIIT significantly increased PPO (25%)
Hasnan et al. [24]	Pre-post study	Exp: HIIT Comp: none	6 weeks 2×/week for 48 min 3×/week for 32 min	8 individuals Mean age: NR	VO_{2peak} PPO	HIIT significantly increased VO_{2peak} (20%) HIIT significantly increased PPO (33%).
Jacobs et al. [11]	Pre-Post Study	Exp: CRT Comp: none	12 weeks 3×/week 40–45 min	10 individuals, 10 M: 0 F Mean age: 39 ± 6 y (range 28–45 y) AIS A T5–L1	VO_{2peak} PPO	CRT significantly increased VO_{2peak} (30%) CRT significantly increased PPO (16%).
Le Foll de Moro et al. [12]	Pre-Post Study	Exp: HIIT Comp: none	6 weeks 3×/week 30 min	6 individuals, 5 M: 1 F Mean age: 29 ± 14 y (range 18–54 y) T6–T12	VO_{2peak} VE_{peak} PPO	HIIT significantly increased VO_{2peak} (36%) HIIT significantly increased PPO (34%) HIIT did not increase VE_{peak}.
Nash et al. [26]	Pre-Post Study	Exp: CRT Comp: none	12 weeks 3×/week 40–45 min	5 subjects, 5 M: 0 F Mean age: 38 ± 4 y (range 34–43 y) AIS A T6–L1	VO_{2peak} PPO	CRT significantly increased VO_{2peak} (30%) CRT significantly increased PPO (30%)
Nash et al. [25]	Pre-Post Study	Exp: CRT Comp: none	16 weeks 3×/week 40–45 min	7 individuals, 7 M: 0 F Mean age: (range 39–58 y) AIS A–B T5–T12	VO_{2peak}	CRT significantly increased VO_{2peak} (10%)
Tordi et al. [27]	Pre-Post Study	Exp: HIIT Comp: none	4 weeks 3×/week 30 min	5 subjects, 5 M: 0 F Mean age: 27 ± 8 y (range 18–40 y) AIS A T6–L4	VO_{2peak} VE_{peak} PPO	HIIT significantly increased VO_{2peak} (19%) HIIT did not significantly increase VE_{peak} HIIT significantly increased PPO (28%)
de Groot et al. [28]	CT	Exp: HIIT Comp: LIIT	8 weeks 3×/week 60 min	6 individuals, 4 M: 2 F Mean age: HIIT—39 ± 2 y and LIIT—52 ± 2 y AIS A–C C5–L1	VO_{2peak} PPO	Both HIIT and LIIT significantly increased VO_{2peak} (50% vs. 17%, respectively) Both interventions significantly increased PPO No significant difference between both groups related to PPO
Gauthier et al. [29]	CT	Exp: HIIT Comp: MICT	6 weeks 3×/week 40 min	9 individuals, 8 M: 1 F Mean age: HIIT—34 ± 3 y (range 31–38 y) and MICT—43 ± 19 y	VO_{2peak} PPO	Neither HIIT or MICT significantly increased any measures or performance or fitness

