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Impacts of aquatic walking on arterial stiffness, exercise tolerance, and physical function in patients with peripheral artery disease: a randomized clinical trial

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Peripheral artery disease (PAD) is an atherosclerotic disease that is associated with attenuated vascular function, cardiorespiratory capacity, physical function, and muscular strength. It is essential to combat these negative effects on health by incorporating lifestyle interventions to slow disease progression, such as exercise. We sought to examine the effects of aquatic walking exercise on cardiovascular function, cardiorespiratory capacity [maximal volume of oxygen consumption ($\dot{V} O_{2max}$)], exercise tolerance [6-min walking distance (6MWD)], physical function, muscular strength, and body composition in patients with PAD. Patients with PAD ($n = 72$) were recruited and randomly assigned to a 12-wk aquatic walking training group (AQ, $n = 35$) or a control group (CON, $n = 37$). The AQ group performed walking and leg exercises in waist-to-chest-deep water. Leg arterial stiffness [femoral-to-ankle pulse wave velocity (legPWV)], heart rate (HR), blood pressure (BP), ankle-to-brachial index (ABI), $\dot{V} O_{2max}$, 6MWD, physical function, muscular strength, body composition, resting metabolic rate (RMR), and flexibility were measured before and after 12 wk. There were significant group X time interactions ($P < 0.05$) after 12 wk for legPWV and HR, which significantly decreased ($P < 0.05$) in AQ, and $\dot{V} O_{2max}$, 6MWD, physical function, and muscular strength, which significantly increased ($P < 0.05$) in AQ, compared with no changes in CON. There were no significant differences ($P > 0.05$) for

BP, ABI, RMR, or flexibility after 12 wk. Interestingly, there was relatively high adherence (84%) to the aquatic walking exercise program in this population. These results suggest that aquatic walking exercise is an effective therapy to reduce arterial stiffness and resting HR and improve cardiorespiratory capacity, exercise tolerance, physical function, and muscular strength in patients with PAD.

NEW & NOTEWORTHY The results of this study reveal for the first time that aquatic walking exercise can decrease arterial stiffness and improve exercise tolerance, cardiorespiratory capacity, and muscular strength in patients with peripheral artery disease (PAD). Aquatic walking exercise training demonstrates relatively high exercise adherence in this population. Aquatic walking exercise training may be a useful therapeutic intervention for improving physical function in patients with PAD.

INTRODUCTION

Peripheral artery disease (PAD) is the manifestation of atherosclerotic plaque in the larger arteries in the legs, which results in impaired blood flow and oxygen (O₂) delivery to the lower extremities (28). PAD affects nearly 12 million people in the United States (52), and the cost associated with PAD is greater than or similar to costs associated with congestive heart failure and cerebrovascular disease (27). Patients with PAD often experience claudication (leg pain), which impairs walking ability, lowers physical activity levels, and results in health-related quality-of-life scores lower than those of patients with coronary artery disease and congestive heart failure (57, 72). Previous studies utilized exercise-training programs to improve walking capacity, exercise tolerance, and overall health in patients with PAD (4, 24, 30, 49). These studies suggest that walking exercise-training programs that consist of 30 – 60 min of light-to-moderate-intensity walking for ~3 times/wk over ~2–6 mo (4, 24, 30, 49, 66) alone can improve exercise tolerance (4, 24, 30, 49), lower-limb blood flow (24, 30), endothelial function (4), and perceived physical function scores (66). Although participating in an exercise program may be beneficial to reduce the risks for further disease progression in patients with PAD, exercise programs that include weight-

bearing gait exercise may induce greater claudication. This may synergistically induce greater claudication, prevent exercise participation, and cause low adherence in exercise programs in this population.

Swim training has been shown to improve blood pressure (BP) and vascular function in healthy older adults (47). We have also previously demonstrated that swim training has beneficial effects on body composition, BP, arterial stiffness, muscular strength, and cardiorespiratory health in postmenopausal women with stage 2 hypertension (76). Additionally, warm water immersion (~28–30°C) has been shown to reduce pain (2, 45), improve blood flow (2, 10), and decrease joint loading and stress on the lower-extremity musculature (10, 56). In fact, it has been suggested that water immersion alone improves blood flow and BP in patients with PAD (64) and water immersion heat therapy may improve exercise tolerance in patients with PAD (1). Therefore, an exercise-training program that takes place in warm water may be an optimal therapeutic intervention for reducing leg pain and improving exercise tolerance in patients with PAD. Thus, water immersion exercise, such as walking exercise training in the water, may be an alternative exercise modality to ground walking exercise for improving overall health and physical function in patients with PAD. To our knowledge, this is the first study that examined the effects of aquatic walking exercise in patients with PAD, and we hypothesized that aquatic walking exercise training would reduce arterial stiffness, resting heart rate (HR), and BP and improve ankle-to-brachial index (ABI), maximal volume of O₂ consumption ($\dot{V} O_{2max}$), 6-min walking distance (6MWD, exercise tolerance), physical function, muscular strength, body composition, resting metabolic rate (RMR), and flexibility in patients with PAD.

METHODS

Participants. Participants were recruited with flyers and clinic referrals in a metropolitan city in South Korea at multiple community health centers where the members were primarily female. Study allocation was determined randomly with a computerized random-number generator (Fig. 1). All participants were female and classified as Fontaine stage I or II PAD with an ABI of 0.7–0.9. All participants were sedentary, defined as participating in under 1 h of regular exercise participation per

week within the previous year. Exclusion criteria included current smoker (smoking within <6 mo), psychiatric conditions, and pulmonary, renal, and thyroid diseases. Exclusion criteria for these diseases were included to avoid any secondary disease effects on the target population used in the present study. All procedures were conducted in accordance with protocols approved by the institutional review board designated by the Ministry of Health and Welfare (PNU IRB-2016_92_HR) and performed in accordance with the Declaration of Helsinki, and all subjects provided written, informed consent prior to experimental measures. All protocols and laboratory procedures took place at the community centers. This study was registered with <https://clinicaltrials.gov/> (NCT03849300).

