Effect of Body Weight–Supported Treadmill Training on Cardiovascular and Pulmonary Function in People With Spinal Cord Injury: A Systematic Review

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Objective: To assess the current evidence with regard to the effects of body weight–supported treadmill training (BWSTT) on cardiovascular and pulmonary function in people with spinal cord injury (SCI) with a focus on outcomes of heart rate (HR), blood pressure (BP), and respiratory parameters. **Methods:** A systematic literature search was conducted through MEDLINE/PubMed, the Cumulative Index to Nursing and Allied Health Literature, and Physiotherapy Evidence Database. Clinical trials involving adults with SCI and focusing on the effects of BWSTT on HR, BP, and respiratory measurements were included. The quality of included studies was assessed using the Downs and Black scale. The level of evidence of each study was identified using the Spinal Cord Injury Rehabilitation Evidence system. **Results:** Nine studies that met inclusion criteria were evaluated and included in this review. Overall, the quality index of all included studies was low. All studies scored less than 21 out of 28 on the Downs and Black scale. The level of evidence varied from level 2 to level 4. Level 4 evidence supports the use of BWSTT to decrease resting and exercise HR and improve heart rate variability. The use of BWSTT to improve respiratory parameters after SCI is supported by one study with level 2 evidence. The evidence that supports the use of BWSTT to improve resting BP is inconclusive. **Conclusion:** There has been low to moderate evidence to support the use of BWSTT in individuals with SCI to improve cardiovascular and pulmonary health. Future randomized controlled trials are needed to investigate the effect of BWSTT on cardiovascular and pulmonary function in people with SCI and compare BWSTT to other physical rehabilitation interventions.
Key words: *body weight–supported treadmill training, blood pressure, heart rate, locomotion training, respiratory parameters, spinal cord injury, walking training*

Spinal cord injury (SCI) is a serious medical condition that leads to loss of or impairment in sensorimotor function, which negatively impacts the quality of life. Individuals with SCI are susceptible to various secondary complications, including deterioration in cardiovascular and respiratory health.[1,2] It has been estimated that the prevalence rate of cardiovascular disease (CVD) in the SCI population (30%-50%) is significantly higher compared to the able-bodied population (5%-10%).[3] A study reported that the SCI population has a 2.72 times higher risk of heart disease and a 3.72 times higher risk of stroke compared to the general population.[4] In terms of morality after CVD, a cohort study that followed individuals with SCI for 5 years after discharge from inpatient rehabilitation found that 37% of individuals died due to cardiovascular causes.[5]

Physical inactivity is associated with a decrease in cardiovascular fitness (eg, elevated heart rate [HR]) and consequently an increased risk of CVD.[6-8] Lack of physical activity or prolonged sitting observed in many SCI survivors due to limited functional mobility can contribute to elevated HR and other risk factors for CVD.[3,6] Elevated resting HR is more common in individuals with SCI at T1 or below (paraplegia) as compared to those with cervical SCI (quadriplegia).[8,9] Studies report that people with SCI, especially those with paraplegia, have higher resting HR compared to able-bodied people.[7-10] Furthermore, the cardiac autonomic system can be altered after SCI due to the

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sedentary lifestyle and lack of mobility resulting from the injury.[11] Heart rate variability (HRV) can be used as a sensitive measure to determine cardiac autonomic function. Reduced HRV after the injury is associated with an increased risk of heart diseases.[12,13] Past studies show reduced HRV in individuals with SCI in comparison with able-bodied individuals.[11,14] Physically inactive individuals with SCI have less HRV than those who are physically active.[11]

High blood pressure (BP) (ie, hypertension) is another factor that can increase the risk of cardiovascular disease.[15] Hypertension is common in people living with long-term SCI, and it is more prevalent in people with paraplegia compared to quadriplegia.[16-18] Previous studies report a high prevalence of hypertension among people with SCI, especially those with paraplegia, as compared to able-bodied people.[16,19] Sedentary lifestyle after SCI plays an important role in the development of hypertension. Other risk factors such as obesity, hypercholesterolemia, diabetes, smoking, and age can also contribute to an increased risk of hypertension after SCI.[16]

The paralysis of the respiratory musculature following SCI can result in an alteration of the mechanical properties of the lung and chest wall.[20] Pulmonary function may decline after SCI because of decreased muscle strength of the diaphragm, respiratory, and abdominal muscles as well as a lack of sufficient mobility.[21] Reduction in pulmonary function after SCI is reflected by decreases in spirometric and lung volume parameters and static mouth pressures.[22] The weakness of respiratory muscles can result in an ineffective cough and a tendency toward mucus retention, which might increase susceptibility to respiratory diseases.[22] Respiratory impairments are more severe in people with cervical injury compared to those with thoracic or lumbar injury due to a disruption in the function of the majority of the respiratory and abdominal muscles.[22] Respiratory deficiency can lead to secondary problems such as respiratory infectious diseases, which are the leading causes of death in people with chronic SCI.[23]

