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ARTICLE

Comparison of peak oxygen consumption response to aquatic and robotic therapy in individuals with chronic motor incomplete spinal cord injury: a randomized controlled trial

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Abstract

Study design: Randomized dual center controlled clinical trial.

Objective: To determine and compare the cardiorespiratory impact of 3 months of aquatic and robotic therapy for individuals with chronic motor incomplete spinal cord injury (CMISCI).

Settings: Two rehabilitation specialty hospitals.

Methods: Thirty-one individuals with CMISCI with neurological level between C2-T12 at least 1 year post injury were randomized to either aquatic or robotic treadmill therapy for 36 sessions. Customized sessions lasted 40–45 min at 65–75% heart rate reserve intensity with peak oxygen consumption (peak VO_2) measured during arm ergometry at baseline and post intervention. Additional peak robotic treadmill VO_2 assessments were obtained before and after training for participants randomized to robotic intervention.

Results: Peak VO_2 measured with arm ergometry was not significantly different with either aquatic intervention (8.1%, $p = 0.14$, $n = 15$) or robotic intervention (−0.7%, $p = 0.31$, $n = 17$). Peak VO_2 measured with robotic treadmill ergometry demonstrated a statistical improvement (14.7%, $p = 0.03$, $n = 17$, two-tailed t-test) across the robotic intervention. Comparison between the two interventions demonstrated a trend favoring aquatic therapy for improving arm ergometry peak VO_2 (ANOVA, $p = 0.063$).

Conclusions: Neither 3-month exercise interventions statistically improved arm cycle ergometry peak VO_2, our cardiorespiratory surrogate marker, although percent improvement was greater in the aquatic exercise condition. Robotic ergometry peak VO_2 did improve for the robotic intervention, confirming previous work. These results suggest that either intervention may hold utility in improving cardiorespiratory fitness in CMISCI, but peak VO_2 measurement technique appears critical in detecting effects.

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Introduction

Aerobic cardiorespiratory fitness is comparatively low in the spinal cord injury (SCI) population, with approximately 25% of otherwise healthy young individuals with SCI failing to achieve oxygen consumption levels sufficient to

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perform many essential activities of daily living (ADLs) [1]. Interventions to effectively increase cardiorespiratory endurance and exercise capacity include arm ergometry [2–4], functional electrical stimulation [5], and robotically assisted treadmill training [6, 7]. Six months, three times weekly, of body weight supported treadmill training produced both glucose and insulin reduction in people with chronic incomplete SCI [8]. However, a Cochrane review of the effect of exercise on carbohydrate and lipid metabolism disorders in people with chronic SCI concluded insufficient evidence exists to determine whether exercise can improve carbohydrate and lipid metabolism [9].

Body weight supported locomotor training with or without robotic assistance has been shown to improve walking and cardiorespiratory fitness for people with chronic motor incomplete spinal cord injury (CMISCI) [10–15]. Jack et al. [13] reported improvement in peak VO_2 uptake on two participants who engaged in body weight supported treadmill training without robotic assistance three times per week for 20 weeks. Kressler et al. [14] performed an extensive single site comparison study of four different approaches to body weight supported locomotor training: (1) manual assistance, (2) transcutaneous electrical stimulation, (3) robotically assisted training, or (4) over ground training with electrical stimulation. The robotically assisted training group failed to display a change in peak VO_2, whereas individuals in the other three groups demonstrated improved peak VO_2 responses after the intervention. The *passive* robotic training paradigm employed in this study utilizing 100% guidance force to provide maximal assistance throughout the step cycle may have contributed to no robotic cardiorespiratory change [16].

We previously reported improvement in peak VO_2 after a 3-month, three times per week coached robotic-assisted body weight supported treadmill training (RABWSTT) [6]. This prospective randomized single center controlled clinical trial involved 18 individuals with CMISCI randomized to progressive robotic therapy or a home stretching control arm. Outcome measures included peak VO_2 measured with both robotic-assisted treadmill walking ergometry and arm ergometry at baseline, 6 weeks, and 3 months. Peak VO_2 measured with robotic treadmill ergometry across the robotic therapy intervention showed a statistically significant improvement of 12.3% from baseline to 3 months ($p = 0.02$) compared to the stretching control group non-significant improvement of 3.9% ($p = 0.37$). Peak VO_2 measured with arm ergometry in the robotic therapy group increased, albeit not significantly, by 8.5% ($p = 0.25$).

We also demonstrated high test-retest reliability of peak VO_2 measurement during robotic treadmill walking ($r = 0.96$, $p = 0.01$) and arm ergometry ($r = 0.95$, $p = 0.01$) in this population [17], as well as a high correlation ($r = 0.87$, $p = 0.01$) between arm cycle ergometry and robotic treadmill peak VO_2 testing. This suggests both techniques assess cardiorespiratory fitness, although different peak VO_2 outcomes are expected when using only upper extremities, or upper and lower extremities and trunk.

