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ORIGINAL ARTICLE

The effect of lower limb strengthening exercise on orthostatic blood pressure and the skeletal muscle pump in older people with orthostatic hypotension

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Abstract

Introduction: Activation of muscles during standing is recommended to activate the skeletal muscle pump, increasing venous return and increasing blood pressure (BP) in people with orthostatic hypotension (OH).
Aim: The aim of this study is to determine if increasing the strength of the lower limb muscles can improve the effectiveness of the venous pump and postural BP in older people with OH.
Methods: Ten older people with OH underwent an 8-week lower limb strengthening intervention. Repeated measurements of orthostatic BP, calf venous ejection fraction (EF) and muscle strength took place before, during and after intervention.
Results: The intervention increased calf muscle strength by 21% (interquartile range: 18–28), $p = 0.018$, from a median baseline of 38 (34–45) kg. Participants had normal levels of venous EF 64% (51–75) at baseline, with little to no venous reflux. The median ejection volume at baseline was 44 (36–58) mL per calf. Despite increasing muscle strength, venous EF did not increase (percentage change −10% (−16 to 24), $p = 0.8$) and systolic BP drop did not improve (percentage change 0% (−17 to 16), $p = 1.0$). Similarly, visual analysis of individual case-series trends revealed increasing muscle strength with no clinically meaningful change in EF or orthostatic BP.
Conclusions: Muscle strengthening exercise does not increase the effectiveness of the skeletal muscle pump and is not an efficacious intervention for OH. As there is little to no venous pooling in the calf during standing in older people with OH, below knee compression is unlikely to be clinically effective.

KEYWORDS
aged, exercise therapy, orthostatic intolerance, venous insufficiency, venous return

1 | INTRODUCTION

Orthostatic hypotension (OH) is a disabling condition characterized by a significant drop in blood pressure (BP) upon standing upright. It affects 20% of community dwelling older people and is associated with reduced quality of life and increased mortality (Angelousi et al., 2014; Saedon et al., 2020).

Nondrug therapies, such as physical counter-manoeuvres (PCMs) are used first line to treat people with OH. PCMs involve voluntary contraction of skeletal muscles to increase venous return. Older people with OH are motivated to use nondrug therapies to avoid medication, with PCMs being one of the most tolerable therapies for this group (Robinson et al., 2018). Whether increasing the strength of these muscles would result in improved venous function and orthostatic BP is unknown.

2 | OBJECTIVES

Determine whether increased muscle strength is associated with improvements in orthostatic BP and skeletal muscle pump venous function, in older people with OH.

3 | METHODS

In this evaluative case series, participants acted as their own controls, with outcomes being evaluated before, during and after the intervention. Participants were randomized to different baseline observation periods by selecting a sealed, opaque envelope with a one-in-three chance of being allocated to the following baseline periods: 4, 3 or 2 weeks.

3.1 | Population

Participants were recruited from a Falls and Syncope clinic in England, were aged 60 years or over, fulfilled international diagnostic criteria for OH and were physically and cognitively able to participate in physical therapy (Freeman et al., 2011). Exclusion criteria were as follows: lower limb ulceration or deep vein thrombosis, participation in lower limb physiotherapy in the preceding 8 weeks and acute illness.

3.2 | Intervention

The 8-week, self-led, home-based exercise programme consisted of three to four 40 min sessions per week, taught to participants by a research assistant. The intervention focussed on progressively increasing strength in the lower limb muscles through voluntary contraction of the calf, quadriceps, hip adductors and abductors, and pelvic muscles with resistance bands for progression (see Supporting Information S1: Appendix VI for more information).

3.3 | Outcomes

Primary outcomes: Change in orthostatic systolic BP (SBP) drop.

Secondary outcomes: Venous ejection fraction (EF), volume (EV), and venous filling index (VFI); calf muscle strength; lower limb strength and function; symptoms, adherence, acceptability and safety.

3.4 | Data collection

Postural BP and muscle strength were measured each week in participant's homes during baseline and intervention. Participants attended a physiology laboratory to calculate the venous measures at baseline, midintervention, end of intervention and 4 weeks following the intervention. As far as possible, the assessments occurred on the same day of the week at the same time and were performed by the same operators.

3.4.1 | Home assessments

Medical history was noted from medical records and the Charlson Comorbidy Score calculated (Charlson et al., 1987).