Table 1 continued

Study, Ref.	Study design	Comparison	Dosage	Participants	Measure of performance/fitness	Main findings
				(range 23–64 y) AIS A–C C6–T11		
Graham et al. [30]	CT	Exp: HIIT Comp: MICT	6 weeks 2×/week-HIIT 3×/week-MICT HIIT: 20 min MICT: 30 min	7 individuals, 6 M: 1 F Mean age: HIIT–49 ± 13 y and MICT—51 ± 1 y AIS A–D C7–L1	VO_{2peak}	Both MICT and HIIT significantly increased VO_{2peak} (17 vs. 7%, respectively)
Hooker and Wells [31]	CT	Exp: VICT Comp: MICT	8 weeks 3×/week 20 min	8 individuals (three completed both protocols with 8 weeks of detraining in between), 6 M: 5 F Mean age: VICT—30 ± 5 y (range 23–36 y) and MICT—31 ± 4 y (range 23–36 y) C5–T9	VO_{2peak} PPO	Either condition did not significantly increase VO_{2peak} Either condition did not significantly increase PPO
Jacobs [32]	CT	Exp: RT Comp: VICT	12 weeks 3×/week RT: NR VICT: 30 min	18 subjects, 12 M: 6 F Mean age: RT—34 ± 8 y (range 25–51 y) and VICT—29 ± 10 y (range 20–50 y) AIS A T6–T10	VO_{2peak} VE_{peak}	RT and VICT significantly increased VO_{2peak} (15% vs. 12%, respectively) No significant difference between modes Neither intervention significantly increased VE_{peak}
Mcleod et al. [19]	CT	Exp: SIT Comp: MICT	5 weeks 3×/week SIT: 10 min MICT: 25 min	20 individuals, 15 M: 5 F Mean age: SIT—47 ± 15 y and MICT—45 ± 17 y AIS A–D C2–L4	PPO	SIT significantly increased PPO (39%) MICT significantly increased PPO (33%) No significant difference in PPO between the groups
Kressler et al. [21]	CT—double blind	Exp: CRT-IPS Comp: CRT-DPS	6 months 3×/week 40–45 min	11 individuals, 9 M: 2 F Mean age: CRT-DPS—37 ± 11 y (range 24–50 y) and CRT-IPS—42 ± 11 y (range 30–58 y) Total CRT—(range 18–55 y) AIS A–D C5–C8	VO_{2peak}	VO_{2peak} significantly increased over time (26%) CRT-IPS group significantly increased VO_{2peak} (35%) CRT-DPS group did not increase VO_{2peak}
Fischer et al. [20]	CT	Exp: RMET Comp: normal training routine	4 weeks 5×/week RMET: 30 min	12 individuals, 10 M: 2 F Mean age: RMET—43 ± 6 y (range 32–48 y) and Control—43 ± 5 y (range 38–50 y). AIS A–B. T2–T8	VO_{2peak} PPO VE_{peak}	VO_{2peak} did not change in either group No significant difference in VO_{2peak} between groups PPO did not significantly change in either group No significant difference in PPO between groups RMET significantly increased VE_{peak} (27%) No significant difference in VEpeak between groups

MICT moderate intensity continuous training, *NR* not reported, *CT* controlled trial, *SIT* sprint interval training, *RT* resistance training, *VICT* vigorous intensity continuous training, *VO_{2peak}* peak oxygen uptake, *HIIT* high-intensity interval training, *CRT* circuit resistance training, *CRT-DPS* circuit resistance training delayed protein supplement, *CRT-IPS* circuit resistance training immediate protein supplement, *VE_{peak}* peak minute ventilation, *PPO* peak power output, *RMET* respiratory muscular endurance training, *LIIT* low intensity interval training, *IPS* immediate protein supplementation, *DPS* delayed protein supplementation, *Exp* experimental, *Comp* comparator, *M* male, *F* female, *y* years, *AIS* American Spinal injury Association Impairment Scale.

Table 2. Methodological quality assessment of CT studies included in the review.

Study, Ref.	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias	Overall quality
Fischer et al. [20]	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low
McLeod et al. [19]	Low	Low	Unclear	Unclear	Low	Low	Low	Low
Graham et al. [30]	Low	Low	Unclear	Unclear	Low	High	High	Unclear
Gauthier et al. [29]	Low	Low	Unclear	Unclear	Low	Low	High	Unclear
de Groot et al. [28]	Unclear	Unclear	Unclear	Unclear	Low	Low	High	Unclear
Jacobs [32]	Unclear	Unclear	Unclear	Unclear	Low	Unclear	Low	Low
Kressler et al. [21]	Unclear	Unclear	Low	Unclear	Low	Unclear	High	Unclear
Hooker and Wells [31]	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low

Table 3. Methodological quality assessment of pre-post studies included in the review.