Aquatic therapy is a rehabilitation technique utilized frequently to improve function for individuals with CMISCI [18, 19]. Limited empirical evidence exists, however. Clinically, the aquatic environment facilitates both gait and cardiorespiratory functional gains. Buoyancy provides natural body weight support; hydrostatic pressure activates sensory receptors, thereby providing increased proprioceptive feedback; viscosity increases resistance to the musculoskeletal and cardiorespiratory systems. Stevens et al. [20] recently reported improved leg strength, balance, walking speeds, distance walked over 6 min, and daily step activity in 11 volunteers with incomplete SCI who participated in an 8-week, three times per week underwater treadmill training program. They did not address aerobic capacity, however.

Given this background, we proposed a randomized clinical trial to assess two rehabilitation techniques for individuals with CMISCI. Our a priori hypotheses anticipated both conditions would improve cardiorespiratory fitness but aquatic therapy (AT) would demonstrate a ten percent greater improvement than robotic-assisted body weight supported treadmill training (RT). We based this on the idea buoyancy facilitates more innervated motor units to contract due to the relative reduction of gravity and hydrostatic pressure assists with blood flow return. Both hydrodynamic principles facilitate a greater work load for individuals with SCI than a land-based exercise program, even body weight supported activities. We assessed the impact of 36 sessions of AT and RT on cardiorespiratory fitness for individuals with CMISCI. This paper represents one component of our overall study examining aquatic and robotic treadmill therapy effects prior to crossover to the alternate intervention upon cardiorespiratory fitness.

Methods

The appropriate institutional review boards (IRBs) as well as the Department of Defense IRB approved this protocol. This trial involved collaborating sites at two rehabilitation specialty hospitals located in different United States cities. Weekly communication occurred between intervention practitioners across both sites, and monthly teleconferences occurred between the principal investigators and practitioners to insure adherence to the protocol and offer optimal programming for participants. During data collection lead investigators visited each others' sites on two occasions and conducted aquatic and robotic training sessions. Additionally, throughout the study weekly phone calls and emails occurred across the entire study period to address

procedural consistency, and the research team met annually at professional conferences to discuss study logistics.

Statement of compliance

We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. This trial was registered under Clinicaltrials.gov identifier NCT01407354.

Participants

Individuals with CMISCI were recruited as a convenience sample from outpatient SCI clinics and through available clinical databases at both centers. The recruitment of individuals for this study occurred over three and a half years. Participants eligible for the study were between the ages of 18 and 65, with a spinal cord injury of at least 12 months, including levels C2 to T12, and classified as an International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) impairment scale of C or D, who could tolerate being upright in a standing frame for at least 30 min. We excluded individuals with a history of long bone fracture, active symptomatic cardiovascular disease, concurrent lower motor neuron injury as determined by physical examination (areflexia), other medical co-morbidities precluding safe participation, or active participation in physical therapy for 3 months prior to enrollment.

Participant screening included a general history and physical examination (done by a spinal cord injury certified physician at each site), an ISNCSCI examination (done by a spinal cord injury specialty trained physical therapist or physician), a resting electrocardiogram, and baseline blood tests including a complete blood count and metabolic profile to screen for occult infection, anemia, renal or liver disease, or uncontrolled diabetes. A 30 min standing frame challenge was performed by a physical therapist. Information collected included The Lower Extremity Motor Score (LEMS), which is derived from five specific bilateral leg muscle scores included in the ISNCSCI examination completion; and the Upper Extremity Motor Score (UEMS) obtained in a similar manner; The Walking Index for Spinal Cord Injury (WISCI-III), which records the physical assistance needed, and devices required, for walking following spinal cord injury. In addition, basic demographic information (age, sex, age at time of injury, time since injury) was collected on all individuals. Participants meeting eligibility criteria and who signed the IRB approved consent forms were block randomized by site using a computer-generated algorithm to treatment with either robotic or aquatic therapy for 36 sessions followed by repeat peak VO_2 testing. A statistician not involved in the study generated the randomization. The randomization was implemented after all baseline testing was completed and was performed by a research coordinator uninvolved in the study execution. For individual subjects, the screening, randomization process, and baseline physiologic testing (see below) took approximately 2 weeks.

Baseline and outcome physiologic testing

Testing was performed by appropriately trained personnel at each site. This included an exercise physiologist and physical therapist at one site, and a blinded physical therapist at the second site. The arm cycle ergometry was performed in a clinical laboratory research setting at each site. The robotic-assisted ergometry testing was performed in clinical treatment space at one facility and in dedicated research space where the respective Lokomat® devices were located.