Participating in regular exercise is necessary to prevent or reduce secondary complications after SCI. Aerobic exercise using arm cycling or functional electrical stimulation (FES) leg cycling has been utilized to improve cardiovascular and pulmonary health in the SCI population. However, exercise using these modalities has shown inconsistent results regarding its effects on cardiovascular and pulmonary health in the SCI population.[24-27] Limitations of these modalities have been discussed in the literature.[28-31] A major limitation of arm cycling or FES leg cycling exercise is the lack of sustainable activities of large leg muscles, leading to insufficient challenges to the cardiopulmonary system.[32,33] As an alternative, body weight–supported treadmill training (BWSTT) is a tool that is widely used in the rehabilitation program for people with neurological conditions. Even though most studies have focused on investigating the effectiveness of BWSTT on motor function and concluded that it might be an appropriate intervention to improve walking ability, promising findings from previous studies have shown that regular walking training using BWSTT can help to improve cardiovascular and pulmonary health in the SCI population.[34-42] Therefore, this systematic review aimed to qualitatively assess the current evidence with regard to the effects of walking training using BWSTT on cardiovascular and pulmonary health among people with SCI. The focus of the study is on the effects of BWSTT on HR and BP measurements and respiratory parameters.

Methods

Search strategy

A systematic literature search was conducted to examine the effect of BWSTT on measures of cardiovascular and pulmonary health in people with SCI. MEDLINE (PubMed), the Cumulative Index to Nursing and Allied Health Literature (CINAHL), and the Physiotherapy Evidence Database (PEDro) were searched. The search was limited to clinical trial studies in humans, with adult patients (≥18 years), and written in English. It was conducted for the time period of January 2004 until May 2018.

The search strategy included the terms for target population (spinal cord injury, paraplegia, quadriplegia or tetraplegia), outcome measures (heart rate, blood pressure, pulmonary function,

Table 1. Key words and combination of key word used in the search

Population	Outcomes	Intervention
• Spinal cord injury • Paraplegia • Quadriplegia/tetraplegia	• Heart rate • Blood pressure • Pulmonary function • Respiratory function • Respiratory parameters	• Locomotor training • Walking training • Gait training • Body weight support treadmill training

Note: "AND" was used between terms in population, outcomes, and intervention columns. The terms in the columns are allied with "OR."

respiratory function, and respiratory parameters), and intervention (locomotor training, walking training, gait training, or body weight support treadmill training). Different combinations of the terms were made using "AND" and "OR" in order to achieve a specific selection of literature (see **Table 1**).

Study eligibility criteria

Inclusion criteria were the following:

1. Studies with adult patients (≥18 years) with traumatic or nontraumatic SCI (cervical, thoracic, and lumbar), complete or incomplete lesions, and American Spinal Injury Association Impairment Scale (AIS) of A, B, C, or D.
2. Treadmill walking training, including manual-assisted BWSTT, robotic-assisted BWSTT, and treadmill walking training in water.
3. Studies focused on measurements of HR and BP and respiratory parameters after a course of treadmill walking training.
4. Clinical trial studies, including randomized controlled (RCTs), quasi-experimental, or pre-experimental trials.
5. Published in English.

Exclusion criteria were (a) overground walking training and (b) animal studies or studies on children.

Study selection

After removing duplicated studies, two independent researchers (R.A and A.A) screened the articles by reading titles and abstracts. Then, the full text of articles relevant to study objectives was read in detail to determine eligibility (see **Figure 1**). Disagreements on study selection were resolved by discussions between two researchers (R.A. and A.A)

Data extraction

The study information was extracted by two reviewers (R.A. and A.A.) independently. The following data were extracted from included studies: author's name, year, study design, sample size, participants' characteristics (gender, age, injury level on the SCI, grade based on AIS, and time since injury), intervention program (length and frequency), and outcomes related to measurements of HR, BP, and respiratory parameters. There were no disagreements between the reviewers regarding data extraction.