Author, Ref.	Question/ objective	Selection criteria	Representative POI	Eligible participants	Sample size	Intervention	Outcome measure	Blinding of outcome assessment	Attendance ratio	Statistical tests	Multiple outcome measures	Group intervention	Overall Quality
Tordi et al. [27]	Y	N	Y	N	N	Y	Y	N	Y	Y	N	NA	Fair
Brurok et al. [23]	Y	N	Y	Y	N	N	Y	N	N	Y	N	NA	Fair
Foll de Moro et al. [12]	Y	N	N	N	N	Y	Y	N	Y	Y	N	NA	Fair
Bougenot et al. [22]	N	N	Y	N	N	Y	Y	N	Y	Y	N	NA	Fair
Hasnan et al. [24]	Y	N	Y	N	N	Y	Y	NR	Y	Y	N	NA	Fair
Nash et al. [26]	Y	Y	Y	Y	N	Y	Y	NR	Y	Y	N	NA	Good
Nash et al. [25]	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	N	NA	Good
Jacobs et al. [11]	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	NA	Good

NA not applicable, *NR* not reported, *N* no, *POI* population of interest, *Y* yes.

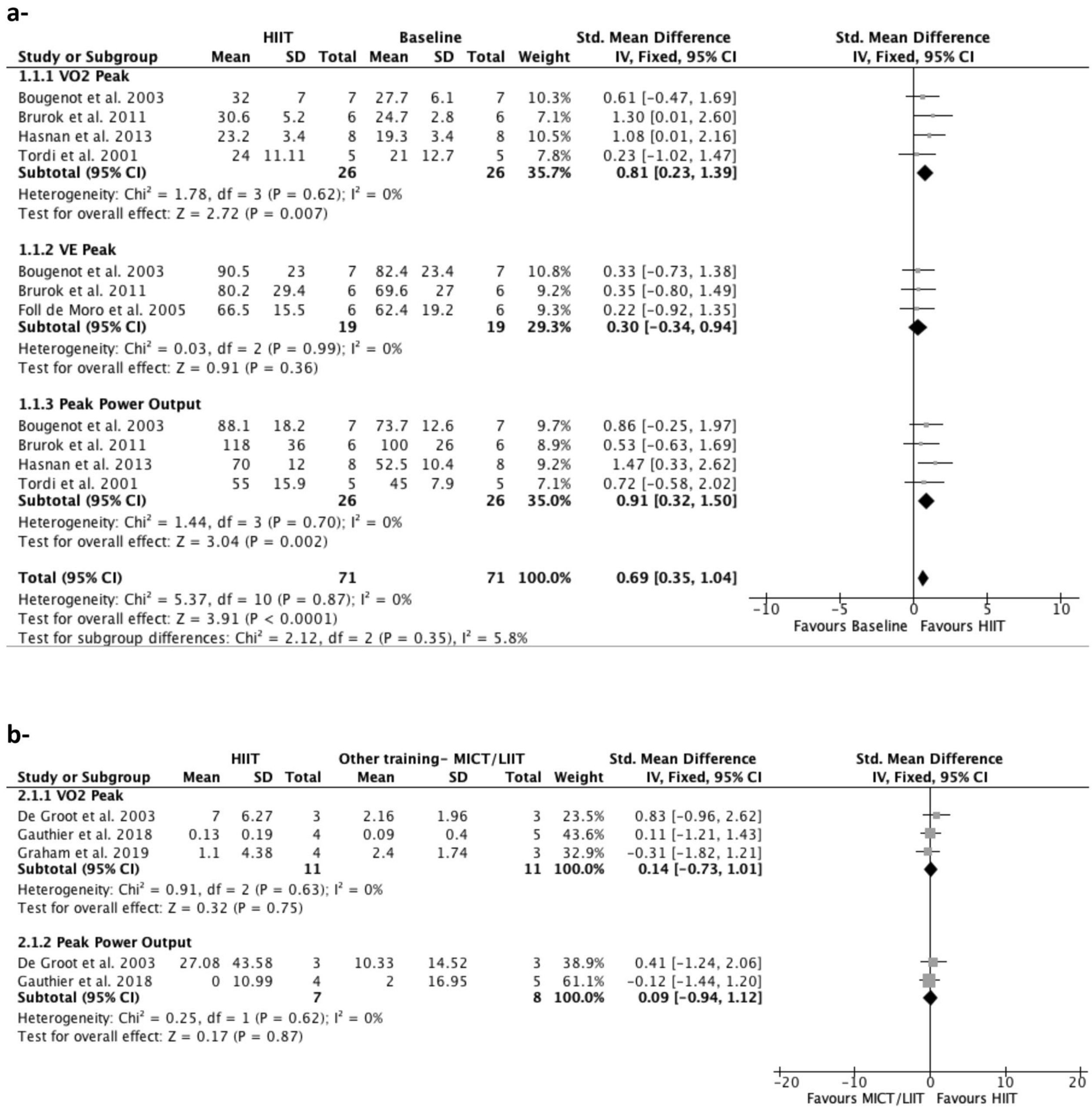

Fig. 2 High-intensity interval training studies. **a** Pre-post studies: standardized mean difference in VO_{2peak}, VE_{peak}, and PPO following HIIT interventions compared to baseline values. **b** Controlled trials: standardized mean difference in VO_{2peak} and PPO between HIIT and low-to-moderate intensity exercise interventions.

Circuit resistance training. Figure 3a includes three pre-post studies examining the effect of a CRT intervention on VO_{2peak} [11, 25, 26]. The three studies were rated as having good overall methodological quality. They were pooled in two meta-analyses