Study design. This study used a two-armed parallel experimental design. Arterial stiffness, resting HR, BP, ABI, $\dot{V} O_{2max}$, 6MWD, physical function scores, handgrip strength, leg strength, anthropo- metrics, RMR, and flexibility were assessed at baseline and after the 12 wk. All measurements were performed at the same time of day (8:00 AM, ± 1 h) after a 12-h fast. The $\dot{V} O_{2max}$ test and 6-min walk test were separated by a period of ~ 24 h to prevent confounding effects of fatigue. After baseline measurements were completed, participants were randomly allocated to either the aquatic walking training group (AQ, $n = 35$) or the control group (CON, $n = 37$). The AQ group participated in a supervised aquatic walking training program for 12 wk that included a warm-up, a main exercise session, and a cooldown. The CON group did not participate in any exercise program or perform any additional exercise. The CON group participants were present and supervised in the laboratory at the same frequency and time of day as the AQ group (10:00 AM, ± 1 h) and performed sedentary activities such as reading books, listening to music, or learning new computer skills, which are among some of the activities these participants normally perform when attending the community center daily. The AQ and CON groups were advised to refrain from changing any dietary habits throughout the study period, and diet logs were given to researchers weekly to monitor caloric intake to ensure that there were no changes in diet throughout the intervention. If researchers noticed differences in caloric intake, they advised participants to maintain their normal diet. Lunch and dinner were provided to participants at the community centers. All participants were supervised by qualified

trainers, and measurements were taken by experienced researchers; researchers who performed the laboratory measurements were blinded to the randomization of subjects.

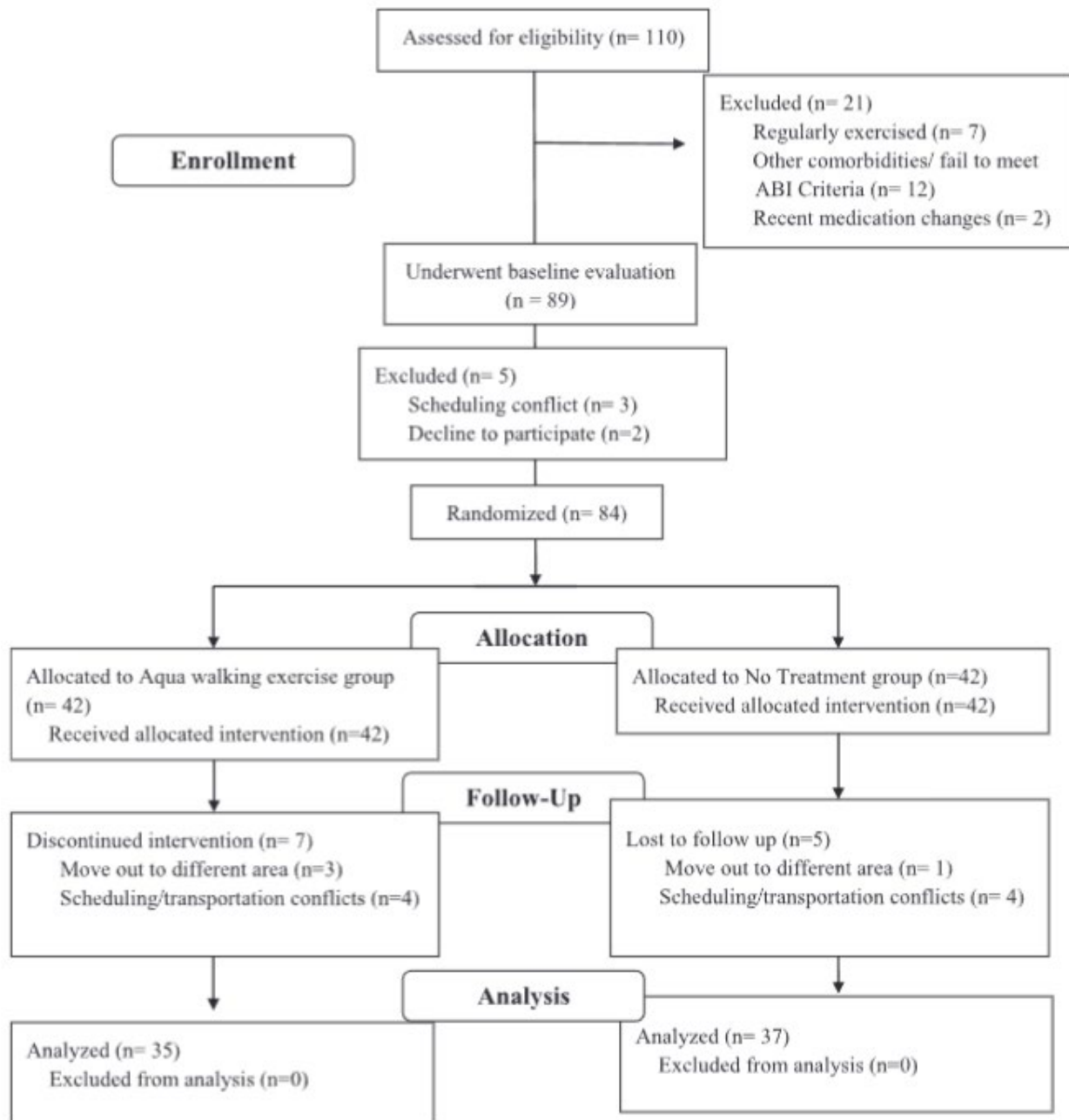


Fig. 1. Study allocation and flowchart. ABI, ankle-brachial index; Aqua, aquatic.