Peak oxygen consumption measurement

Peak aerobic capacity was assessed under two conditions: (1) arm ergometry and (2) robotic treadmill walking. A COSMED Quark Cardiopulmonary Metabolic Cart (CPET) measured oxygen consumption during the peak aerobic tests (arm ergometry and robotic treadmill walking) with the unit calibrated per manufacturer guidelines before each test. A Hans Rudolph half mask with a flow meter attachment was positioned over the participant's nose and mouth region, permitting the collection of continuous air flow and gas concentrations. This configuration connected to the metabolic cart and a computer software program integrating the flow and gas data to calculate oxygen consumption values. We determined peak oxygen consumption by averaging the highest values observed from three consecutive 10-s sampling periods.

Arm ergometry peak VO_2 test

We conducted the arm ergometry test with a Monark upper extremity arm cycle ergometer with participants positioned in front of the device in a standard chair or personal wheelchair. The ergometer height aligned the axis of rotation with the shoulder joint with seating adjustments made to bring the pelvis in a neutral position. Participants sat quietly for 5 min before performing a 3-min warm-up phase at zero watts (no resistance) with the pedal cadence at 50 rpm. Work rates increased by 5 watts every minute after the warm-up phase with pedal cadence remaining constant at 50 rpm. The session terminated at volitional fatigue or if the participant failed to maintain the pedal cadence at 50 rpm at any given work rate.

Robotic-assisted body weight supported peak VO_2 test

We used a robotic device, the Lokomat® Robotic Treadmill training device (Hocoma, Inc.), with a computer interface for the robotic treadmill walking ergometry test. All participants were measured and configured in the device according to manufacturer guidelines. Participants were positioned safely with as much body weight as possible and were instructed to limit movement and communication for a 5-min period prior to the initiation of the treadmill test to collect baseline VO_2 and heart rate values. Next, participants performed a 3-min warm-up phase at his or her optimal treadmill speed and body weight support (BWS). We determined the optimal work rate (speed and BWS) during a 20-min acclimation training session, which determined treadmill speed and BWS for an optimal gait pattern. We changed this work rate each minute, first by decreasing BWS by 10% increments, next by increasing speed by 0.2 kilometers/hour, and then by decreasing guidance force by 10% increments. Participants walked until they reached volitional fatigue or failed to maintain a safe gait pattern (e.g., without tripping or stumbling).

The testers that performed these peak VO_2 tests at the second site were trained in the standardized implementation of these tests by an exercise physiologist (author WS) with previous expertize in these types of studies, who performed all of the testing at the first site. Because of the relatively small size of the research teams at one site, blinding of testers was not practicable. The second site was able to employ an external therapist for testing other than robotic peak VO_2.

Interventions

The interventions were performed by a team of skilled physical or occupational therapists at each site. During each training session for both groups, heart rate was assessed by palpation and with a heart rate monitor to guide tasks to stimulate the desired exercise intensity (65–75% heart rate reserve (HRR)) as determined during the baseline peak VO_2 test. The Borg scale (6–20) was also administered to all participants to obtain subjective feedback regarding the exercise intensity and was used as an additional tool to adjust exercise intensity during and between sessions [21].

Robotic therapy (RT) intervention

Participants reported to the rehabilitation facility up to three days per week during the robotic training intervention using Lokomat®. An acclimation session was performed to determine the robot manufacturer guideline anatomical settings, and optimal treadmill speed, body weight support, and guidance force settings before conducting robotic ergometry testing and the intervention. To allow endurance and skin tolerance to build, the first robotic session duration was 20 min, and then increased by 5-min in subsequent visits until the exercise duration reached 45 min. During each session participants performed a 5-min warm-up, followed by customized, coached gait training tasks, and a 5-min cool-down. During each training session, the Polar heart rate monitor, as well as palpated heart rate, guided clinician application of treadmill speed, body weight support, guidance force adjustments, and coaching to stimulate the desired exercise intensity. The overall protocol for adjustment of the robotic treadmill parameters is depicted in Figure1. Stimulus intensity was adjusted in an individualized way in order to achieve 65 to 75% HRR.

Aquatic therapy (AT) intervention

Aquatic therapy sessions consisted of up to three, 45-min sessions per week. Training started conservatively at 50% of HRR and advanced to 65–75% HRR (measured also by a Polar heart rate monitor and palpation) as determined by the adjusted-for-aquatic-immersion Karvonen formula [22]. The initial session duration was 20 min, with each subsequent session increased by 5–7 min until 45 min was reached. Multiple factors influence heart rate during aquatic activity, and the aquatic-immersion-adjusted Karvonen heart rate addressed these components such as depth of immersion and water temperature. Each session consisted of 5-min warm-up and cool-down periods, and equal training time of mobility, cardiorespiratory, and strengthening components with rest periods of 1- to 3-min as needed. Participant ability and motor function directed our customized and individualized exercise routines, but followed the protocol guidelines (Table 1). Water positioning (standing, sitting, horizontal, depth), floatation and resistance devices used, and heart rate and Borg exertion scale reports were assessed and recorded daily. Therapists encouraged each participant to work at 65–75% intensity level throughout each aquatic exercise session.