with results expressed as MD. VO_{2peak} was statistically different following the CRT intervention (MD = 0.38; 95% CI 0.19–0.57; $P < 0.01$). Figure 3a includes two pre-post studies examining PPO. Results also revealed statistically significant mean changes (MD = 20.17; 95% CI 8.26–32.08; $P < 0.01$).

Vigorous intensity continuous training. Figure 3b includes two CTs that examined the effects of VICT compared to MICT or resistance training (RT) [31, 32]. Both studies showed a low risk of bias. They were pooled in a meta-analysis with the results expressed as SMD. The meta-analysis of VICT did not show a significant between-group difference for VO_{2peak} (SMD = −0.03; 95% CI −0.76–0.70; $P > 0.05$).

Trials not included in meta-analysis. The reasons these studies were excluded from meta-analysis were missing data, grouping differences, or design differences. The CT by Fischer et al. did not reveal significant improvements related to VO_{2peak} or PPO, however, 4 weeks of RMET significantly improved VE_{peak} [20]. Similarly, the double-blind CT by Kressler et al. revealed statistically significant improvements in VO_{2peak} following a 6-month CRT protocol [21]. Further, individuals who ingested protein immediately following training significantly improved VO_{2peak} compared to individuals who did not. The CT by Mcleod et al. revealed significant PPO improvements following a 5-week SIT protocol compared to MICT [19].

