Efficacy of Hydrotherapy on Arterial Blood Pressure in patients with peripheral artery disease: A systematic review and meta-analysis

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Research Article

Keywords: Hydrotherapy, peripheral arterial disease, systematic review

Posted Date: May 3rd, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2869628/v1

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Abstract

Background

Hydrotherapy is an effective therapeutic modality in controlling pain and increasing blood flow, but its effect on Peripheral arterial diseases (PAD) is still unclear.

Aim

The aim of this systematic review was to investigate the effect of hydrotherapy on the arterial blood pressure in patients with PAD.

Method

A systematic review searches were conducted on the PubMed, Scopus, Physiotherapy Evidence Database (PEDro) and EBSCO databases from 2015 till 2022. Studies were eligible if randomized controlled trails (RCTs) investigating the effect of hydrotherapy on arterial blood pressure in patients with PAD. Qualitative data was extracted from six studies. Methodological quality was used to assess the risk of bias using the PEDro scale.

Results

A Meta-analysis was conducted on 6 RCTs (214 patients: 204 patients with PAD and 10 healthy subjects) to calculate the standardized mean difference (SMD) with 95% confidence interval (CI), and overall effect size (ES) of the ankle brachial index (ABI), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), 6-min-walk test (6MWT) distance, resting heart rate (RHR). The Meta-analysis showed that hydrotherapy had non-significant effects on the SBP (SMD 0.01 [95% CI -0.26-0.27]), the DBP (SMD − 0.18 [95% CI -0.58-0.22]), the ABI (SMD 0.08 [95% CI -0.57-0.73], 6MWT (SMD 0.45 [95% CI -0.19-1.08]), RHR (SMD − 0.19 [95% CI -0.52-0.14]).

Conclusion

The results of this review could not conclude the non-significant effects of the hydrotherapy in improving the SBP, ABI, DBP, RHR, and the 6MWT distance in patients with PAD.

1. Introduction

Peripheral arterial disease (PAD) is a continuously increasing prevalence[1] circulatory problem characterized by reduced blood flow to the affected upper or lower limbs secondary to narrowing in the peripheral arteries. Patients with PAD suffer frequent leg claudication pain that negatively impacts the walking and functional abilities as well as the muscles strength and functional balance [2]. The PAD-associated pain may progress from being exacerbated with activities to be elicited during rest, that, with other micro or macrovascular disorders elsewhere can predispose to elevated cardiovascular mortality risk [3]. The PAD accelerates the functional ability decline [4], predispose to deteriorated health-related quality of life [5]. Patients with PAD also manifest abnormally elevated blood pressure [6], and resting heart rate (RHR) that is related to reduced vagal tone, that in turn can cause adverse cardiac insults in patients with PAD [7]. The ankle-brachial index (ABI) provides clear diagnostic tool for the PAD severity. The presence of PAD increases with increasing age [8]. Although its beneficial effects; previous trials reported absence of a significant effect of the exercise therapy on the ABI in patients with PAD [9, 10].

Varieties of conservative therapeutic procedures are available for treatment of the PAD, with the exercise is strongly recommended to control the PAD-associated claudication [9]. Interventions targeting slowing down of the resting heart rate will favorably reduce the potential of arising cardiac events in patients with PAD and can even ameliorate the disease progression [11]. Supervised exercise in patients with PAD can effectively reduce the arterial stiffness [12, 13] control the abnormally increased blood pressure [9], increase the exercise tolerance[14], walking capacity[15,16], and pain-free walking duration[10, 16].

Although the effectiveness of the therapeutic exercise in alleviating the PAD disease burden, enhancing the overall health, limiting the rate of disease progression, and enhancing the functional capacity [17], but the commonly encountered walk-induced intermittent claudication is a major barrier for exercise participation in patients with PAD [18]. The claudication-related limitations significantly contribute to the low treatment- adherence rate in patients with PAD [18], about only one-third of the PAD patients adhere and complete the prescribed exercise program [19]. The unavoidable "weight bearing" during the exercises training is another factor predisposes to the increased claudication in patients with PAD during exercise training and thus further reduces the adherence to exercise [11, 6, 14, 15, 20, 21] especially in patient with multiple comorbidities.

Hydrotherapy stands as an alternative therapeutic option for patient with PAD [18], where buoyancy eliminates the weight-bearing stress [22, 23], with relatively higher adherence rate to the training program compared with the on-land training [21]. Quite recent evidence supports the effectiveness of performing exercises on water as a therapeutic procedure during the rehabilitation program for patients with cardiovascular disorders and functional deterioration [24–27].

Performing exercise on warm water can ameliorate the arterial stiffness [21], reduce pain and increase peripheral arterial blood flow [28], reducing the RHR, improving the cardiopulmonary capacity, muscular strength, and physical function [21]. Moreover, patients with PAD benefits just water immersion in improving exercise tolerance[9], blood flow and controlling the abnormally elevated blood pressure [29].