Assessment of quality study and level of evidence

Included studies were assessed using the modified Downs and Black scale to determine their methodological quality. The Downs and Black scale is composed of 27 questions to assess the quality of a study across five categories, including reporting (10 questions), external validity (3 questions), internal validity (bias and confounding; 13 questions), and power (one question) (see **Appendix**).[43] The total score of the scale ranges from 0 to 28. A higher score indicates a better quality of methodology. From the percentage of derived total score, studies were classified as high (>75%), moderate (50%-74%), or low quality (<50%). The level of evidence of each study was identified using the Spinal Cord Injury Rehabilitation Evidence (SCIRE) system, a five-level system that differentiates between studies of differing quality and incorporates the types of research designs commonly used in rehabilitation research (see **Table 2**).[13] This scale has been used

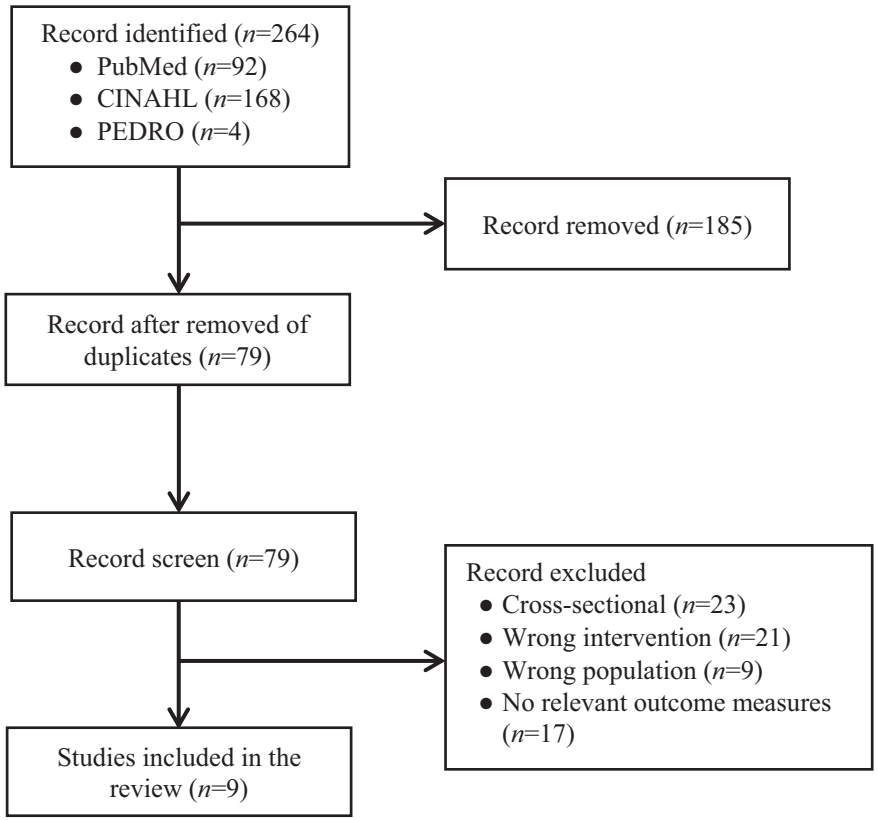

Figure 1. Flowchart of the literature search and selection process.

Table 2. Level of evidence and criteria based on the Spinal Cord Injury Rehabilitation Evidence (SCIRE) system

Level of evidence	Criteria
Level 1	• **RCT:** PEDro score ≥ 6. Includes crossover design with randomized experimental conditions and within-subjects comparison.
Level 2 (n = 2)	• **RCT:** PEDro score ≤ 6. • **Prospective controlled trial:** Nonrandomized. • **Cohort:** Longitudinal study using at least two similar groups with one group being exposed to a condition.
Level 3	• **Case-control studies:** Retrospective study comparing control conditions.
Level 4 (n = 7)	• **Pre-post:** Trial with a baseline measure, intervention, and a post-test using a single group of subjects. • **Posttest:** Posttest with two or more groups using a single group (intervention followed by a posttest with no retest or baseline assessment).
Level 5	• **Observational:** Study using cross-sectional analysis to interpret relations. • **Case report:** Pre-post or case series involving one subject.

Note: The PEDro scale is developed by the Physiotherapy Evidence Database to determine the quality of clinical trials (high quality = score 6-10, fair quality = 4-5, poor quality = score ≤ 3). RCT = randomized controlled trail.

in published systematic review studies of exercise training in people with SCI.[44,45] Two researchers evaluated and scored studies independently. In case of disagreement between two evaluators, a consensus was made through discussion.

Results

An overview of the results of the literature search and screening process is provided in **Figure 1**. The electronic database search retrieved 264 articles. Removal of duplicates within and between the individual databases left 79 articles for further examination. Of the 79 retrieved articles, 53 articles were excluded after screening for titles and abstracts. The remaining 26 articles were screened by reading the full text to determine eligibility. Specific reasons for article exclusion are presented in **Figure 1.** Nine articles were evaluated in detail and are included in this review study.