Statistical analysis

Prior to initiation of the study, a sample size analysis was performed. There was no prior data available on RT or AT in individuals with CMISCI on which to base a power calculation. There was however, prior work on cardiorespiratory fitness in a spinal cord injured cohort using aerobic wheelchair propulsion as the exercise intervention. Gass et al. [23] in this early work, physically trained seven spinal cord injured individuals for 7 weeks, five times per week (35 sessions) using wheelchair pushing on a treadmill and measured VO_{2max} before and after the intervention. They found a 35% increase in VO_{2max}. This study involved

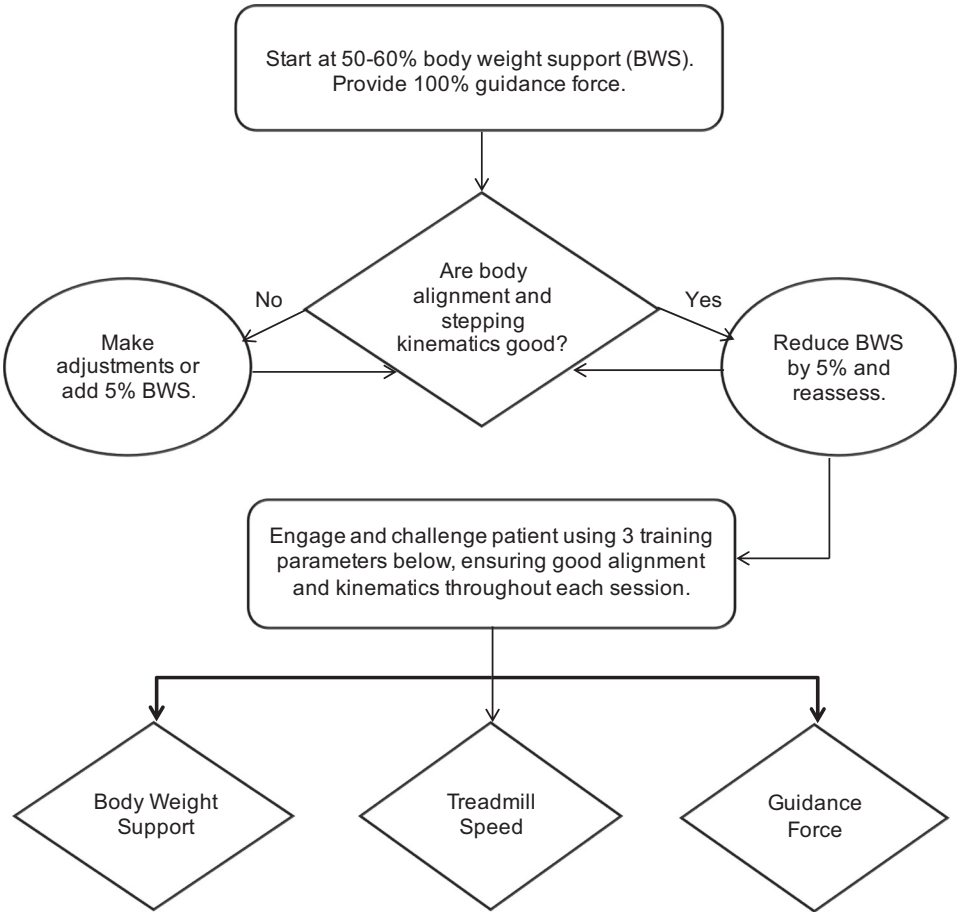

Fig. 1 Robotically Assisted Treadmill Training Protocol using Lokomat®: First session and start of each subsequent session

a similar intensity of exercise experience as what had been proposed for the current work. Based on that prior result, with an alpha of 0.05 and power of 0.8, 28 total participants were estimated to be needed for this study.

We used Microsoft Excel to manage data throughout the trial, checking for data completeness, regularity, and coding. All statistical analyses utilized SPSS version 22. Descriptive statistics, *t*-tests and ANOVA were performed. Descriptive statistics detailed demographics within the sample and independent means. Means and standard deviations were generated for the primary outcome measure (peak VO_2). Paired sampled *t*-tests were performed to determine if peak VO_2 changes occurred in groups pre- and post-intervention. Significance was set a priori with alpha $= 0.05$. A modified intention to treat analysis was performed in which all participants with available data were analyzed according to their group allocations.