A recent systematic review assessed the effect of heat therapy on arterial shear rate, blood flow rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), six-minute walk test (6MWT) and ABI in patients with PAD and intermittent claudication. There was no comparison between the intervention and
control groups and there was no pooled data in different outcomes in this systematic review [30]. The recent review showed that the 6MWT distance was improved only in whole body immersion in patient with PAD, but a recent randomized controlled trial (RCT) showed non-significant difference in the 6MWT distance between the supervised exercise and the heat therapy procedures [9]. Therefore, the effect of hydrotherapy on patients with PAD is still unclear, contradiction exists, and there is no meta-analysis done in this area. Therefore, the aim of this systematic review with a meta-analysis was to investigate the effect of hydrotherapy on the arterial blood pressure in patients with PAD.

2. Methods

2.1. Study design

The current study design was a systematic review and meta-analysis, which was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The protocol of this systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) with a registration number (CRD42022341815).

2.2. Search strategy

A systematic search for original articles was performed from 2015 till 2022 via the following databases: PubMed, Scopus, EBSCO, and Physical Therapy evidence database (PEDro) databases. Searching was also performed on additional methods including websites like Google scholar, ResearchGate or the reference list from all full text paper which considered eligible in the current review.

The search included the following terms: Hydrotherapy [MeSH] OR Aquatic Therapy OR Therapeutic Irrigation OR Pool Therapy OR Water Exercise Therapy OR Aquatic Exercise Therapy OR Whirlpool Baths AND Peripheral Arterial Disease [MeSH] OR Peripheral Vascular Diseases OR Peripheral Arterial Occlusive Diseases PR Chronic Limb-Threatening Ischemia. In search filters were used: search key words in (Abstract &title), Article Type (Clinical Trial, Randomized Controlled Trial), Species (Humans), Language (English), year (2015–2022).

2.3. Eligibility study

Any article was eligible to be included if it was: A randomized controlled study (RCTs), Clinical Trial, a full text was written in English, investigating the effect of hydrotherapy on patients with PAD with no restriction on sex and race. The primary outcome measures were SBP and DBP. Studies were excluded if they: non-RCTs study designs (as case study and observational studies), any study with no control group, studies published before 2015, both treatment groups received hydrotherapy, or included participants with other chronic diseases rather than the PAD.

2.4. Study selection

Two reviewers (AK & AA) independently completed the databases search and selection of studies including screening the title and abstract then screening the full text. All studies that matched the inclusion criteria were carefully assessed for final decision and the process of the selection of the included studies explained in the PRISMA flow chart (Fig. 1). The third reviewer (MS) consulted in the meeting if there was any disagreement between the two reviewers’ results.

2.5. Data extraction

Data was extracted from all included studies as following: Population (disease), study author and date, participants data (age, sex, and sample size in both experimental and control groups), the intervention and the co-interventions used in the experimental and control group, outcome measures used in experimental and control groups, main findings of the study included. To conduct the meta-analysis, mean, standard deviation (SD), and sample size were reported for each variable for all included studies in both experimental and control groups.

2.6. Evaluation of methodological quality

To assess the methodological quality for included studies, PEDro scale was used. PEDro scale was widely used in the assessment of the risk of bias for the RCTs studies[31]. The scale consists of 11 items of yes/no answer. The first item evaluated the external validity and was not included in the total score. Items from two to 11 were used to rate the methodological quality of a total score of 10 [32]. The included study was rated as high (≥ 6), fair (4–5), or low quality if it had score ≤ 3 [33]. Two reviewers (AK & MS) independently assessed the risk of bias using the PEDro scale. The third reviewer (AA) reviewed any study if there was any disagreement between the two reviewers.

2.7. Quality of evidence

The quality of evidence was assessed by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system by the third reviewer (MA). GRADE has five main categories that used a three subscale for rating the quality of Evidence. The five categories were the study limitation, the indirectness, the impression, the inconsistency, and the publication bias. Each may be rated as very serious, serious, or not serious. The total score may be high quality, moderate quality, low and very low quality of evidence. The total score may help to ensure how the effect estimate is closely related to the true effect of the intervention[34–36].

2.8. Data Analysis

Qualitative analysis was applied and presented in tables, and quantitative synthesis was presented as a forest plot by performing a meta-analysis. The primary outcomes SBP and DBP were used in the meta-analyses to assess the effectiveness of hydrotherapy on patients with PAD. The secondary outcomes were 6MWT, ABI and the RHR.
The meta-analysis was performed using the review manager (version 5.4, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) software, forest plots were conducted by calculating the effect size through collecting the mean, standard deviation, and sample size for experimental and control groups of the included studies. The standardized mean difference (SMD) was presented as the effect size (ES), and the corresponding 95% CI was computed. The estimated effect size was rated as: small (0.2), medium (0.5), and large (0.8) ES. The $I^2$ test was conducted to test and quantify the heterogeneity among the studies. To categorize the heterogeneity in the $I^2$ test: small ($I^2 \leq 25$%), medium ($I^2 26\%-50$%) and high ($I^2 \geq 75$%) heterogeneity [38]. A sensitivity analysis was used to assess the consistency of the results if heterogeneity was high.