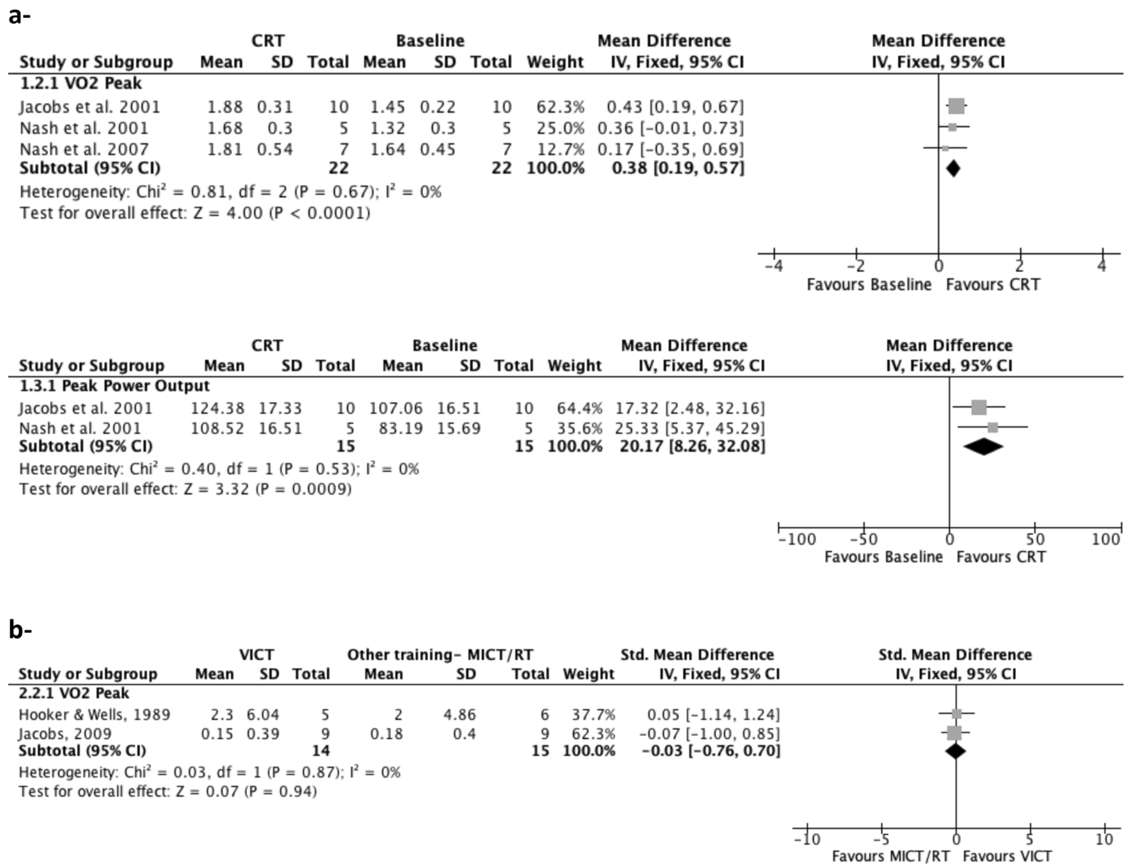

Fig. 3 Circuit resistance training and vigorous intensity continuous training studies. a Pre-post studies: mean difference in VO_{2peak} and PPO following CRT interventions compared to baseline values. **b** Controlled trials: standardized mean difference in VO_{2peak} and PPO between vigorous intensity continuous training and moderate intensity continuous and resistance training.

DISCUSSION

As the need to discover more effective modes of achieving cardiovascular fitness in PwSCI becomes essential, the purpose of this systematic review and meta-analysis was to investigate the literature related to the effectiveness of vigorous training interventions on cardiorespiratory fitness of PwSCI. Our meta-analysis of pre-post studies indicates significant differences of VO_{2peak} and PPO after HIIT and CRT. The differences were also clinically significant as all increments in VO_{2peak} after HIIT and CRT exceed 6%. Every 6% increase in VO2peak has been related to reduced cardiovascular complications including reduced cardiovascular mortality [33]. No significant differences were observed when vigorous intensity exercises were compared to low and moderate intensity exercises.