Results

We screened a total of 68 individuals with 31 excluded as per exclusion criteria ($n = 14$), declining to commit to full participation ($n = 13$), or for other reasons ($n = 4$). Thirty-seven individuals were randomized to either RT ($n = 20$) or AT ($n = 17$). Figure 2 represents a Consolidated Standards of Reporting Trials (CONSORT) diagram. Of the 20 individuals randomized to RT, 18 completed this intervention. One individual was removed from the study after failing to comply with the medical staff's request to address a non-study related medical condition. Another individual was dismissed after experiencing recurring anxiety episodes in the robotic device. Two individuals failed to complete the AT treatment. One individual completed 24 aquatic exercise sessions before experiencing a non-study related ankle fracture. Another AT participant was withdrawn due to health and bowel management issues. One individual in the RT group was not included in the ergometry final analysis because he could not complete the arm ergometry test secondary to upper extremity spasticity. Except for the previous participants who dropped out for medical reasons, all individuals completed the protocol with no drop outs due to the exercise intensity or demand. Ultimately, participants completed 97% of the exercise interventions, namely 36 sessions under each exercise condition with 20% of the sessions rescheduled to complete the protocol prescribed exercise visits.

Table 1 Aquatic Exercise Guidelines used in this protocol. These guidelines were customized by the therapist based on individual participant's impairments and abilities

Overall Aquatic Exercise Guidelines				
• Water depth: work at the level that provides highest level of function while challenging core stability and balance • Position in water: upright, horizontal, semi reclined based on individual needs, and abilities • Activities: Gait training, cardiovascular conditioning, and strengthening activities • Water temperature 87 to 90 degrees Fahrenheit • 40–45 min of continuous exercise is goal with 1 min rest/change of activity • Effort level goal: minimum 60% max aquatic adjusted heart rate for strengthening and cardiovascular component at 65 to 75% max aquatic adjusted heart rate (moderate to high moderate on perceived exertion scales). Max heart rate was determined during baseline peak arm ergometer test.				
Activity	**Frequency/Reps/Sets**	**Duration (minutes)**	**Potential equipment**	**Comments**
Warm-Up: Water walking	1 set @: forward, backward, sideward	5 minutes	No ↑ surface area to start, slowly ↑ to include paddles for UEs and wrap cuffs for LEs	Core stability focus, open chest expansion in all planes
LE muscle group	8 reps, 1–3 sets both legs for each of the following muscle groups: hip flex/ext/ABD/ADD; knee flex/ext	9 minutes	Use small to increasing in surface area cuffs	Start facing wall 2 hand support; turn parallel one hand support; move away from wall no UE support
Cardio function	Lunge walking/semi reclined paddling/kickboard	7 minutes	As needed to support participant in functional cardio positions	
Cardio function	Step ups, push off wall tethered, cycling UE and LE seated/semi reclined, adapted swim strokes	7 minutes	As needed to support participant in functional cardio positions	
Cool-down	Water walking/Ai Chi	5 minutes		Address any tight muscle groups as needed

min minutes, *UE* upper extremity, *LE* lower extremity, *flex* flexion, *ext* extension, *ABD* abduction, *ADD* adduction.

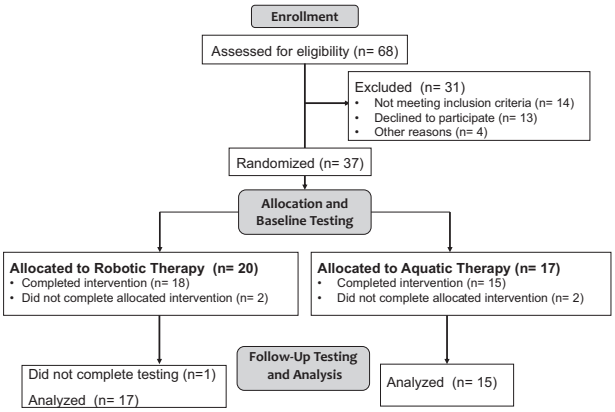

Fig. 2 CONSORT diagram of enrollment of participants into the study

Table 2 Baseline demographics

	Aquatic ($n = 15$)	Robotic ($n = 18$)
Age (yrs)	46.9 ± 9.9	45.4 ± 12.9
Body weight (kg)	87.7 ± 20.7	79.33 ± 20.2
Time since injury (yrs)	12.2 ± 12.6	6.6 ± 4.3
Tetraplegics	11 (73%)	12 (67%)
Paraplegics	4 (27%)	6 (33%)
WISCI (0–20)	9.5 ± 7.6	11.7 ± 6.5
LEMS (0–50)	31.2 ± 11.9	32.4 ± 10.7
UEMS (0–50)	42.9 ± 8.0	41.7 ± 9.7
Community ambulation	10 (67%)	16 (83%)

Participants completing intervention are included

Values are mean ± standard deviation for continuous variables or percentages for categorical variables

Yrs years, *kg* kilogram, *WISCI* Walking Index for Spinal Cord Injury, *LEMS* lower extremity motor score, *UEMS* upper extremity motor score

Baseline demographics

Table 2 displays baseline demographic data for the two groups, including all enrollees including the following: age, body weight, time since injury (TSI), WISCI-III score, LEMS, UEMS, and arm ergometry peak VO_2.