3. Results

3.1. Study selection

A total of 141 studies searched in the included Five databases. After removing the duplications, 114 studies remained. Of the 114; only 21 studies were initially eligible after the abstract screening and only 8 studies were eligible after the full text screening, with two of them were excluded because of the patients had not only PAD, so the finally included studies in this systematic review were 6 studies. The PRISMA flow diagram represented in Fig. 1 explaining the steps of searching and the procedures of studies selection.

3.2. Study characteristics

Six studies published after 2015, including 214 patients: 204 patients with PAD and 10 healthy subjects. 105 patients were in the experimental group and 99 patients, and 10 healthy subjects were in the control group. Conflicting results were noticed regarding effects of the hydrotherapy treatment on the SBP, DBP, ABI, RHR, and 6MWT.

A previous RCTs showed significant reduction in the SBP, and the DBP, with significant increase in the HR during (all $p < .001$) and 30 minutes post hot water immersion (all $p \leq .03$). Furthermore, there were significant reduction in the ambulatory values of the SBP ($p = .001$), and the DPB ($p = .047$) in patients with PAD [29]. Another RCT reported that the SBP respond favorably and was significantly reduced (-7 mmHg, $p < .001$) in response to the hot water immersion (spa bathing and calisthenics exercise), more than ($p = .049$) the land-based (supervised walking and gym-based exercise) training program (-3 mmHg, $p = .078$). The DBP respond favorably to both interventions (-4 mmHg, $p = .002$ for both groups), with non-significant between-groups differences ($p = .229$), additionally; no significant changes on the peak HR were recorded in either group ($p = .363$), with non-significant differences between-groups ($p = .154$), and there were still non-significant differences between groups ($p = .668$) in the covered 6MWT distance [9].

In another study explored the effects of aquatic exercise training (AQET) on the HR, BP, ABI, and 6MWT in patients with PAD reported conflicting results opposed the previously reported findings. The post-study mean values of the resting HR was significantly reduced (-2.3 beat/min, $p < .05$) in the AQET group compared to non-significant decrease (-1 beat/min, $p > .05$) in the control group. The 6MWD was significantly increased (+ 50 m, $p < .05$) in the AQET group compared to non-significant decrease (-2 m, $p > .05$) in the control group, where there were non-significant differences for the SBP, DBP and the ABI ($p > .05$) in patients with PAD[21]. A single session of 90 min of leg heat therapy using warm water decreased the SBP (-7 mmHg, $p < .05$) but not the DBP in patients with PAD compared to shame treatment [39].