The first of our meta-analyses revealed the effectiveness of HIIT. HIIT resulted in significant improvements in VO_{2peak} and PPO over time. These findings are in accordance with Nightingale's position that HIIT is both an optimal and viable exercise option for PwSCI [10]. After HIIT, VO_{2peak}, and PPO significantly improved with no adverse consequences reported by participants, and low evidence of musculoskeletal injury or autonomic dysreflexia complications. Brurok et al. reported latent shoulder dysfunction in two participants during the HIIT intervention, but following rest and therapy, they were able to safely complete the intervention [23]. Overall, our findings are in agreement with the review by Batacan et al. [34] that showed similar improvements in VO_{2peak} among able-bodied adults following HIIT. As these pre-post experiments did not utilize a control group, results should be interpreted with caution, and it is difficult to conclude whether cardiovascular improvements were due solely to the intervention.

The meta-analysis comparing HIIT with low-to-moderate intensity exercise did not reveal significant differences in cardiorespiratory adaptations. SMD in VO_{2peak} and PPO was not different across exercise modes. We must note that sample sizes were small across studies as many experimental groups did not consist of more than three participants. Further examination of these studies also indicates a high risk of bias as differences in group pre-training fitness levels appear to exist. For example, in Graham et al.'s study on HIIT versus MICT, pre-intervention fitness levels were higher in the HIIT group than the MICT group [30]. Low-fitness groups typically experience the greatest improvements from exercise interventions [35].

Further examination of the various HIIT interventions also suggests that exercise volumes may have influenced HIIT's efficacy. For example, the most demanding HIIT protocol, by de Groot et al. elicited the largest VO_{2peak} improvement (50%) [28], while the least demanding HIIT protocol, by Graham et al. elicited minimal improvements (7%) [30]. In Graham et al.'s study, exercise protocols were 225% greater in duration for the MICT group (90 min/week) than the HIIT group (40 min/week), which may also explain why greater improvements were observed in the MICT group. While the PAG-SCI recommend at least 90 min per week of moderate intensity aerobic exercise, the guideline prescribes just 40 min of moderate intensity aerobic exercise if two strength sessions are incorporated into the weekly exercise program [2]. As 40 min of vigorous intensity exercise revealed minimal improvements, it seems logical that moderate intensity aerobic exercise of the same duration would also be ineffective [3]. According to Collins et al. when vigorous and moderate handcycling efforts are matched for time, vigorous intensity workloads are ~40% greater

[36]. Therefore, if only 40 min/week of aerobic exercise is going to be prescribed, future recommendations must emphasize a need to raise overall exercise intensities to reach adequate exercise volumes [10].

The meta-analysis also revealed significant improvements in VO_{2peak} and PPO after exposure to CRT. Unlike HIIT, CRT has not revealed clear benefits for improving cardiorespiratory fitness in able-bodied individuals. For example, Myers et al. revealed significant improvements in both VO_{2peak} and PPO following a 5-week CRT [37], but Maiorana et al. [38] did not observe any cardiorespiratory improvements following a 10-week CRT intervention. However, Myers et al. [37] studied CRT in able-bodied females only, while Maiorana et al. studied it in able-bodied males only [38]. Our meta-analysis only included pre-post CRT studies among males with SCI [11, 25, 26], highlighting the need for more robust work examining CRT in both genders with SCI.

No differences in cardiorespiratory adaptations emerged when VICT was compared to moderate continuous or RT. Although differences were low, across studies, it must be noted that Hooker and Wells' study was unusual and utilized three out of six participants in both the vigorous and moderate intensity protocols by separating their interventions with an 8-week detraining period [31]. While this technique increases the overall sample size, detraining periods may be insufficient in preventing carry-over effects as trained groups present better fitness and regain adaptations much easier than untrained groups [39]. Additionally, aerobic adaptations may be less affected by detraining [40]. Therefore, the use of detraining strategies makes their findings difficult to interpret. It also seems plausible that VICT and RT elicited similar results due to the peripheral adaptations associated with both RT and vigorous endurance training. The rest periods of RT also enable participants to tolerate greater loads which over time stimulates peripheral muscle and mitochondrial growth [6].

