One-year of isometric exercise training for blood pressure management in men: a prospective randomized controlled study.

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Conflicts of Interest and Source of Funding: None

Running Title: Longitudinal IET and blood pressure

Keywords: Blood pressure, hypertension, isometric exercise training

Word Count: 2427

Abbreviations

BP – blood pressure

IET – isometric exercise training

CO – cardiac output

dBP – diastolic blood pressure

ECG – electrocardiogram

HR – heart rate

mBP – mean blood pressure

sBP – systolic blood pressure

SV – stroke volume

TPR – total peripheral resistance

Abstract

Objective: Isometric exercise training (IET) over 4-12 weeks is an effective anti-hypertensive intervention. However, blood pressure (BP) reductions are reversible if exercise is not maintained. No work to date has investigated the long-term effects of IET on resting blood pressure.

Methods: We randomised 24 unmedicated patients with high-normal BP to a 1-year wall squat IET intervention or non-intervention control group. Resting BP and various clinically important haemodynamic variables including heart rate (HR), stroke volume (SV), cardiac output (CO) and total peripheral resistance (TPR) were measured pre and post the 1-year study period.

Results: 1-year of IET produced statistically significant reductions in resting systolic (-8.5±5 mmHg, $p<0.001$) and diastolic (-7.3±5.8 mmHg, $p<0.001$) BP compared to the control group. There was also a significant reduction in resting HR (-4.2±3.7 $b \cdot min^{-1}$, p=0.009) and significant increase in SV (11.2±2.8 ml, p=0.012), with no significant change in CO (0.12±2.8 $L \cdot min^{-1}$, p=0.7). TPR significantly decreased following IET (-246±88 $dyne \cdot s \cdot cm^{-5}$, p=0.011). Adherence to the IET sessions was 77% across all participants (3x IET sessions per week), with no participant withdrawals.

Conclusion: This novel study supports IET as an effective long-term strategy for the management of resting BP, producing clinically important, chronic BP adaptations in patients at risk of hypertension. Importantly, this work also demonstrates impressive long-term adherence rates, further supporting the implementation of IET as a means of effective BP management in clinical populations.

Introduction

Isometric exercise training (IET) is now well established as an efficacious anti-hypertensive intervention, capable of producing greater reductions in resting blood pressure (BP) when compared to the standard recommendations of exercise guidelines [1]. Specifically, recent meta-analysis evidence has shown statistically significant systolic and diastolic BP (sBP and dBP) reductions of 8.5 and 4.1 mmHg, respectively, following relatively short-term (4-12 weeks) IET interventions [2]. The magnitude of these reductions are comparable to standard anti-hypertensive pharmacotherapy [3], with the added benefit of no adverse side effects and reduced costs. Given that hypertension is the leading attributable risk factor for cardiovascular disease and all-cause mortality [4], with a prevalence of greater than 1.1 billion worldwide [5,6], IET may have substantial clinical implications for the future management of resting BP.

A number of trials have demonstrated clinically significant reductions in sBP and dBP following as little as 4-weeks of IET [7–10]; however, no work to date has investigated the efficacy of an IET intervention beyond 12-weeks in duration. Consequently, there is currently no evidence to support long-standing adaptations in resting BP or the long-term adherence to IET. Research from Millar et al. [11] demonstrated linear negative trends in resting sBP and dBP over an 8-week intervention with no plateau in reductions over this timeframe. In addition, a meta-analysis from Inder et al. [12], reported larger reductions in sBP in participants undertaking ≥8 weeks of IET compared to <8 weeks of IET. However, while this work may indicate greater reductions from a longer intervention duration, conclusive inferences cannot be made through the extrapolation of such limited data. As such, prospective randomised controlled trials are required to truly understand the long-term effectiveness of IET. Furthermore, the potential future clinical implementation of IET is, at least somewhat, based on the presumption that adherence to IET is likely to be greater than that of other exercise modes due to its time-efficient and practical nature. However, without sufficient longitudinal investigation of IET, the validity of this presumption is not known. This study aimed to perform the first longitudinal randomised controlled study, measuring the effects of a 12-month IET intervention on resting BP in patients with high normal BP. We also aimed to measure important mechanistic haemodynamic variables including cardiac output (CO) and total peripheral resistance (TPR).