Exercise program. Participants in the AQ group participated in an aquatic

walking exercise-training program for 12 wk, 4 days/ wk, for 60 min/day (Table 1), and this was adapted from previous literature for older individuals and patients with PAD (2, 47). Sessions were conducted in waist-to-chest-deep water (28 –30°C) in a group setting (2). Participants were allowed to use flotation devices as needed for safety purposes. Participant HR was monitored using a wearable Polar HR monitor (Polar Electro Oy, Kempele, Finland) during all exercise sessions to maintain the appropriate training intensity. The aquatic walking exercise-training program intensity was established using heart rate reserve (HRR) and Borg’s revised rating-of-perceived exertion scale (RPE, 0 –10 scale). HRR was calculated as $\{HRR = [\%intensity\ desired \times (HR_{max} - HR_{rest})] + HR_{rest}\}$, where HR_{max} is maximum HR and HR_{rest} is resting HR. The intensity of the program increased every 4 wk: *weeks 1–4* were at 50 –60% HRR and 6 –8 RPE, *weeks 5–8* were at 60 –70% HRR and 6 –8 RPE, and *weeks 9–12* were at 70 –85% HRR and 6 –8 RPE. Each training session was supervised, and each trainer was assigned to work with 10 participants during the sessions. HR monitors and RPE were checked every 5 min during the sessions. If the HR or RPE was too low or too high according to the intensity level, the participants were encouraged to either increase or decrease their effort during the exercise-training session.

The program was divided into three sections including a warm-up (10 min), the main exercise component (40 min), and a cooldown (10 min; Table 1). Both the warm-up and cooldown included underwater stretching that emphasized lower-limb muscles (quadriceps, ham-strings, hip abductors/adductors, and hip flexors) and low-intensity gait training (forward, backward, and lateral movement; 2). The main exercises were performed for a total of 40 min. The first 10 min of main exercises included simple movement patterns such as hip flexion-extension, hip abduction-adduction, and knee flexion-extension (2). The next 30 min of the main exercise session consisted of water walking exercises (forward, backward, and lateral; 2).

Arterial stiffness, HR, BP, and ABI. Participants rested in a supine position for 5 min. Femoral-to-ankle pulse wave velocity (legPWV), a measurement of peripheral arterial stiffness, was measured using applanation tonometry (TU-100 and VP-2000; Omron Healthcare, Kyoto, Japan). A pulse wave sensor was placed on the femoral

artery, while the cuffs with pulse wave sensors on the ankles and electrocardiogram (ECG) electrodes remained in place from the ABI measurement. BP, ECG, and pulse waveforms were simultaneously recorded for 10–30 s. Data analysis was performed according to the Clinical Applications of Arterial Stiffness Task Force III (69).

Participants rested in a seated position for 5 min. Resting HR and systolic and diastolic BP were measured in duplicate using radial artery palpation and an automated sphygmomanometer (BP-200; Omron Healthcare), respectively, before and after 12 wk. The average of the two measurements was recorded as the resting values. If the measurements differed by >5 mmHg, an additional measurement was taken, and the two closest readings (differing by <2 mmHg) were averaged (50). The interclass correlation coefficient in our laboratory for systolic and diastolic BP calculated on two measurements is =0.97.

Participants rested in a supine position for 5 min. ABI was measured using the VP-2000 (Omron Healthcare). ECG electrodes were placed on the forearms. BP cuffs with pulse wave sensors were wrapped around both arms (brachial artery) and ankles (posterior tibial artery). Measurements were recorded for 10–30 s.

Cardiorespiratory capacity and 6MWD. The Cornell modified Bruce treadmill test was used to determine $\dot{V}O_{2\max}$ (32). This Bruce protocol modification has been proven to be valid and reproducible (48) and has been used in disease populations (76). The modified Bruce test consists of eleven 2-min stages that progress from 1.7 miles/h and 0% grade to 5 miles/h and 18% grade (48). The treadmill test was ended when the participants reached volitional fatigue. Expired gases were measured with a metabolic cart (OxyCon Pro; Viasys Healthcare, Conshohocken, PA).

The 6-min walk test was used to determine maximal walking distance, or exercise tolerance. Participants were asked to walk as many laps as possible around a 100-m track for 6 min.

Physical function. Physical function was assessed collectively using physical function questionnaires from the Medical Outcomes Study Short Form 36 General Health Survey (MOS SF-36; 73). Other parameters (i.e., not physical function domain) were not assessed using the MOS-SF 36. Physical function questionnaires from the MOS SF-36 are valid and reliable surveys that are often used for assessing physical

function in patients with PAD (22, 24, 66, 73).

Muscular strength. Upper-body muscular strength was determined using maximal isometric handgrip strength with a standard handgrip dynamometer (Jamar, Bolingbrook, IL). Measurements of the dominant hand were taken three times, and the best of the three trials was recorded as the measurement.

Lower-body muscular strength was assessed using one-repetition maximum (1RM) on a leg extension machine (Cybex 6000; Lumex, Albertson, NY). The 1RM was measured with the dominant leg, and the 1RM was achieved within five or fewer attempts. The highest weight lifted using the proper form was recorded as the 1RM.

Anthropometrics. Anthropometric measurements, including height, total body mass, body mass index (BMI), and body composition, were measured before and after 12 wk. Height was measured using a standard stadiometer to the nearest 0.1 cm. Body composition was estimated using bioelectrical impedance analysis (InBody230; Biospace, Seoul, Korea), which simultaneously recorded total body mass (nearest 0.1 kg) and body fat (nearest 0.1%; 60). BMI was calculated as body mass divided by the height squared (kg/m^2).

Table 1. *Aquatic walking training program*

Order	Exercise	Duration, min	Intensity	Frequency, times/wk
Warm-up	Stretching and gait training	10		4
Main exercise	Hip flexion-extension, hip abduction-adduction, knee flexion-extension, and water walking	40		4
	Weeks 1-4		50-60% HRR; 6-8 RPE	
	Weeks 5-8		60-70% HRR; 6-8 RPE	
	Weeks 9-12		70-85% HRR; 6-8 RPE	
Cool down	Stretching and gait training	10		4

HRR, heart rate reserve; RPE, rating of perceived exertion.