Six-weeks of leg heat therapy using heated water significantly decreased the SBP (-6 mmHg, $p = .0042$) and the DBP ($p = .0168$) in the heat therapy group. The post-hoc analysis detected significant differences between-groups (treatment versus shame) on the SBP ($p = .0178$), but not on the DBP. Furthermore, results could not conclude significant group differences in either the SBP or the DBP in the mean changes. The Leg heat therapy did not increase the 6MWT distance ($p = .80$) and did not reduce the ABI ($p = .75$) in the 6 intervention weeks [40]. A Randomized controlled study examined the effectiveness of performing 12 weeks of the exercise training in heated water on the BP, RHR, ABI, and the 6MWT distance compared with the land-based exercise training in patients with PAD. Results revealed significant reduction in the SBP, DBP, and RHR, significant increase in the 6MWT ($p < .05$), with non-significant increase in the ABI in the heated water group ($p > .05$). The results did not conclude between-groups significant differences in the ABI ($p > .05$) (Table 2) [41].
Table 1: Summary of included RCT intervention studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample characteristics</th>
<th>Intervention and co-intervention</th>
<th>Measured variables</th>
<th>Summary of results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thomas, 2017²⁹</td>
<td>21 participants</td>
<td>Participants randomized to 11 PAD patients performed 1 week to 3 weeks, 30 min exercise including 3 min treadmill walk at 3km/h under waist level (Active and passive sessions) and 10 control subjects for passive immersion with only 3 min treadmill exercise and passive immersion.</td>
<td>BP, HR</td>
<td>Elderly individuals to reduce blood pressure and rising heart rate significantly ($p = .001$) in both groups except the SBP was higher in PAD group and significantly different than control group ($p = .04$).</td>
</tr>
<tr>
<td>Akerman, 2019⁹</td>
<td>22 PAD patients</td>
<td>22 PAD patients randomized to 11 in the heat therapy group and 11 in the supervised exercise group for 12 weeks each. The exercise time was: For supervised exercise 90 min including 30 min walking and 60 min circuit exercise for 2 days/week. For heat therapy group 3–5 days per week for 30 min, followed by 30 min of calisthenics in spa bath including resistance exercises.</td>
<td>ABI, BP, 6MWT</td>
<td>Systolic BP was reduced more following heat (7 mmHg, $p = .001$) than following exercise (3 mmHg, $p = .078$), and diastolic BP decreased by 4 mmHg in both groups ($p = 0.002$). There were no significant changes in, ankle-brachial index ($p = .459$), or measures of vascular health. There were no differences in the improvement in functional or BP outcomes between heat and exercise in individuals with PAD.</td>
</tr>
<tr>
<td>Park, 2019²¹</td>
<td>72 Female PAD</td>
<td>72 female PAD patients randomized to 35 in the aquatic therapy group and 37 in the control group (no treatment). Participants in the intervention group participated in an aquatic walking exercise-training program for 12 weeks, 4 days/week, for 60 min/day.</td>
<td>ABI, BP, 6MWT, RHR</td>
<td>The HR significantly decreased, whereas 6MWD significantly increased, compared with pre-exercise program and control group. There were no significant differences for BP ($p = .63$) and ABI after 12 weeks.</td>
</tr>
<tr>
<td>Monroe, 2021³⁹</td>
<td>16 PAD patients</td>
<td>90 min of single leg heat therapy for 16 patients randomized cross over to leg heat therapy and shame treatment. Leg heat therapy was applied for 90 min, 3 times/week for 6 weeks for a total of 18 sessions. Cardiopulmonary exercise test done after leg heat therapy.</td>
<td>BP</td>
<td>A single session of 90 min of leg heat therapy reduced SBP ($p = .05$) but not DBP in patients with PAD compared to shame treatment.</td>
</tr>
<tr>
<td>Monroe, 2020⁰⁰</td>
<td>30 PAD patients.</td>
<td>PAD patients randomly to 15 in the control/sham group and 15 in the leg heat therapy group</td>
<td>ABI, BP, 6MWT</td>
<td>6 weeks of supervised leg HT increased physical functioning but had no effect on vascular reactivity and 6-min walk distance and in patients with PAD. Leg HT did not improve 6-min walk distance ($p = 0.80$), ABI ($p = 0.75$) and BP in 6 weeks.</td>
</tr>
<tr>
<td>Park, 2020⁴¹</td>
<td>53 Female PAD patients</td>
<td>The HWET group participated in a supervised heated-water exercise therapy program for 12 week, 4 days/week, for 60 min/day. The LBET group participated in supervised treadmill therapy program for the same period.</td>
<td>ABI, BP, RHR, 6MWT</td>
<td>Walking distance increased and systolic and diastolic blood pressure decreased in both groups and the change in HWET was greater than LBET, which indicate that HWET better then LBET in walking distance, blood pressure and resting heart rate but not in ABI.</td>
</tr>
</tbody>
</table>

PAD = Peripheral artery disease, ABI = Ankle-brachial index, BP = Blood pressure, RCT = Randomised control trial, HWET = heat-water exercise therapy, LBET = land-based exercise therapy, 6MWT = 6 Minute walk test, RHR = Resting heart rate, HR = Heart rate, 6MWD = 6 Minute Walk Distance, HT = Heat therapy.
Table 2
Methodological quality assessment of included studies (PEDro scale).

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Eligibility criteria a</th>
<th>Random allocation</th>
<th>Concealed allocation</th>
<th>Baseline comparability</th>
<th>Blind subjects</th>
<th>Blind therapists</th>
<th>Blind assessors</th>
<th>Adequate follow-up</th>
<th>Intention-to-treat analysis</th>
<th>Between-group comparisons</th>
<th>Point estimate and variability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thomas, 2017</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Akerman, 2019</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Park, 2019</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Monroe, 2020</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Monroe, 2021</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Park, 2020</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>

a Not included in the final score.

3.3. Evaluation of methodological quality

Assessment of the methodological quality by PEDro scale revealed four high quality studies [9, 40, 21, 29] and two fair quality studies [39, 41]. The cause of lowering the score for the PEDro scale was that most of the included studies did not mention the concealed allocation, blind subjects, blind therapists, and the intention-to-treat analysis (Table 3).

Table 3
Quality of evidence (GRADE)