Three-month intervention results

A summary of peak VO_2 results is provided in Table 3. More detailed exercise data are provided several supplemental files (Supplementary Tables 1, 2, and 3 and Supplementary Figures 1 and 2). Neither aquatic exercise nor robotic exercise produced statistical improvement in peak VO_2 when measured by arm cycle ergometry. However, with robotic intervention and using robotic peak VO_2 assessments, peak VO_2 did improve significantly (2.07

Table 3 Summary table of peak VO_2 results after 3 months of intervention.

Group	Intervention	Assessment method	Prepeak VO_2 (ml/kg/min)	Postpeak VO_2 (ml/kg/min)	Delt absolute (ml/kg/min)	Delta (%)	Pre/post *t*-test *p*-value
Aquatic ($n = 15$)	Aquatic (3 months)	Arm Ergometer peak VO_2	13.33 ± 3.06	14.31 ± 3.88	0.98	8.1%	0.14
Robotic ($n = 17$)	Robotic (3 months)	Arm Ergometer peak VO_2	16.48 ± 5.39	16.18 ± 5.11	−0.30	−0.70%	0.33
Robotic ($n = 17$)	Robotic (3 months)	Robotic peak VO_2	14.88 ± 4.30	16.95 ± 6.08	2.07	14.7%	**0.03**

Assessment column indicates the circumstance under which peak VO_2 measurements were performed. Peak VO_2 measurements are ± standard deviation. Delta is provided in absolute and percent change. *p*-values are based on a two-tailed *t*-test. Note that the *n* for the Robotic group is one less in this summary table than that presented in Table 2. This is due to one participant not able to complete the arm ergometer test. Bolded value represents statistical significance

Table 4 Responders vs. non-responders (as defined by a 10% increase in peak VO_2) across the 3-month exercise intervention

A: Aquatic group (Arm Ergometer VO_2)	Responders ($n = 6$)	Non-responders ($n = 9$)
Age (yrs)	44.3 ± 10.7	48.6 ± 8.3
Time since injury (yrs)	4.0 ± 2.9	17.7 ± 12.9
Weight (kg)	77.3 ± 21.6	94.5 ± 15.4
LEMS (0–50)	35.2 ± 11.6	28.6 ± 10.6
Baseline VO_2 (ml/kg/min)	13.1 ± 3.2	13.4 ± 2.8
B: Robotic group (Arm Ergometer VO_2)	Responders ($n = 2$)	Non-responders ($n = 15$)
Age (yrs)	50.0 ± 11.0	46.0 ± 12.1
Time since injury (yrs)	4.5 ± 1.5	6.9 ± 4.5
Weight (kg)	80.9 ± 8.2	79.0 ± 21.3
LEMS (0–50)	27.5 ± 6.5	33.0 ± 11.0
Baseline VO_2 (ml/kg/min)	8.9 ± 0.8	17.5 ± 4.7
C: Robotic group (Robotic Treadmill VO_2)	Responders ($n = 11$)	Non-responders ($n = 6$)
Age (yrs)	44.8 ± 14.5	45.2 ± 8.9
Time since injury (yrs)	5.4 ± 2.8	7.2 ± 4.5
Weight (kg)	78.7 ± 21.9	84.3 ± 12.6
LEMS (0–50)	33.6 ± 11.4	31.7 ± 8.7
Baseline VO_2 (ml/kg/min)	14.5 ± 5.1	15.6 ± 1.2

Data are presented in three sections: A and B—arm ergometry peak VO_2 results for Aquatic and Robotic groups, respectively, and C-robotic treadmill peak VO_2 results for Robotic group

Yrs years, *kg* kilograms, *ml* mililiters, *LEMS* lower extremity motor score

ml/kg/min,14.7%, $p = 0.03$, $n = 17$). The effects of AT and RT on the primary outcome measure, namely arm ergometry measured peak VO_2, were compared using a univariate ANOVA with the arm cycle ergometry being the consistent dependent variable. Even though it did not reach statistical significance ($p = 0.063$), AT provided a larger arm cycle ergometry peak VO_2 change than RT.