A summary of the study designs, participants' characteristics, interventions, and outcome measures for each of the nine studies reviewed is provided in **Table 3**. The number of participants in the included studies ranged from 6 to 52 participants; a total of 121 participants took part in those studies. They included individuals with incomplete SCI, complete SCI, or both. The duration of interventions ranged from 2 to 5 times per week for 4 weeks to 6 months. Seven studies examined the effects of walking training on HR measurements.[34-40] Four studies examined the effects of walking training on BP measurements.[34-36,40] Three studies examined the effects of walking training on respiratory parameters.[36,41,42]

Quality assessment for included studies

The results of the quality review are presented in **Table 4**. Overall, the quality index of all included studies was low. All studies scored less than 21 out of 28 on the Downs and Black scale. All studies fulfilled most of the criteria for reporting. The objectives of the study, the main outcomes, the characteristics of the patients, the interventions of interest, and the main findings were clearly described in these studies.[34-42] However, all studies[34-37,39-42] except one[38] were rated poorly on the measurements of the internal validity (bias and confounding) because of lack of control group and randomization. Two studies were scored poorly on the measurement of the external validity because only men were included, and this might have an influence on the generalizability of findings.[38,40] All studies did not report estimation of sample size; thus, they were rated poorly on the measurements of the power.[34-42]

Levels of evidences for included studies

The level of evidence varied from level 2 to level 4 (see **Table 3**). Two studies included a control group.[38,42] One of the studies was a randomized crossover study design with small sample size and was classified as level 2.[38] The other study was a prospective study with a control group (ie, quasi-experimental study design) and was also categorized as level 2.[42] The remaining seven studies used a single group, pre- and post-test study design and were placed at level 4.[34-37,39-41] The sample sizes of all studies[34-41] were small (range, 6-12) except one study[42] that included 52 participants.

Discussion

To the best of our knowledge, this review is the first to systematically synthesize the evidence regarding the effects of BWSTT program on measurements of HR, BP, and respiratory parameters in people with SCI. An exhaustive search found nine studies that met inclusion/exclusion criteria. Given the heterogeneous nature of the SCI population and low research quality, there is weak to moderate evidence to support the effects of BWSTT on improving HR measures and respiratory parameters; however, the evidence regarding BP measures is still lacking or needed.

Heart rate measurements

Changes in HR were measured pre- and post-BWSTT in seven single group studies.[34-40] One study[40] included only individuals with motor complete cervical SCI (ie, quadriplegia) and found no changes in resting HR after BWSTT (two sessions per week for 3 months). On the contrary, another study[34] that included both motor

Table 3. Summary of the studies, participant characteristics, interventions, outcome measures, and main findings ($N = 9$)

Author	Study design	Evidence level	Participants	Intervention	Outcome measures	Main findings
Ditor et al, 2004[34]	Single group, pre- and posttest	Level 4	8 individuals with chronic cervical SCI [6 men, 2 women; mean age, 27.6 y; SCI level: C4-C5; AIS: B-C; mean postinjury, 9.6 y]	BWSTT with manual assistance [3x/wk for 6 mo]	• HR • BP • HRV • BPV	• Significant reduction in the resting HR • No significant change in resting BP • Significant reduction in the resting LF to HF ratio of HRV • Significant decrease in resting LFSBP of BPV
Ditor et al, 2005[35]	Single group, pre- and posttest	Level 4	6 individuals with chronic SCI [4 men, 2 women; mean age, 37.77±15.4 y; SCI level: C4-T12; AIS: A-B; mean postinjury, 7.67±9.4 y]	BWSTT with manual assistance [3x/wk for 4 mo]	• HR response measures • HRV and BPV • Resting measures of arterial dimension and function	• No significant changes in resting HRV and BPV • However, subgroup of individuals who had HR response to training showed improvements in HRV (ie, ¯ LF to HF ratio due to HF and ¯LF) and reductions of BPV (ie, ¯LFSBP) • Significant increase in femoral artery compliance
Soyupek et al, 2009[36]	Single group, pre- and posttest	Level 4	8 individuals with SCI [6 men, 2 women; mean age, 40.75±13.93 y; SCI level: C6-L1; AIS: B-D]	BWSTT with manual assistance [5x/wk for 6 wk]	• Cardiovascular parameters (resting HR and BP) • Pulmonary function test • Depression	• Significant decrease in resting HR • No significant change in resting SBP • Significant improvement only in FVC and IC
Hoekstra et al, 2013[37]	Single group, pre- and posttest	Level 4	10 individuals with chronic SCI [4 men, 6 women; mean age, 49±14 y; SCI level: C3-L2; AIS: C-D; mean postinjury, 9±10 y]	BWSTT with robotic assistance [2-3x/wk; total of 24 sessions]	Cardiopulmonary fitness, including: • Resting, submaximal, and peak VO2 and O2 pulse • Resting, submaximal, and peak HR Walking training intensity: • %HR reserve • %VO2 reserve • METs	• Significant decrease in resting and submaximal HR after training • Three subjects met the recommended guidelines of exercise intensity based on % VO2 reserve • Two subjects met the recommended guidelines of exercise intensity based on % HR reserve • Two subjects met the recommended guidelines of exercise intensity based on METs • Rest of subject's exercise at low intensity
Millar et al, 2009[38]	Randomized crossover	Level 2	6 individuals with chronic SCI [6 men; mean age, 37.1±7.7 y; SCI level: C5-T10; AIS: A-C; mean postinjury, 5.0±4.4 y]	Group 1: BWSTT with manual assistance Group 2: Passive HUTT [3x/wk for 4 wk]	• Resting HR • HRV • HR complexity • Detrended fluctuation analysis of HR behavior	• Decrease in resting HR after BWSTT and HUTT, but was not significant • A trend toward improvement of HRV, as reflected by reduced LF/HF ratio, after BWSTT • Significant increase in HR complexity and reduction in the fractal scaling distance score