<table>
<thead>
<tr>
<th>Outcome measured</th>
<th>N. of part. (studies)</th>
<th>Study limitation</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Publication bias</th>
<th>Overall quality of evidence</th>
<th>Effect Estimate [95% CI]</th>
<th>Effect size</th>
<th>Direction</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td>230 (6)</td>
<td>Serious a</td>
<td>Serious b</td>
<td>Not serious</td>
<td>Serious c</td>
<td>Very Low d</td>
<td>0.01 [-0.26, 0.27]</td>
<td>Small</td>
<td>No favour</td>
<td></td>
</tr>
<tr>
<td>DBP</td>
<td>230 (6)</td>
<td>Serious a</td>
<td>Serious b</td>
<td>Not serious</td>
<td>Serious c</td>
<td>Very Low d</td>
<td>-0.18 [-0.58, 0.22]</td>
<td>Small</td>
<td>Hydrotherapy</td>
<td></td>
</tr>
<tr>
<td>6-min walk test</td>
<td>124 (3)</td>
<td>Serious a</td>
<td>Serious b</td>
<td>Not serious</td>
<td>Serious c</td>
<td>Very Low d</td>
<td>0.45 [0.19, 1.08]</td>
<td>Medium</td>
<td>Hydrotherapy</td>
<td></td>
</tr>
<tr>
<td>Resting heart rate</td>
<td>146 (3)</td>
<td>Serious a</td>
<td>Serious b</td>
<td>Not serious</td>
<td>Serious c</td>
<td>Very Low d</td>
<td>-0.19 [-0.52, 0.14]</td>
<td>Small</td>
<td>Hydrotherapy</td>
<td></td>
</tr>
<tr>
<td>Ankle brachial index</td>
<td>177 (4)</td>
<td>Serious a</td>
<td>Serious b</td>
<td>Not serious</td>
<td>Serious c</td>
<td>Very Low d</td>
<td>0.08 [-0.57, 0.73]</td>
<td>Small</td>
<td>No favour</td>
<td></td>
</tr>
</tbody>
</table>

GRADE, Grading of Recommendations Assessment, Development and Evaluation; SMD, Standard Mean Difference; CI, Confidence Interval.

a Allocation concealment was not clearly reported; lack of blinding of participants or assessors and therapists; attrition bias due to incomplete outcome data.

b Significant heterogeneity in meta-analysis, I² > 75%.

c Small sample size with wide confidence interval, (sample size less than 400 participants).

d Very low quality of evidence: the true effect might be different from the estimated effect with very limited confidence to the estimated effect.

3.4. Quality of evidence

The GRADE assessment showed an overall very low level of evidence score with small effect size on SBP, DBP, RHR, ABI and medium effect size on 6MWT (Table 3). The causes for downgrading were related to the presence of study limitation, inconsistency, and imprecision. The reason for serious score in the study limitation was due to lack of allocation concealment, blinding of participants or therapists, attrition bias due to incomplete outcome data regarding to
the intention to treat analysis procedures [42]. The significant heterogeneity among the included studies was the main cause for serious downgrading of the core for the inconsistency [43]. Small sample size (less than 400 participants) with wide confidence interval was responsible for downgrading the imprecision score [44].

3.5. Data synthesis

A descriptive synthesis was performed, and data was extracted and represented in Table 1. A total of six studies were included in the meta-analysis [9, 41, 21, 29, 39, 40]. All the included studies (6 studies) measured the SBP and DBP while only three studies measured the 6MWT [9, 40, 21] and only three studies measured the RHR [21, 29, 39] and four studies measured the ABI [9, 21, 29]. Forest plot showed a favor to hydrotherapy in DBP, 6MWT and RHR. The estimate effect size showed a medium effect size in 6MWT with small effect size to the remaining variables (Table 3). Test of the overall effect of hydrotherapy on the outcome measured variables showed non-significant effect (P < .05). Heterogeneity was significant in the SBP (I² = 64%) and ABI (I² = 76%) (Figs. 2,6). On the other measured outcomes, heterogeneity reported a percentage of I² = 53% in the DBP and I² = 61% in 6MWT with non-significant (Figs. 3–5).

4. Discussion

This is the first systematic review with a meta-analysis to investigate the effects of hydrotherapy on SBP, DBP, RHR, ABI, and the 6MWT distance in patients with PAD. The results of the current systematic review showed that there were no significant differences between the patients with PAD and the control groups in response to the hydrotherapy on the SBP (SMD 0.01 [95% CI -0.26-0.27], p = .95; very low-quality evidence), increasing the ABI (SMD 0.08 [95% CI -0.57-0.73], p = .81; very low-quality evidence), reducing the DBP (SMD = 0.18 [95% CI -0.58-0.22], p = .37; very low-quality evidence), increasing the 6MWT distance (SMD 0.45 [95% CI 0.19-1.08], p = .17; very low-quality evidence), reducing the RHR (SMD = 0.19 [95% CI -0.52-0.14], p = .26; very low-quality evidence).

Results of the current review regarding effects of the hydrotherapy on the SBP contradicts the previously reported results. Neff et al., reported significant reduction in SBP in response to the aquatic-based thermotherapy program by about 11 mmHg [36]. Observed SBP reduction by 7.3%, no change in the DBP in response to 25-min moderate intensity aquatic walking program [45–47], reported that the average reduction in the SBP and the DBP were 5 mmHg and 1 mmHg respectively in response to moderate to high intensity aquatic exercise program in older women[47].