Responders vs. non-responders analysis

To determine whether participant characteristics existed to identify a positive response to either of these two interventions, we assessed responder and non-responder groups. We defined a "responder" as a participant who exhibited a 10% or greater peak VO_2 change. This definition was based on our prior work in this population [6], as well as previously published literature in a stroke survivor population [24] that demonstrated a reduced cardiorespiratory risk with 10% change. A responder vs. non-responder comparison produced no apparent statistically significant demographic factors predicting greater cardiorespiratory response (Table 4). It should be noted, however, that when robotic

treadmill peak VO_2 was compared to the arm ergometry peak VO_2, the responder/non-responder ratio changed considerably (from 2:15 to 11:6). We repeated the responder/non-responder comparison using percentage cutoffs ranging from 5 to 9% improvement in peak VO_2 based on our overall average improvement in arm ergometry VO_2 and were unable to identify demographic factors that identified who would respond. Nonetheless, there were some trends noted, namely responders tended to be younger, more recently injured, and lighter weight than non-responders in the aquatic therapy group, and in the robotic therapy group when measurements were made with robotic ergometry.

Discussion

Aquatic exercise in peak arm ergometry VO_2 demonstrated an average improvement of 8.1% with a wide variance. Our previous robotic treadmill intervention was conducted at 80–85% of HRR, in contrast to the lower intensity (65–75%) of this current study. The lower intensity (65–75% HRR) was perhaps sufficient to induce a change in peak VO_2 during robotic exercise, but may be insufficient to stimulate a change in cardiorespiratory fitness detectable via arm ergometry. This lack of sensitivity suggests that arm ergometry testing may not be the best tool to detect change in cardiorespiratory fitness following non-arm ergometry training interventions. This is despite previous work identifying a moderate correlation ($r = 0.87$) between arm ergometry and robotic VO_2 measurement, although that study was not interventional [17].

Arm ergometry is an accepted measurement tool for assessing cardiorespiratory fitness in individuals with gait disturbances limiting treadmill testing [25, 26]. It may not however, be the most sensitive technique. The sensitivity difference may be due to differing muscle group activation during both the exercise intervention and cardiorespiratory testing. With coached robotic treadmill training and testing, the same leg and possibly trunk musculature are being activated as much as possible. In the water, upper extremity, trunk and preserved lower extremity musculature are recruited and augmented by gravity reduction and other hydrodynamic principles such as hydrostatic pressure, viscosity, and turbulence. Cardiorespiratory testing using arm ergometry recruits primarily the upper extremity and partial trunk musculature. Even though peak VO_2 measurement is intended to assess primarily cardiorespiratory fitness, the technique used relies on specific musculature, perhaps limiting test sensitivity when the exercise intervention and the testing paradigm are not muscularly matched (such as when using arm ergometry to measure outcomes in robotic treadmill exercised individuals). This is particularly true since we included both paraplegic and tetraplegic individuals in the protocol, and impaired upper extremity function may have limited arm ergometry ability and performance in those with tetraplegia.

This study reproduced our previous findings that robotic treadmill therapy three times per week over 12 weeks improves cardiorespiratory fitness as measured by robotic treadmill peak VO_2 measurements. The robotic treadmill peak VO_2 improvement in this study across robotic randomized intervention was 14.7%, similar to the 12.3% improvement reported in our prior single intervention protocol [6].

Specificity of intervention-test is reported with non-SCI participants. Pogliaghi et al. [27]. measured arm and leg cycling peak VO_2 responses in healthy older males randomized to a 12-week arm or leg cycling intervention. Both groups displayed increases in peak VO_2 responses post-intervention regardless of the exercise test modality. However, significantly higher peak VO_2 responses occurred in the test modality specific to the training intervention. Another study by Bhambhani et al. [28] showed significantly improved peak VO_2 responses in individuals with SCI randomized to an 8-week leg or arm cycling program with improvements only demonstrated by the test modality that matched the intervention phase for the respective randomized groups. Similarly, in a study of participants with peripheral arterial disease randomized to either arm or leg crank exercise, the improvement in peak VO_2 was more robust when tested by the matched (arm or leg ergometry) technique [29]. To accurately capture cardiorespiratory adaptations our results combined with previous findings and literature stress the importance in selecting testing assessments specific to the training intervention. Both the robotic and aquatic testing data show task specificity is an important factor to consider when choosing test modalities to assess cardiorespiratory outcome before and after training those with incomplete SCI. Additionally, it is important to consider which cardiorespiratory training modality is more available for a given client. Rehabilitation institutions with wellness programs may include body weight support cardiorespiratory training, although these devices are not ubiquitous. Aquatic exercise is more likely to be readily available in a community setting and under some circumstances (depending on individual impairment and water safety) may be performed in a group format.