BP recordings were taken at the end of a 10 min supine rest and then repeated immediately upon standing, and after 1, 2 and 3 min using intermittent brachial artery BP (GE CARESCAPE V100 Vital Signs Monitor).

Symptoms were recorded using the Orthostatic Hypotension Questionnaire (OHQ) (Kaufmann et al., 2012). Exercise diaries were reviewed to monitor adherence and safety.

Isometric calf muscle strength (ICMS) was measured using a dynamometer (Jamar®). Participants were seated with their hip flexed and knee fully extended, while plantar flexing the foot against the dynamometer, fixed in place against a wall. The best of three attempts was noted. The left leg was used throughout the study for each participant.

Five times sit to stand (5STS) was performed to measure lower limb muscle strength and function at each visit. This measures how long it takes an individual (in seconds) to stand five times from a standard height chair without using their arms.

3.4.2 | Vascular physiology studies

ICMS and 5STS were repeated at the physiology laboratory visits. The postural BP was also repeated using continuous noninvasive BP measurement (CNSystems, Taskforce Monitor).

Air plethysmography (APG, ACI Medical Inc.) determined the EV, EF and VFI of the calf. The procedure included: a 10 min supine rest with the APG cuff lightly inflated around the calf, with study leg placed at a level above the heart; a calibration volume marked using a 100 mL syringe; a controlled move to standing guided by two operators; once the APG volume reached a raised plateau the participant performed three tiptoe manoeuvres, each separated by 1 min. The participant then returned to the supine position with their study leg in the original starting position. Both legs were studied, starting with the right leg. Data were recorded for analysis (Matlab, MathWorks Inc.). EF values can be categorized as follows: >60% good; 40%–60% borderline; <40% poor (Nicolaides, 2000).

3.5 | Data analysis

The target sample size for study completion was 10 participants, with attrition estimated at 30%, the recruitment target was 15. As a case series design, repeated measures are plotted on time-series graphs to identify clinically meaningful changes, with an increasing number of observations providing greater power. The case series design is a useful method to establish the preliminary efficacy of an intervention, especially those with a behavioural component (Dallery & Raiff, 2014). The method aims to identify signals of clinical, rather than statistical, significance. As this can be open to bias, statistical analyses are reported alongside visual analyses.

Data are summarized using median with inter-quartile range. Changes in outcomes were compared between baseline and Week 8 (end of intervention) and tested using a one-sample Wilcoxon's test with significance level set at <0.05. EV and EF were calculated as the maximum volume change with tiptoe compared to the venous volume level from standing (compared to supine level). The VFI was determined using the rate of change of venous filling on standing (mL/s). The mean of left and right values were calculated for each measure. Out of range EF and EV values due to artefact/interference were excluded.

3.6 | Approvals

This study was approved by UK Health Research Authority (18/NE/0173) and registered with the ISRCTN (ISRCTN45337422). All participants provided written informed consent.

4 | RESULTS

4.1 | Recruitment

Fourteen participants were recruited between September 2018 and September 2019, four of which withdrew. Case 8 missed the Week 8 assessment; as this was key to determine end of intervention effects, they are excluded from statistical analysis, but included in visual analysis for BP and strength (Supporting Information S1: Appendix I).

Baseline characteristics of the participants are summarized in Table 1. All were community-dwelling and there were no changes to participant medications during the study period.

TABLE 1 Characteristics of participants at baseline (*N* = 10).

Age (years)	72 (69–80)
Male	8
Orthostatic symptoms (OHQ)	1.5 (0–3)
Charlson comorbidity score	3 (1–4)
Hypertension	4
Parkinson's disease or MSA	2
Type 2 diabetes	3
Standing SBP (mmHg)	94 (83–101)
SBP drop (mmHg)	48 (34–73)
Standing diastolic BP (mmHg)	63 (57–74)
Diastolic BP drop (mmHg)	29 (14–42)
Vasoactive medications taken by participants*	
Fludrocortisone	3
Diuretic	1
Angiotensin converting enzyme inhibitor	2
Alpha blocker	2
β-blocker	2
Isosobide mononitrate	1
Levodopa	2

Note: Median values are displayed with the interquartile range.
Abbreviations: MSA, multisystem atrophy; OHQ, Orthostatic Hypotension Questionnaire; SBP, systolic blood pressure.
*Each participant took the same medication at each timepoint.