According to the current systematic review and meta-analysis; there was non-significant reduction in the SBP in response to the hydrotherapy treatment. The current review findings came in accordance with that of Park et al (2019) who concluded non-significant differences on the BP (p = .63) and ABI after 12 weeks between AQWET and control groups [21]. The non-significant SBP reduction in response to the hydrotherapy, especially warm water therapy can be explained on the moderate and significant heterogeneity between the included studies in this review, so it is important to do more research with less heterogeneity, high quality, and large sample size to draw a conclusion on the effect of the hydrotherapy on the SBP in patients with PAD. On the other hand, the current study findings contradict that of Tomas et al (2017) who reported significant hemodynamic and cardiovascular responses to the hot water in PAD patients [29] this contract can be resolved when considering that they evaluated the acute post-immersion responses.

Although the non-significant results regarding the hydrotherapy-related effects on the evaluated variables, but still there is some evidence showed that the heat is associated with variations in the endothelium and smooth muscles activity [48], reduction in the systematic vascular resistance [49, 50], control of the baroreflex and the renin-angiotensin system activation [51, 52], blood flow shift from the core towards the peripheral arteries [53, 50], and transient increase in the anti-inflammatory chemokines and cytokines concentrations as IL-10 and IL-6 [54]. The immersion-related hydrostatic effects can also increase the venous return, with about 700 mL of blood is directed from periphery towards the thorax, [55, 56] that are cumulatively with the previously mentioned alternations lead to better vascular compliance, that ends in reducing the peripheral arterial resistance [57]. The significant heterogeneity between the included studies in the current review can explain the absence of these alterations-related effects in the current review.

The results of the current review regarding effects of the hydrotherapy on the DBP and RHR contradicts that of Neff et al., who reported significant reduction in DBP in response to the aquatic-based thermotherapy program by about 6 mmHg and significant increase in the RHR, [45] this response is an acute post-intervention response (within two hours post-treatment) to a single (90 minutes) session treatment, so the results cannot be generalized as a long-standing chronic effect. Park et al (2019) study showed that the RHR was significantly reduced after 12 weeks, but a clear conclusion was still unclear because results came from only single study with small sample size [21].

The 6MWT distance results clarified non-significant differences between study and control groups, coming in accordance with Neff et al., who reported no differences between intervention (327 m) and control (325 m) groups [45]. Previously published RCTs reported the same conclusion [58, 59].

The current review results of the 6MWT contradict that of Kapusta and Irzmanski (2022) who reported significant increase in the 6MWT distance in patients with chronic lower limbs arterial disorders after a 3-weeks of supervised rehabilitation program. The significant improvement in the covered 6MWT distance can be relayed on the combined effects of the individually-tailored exercise training program in addition to the 10 whirlpool treatment sessions [60].

The current review results clarified non-significant effect of hydrotherapy on DBP and RHR, ABI and the 6MWT and these findings are aligned with Akreman study [9] who reported that blood pressure and functional performance responses were not significantly different in response to either heat or supervised exercise for 12 weeks, which suggest that heat therapy can be used as an alternative to the supervised land-based exercise program and it is useful to use it particularly with patients with PDA who cannot adhere supervised exercise program. Moreover, Park et al (2019) study showed that there were non-significant differences in the SBP, DBP and the ABI (p > .05) between the AQWET and the control groups after 12 weeks in patients with PAD [21], and these findings are in alignment with the results of the current review. Monroe et al (2020) reported that the leg heat therapy can significantly improve the SBP but not the DBP (p > .05), the 6MWT distance (p = .80) or the ABI (p = .75) after the 6 intervention weeks [40], which most came in alignment with the current review results but other are contradicted with the current review results.
Results of a quiet recent systematic review [30] were not aligned with the current review results as it suggested significant differences in the 6MWT, the possible reason is that they did pooled the studies together and one or two studies could not be sure about the results, they did not measure the difference between the PAD and control groups, and they reported that their results could not give clear conclusions for patients with PAD due to small number of studies and large heterogeneity between the types of the interventions in the intervention and control groups.

Future research is warranted to further clarify the hydrotherapy treatment programs optimum details and criteria required to obtain significant effects on the dependent variables in patients with PAD. Future research with well-defined treatment parameters (mode, intensity, frequency, and duration), inclusion and exclusion criteria, with more extended treatment time (more than 12-weeks) are needed to objectively assess the effectiveness of the hydrotherapy treatment programs and to determine the optimal hydrotherapy treatment parameters for patients with PAD. Finally, more comparative studies with sufficient sample size are required to objectively draw a clear conclusion and clarify the degree of effectiveness of the hydrotherapy treatment program when delivered to patients with PAD.

4.1. Study limitations

Although the strength of current systematic review was to include a meta-analysis and pooled the data together; but number of limitations were encountered. First is that there was moderate heterogeneity in most of the obtained results, and the control group (that was presented by healthy subjects) differed from the intervention PAD group in some studies. The hydrotherapy program parameters' variability across screened studies (that was differ from one study to another) and the length of treatment (that varied from 30 min in a single session to reach 12-weeks) were other limitations.