At this time, no peak VO_2 minimal clinically important difference is established for individuals with SCI [30, 31]. One aspect of the importance of improvement in peak VO_2 in people with CMISCI rests in the potential for greater capability and endurance in activities of daily living (ADL) performance. A study of individuals with paraplegia showed that improvement in peak VO_2 positively correlated with self-reported physical activity [32]. The other benefit

of improving peak VO_2 is the potential reduction in cardiorespiratory disease and coronary heart disease, as demonstrated in the able-bodied population [33].

Study limitations

A relatively small sample size limited the study, although given the intensity of the intervention, recruitment of 37 participants across the two centers represents one of the larger SCI randomized exercise trials. Because of the complexity and length of the study, compliance with the schedule, especially over winter months, was a challenge, with a rescheduling rate approaching 20%. Both robotic treadmill training and aquatic intervention protocols were designed to allow therapists to customize training based on individual participant needs while meeting this set study exercise structure. Dosage of each intervention remained consistent within the designed protocol, but different activities were utilized to optimize individual interventions. For example, a participant requiring increased hip flexion practiced flexion activities while another participant with preserved hip extension performed other activities such as hip abduction with both individuals maintaining the prescribed dosage intensity and time. Equipoise was maintained and interventions reflected customized clinical care within the study protocol structure.

We would have preferred to collect peak VO_2 test during aquatic therapy itself, but the necessary equipment was not available at the time of this study. Our laboratory is currently evaluating the reliability and validity of peak VO_2 responses obtained during deep water aerobic activities in individuals with SCI. Preliminary results show reliable and valid peak VO_2 under these conditions [34]. We additionally determined 65–75% HRR was potentially insufficient to maximize the change in cardiorespiratory fitness. When physically possible for participants, we recommend 75–85% HRR for all cardiorespiratory training occurring in deep water thereby facilitating a greater cardiorespiratory response [35].

Blinding of the testers performing the peak VO_2 measurement did not occur at both sites given the study complexities and manpower needs. Potential bias may be one concern but with multiple concurrent participants testers were evaluating individuals receiving different interventions on a regular basis. Furthermore, the testers held no direct knowledge of the preintervention results at the time of the post intervention testing.

The heterogeneity of our study participants, even with well described inclusion criteria, creates issues in determining and assessing meaningful cardiorespiratory change. Our struggle to identify homogeneous subgroups who could optimally benefit from one intervention or the other is not novel in clinical rehabilitation research [36, 37].

To optimize best care, it would be helpful to understand not only the intensity, frequency, and specific intervention parameters but also the duration, or how many visits facilitate best care to improve cardiorespiratory and cardiovascular health. Another important area to investigate is the exercise parameters that will maintain the improved cardiorespiratory health for individuals with SCI. As mentioned previously the large fitness variance in the SCI population (due to many factors) creates difficulties with exact rehabilitative and wellness intervention dosage. Although exercise guidelines are available for individuals with SCI, further refinement is needed [38].

Aquatic and robotic treadmill therapies are can safely improve cardiorespiratory fitness in individuals with CMISCI. The cardiorespiratory effect of coached robotic treadmill therapy provided a significant improvement as measured by a peak VO_2 robotic treadmill testing paradigm, but not with an arm ergometry paradigm. In order to optimize the sensitivity of testing, it is best to match the intervention with the testing approach. Although not everyone responded to aquatic or robotic exercise intervention, this dataset suggests that younger age, a more recent time since injury, and lower body weight may facilitate increased cardiorespiratory improvement.

Data archiving

Data generated and analyzed during this study are included in this published article and its supplementary information files. This study is registered under ClinicalTrials.gov Identifier: NCT01407354, and some of the summary data are available at that repository as well.

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Author contributions PHG was responsible for co-study design, co-submitting the application for funding, screening, and medical supervision of participants at one center, writing the initial draft of the manuscript, and submission of completed manuscript. WS was responsible for daily study execution, robotic treadmill training and collection of all VO_2 data at one center, initial statistical evaluation of the collected data, and major editing of the manuscript. LVH was responsible for co-design of the robotic treadmill algorithm and training, regulatory management and daily oversight including robotic treadmill training and aquatic therapy, VO_2 data collection, screening and recruitment of participants at the second center, and review of the manuscript. KT was responsible for co-study design, medical oversight

at the second center, co-authorship of the original funding application, and review of the manuscript. WMS was responsible for statistical analysis of the overall study. PRG was responsible for co-study design, co-submitting the application for funding, daily oversight of the dual center study, the design of the aquatic intervention, direct supervision of the aquatic intervention at one center and indirect at second site, initial statistical assessment with WS, and critical partial writing and review of the manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research.

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