Table 2. Participant characteristics and anthropometrics before and after 12 wk of control or aquatic walking exercise training

	CON			AQ		
	Pre	Post	Δ	Pre	Post	Δ
Age, yr	71.0±8.0	71.0±8.0		70.0±10.0	70.0±10.0	
Mass, kg	55.1±5.1	54.9±5.3	-0.2±0.2	54.1±7.1	55.9±7.4	1.8±0.4
Height, cm	162.1±7.3	162.1±7.3		160.1±5.9	160.1±5.9	
BMI, kg/m ²	21.3±3.2	21.7±4.1	0.4±0.9	20.4±2.1	21.8±2.8	1.4±0.7
Body fat, %	30.9±4.7	30.5±5.2	-0.4±0.5	29.7±3.6	28.5±3.9	-1.2±0.3
Lean body mass, kg	38.1±4.2	38.2±4.5	0.1±0.3	38.0±4.4	40.0±4.9	2.0±0.5
ABI	0.8±0.3	0.8±0.3	0.1±0.1	0.8±0.2	0.8±0.3	0.1±0.1

Values are means ± SD; no. of participants (*n*) = 37 for control group (CON) and 35 for aquatic walking training group (AQ). Δ, change; ABI, ankle-brachial index; BMI, body mass index; Pre and Post, before and after 12 wk of control/aquatic walking exercise training, respectively.

Resting metabolic rate. RMR was estimated using a metabolic cart (OxyCon Pro; Viasys Healthcare). Subjects remained in the supine position and were instructed to breathe normally and not to fall asleep during the measurement, and the measurements were performed for 30 min.

Flexibility. Flexibility was measured using the Young Men's Christian Association (YMCA) sit-and-reach test. Each participant was given three attempts to reach as far as possible with proper form, and the best of the three trials was recorded as the score.

Statistical analysis. The Shapiro–Wilk test was used to determine data normality. Independent *t* tests were used to determine any baseline differences between the AQ and CON groups. A two-way analysis of variance (ANOVA) with repeated measures [group (AQ and CON) X time (pre- and post-12 wk)] was used to determine the difference of changes between pre- and post-aquatic walking training program within and between groups on the dependent variables. When a significant interaction was noted, paired *t* tests were used for post hoc comparisons. All analyses were performed using SPSS 24 (SPSS, Chicago, IL). Data are presented as means ± SD. Statistical significance was set to *P* < 0.05. Additionally, correlations between variables were assessed with Pearson product-moment correlations. A power analysis calculation was used to determine that a minimum sample size of 64 (32 in each group) would allow for the observation of a difference of 3–5% between groups (AQ vs. CON) for PWV with a power of 90% (3, 47).

RESULTS

No participants reported any unfavorable symptoms or adverse side effects resulting from the aquatic walking training program. Of the 84 participants included in the study interventions, 72 participants completed the trial (AQ, $n = 35$; CON, $n = 37$) and were included in the analysis (Fig. 1 and Table 2). Participant comorbidities included diabetes mellitus, hypertension, dyslipidemia, heart failure, and other conditions such as previous myocardial infarction, cardiac valve dysfunction, arrhythmias, and knee and/or hip arthritis (Table 3). Participants in the AQ group demonstrated 84% adherence to the supervised 12-wk aquatic walking training program. There were no significant differences between groups ($P > 0.05$; Tables 2 and 4). There were significant group X time interactions ($P < 0.05$) for legPWV, resting HR, $\dot{V}O_{2\max}$, 6MWD, physical function, handgrip strength, and leg strength. After the exercise program in the AQ group, legPWV [change (Δ) -2.6 ± 0.7 m/s] and resting HR (Δ -2.3 ± 1.4 beats/min) significantly decreased ($P < 0.05$), whereas $\dot{V}O_{2\max}$ (Δ 2.4 ± 1.0 mL \cdot kg $^{-1}\cdot$ min $^{-1}$), 6MWD (Δ 50.0 ± 8.0 m), physical function score (Δ $6.0 \pm 9.0\%$), handgrip strength (Δ 1.2 ± 0.1 kg), and leg strength (Δ 1.9 ± 9.1 kg) significantly increased ($P < 0.05$), compared with pre-exercise program and CON (Fig. 2, A–D, and Table 4). There was a moderate relationship ($r = 0.5$, $P < 0.05$) between $\dot{V}O_{2\max}$ and 6MWD (Fig. 3) and a weak-to-moderate relationship ($r = -0.3$, $P < 0.05$) between legPWV and 6MWD (Fig. 4). There were no significant differences ($P > 0.05$) for BP, ABI, anthropometrics, RMR, flexibility, or caloric intake after 12 wk (Tables 2 and 4).

DISCUSSION

This study was conducted to investigate the impacts of aquatic walking exercise training on arterial stiffness, resting HR, BP, ABI, cardiorespiratory capacity, exercise tolerance, physical function, muscular strength, body composition, RMR, and flexibility in patients with PAD. There are several novel findings from this study that may be clinically beneficial for this population. First, there were significant reductions in arterial stiffness and resting HR after the 12-wk exercise program. Second, cardiorespiratory capacity, exercise tolerance, and muscular strength all significantly improved after the exercise program. Additionally, self-reported physical function, a marker of quality of life, was significantly improved following training. To our knowledge, this is the first study to show

the beneficial effects of a 12-wk aquatic walking training program on arterial stiffness, resting HR, cardiorespiratory capacity, exercise tolerance, physical function, and muscular strength in patients with PAD.

Table 3. *Participant comorbidities and medications*

Comorbidity or Condition	CON	AQ
Diabetes mellitus	12	13
Hypertension	37	35
Dyslipidemia	30	29
Arthritis	28	29
Cardiac/other vascular diseases	12	11
Medication	CON	AQ
Angiotensin-converting enzyme inhibitors	13	9
ANG II receptor blockers	7	11
Diabetic medication/insulin therapy	12	13
Beta-Blockers	9	8
Calcium channel blockers	4	7
Diuretics	6	10
Nonsteroidal anti-inflammatory medication	19	21

No. of participants (*n*) = 37 for control group (CON) and 35 for aquatic walking training group (AQ).