In the meta-analysis, no specific mode of vigorous training was more effective than low-to-moderate modes of training. These findings do not support our hypothesis that HIIT and other vigorous modes that incorporate recovery periods better optimize cardiorespiratory fitness in PwSCI. Moving forward, more work with broader demographics and sample sizes is needed to validate the current results.

The three studies which were left out of the meta-analysis showed meaningful cardioprotective benefits. According to Kressler et al. VO_{2peak} significantly improved following a 6-month CRT intervention, with greatest improvements in those who ingested protein immediately post workout [21]. As adequately timed protein supplementation enhances muscle anabolism in able-bodied populations [41], this finding further supports the idea that peripheral adaptations enhance cardiovascular fitness in PwSCI. McLeod et al. observed greater improvements in PPO following a 5-week SIT intervention in patients with acute SCI [19]. However, due to the acute nature of the SCI, it is difficult to determine if improvements in PPO were due to the training intervention or the typical rehabilitation and recovery processes which follow SCI. Lastly, Fischer et al. observed significant improvements in VE_{peak} following RMET [20]. The unique RMET protocol used prevented inclusion of this study in the meta-analysis. It should also be noted that all participants in this study were competitive hand-cyclists. Due to the ceiling effects of chronic training, improvements in VE_{peak} support RMET as a potential effective option for the general populations of PwSCI.

Limitations

There are several limitations in this systematic review and meta-analysis. First, individuals of various injury levels and AIS classifications were included. Due to the complex nature of a SCI, an individual with a complete high-thoracic level injury and tetraplegia will likely have different cardiovascular responses to exercise than someone an incomplete and/or lower-level injury and full torso and autonomic (i.e., heart rate, respiratory rate, etc.) function [42]. Therefore, results should be interpreted with caution as response to exercise will vary depending on level of injury and/or AIS classification [43]. Next, only five CTs were eligible for meta-analysis. This low number reduces generalization of the findings. Further, the protocols and durations between similar training styles differed across studies. For example, both Gauthier et al. and de Groot et al. used HIIT in their protocols, however, Gauthier et al. conducted HIIT utilizing manual wheelchair propulsion for 6 weeks [29], while de Groot et al. conducted HIIT on an upper-body cycle ergometer for 8 weeks [28]. Another important limitation of this review is the inclusion of pre-post interventions. We cannot fully determine the true effect of vigorous intensity training based on pre-post studies.

CONCLUSION

This systematic review and meta-analysis revealed significant improvements in cardiorespiratory fitness in PwSCI after engaging in HIIT and CRT. As nearly all vigorous intensity interventions appeared to produce clinically significant improvements in cardiorespiratory fitness, PwSCI may benefit from incorporating vigorous intensity exercises into their weekly physical activity regimes. However, no statistically significant differences were found when comparing these strenuous exercise modalities to standard moderate intensity training. Many of the reviewed CTs included small sample and participants with low fitness, highlighting the need for higher quality study designs examining the effect of different exercise intensities on fitness. Future randomized CTs should focus on increasing sample sizes and recruiting active PwSCI. Nonetheless, this systematic review and meta-analysis highlights the importance of physical activity in improving cardiorespiratory fitness in PwSCI.

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AUTHOR CONTRIBUTIONS

JP was responsible for screening the potentially eligible studies, data extraction, assessing the quality of the included studies, interpreting studies, and writing the initial paper. LA was responsible for designing the initial review protocol, registering the protocol, conducting the search, mediating any data extraction discrepancies, interpreting results, reviewing data extraction, and providing feedback on the paper. LR contributed to the study idea and provided feedback on the initial review protocol, results interpretation, and paper. KD was responsible for screening the potentially eligible studies, data extraction, and writing the initial paper. AA was responsible for performing the quality assessment for the included studies. AS was responsible for identifying key data outcomes, assisting with eligible studies, interpreting results, and providing feedback on the paper. IR contributed to the study idea and provided feedback on the results interpretation and paper.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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