Table 3. Summary of the studies, participant characteristics, interventions, outcome measures, and main findings (N = 9) (CONT.)

Author	Study design	Evidence level	Participants	Intervention	Outcome measures	Main findings
Stevens et al, 2015[39]	Single group, pre- and posttest	Level 4	11 individuals with chronic incomplete SCI [7 men and 4 women; mean age, 48±12 y; SCI level: C2-L2; AIS: C-D; mean postinjury, 5±8 y]	Underwater treadmill training [3x/wk for 8 wk]	• Exercise HR during training period 1 (wk 2-3), 2 (wk 4-5), and 3 (wk 6-7)	• Significant decrease in mean exercise HR during each training period 1, 2, and 3 • All participants experience a decrease in daily walking HR for each 2-week block period
Carvalho et al, 2005[40]	Single group, pre- and posttest	Level 4	12 individuals with complete cervical SCI [12 men; mean age, 33.8±33.73 y; SCI level: C4-C7; AIS: A; median postinjury, 77.58 months]	BWSTT with manual assistance and NES [2x/wk for 3 months]	• HR and BP at rest, during treadmill walking and during the recovery phase pre- and posttraining	• Significant increase in HR and SBP from rest to walking training • After 3 months walking training, significant increase in SBP at rest and during walking training, but in recovery phase • No significant changes in HR at rest, during walking training, in recovery phase after 3 months walking training
Terson de Paleville et al, 2013[41]	Single group, pre- and posttest	Level 4	8 individuals with chronic SCI [7 men, 1 woman; mean age, 37±18 y; SCI level: C3-T12; AIS: A-D; mean postinjury, 25±12 months]	BWSTT with manual assistance [5x/wk; total of 62±10 sessions]	• Pulmonary function test • EMG signal of respiratory muscles during respiratory tasks as follows: • MIPT • MEPT • Cough	• Significant increase in FVC, FEV1 • Significant increase maximum inspiratory pressure (PI max) and maximum expiratory pressure (PE max) • Significant increase in EMG activity and motor unit recruitment rate of all respiratory muscles during respiratory tasks after training
Tiftik et al, 2015[42]	Quasi-experimental study	Level 2	52 individuals with SCI [Group A: 19 men and 7 women; mean age, 31.2±12.7 y; SCI level: 7 C1-C8, 6 T1-T12, 13 L1-S4/5; mean postinjury, 10.6±13.5 months] [Group B: 21 men and 5 women; mean age, 35.6±15.0 y; SCI level: 10 C1-C8, 9 T1-T12, 7 L1-S4/5; mean postinjury, 14.5±12.5 months]	Divided into two groups: Group A: BWSTT + rehabilitation program Group B: rehabilitation program alone [3 sessions/wk for 4 wk]	• Pulmonary function test	• Significant increase in FVC, FEV1, vital capacity, % vital capacity, peak expiratory flow rate, and maximum voluntary ventilation

Note: AIS = American Spinal Injury Association Impairment Scale; BP = blood pressure; BPV = blood pressure variability, BWSTT = body weight–supported treadmill training; EMF = electromyography; FEV1 = forced expiratory volume 1 second; FVC = forced vital capacity; HF = high-frequency power; HR = heart rate; HRV = heart rate variability; HUTT = head-uptilt training; IC = inspiratory capacity; LF = low-frequency power; METs = metabolic equivalents; MEPT = maximum expiratory pressure task; NES = neuromuscular electrical stimulation; SBP = systolic blood pressure.