Arterial stiffness, resting HR, and BP. Increased arterial stiffness has been reported in patients with PAD (80). Previous studies have shown that arterial stiffness was reduced following ground and treadmill walking interventions in overweight adults (34) and young men and women with prehypertension (8). To our knowledge, no studies have examined the impacts of aerobic exercise training on arterial stiffness in patients with PAD. In the present study, legPWV was used to assess arterial stiffness, and arterial stiffness was significantly reduced following the aquatic walking exercise training (from 12.8 ± 1.6 to 10.2 ± 0.9 m/s). Increased nitric oxide bioavailability has been reported to be a key player in determining arterial elasticity (35). It has been previously reported that reductions in peripheral PWV following exercise programs have been partially attributed to improvements in nitric oxide bioavailability, suggesting an improvement in vasodilatory function in response to exercise training (23, 36, 60). Improved nitric oxide bioavailability may be a potential mechanism in the present study, given that ABI remained the same before and after the exercise program, suggesting a lack of structural change within the vasculature. However, nitric oxide bioavailability and vasodilatory capacity were not directly examined in this study and warrant further

investigation.

Table 4. Participant heart rate, blood pressure, resting metabolic rate, handgrip strength, leg strength, arterial stiffness, cardiorespiratory capacity, 6-min walking distance, flexibility, and physical function before and after 12 wk of control or aquatic walking exercise training

	CON			AQ		
	Pre	Post	Δ	Pre	Post	Δ
Resting HR, beats/min	71.2 \pm 5.0	70.2 \pm 10.0	-1.0 \pm 5.0	70.2 \pm 7.8	67.9 \pm 9.1 [†]	-2.3 \pm 1.4
SBP, mmHg	131.8 \pm 15.0	132.4 \pm 9.0	0.6 \pm 6.0	133.4 \pm 12.9	130.4 \pm 8.2	-3.0 \pm 4.0
DBP, mmHg	91.8 \pm 8.0	90.7 \pm 11.0	1.1 \pm 3.0	87.8 \pm 6.8	82.7 \pm 10.0	-5.1 \pm 3.2
RMR, kcal	1029.8 \pm 52.4	1022.8 \pm 44.2	-6.8 \pm 8.2	1003.3 \pm 44.6	1021.5 \pm 40.5	18.2 \pm 4.1
Handgrip strength, kg	25.8 \pm 2.8	25.1 \pm 1.2	-0.7 \pm 1.6	24.8 \pm 3.7	26.0 \pm 3.7 [†]	1.2 \pm 0.0
Leg strength, kg	46.1 \pm 8.1	45.2 \pm 12.1	-0.9 \pm 4.0	45.4 \pm 11.9	47.3 \pm 20.9 [†]	1.9 \pm 9.0
legPWV, m/s	12.4 \pm 1.3	12.3 \pm 1.1	-0.1 \pm 0.2	12.8 \pm 1.6	10.2 \pm 0.9 [†]	-2.6 \pm 0.7
VO _{2max} , mL·kg ⁻¹ ·min ⁻¹	19.2 \pm 2.2	17.8 \pm 5.3*	-1.4 \pm 3.1	18.1 \pm 6.1	20.5 \pm 5.2 [†]	2.4 \pm 0.9
6MWD, m	360.0 \pm 90.0	358.0 \pm 92.0	-2.0 \pm 2.0	390.0 \pm 80.0	440.0 \pm 88.0 [†]	50.0 \pm 8.0
Sit-and-reach test result, cm	15.4 \pm 6.1	15.2 \pm 3.3	-0.2 \pm 2.8	14.3 \pm 8.3	15.9 \pm 6.3	1.6 \pm 2.1
Physical function score, %	47.0 \pm 24.0	46.0 \pm 21.0	-1.0 \pm 3.0	46.0 \pm 22.0	52.0 \pm 31.0 [†]	6.0 \pm 9.0

Values are means \pm SD; no. of participants (n) = 37 for control group (CON) and 35 for aquatic walking training group (AQ). Δ , change; DBP, diastolic blood pressure; HR, heart rate; legPWV, femoral-to-ankle pulse wave velocity; 6MWD, 6-min walking distance; Pre and Post, before and after 12 wk of control/aquatic walking exercise training, respectively; RMR, resting metabolic rate; SBP, systolic blood pressure, \dot{V} O_{2max}, maximal volume of oxygen consumption. * P < 0.05 different from Pre. [†] P < 0.05 different from CON.

Additionally, skeletal muscle capillary density has been shown to improve following aerobic exercise training (38). An improvement in muscle quality, specifically an increase in skeletal muscle capillarization, may be a contributing factor in the reduction in peripheral arterial stiffness by reducing systemic vascular resistance (21, 28a, 60), although the relationship warrants further research.

Increased levels of arterial stiffness have been shown to be associated with shorter walking distances in patients with PAD, and the relationships between both central (11, 74) and systemic (5) arterial stiffness and walking distance in patients with PAD have been previously investigated. We also found that following 12 wk of aquatic walking exercise training, the change in legPWV was found to be moderately associated

with the change in 6MWD in this population (Fig. 4). This suggests that the change in arterial stiffness may be associated with the change in walking distance.

Patients with PAD have been shown to demonstrate attenuated vagal tone (68), and attenuated vagal tone has been shown to be associated with the occurrence of adverse cardiac events in patients with PAD (14, 39). Additionally, resting HR is inversely associated with vagal tone (79), and a high resting HR has been shown to play a role in the progression of cardiovascular diseases (20). Therefore, utilizing an intervention to reduce resting HR and improve vagal tone in patients with PAD may be beneficial for protection against cardiac events and slowing disease progression. Resting HR has been shown to be significantly lower following aerobic exercise- training programs in young, middle-aged, and older subjects (33, 60, 76). A previous study involving patients with PAD demonstrated that HR at a submaximal exercise intensity was reduced after 12 wk of treadmill training, and this was partially attributed to an increase in maximal $\dot{V}O_2$; however, the effect of treadmill training on resting HR was not examined (31). In the present study, we demonstrated that resting HR was significantly reduced ($\Delta -2.3 \pm 1.4$ beats/min) following the 12-wk aquatic walking training program. The reduction in resting HR may be partially attributed to an increased activation of the parasympathetic nervous system and inhibition of the sympathetic nervous system at rest, and these possible mechanisms in response to endurance exercise training have been previously reported in both healthy and disease populations (15, 37, 82). This improvement in parasympathetic tone over sympathetic activation may be beneficial to slow the progression of PAD (40). However, autonomic nervous system interplay was not examined in this study, and further investigation is warranted to examine the contribution of the exercise training-induced improvements in autonomic function and disease progression in PAD.