4.2. Conclusion

The results of this review could not conclude the non-significant effects of the hydrotherapy in improving the SBP, ABI, DBP, RHR, and the 6MWT distance in patients with PAD. Well-constructed studies are required to provide strong evidence about the effectiveness of hydrotherapy in patients with PAD. More extended treatment time and frequencies may be required to clarify the gap in our understanding about the effectiveness of hydrotherapy in patients with PAD.

Abbreviations

ABI
Ankle-brachial index
AQET
Aquatic exercise training
DBP
Diastolic blood pressure
ES
Effect size
GRADE
Grading of Recommendations Assessment, Development, and Evaluation
PAD
Peripheral arterial disease
PEDro
Physical Therapy evidence database
PRISMA
Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO
Prospective Register of Systematic Reviews
RCT
Randomized controlled trial
RHR
Resting heart rate
6MWT
Six-minute walk test
SD
Standard deviation
SMD
Standardized mean difference
SBP
Systolic blood pressure.

Declarations

Acknowledgements
Funding
Not applicable.

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Contributions
All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by A K, A A, M A, and O K. The first draft of the manuscript was written by A K and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript. The First Author A K had the idea for the article, who reviewed the literature search and data analysis, and who drafted and/or critically revised the work.

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Ethics declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Availability of data and materials
Datasets are available through the corresponding author upon reasonable request.

References


**Figures**
Figure 1

PRISMA Flow diagram of the selected studies

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Hydrotherapy</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Std. Mean Difference</th>
<th>IV, Fixed, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thomas et al., 2017</td>
<td>121</td>
<td>20</td>
<td>11</td>
<td>110</td>
<td>101</td>
<td>8.0%</td>
<td></td>
<td></td>
<td>1.07 [0.14, 2.90]</td>
<td>2017</td>
<td></td>
</tr>
<tr>
<td>Ackerman et al., 2019</td>
<td>145</td>
<td>7</td>
<td>11</td>
<td>150</td>
<td>111</td>
<td>9.5%</td>
<td></td>
<td></td>
<td>-0.52 [-1.37, 0.32]</td>
<td>2019</td>
<td></td>
</tr>
<tr>
<td>Park et al., 2010</td>
<td>136.4</td>
<td>8.2</td>
<td>35</td>
<td>124</td>
<td>67</td>
<td>32.2%</td>
<td></td>
<td></td>
<td>-0.23 [-0.69, 0.23]</td>
<td>2010</td>
<td></td>
</tr>
<tr>
<td>Park et al., 2020</td>
<td>128</td>
<td>9</td>
<td>25</td>
<td>125</td>
<td>25</td>
<td>23.6%</td>
<td></td>
<td></td>
<td>-0.31 [-0.68, 0.05]</td>
<td>2020</td>
<td></td>
</tr>
<tr>
<td>Menon et al., 2020</td>
<td>150</td>
<td>3</td>
<td>15</td>
<td>149</td>
<td>25</td>
<td>13.6%</td>
<td></td>
<td></td>
<td>0.08 [-0.68, 0.83]</td>
<td>2020</td>
<td></td>
</tr>
<tr>
<td>Menon et al., 2021</td>
<td>140</td>
<td>11</td>
<td>16</td>
<td>130</td>
<td>12</td>
<td>13.1%</td>
<td></td>
<td></td>
<td>0.65 [0.12, 1.97]</td>
<td>2020</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI): 116
Heterogeneity: Chi² = 1.93, df = 5 (P = 0.93), I² = 0%
Test for overall effect: Z = 0.08 (P = 0.93)