Table 4. The quality of included studies based on the modified Down and Black scale

Authors	Reporting										External validity-bias			Internal validity-bias							Internal validity-confounding						Power	Total score
Question	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	
Ditor et al, 2004[34]	1	1	1	1	0	1	1	1	0	1	0	0	1	0	0	1	0	1	1	1	0	0	0	0	0	0	0	13
Ditor et al, 2005[35]	1	1	1	1	0	1	1	1	0	1	0	1	1	0	0	1	0	1	1	1	0	0	0	0	0	0	0	14
Soyupek et al, 2009[36]	1	1	1	1	0	1	1	0	0	0	0	1	1	0	0	1	0	1	0	1	0	0	0	0	0	0	0	11
Hoekstra et al, 2013[37]	1	1	1	1	0	1	1	0	0	1	0	1	1	0	0	1	0	1	0	1	0	0	0	0	0	0	0	12
Millar et al, 2009[38]	1	1	1	1	0	1	1	0	0	1	0	0	1	0	0	1	0	1	0	1	1	0	1	1	0	0	0	15
Stevens et al, 2015[39]	1	1	1	1	0	1	1	1	0	1	0	1	1	0	0	1	0	1	0	1	0	0	0	0	0	0	0	13
Carvalho et al, 2005[40]	1	1	1	1	0	1	1	0	0	0	0	0	1	0	0	1	0	1	0	1	0	0	0	0	0	0	0	10
Terson de Paleville et al, 2013[41]	1	1	1	1	0	1	1	0	0	0	0	1	1	0	0	1	0	1	0	1	0	0	0	0	0	0	0	11
Tiftik et al, 2015[42]	1	1	1	1	0	1	1	0	0	1	0	1	1	0	0	1	0	1	0	1	0	0	0	0	0	0	0	12

Note: 1 = "yes"; 0 = "no" or "unable to determine"

incomplete and complete cervical SCI reported a significant decrease in resting HR after 6 months of BWSTT with three sessions per week. Two studies with mixed SCI lesion levels (ie, quadriplegia and paraplegia)[36,37] also reported a significant decrease in resting HR after 6 weeks or 24 sessions over 10 to 16 weeks of BWSTT. Two other studies with mixed SCI lesion levels[35,38] reported a nonsignificant decrease in resting HR after 4 months or 4 weeks of BWSTT. Exercise HR was measured in two studies[37,39] with incomplete and mixed SCI lesion levels and was significantly decreased after 24 sessions of BWSTT.

The intensity and duration of BWSTT may influence HR adaptation. One study[38] found no significant decrease in resting HR, but the duration of this study was very short (4 weeks of BWSTT) as compared to the other studies[34,36,37] (8 weeks to 6 months of BWSTT). Authors of this study did not provide information about the intensity of training. Also, it might be challenging to find a significant change in HR after 4 weeks of exercise. It has been shown that at least 6 to 8 weeks of walking training would be ideal for producing HR adaptation.[36,37] Furthermore, moderate to high intensity of arm aerobic exercise for 8 weeks has been shown to improve cardiopulmonary fitness in individuals with SCI.[46] Future studies in walking training should focus on the impact of the training intensity on HR outcomes.

Completeness of injury (incomplete or complete SCI) might also have an influence on HR response to walking training. In two studies[35,40] that included only individuals with motor complete injuries, BWSTT did not produce a significant decrease in resting HR. In Ditor's study,[35] only participants who had HR response (ie, increased HR) during walking training showed a decrease in resting HR. It seems that HR response and voluntary contraction of leg muscles during BWSTT are essential factors for inducing HR adaptation.[35] A repetitive and intensive locomotor training has been shown to improve the activity of leg muscles even in persons with motor complete SCI.[47,48] It is still unknown how significantly increased activity of leg muscles after a course of walking training can contribute to HR adaptation.

Compared to arm cycling exercise, walking training can trigger the activity of larger muscles in the body (ie, leg and trunk muscles) through activation of central pattern generators located within the spinal cord.[49-51] In addition, being in upright posture during walking training can provide greater stress and challenge to the cardiovascular system. It has been shown that in individuals with SCI, HR and oxygen uptake were significantly higher during BWSTT in comparison to exercise in a sitting position.[32,33] Consequently, walking exercise might induce a greater positive adaptation in HR than conventional exercise approaches such as cycling or FES leg cycling exercise.[52] However, the efficacy of walking training compared to other exercise approaches has not been studied.