Elevated BP has been shown to be an important predictor for the risks of cardiovascular events in patients with PAD (58), and nearly 55% of patients with PAD exhibit hypertension (18). Aerobic exercise interventions have been shown to reduce BP and risks for other cardiovascular disease conditions in humans (60, 62, 76). Therefore, using aerobic exercise training as a therapeutic treatment to reduce BP in patients with PAD, such as aquatic walking exercise training, may result in decreased

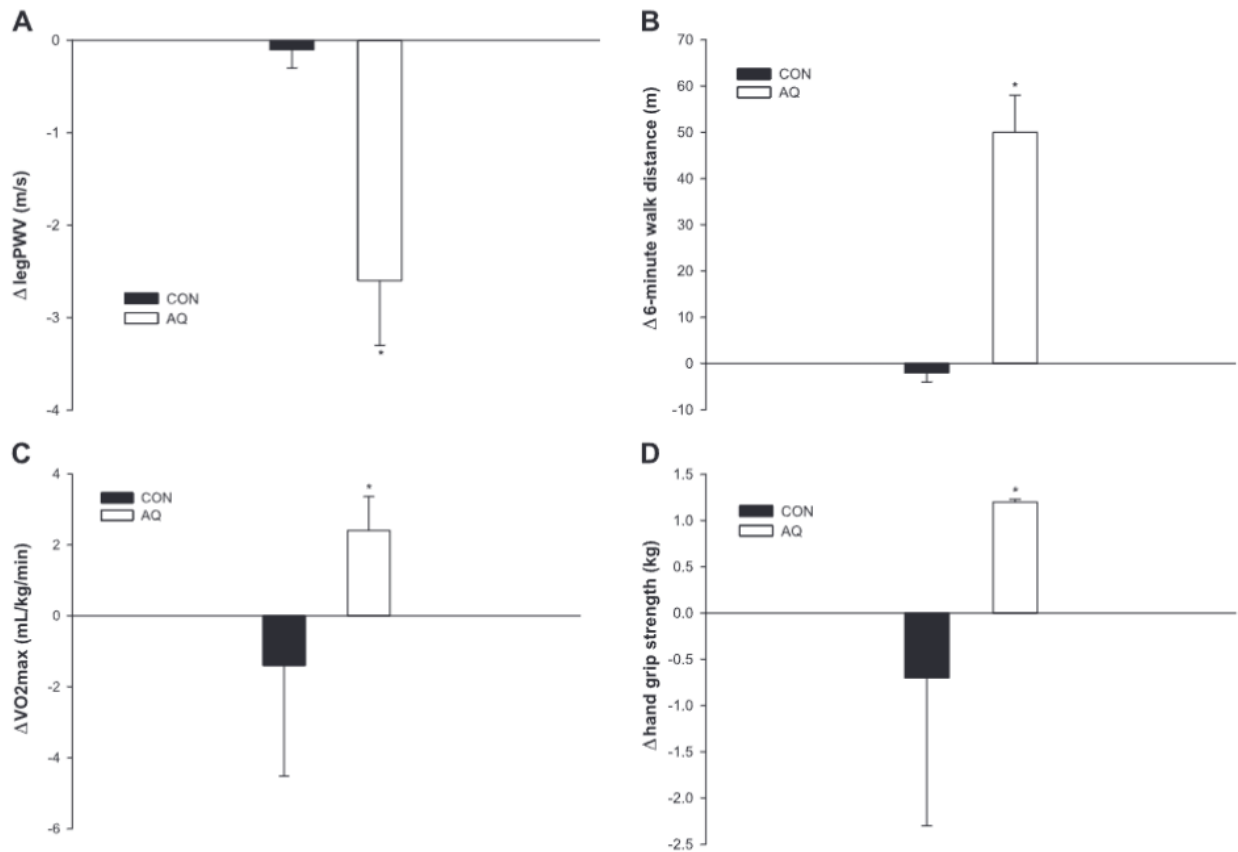


Fig. 2. *A*: change in femoral-to-ankle pulse wave velocity (legPWV, m/s) before and after 12 wk in the control (CON) and aquatic walking training (AQ) groups. legPWV significantly decreased in the AQ group compared with CON. *B*: change in distance walked during the 6-min walk test (m) before and after 12 wk in the CON and AQ groups. Maximal walking distance significantly increased in the AQ group compared with CON. *C*: change in maximal volume of oxygen consumption ($\dot{V}O_{2\max}$, mL·kg⁻¹·min⁻¹) before and after 12 wk in the CON and AQ groups. $\dot{V}O_{2\max}$ significantly increased in the AQ group compared with CON. *D*: change in handgrip strength (kg) before and after 12 wk in the CON and AQ groups. Handgrip strength significantly increased in the AQ group compared with CON. Values are presented as means \pm SD. CON, $n = 37$; AQ, $n = 35$. * $P < 0.05$ different from CON.

risks for further disease manifestation. In the present study, the AQ group showed a trend for reduced systolic BP (from 133.4 ± 12.9 to 130.4 ± 8.2 mmHg, $P = 0.063$) and diastolic BP (from 87.8 ± 6.8 to 82.7 ± 10.0 mmHg, $P = 0.058$) following the 12-wk exercise program, and these values are considered to be clinically relevant. Reductions in both systolic BP and diastolic BP by at least 2 mmHg have been shown

to play a clinically relevant role in reducing the incidence of cardiovascular disease (60, 67, 75, 77). Additionally, BP reduction may play a role in pain management in patients with PAD. In PAD, reduced O₂ perfusion in the skeletal muscle due to impaired leg blood flow leads to ischemia, resulting in claudication (81). Reduced BP has been shown to indicate reduced vascular resistance, which plays a role in improving blood perfusion in the skeletal muscle (81). Therefore, even a slight reduction in systemic BP may be beneficial for greater blood flow and perfusion at rest and during exertion in the AQ group, potentially resulting in less leg pain.