4.2 | Primary outcome

4.2.1 | Orthostatic SBP drop

SBP drop over the baseline, intervention and follow-up period are summarized in Figure 1. Time series trends are illustrated in supplemental Supporting Information S1: Appendix II. Cases 1, 5 and 8 show a trend for improvement in SBP drop over the intervention period, followed by an increase in SBP drop after the intervention ended. However, visual analysis demonstrates wide variation in SBP drop, even during the baseline period.

The median SBP drop at the end of baseline was 54 (32–75) mmHg. At end of intervention this was 50 (26–55) mmHg, which was not statistically different to baseline ($p = 0.477$). The

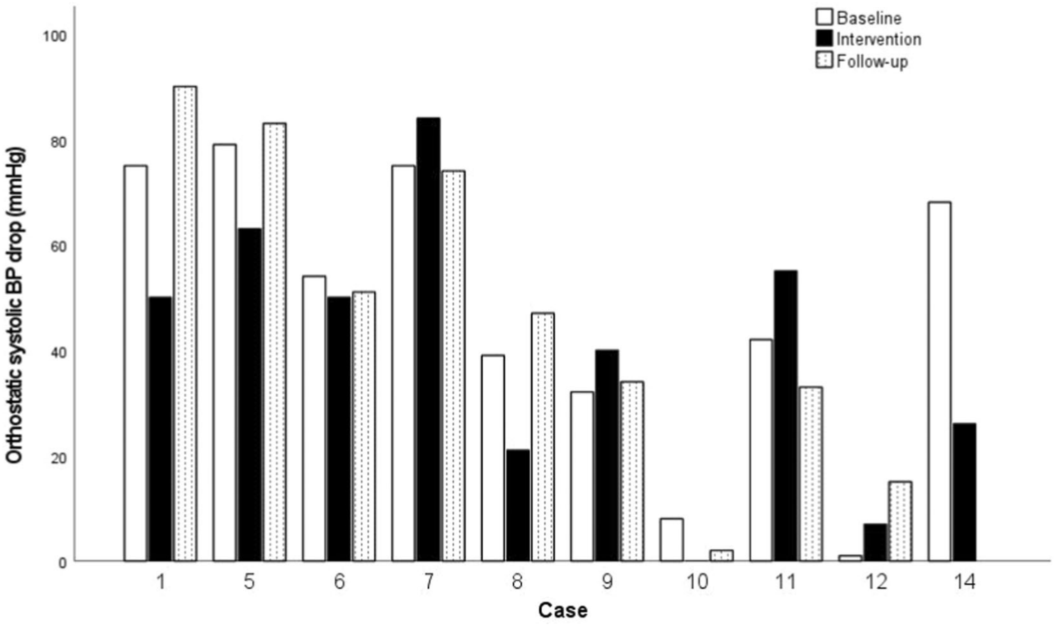

FIGURE 1 Summary of participant orthostatic systolic BP drop (mmHg) at baseline, end of intervention and follow-up (for Case 8, data for Week 8 were missing and substituted with Week 7 data; follow-up data missing for Case 14).

median percentage change in SBP drop from pre- to postintervention was 0 (−17 to 16) % ($p = 1.0$).

4.3 | Secondary outcomes

4.3.1 | Venous muscle pump

Visual analysis of the time series (Supporting Information S1: Appendix III) demonstrates no clear trend for improvement in EF, with five cases demonstrating an increase in EF, three cases with a decreasing EF and two cases with inadequate data.

Case 9 was found to have highly variable measurements from which it was difficult to extract reliable measures and was excluded from the analysis. For the remaining eight participants, the median baseline EF was 64% (51–75) and at end of intervention the change was −6% (−11 to 12), giving an overall percentage change from baseline of −10% (−16 to 24), ($p = 0.834$). Four had EF values at baseline assessment that would be considered borderline/poor for calf muscle pump function but with intervention this reduced to two participants who could be classed as borderline.

The median EV at baseline was 44 (36–58) mL and at end of intervention the change was +3 (0–5) mL, giving an overall percentage change from baseline of +9% (1–16), ($p = 0.183$).