In relation to cardiac autonomic function, one study[34] showed an improvement in HRV, as reflected by a significant reduction in the ratio of low-frequency power to high-frequency power, in individuals with incomplete cervical SCI after 6 months of BWSTT. Two studies[35,38] reported a trend toward an improvement in HRV after 4 weeks or 4 months of BWSTT. The duration of one of these studies that found nonsignificant improvement in HRV after training was very short (ie, 4 weeks).[38] It might be difficult to find a significant improvement in HRV within a short term of training. However, this study has noted a significant improvement in HR complexity after training, which is an indirect measurement of cardiac autonomic function.[38] The other study included only individuals with motor complete SCI, and only participants who showed HR response (ie, increased HR during training) to BWSTT improved their HRV after 4 months of training.[35]

The findings of these studies[34,36,37,39] suggest that BWSTT might result in decreased resting and exercise HR and improved cardiac autonomic function in individuals with SCI. These studies that support the use of BWSTT in improving HR measurements had a single group, pre- and post-test study design. Therefore, level 4 evidence is given for the use of BWSTT to improve HR measurements following SCI.

Blood pressure measurements

Four studies[34-36,40] investigated the effects of BWSTT on changes in BP measurements in individuals with SCI. Two studies[35,36] included

individuals with cervical, thoracic, or lumbar SCI, and the other two studies[34,40] targeted only individuals with cervical SCI. In the studies with mixed SCI levels, no significant changes in resting BP were observed in individuals with motor incomplete SCI after 6 weeks of BWSTT[36] or in motor complete SCI after 4 months of BWSTT.[35] In the studies of cervical SCI, one study observed no significant change in resting BP in motor incomplete SCI after 6 months of BWSTT.[34] Another study with motor complete cervical SCI reported a significant increase in resting BP after 3 months of BWSTT combined with neuromuscular electrical stimulation.[40] The authors of this study suggested that the increase in resting BP might be due to improvement in sympathetic activity after the BWSTT.[40]

It is well known that regular exercise at moderate/high intensity can lead to a decrease in resting BP.[53,54] Past studies indicated that regular exercise might decrease resting BP in people with paraplegia (SCI at T1 or below) for whom the prevalence rate of hypertension is high.[6,55] However, people with cervical SCI (quadriplegia) tend to have abnormally lower resting BP compared to able-bodied individuals and those with thoracic or lumbar SCI (paraplegia) due to impaired cardiovascular autonomic function after SCI.[16-18] Additional reduction in BP after a period of exercise in people with quadriplegia might provoke symptoms of hypotension.[40] A physical exercise program of FES leg cycling for several months increased resting BP in people with quadriplegia.[56] The use of BWSTT in people with quadriplegia may or may not lead to an increase in resting BP, as shown in two reviewed studies.[34,40] Studies that included participants with quadriplegia and paraplegia[35,36] were therefore inconclusive in terms of changes in BP due to the fact that resting BP may change in opposite directions in these populations.

As discussed previously, the four studies[34-36,40] that reported outcomes in resting BP after BWSTT were inconclusive due to their heterogeneity in terms of study participants and the response of the participants. In addition, all four studies had small sample sizes, ranging from 6 to 12 participants. This limited number of studies, small sample sizes, different levels of SCI, and variable responses to walking exercise allow no conclusions to be drawn regarding the effects of BWSTT on resting BP. Future clinical trials need to include large sample sizes and focus on either paraplegia or quadriplegia.

Two studies[34,35] also measured BP variability pre- and post-BWSTT training. One study[34] reported a significant decrease in low-frequency systolic BP (SBP) in individuals with incomplete cervical SCI after 6 months of BWSTT. The other study from the same investigation team found no significant changes in measurements of BP variability in individuals with motor complete cervical or thoracic SCI after 4 months of BWSTT.[35] No conclusion can be made at present.

Respiratory parameters

Only three out of nine studies that were included in this review measured pulmonary function as an outcome.[36,41,42] In all three studies, there were improvements in some of the respiratory parameters after a course of walking training. Soyupek et al[36] found significant increases in forced vital capacity (FVC) and inspiratory capacity (IC) in individuals with motor incomplete SCI after 6 weeks of BWSTT. Another prospective study with a control group showed that vital capacity (VC), VC%, FVC, forced expiratory volume in one second (FEV1), and forced expiratory flow rate 25% to 75% were significantly increased in participants who received 4 weeks of BWSTT (the experimental group) but not in those who received standard rehabilitation program (the control group).[42] Both groups showed a significant increase in maximum voluntary ventilation.[42] However, this study did not use a random procedure in assigning the participants into one of two groups.