Cardiorespiratory and O₂ consumption capacity in the skeletal muscle. $\dot{V} O_{2max}$ represents both cardiorespiratory capacity and O₂ consumption capacity in the skeletal muscle. Attenuated $\dot{V} O_{2max}$ values have been shown to be associated with decreased physical function in older individuals (78), and patients with PAD specifically exhibit low $\dot{V} O_{2max}$ values (54). An improvement in cardiorespiratory capacity by 1 metabolic equivalent (1 MET, 3.5 mL O₂·kg⁻¹·min⁻¹) has been shown to decrease risk for cardiovascular disease by nearly 20% (55) and has been shown to be associated with improved physical function (19). Therefore, improving $\dot{V} O_{2max}$ in patients with PAD may be a viable option for decreasing risk for further disease manifestation and improving physical function. Although $\dot{V} O_{2max}$ has been shown to improve following aerobic exercise training in clinical populations (29, 76), $\dot{V} O_{2max}$ improvements following aerobic exercise-training programs in patients with PAD remain inconsistent. A previous study demonstrated that $\dot{V} O_{2max}$ was not significantly improved following 6 wk of supervised treadmill walking in patients with PAD (54). On the contrary, a study examining the effects of 24 wk of arm-cranking and leg-cranking exercise exhibited significant improvements in $\dot{V} O_{2max}$ in patients with PAD (83). The present study demonstrated a significant improvement in $\dot{V} O_{2max}$ following 12 wk of aquatic walking exercise training. Therefore, the findings from this study suggest that aquatic walking training is an effective exercise modality for improving $\dot{V} O_{2max}$, which may help enhance the performance of activities of daily living and physical function in this population.

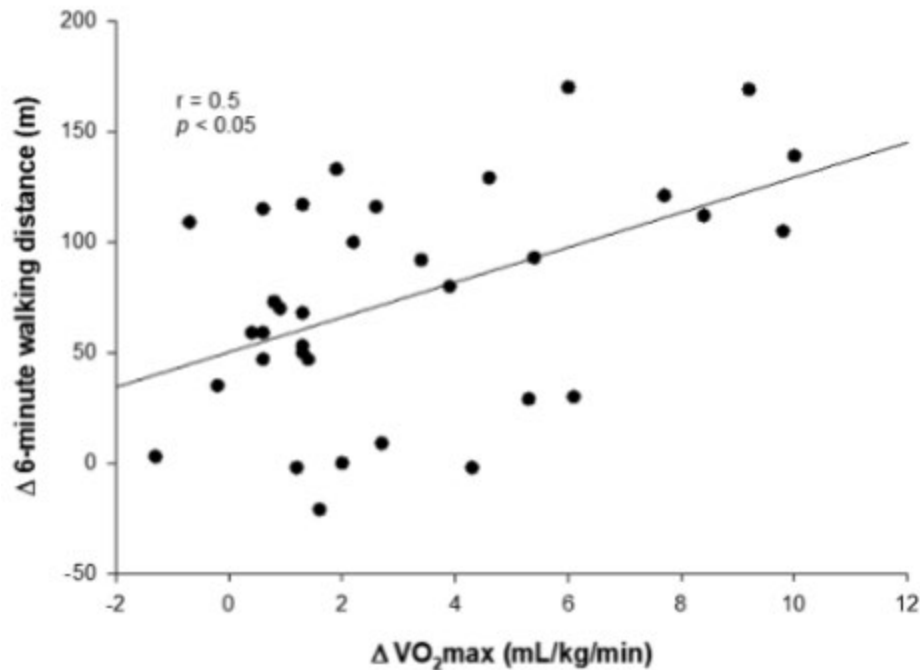


Fig. 3. Relationship between change in 6-min walking distance (m) and change in cardiorespiratory capacity [maximal volume of oxygen consumption ($\dot{V}O_{2max}$), mL·kg⁻¹·min⁻¹], $P < 0.05$.

In addition to improvements in $\dot{V}O_{2max}$, an improvement was seen in 6MWD following the 12-wk aquatic walking program, which indicates an improvement in exercise tolerance. Previous studies demonstrated significant improvements in 6MWD in patients with PAD following 12 wk (61) to 6 mo (24) of treadmill walking by 12 and 14%, respectively. The present study demonstrated a 13% improvement in 6MWD, and therefore the aquatic walking training program provides similar improvements in walking distance compared with treadmill walking interventions (20, 61).

$\dot{V}O_{2max}$ and 6MWD were moderately correlated in this study (Fig. 3), suggesting an association between cardiorespiratory capacity and exercise tolerance in this population. $\dot{V}O_{2max}$ and 6MWD have been reported to be associated in healthy adults and in patients with pulmonary disorders and diseases (12, 13, 16, 53). The present study indicates that $\dot{V}O_{2max}$ and 6MWD are associated measures in patients with PAD, which is similar to the findings in healthy adults and patients with pulmonary disorders and diseases.

Compared with treadmill walking, aquatic walking may be a more comfortable

exercise intervention for these patients because of the decrease in joint loading and stress while increasing muscle relaxation due to water temperature (2, 10, 45, 64). Additionally, patients with PAD often exhibit poor balance and have a higher prevalence of falling compared with non-PAD controls (25), and walking-induced fatigue has been shown to lead to increased fall risk in the elderly (44). Although treadmills have handrails that can be used for better support to prevent falls due to poor balance and/or fatigue, handrail use has been shown to blunt metabolic response, which can negatively impact physiological improvements in response to exercise-training programs (9). Our findings showed similar benefits on $\dot{V}O_{2\max}$ and 6MWD compared with previously reported treadmill programs (26), making the aquatic walking intervention a similarly effective and potentially more comfortable alternative exercise intervention for patients with PAD.

Physical function. Exercise programs have been shown to improve physical function and performance of activities of daily living in frail older adults (17) and in patients with PAD (42, 66). Two previous studies examining 12–24 wk of treadmill walking for patients with PAD reported significantly improved physical function scores (42, 66). Our findings are well aligned with these two previous studies, because the participants in the AQ group reported significantly improved physical function scores following the 12-wk aquatic walking training program. The improvement in physical function scores, a marker of quality of life, may be partially attributed to improvements in cardiorespiratory capacity, exercise tolerance, muscular strength, and arterial stiffness (19). Studies have reported that physical training improvements and increased muscular strength are associated with improved ability to perform activities of daily living (70, 71). Reduced arterial stiffness may have also played a role in improving physical function in the present study. An optimal level of arterial stiffness is important for both proper BP regulation and O₂ delivery to the muscle during physical activity, such as walking or other activities of daily living (65). Therefore, reduced arterial stiffness may potentially allow patients with PAD to have improved physical performance and also to continue their physical activity for a longer period of time with less leg pain.