For VFI the median baseline was 1.5 (1.2–1.7) mL/s and at end of intervention the VFI was −0.1 (−0.3 to 0.3) mL, giving an overall percentage change from baseline of −6% (−2 to 21), ($p = 0.80$). One of the participants had an abnormal VFI due to previous lower limb surgery, which could account for an abnormal VFI. There was no evidence of significant venous reflux on standing in all the other subjects.

4.3.2 | Orthostatic symptoms

Visual interpretation of individual time series graphs identifies no clinically significant change in symptoms following the intervention (Supporting Information S1: Appendix IV).

The median composite OHQ score at baseline period was 2 (1–3) and the end of the intervention period it was 1 (0–2.75), the difference was not statistically significant ($p = 0.74$).

4.3.3 | Lower limb strength

Calf muscle strength

Overall, visual analysis of the time series graphs indicates a trend for increasing ICMS in seven cases (Supporting Information S1: Appendix V). ICMS appears to decrease over time in one case and two cases have no discernible trend.

The median baseline calf muscle strength was 38 (34–45) kg and at end of intervention the change was +10 (7–13) kg, giving an overall percentage change from baseline of +21 (18–28) %, $p = 0.018$.

5STS

The median baseline 5STS was 12.6 (10.7–13.9) s and at end of intervention the change was −0.3 (−2.6 to 0.6) s, giving an overall percentage change from baseline of −4.2 (−15.0 to 3.9)%, ($p = 0.286$).

4.3.4 | Adverse events and adherence to intervention

No adverse events were reported. Self-reported adherence to the intervention was adequate in all participants (performing exercises for at least 40 min for at least 3 times a week).

5 | DISCUSSION

In this case series analysis, there is a clear trend that the exercise intervention increased ICMS. However, this increase in muscle strength did not translate into an improvement in venous EF, orthostatic BP drop or symptoms.

In theory, lower limb muscle strengthening should be a beneficial therapy for OH in older people. Studies in community dwelling older people have found lower calf mass is associated with an increased likelihood of OH and lower limb strengthening exercises in older people with OH improved the duration of the upright position during tilt-testing(Kobayashi & Yamada, 2012; Zion, et al., 2003). Similarly, observational studies report a strong association between sarcopenia and orthostatic intolerance in older people (Soysal et al., 2020).

There are several possible reasons why the increased muscle strength and EF does not have a strong link with orthostatic BP. Firstly, there was wide variation in orthostatic BP values, even during baseline. This variability limits the ability to identify underlying trends. To overcome this, a significantly greater number of observations would be needed. Postural BP is controlled by several complex interacting mechanisms which include pre- and postganglionic autonomic reflexes, cardiac and vascular responses and neurohormonal mechanisms. The skeletal muscle is only one component of this complex physiological process and as such, an intervention focussed on only one component may have a limited impact. This may be particularly true for older people with OH who may have a more multifactorial aetiology.

The majority of venous pooling may occur in the pelvis and thighs, but the measurement of venous physiology in these areas is not straight-forward (Ludbrook, 1966). However, the exercise intervention targeted the whole lower limb to increase strength throughout these muscles and did not improve postural BP. Nevertheless, the calf muscle pump should not be used in isolation as a manoeuvre to treat OH.

An interesting finding from this study is that the levels of venous reflux seen were largely within normal limits, challenging the commonly held view that those with OH have significant venous pooling in the lower limbs. It is also notable that the observed EF of venous blood was similar to previous reports of EF in younger healthy people (Ludbrook, 1966). It is likely that the small volume of blood ejected from the calf muscle would have a negligible impact on venous return and BP. In addition, given the low levels of venous reflux, it is unlikely that below-knee compression garments will be clinically effective.

6 | LIMITATIONS

This is an early phase, single case series design aiming to identify preliminary evidence of efficacy, as such the number of participants is low. However, the intra-participant power is increased with the high number of repeated observations. The symptom severity of participants in the study was relatively low, likely because participants were already receiving treatment for their condition, but it is possible that the nature of the study resulted in those with more severe symptoms declining to volunteer. Although the intervention did result in increased muscle strength, it is possible that a longer intervention could have increased strength further and perhaps this would have improved the venous EF.

7 | CONCLUSION

There is little to no excess venous pooling in the calf of older people with OH. Lower limb strengthening exercise does not improve the efficacy of the muscle pump and does not improve standing BP in older people with OH.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Deidentified data are available upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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