In addition to measuring pulmonary function, a study explored the underlying mechanisms of improvement in pulmonary function after walking training.[41] They reported significant increases in FVC, FEV1, and maximum expiratory pressure after 62±10 sessions of BWSTT. Also, the amplitude and motor unit recruitment of all respiratory muscles during respiratory tasks significantly increased after training as compared to baseline measures. The findings of the study

suggest that BWSTT could induce neuroplasticity in spinal neural circuitry that is responsible for the activation of respiratory muscles.

In comparison to exercises in sitting position, upright posture during walking training can trigger the activity of trunk muscles including abdominal muscles, which play an important role in respiration.[49-51] It is also a highly effective stressor of the cardiopulmonary system since the lungs need to work harder to deliver more oxygen to larger working muscles.[57] Furthermore, it has been shown that walking training increases the connectivity of neural spinal circuity between motor cortex and leg muscles.[58] The increased muscle activity of inspiratory and expiratory muscles after BWSTT may be explained by neuroplastic changes within the neural spinal circuity that controls respiration.[41] All of those factors might induce greater adaptive changes in pulmonary function. Based on this information mentioned, the use of BWSTT to improve pulmonary function after SCI is supported by one study[42] with level 2 evidence.

Conclusion

To maintain cardiovascular and pulmonary health after SCI, it is crucial for people with SCI to engage in regular physical activity. There is some evidence that the use of BWSTT as an exercise in individuals with SCI has positive effects on cardiovascular and pulmonary health by improving resting and exercise HR and respiratory parameters. No clear evidence is currently available about which type of physical rehabilitation produces the best results. In addition, it is not clear whether BWSTT leads to a better outcome in cardiovascular and pulmonary function compared to conventional physical rehabilitation methods, such as arm cycling or FES leg cycling exercise. Furthermore, current studies have not provided information about the effects of the intensity level of walking training on these outcome measurements. Because of limited studies, further investigations are necessary. Future randomized controlled trial studies are needed to investigate the effects of BWSTT on cardiovascular and pulmonary health compared to other physical rehabilitation interventions. Further studies also should investigate the influence of walking training intensity (ie, walking speed or amount of body weight support) on cardiovascular or pulmonary health.

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APPENDIX

Modified Downs and Black Checklist for the Assessment of the Methodological Quality of Studies

Item	Criteria	Possible answers
Reporting		
1	Is the hypothesis/aim/objective of the study clearly described?	Yes = 1 No = 0
2	Are the main outcomes to be measured clearly described in the Introduction or Methods section?	Yes = 1 No = 0
3	Are the characteristics of the patients included in the study clearly described?	Yes = 1 No = 0
4	Are the interventions of interest clearly described?	Yes = 1 No = 0
5	Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Yes = 2 Partially = 1 No = 0
6	Are the main findings of the study clearly described?	Yes = 1 No = 0
7	Does the study provide estimates of the random variability in the data for the main outcomes?	Yes = 1 No = 0
8	Have all important adverse events that may be a consequence of the intervention been reported?	Yes = 1 No = 0
9	Have the characteristics of patients lost to follow-up been described?	Yes = 1 No = 0
10	Have actual probability values been reported (eg, 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	Yes = 1 No = 0
External validity		
11	Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes = 1 No = 0 Unable to determine = 0
12	Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes = 1 No = 0 Unable to determine = 0
13	Were the staff, places, and facilities where the patients were treated representative of the treatment the majority of patients receive?	Yes = 1 No = 0 Unable to determine = 0
Internal validity – bias		
14	Was an attempt made to blind study subjects to the intervention they have received?	Yes = 1 No = 0 Unable to determine = 0
15	Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes = 1 No = 0 Unable to determine = 0
16	If any of the results of the study were based on "data dredging," was this made clear?	Yes = 1 No = 0 Unable to determine = 0
17	In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies is the time period between the intervention and outcome the same for cases and controls?	Yes = 1 No = 0 Unable to determine = 0

Item	Criteria	Possible answers
18	Were the statistical tests used to assess the main outcomes appropriate?	Yes = 1 No = 0 Unable to determine = 0
19	Was compliance with the intervention/s reliable?	Yes = 1 No = 0 Unable to determine = 0
20	Were the main outcome measures used accurate (valid and reliable)?	Yes = 1 No = 0 Unable to determine = 0
Internal validity – confounding		
21	Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?	Yes = 1 No = 0 Unable to determine = 0
22	Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes = 1 No = 0 Unable to determine = 0
23	Were study subjects randomized to intervention groups?	Yes = 1 No = 0 Unable to determine = 0
24	Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?	Yes = 1 No = 0 Unable to determine = 0
25	Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes = 1 No = 0 Unable to determine = 0
26	Were losses of patients to follow-up taken into account?	Yes = 1 No = 0 Unable to determine = 0
Power		
27	Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?	Yes = 1 No = 0 Unable to determine = 0