Figure 2

Forest plot to the effect of hydrotherapy on Systolic Blood Pressure,

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Hydrotherapy</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Std. Mean Difference</th>
<th>IV, Random, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thomas et al., 2017</td>
<td>84</td>
<td>10</td>
<td>11</td>
<td>57</td>
<td>51</td>
<td>12.2%</td>
<td></td>
<td></td>
<td>0.64 [-0.68, 1.74]</td>
<td>2017</td>
<td></td>
</tr>
<tr>
<td>Ackerman et al., 2019</td>
<td>82</td>
<td>7</td>
<td>11</td>
<td>85</td>
<td>11</td>
<td>13.2%</td>
<td></td>
<td></td>
<td>-0.41 [-0.26, 0.45]</td>
<td>2019</td>
<td></td>
</tr>
<tr>
<td>Park et al., 2010</td>
<td>92.7</td>
<td>10</td>
<td>25</td>
<td>97</td>
<td>11</td>
<td>22.1%</td>
<td></td>
<td></td>
<td>-0.76 [-0.32, 0.37]</td>
<td>2010</td>
<td></td>
</tr>
<tr>
<td>Menon et al., 2020</td>
<td>80</td>
<td>3</td>
<td>15</td>
<td>80</td>
<td>6</td>
<td>15.6%</td>
<td></td>
<td></td>
<td>0.00 [-0.42, 0.72]</td>
<td>2020</td>
<td></td>
</tr>
<tr>
<td>Menon et al., 2021</td>
<td>72</td>
<td>12</td>
<td>18</td>
<td>75</td>
<td>16</td>
<td>18.3%</td>
<td></td>
<td></td>
<td>-0.25 [-0.65, 0.14]</td>
<td>2020</td>
<td></td>
</tr>
<tr>
<td>Park et al., 2020</td>
<td>84</td>
<td>8</td>
<td>28</td>
<td>85</td>
<td>10</td>
<td>20.3%</td>
<td></td>
<td></td>
<td>-0.11 [-0.65, 0.43]</td>
<td>2020</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI): 116
Heterogeneity: Tau² = 0.13, Chi² = 10.67, df = 5 (P = 0.08), I² = 53%
Test for overall effect: Z = 0.89 (P = 0.37)
Forest plot to the effect of hydrotherapy on Diastolic Blood Pressure.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Hydrotherapy Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Std. Mean Difference</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akerman et al., 2019</td>
<td>414.52</td>
<td>11</td>
<td>385.83</td>
<td>11</td>
<td>27.4%</td>
<td>0.42 [-0.44, 1.25]</td>
<td>2018</td>
<td></td>
</tr>
<tr>
<td>Park et al., 2019</td>
<td>449.90</td>
<td>17</td>
<td>559.52</td>
<td>26</td>
<td>40.9%</td>
<td>0.96 [-0.42, 1.39]</td>
<td>2019</td>
<td></td>
</tr>
<tr>
<td>Neves et al., 2020</td>
<td>487.108</td>
<td>15</td>
<td>420.138</td>
<td>15</td>
<td>31.8%</td>
<td>-0.18 [-0.52, 0.16]</td>
<td>2020</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>63</td>
<td>61</td>
<td>100.0%</td>
<td>61</td>
<td>0.45 [-0.19, 1.09]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.18; Chi² = 5.31; df = 2 (P = 0.07); I² = 52%
Test for overall effect: Z = 1.38 (P = 0.17)

Figure 4

Forest plot to the effect of hydrotherapy on 6-minute walk test.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Hydrotherapy Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Std. Mean Difference</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thomas et al., 2017</td>
<td>61.13</td>
<td>11</td>
<td>89.17</td>
<td>16</td>
<td>14.8%</td>
<td>-0.51 [-1.38, 0.36]</td>
<td>2017</td>
<td></td>
</tr>
<tr>
<td>Park et al., 2019</td>
<td>87.39</td>
<td>10</td>
<td>70.2</td>
<td>10</td>
<td>37</td>
<td>-0.24 [-0.70, 0.23]</td>
<td>2019</td>
<td></td>
</tr>
<tr>
<td>Park et al., 2020</td>
<td>71.5</td>
<td>28</td>
<td>71.7</td>
<td>25</td>
<td>36.6%</td>
<td>0.09 [-0.54, 0.54]</td>
<td>2020</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>74</td>
<td>72</td>
<td>100.0%</td>
<td>72</td>
<td>-0.19 [-0.52, 0.14]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.96; Chi² = 1.04; df = 2 (P = 0.69); I² = 0%
Test for overall effect: Z = 1.13 (P = 0.26)

Figure 5

Forest plot to the effect of hydrotherapy on Resting heart rate.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Hydrotherapy Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Std. Mean Difference</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akerman et al., 2019</td>
<td>0.54</td>
<td>0.15</td>
<td>11</td>
<td>0.69</td>
<td>0.11</td>
<td>11</td>
<td>-1.10 [-2.81, -0.19]</td>
<td>2019</td>
</tr>
<tr>
<td>Park et al., 2019</td>
<td>0.46</td>
<td>0.22</td>
<td>7</td>
<td>0.3</td>
<td>0.37</td>
<td>7</td>
<td>0.09 [-0.41, 0.59]</td>
<td>2019</td>
</tr>
<tr>
<td>Monereo et al., 2020</td>
<td>0.7</td>
<td>0.3</td>
<td>15</td>
<td>0.5</td>
<td>0.15</td>
<td>15</td>
<td>0.37 [0.21, 0.54]</td>
<td>2020</td>
</tr>
<tr>
<td>Park et al., 2020</td>
<td>0.83</td>
<td>0.28</td>
<td>8</td>
<td>0.81</td>
<td>0.5</td>
<td>25</td>
<td>0.28 [-0.25, 0.83]</td>
<td>2020</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>0.89</td>
<td>0.88</td>
<td>100.0%</td>
<td>0.89</td>
<td>0.68 [0.57, 0.73]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.32; Chi² = 12.33; df = 3 (P = 0.006); I² = 75%
Test for overall effect: Z = 0.25 (P = 0.81)

Figure 6

Forest plot to the effect of hydrotherapy on Ankle Brachial pressure Index.