Muscular strength. Muscular strength is important in performing activities of

daily living and is also strongly associated with protective effects against arterial stiffness, hypertension, and other cardiovascular diseases (41, 59, 75). Leg strength has been found to be associated with improved functional performance and higher ABI in patients with PAD (43), and poor grip strength has been used as an identifier of frailty in patients with vascular disease (51). Additionally, low handgrip strength has also been associated with lower physical function in the elderly (46). Both handgrip strength and leg strength significantly increased after 12 wk of aquatic walking training. It is likely that the improvements in handgrip and leg strength may be partially attributed to the water resistance component of the aquatic walking program (76). These improvements in strength then may, by extension, contribute to improved muscular performance, physical function, and cardiovascular health in patients with PAD.

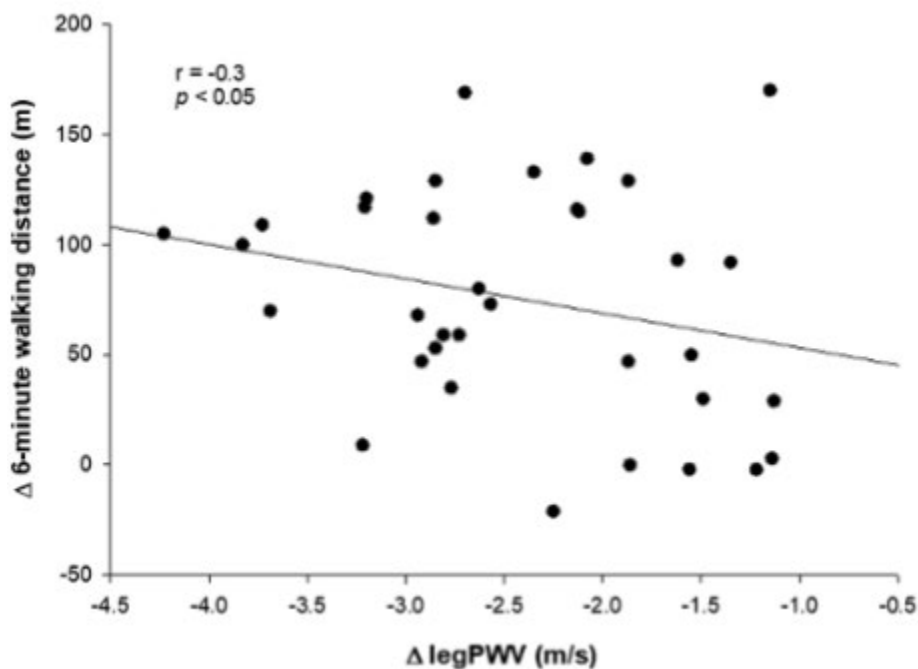


Fig. 4. Relationship between change in 6-min walking distance (m) and change in femoral-to-ankle pulse wave velocity (legPWV, m/s), $P < 0.05$.

Body composition. There were no significant changes in body composition or BMI in the AQ group after the 12-wk aquatic walking exercise-training program; however, there was a trend for higher BMI ($P = 0.061$) and lower body fat percentage ($P = 0.064$). The non-statistically significant increase in BMI may be attributable to an increase in muscle mass, which is supported by the significant improvements in upper-body and lower-body strength and a trend for increased lean body mass ($P = 0.062$) in the present study. However, limb muscle mass was not directly examined, and the effects of this aquatic walking exercise-training program on muscle mass have yet to be elucidated.

Limitations. The present study poses several limitations. First, the exercise-training program was 12 wk in duration, and the sustainability of the improvements seen was not directly examined. However, the aquatic walking training program had a relatively high adherence rate (84%), and these participants may potentially continue this program as their preferred method of exercise therapy to improve muscle function and cardiovascular health. Second, the mechanism(s) underlying reduced arterial stiffness was not directly examined. Future studies with this exercise program warrant the examination of potential mechanisms for this improvement, such as endothelial function assessment and structural changes (i.e., vessel diameter) with Doppler ultrasound, changes in vasoactive substances, and/or assessment of skeletal muscle mitochondrial function. Third, the safety of the protocol was not investigated, although there were no injuries or incidents to report. Entering and exiting the water may pose the risk of slipping or falling if these participants are not properly taught or supervised. This intervention was supervised, and safety personnel were available at all times to assist the participants. Additionally, the water depth was at the level of the sternum for these participants as an additional safety precaution. Finally, the subject pool was limited to patients with mild PAD (Fontaine stage I/II), women, and nonsmokers. This intervention was used to examine the efficacy of this aquatic exercise program in patients with mild claudication (no tissue loss or gangrene). Therefore, these results may not be generalized to patients with severe forms of PAD, men, and/or current smokers, and future investigation for these populations is warranted.

Conclusions and clinical implications. Our findings reveal that aquatic walking is

an effective therapeutic exercise modality for reducing arterial stiffness and resting HR and improving cardiorespiratory capacity, exercise tolerance, physical function, and muscular strength in patients with PAD. Additionally, this exercise modality has relatively high adherence in these patients. These results support that aquatic walking may serve as a new and potentially more comfortable exercise modality for the treatment and prevention of further disease manifestations in this population.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

S.-Y.P. and Y.-S.K. conceived and designed research; S.-Y.P. and Y.-S.K. performed experiments; S.-Y.P., Y.-S.K., and E.J.P. analyzed data; S.-Y.P., Y.-S.K., and E.J.P. interpreted results of experiments; S.-Y.P. and E.J.P. prepared figures; S.-Y.P., Y.-S.K., and E.J.P. drafted manuscript; S.-Y.P., Y.-S.K., and E.J.P. edited and revised manuscript; S.-Y.P., Y.-S.K., and E.J.P. approved final version of manuscript.

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