Methods

Participant population and ethical approval

Twenty-four male participants (mean age 46 ± 8 years) were recruited to this single-centre prospective, randomised controlled trial. Participants were physically inactive and classified as high normal in accordance with the relevant guidelines [13]. None of the participants were under any acute or chronic pharmacotherapy and all presented with a normal clinical cardiovascular examination and 12-lead electrocardiogram (ECG) with no cardiac or metabolic disease. All participants were non-smokers. Written informed consent was obtained from all participants before testing and this study conformed to the Declaration of Helsinki principles with approval from the local ethics committee (Ref:12/SAS/122).

Study Procedures

Eligible participants were randomly allocated to a 12-month IET intervention or to the control group. Participants assigned to the IET group were required to attend the Canterbury Christ Church University laboratory on three separate occasions, while the control group attended twice. The IET group performed an extra initial visit which comprised an incremental isometric wall-squat test to determine the individualised knee joint angle for appropriate IET intensity prescription, as previously described [7]. The remaining sessions involved the acquisition of the relevant pre- and post-intervention cardiovascular parameters. All participants were required to maintain normal dietary and circadian routines throughout the study and each phase of testing, as well as refrain from alcohol and caffeine consumption for 24-hours and fast for at least 4 hours before testing.

Resting clinic blood pressure

Resting clinic brachial artery BP was acquired using a validated automated device (Dinamap Pro 200 Critikon; GE Medical Systems, Freiburg, Germany) and according to current guidelines [13]. All measures were recorded in a temperature-controlled room at the same time of day (±1-hour) pre and post the 12-month IET intervention and control period.

Haemodynamics

All haemodynamic variables were acquired using the Task Force® Monitor, which is a validated non-invasive beat-to-beat monitoring system that provides automatic calculations of all outputs. Heart rate (HR) was acquired through a six-channel ECG and stroke volume (SV) was recorded via impedance cardiography through three electrode bands, two of which were in line with the xiphoid process and adjacent to the thorax and the other placed on the nape of the neck. Cardiac output (CO) was automatically derived from HR and SV. Total peripheral resistance (TPR) was separately calculated in accordance with Ohm's law. Both CO and TPR were indexed to body surface area following acquisition of participant height and mass using a SECA 213 stadiometer and SECA 700 mechanical column scales (SECA GmbH & Co., Hamburg, Germany) respectively. All measures were recorded following 15 minutes of supine rest with a continuous recording period of 5 minutes.

Isometric exercise training intervention

Participants allocated to the training group performed 3 weekly wall squat IET sessions at 95% HR peak for 12-months in an unsupervised home-based setting. As previously described [14–16], each participant performed a maximal incremental wall squat test with beat-to-beat HR recording in order to determine HR peak corresponding to the prescribed knee angle. Following this test, participants were issued a 'Bend and Squat' device, which is a simple device developed in-house allowing for the alignment of a participant's feet and back placement into the correct position to elicit the appropriate HR response [9]. Using the Bend and Squat device, the home-based wall squat protocol involved participants resting their back against a fixed wall with their feet placed parallel and shoulder width apart, while their arms remained relaxed down by their side (see Supplement File for further details). Each session involved of 4 x 2-min bouts of isometric wall squat, separated with 2-min rest intervals, with at least 48-hours recovery between every session [7–9]. To allow for close monitoring of intensity and adherence, all participants recorded HR and rate of perceived exertion data following each IET bout and uploaded their data to a personal online database which was monitored by the investigators. The control group were required to maintain their usual routine and daily activities, abstaining from any form of exercise they did not habitually perform for the full 12-month period. The control group were routinely contacted by the investigators to confirm maintenance of circadian habits.

Sample size estimation

Based on previous studies utilizing this protocol, we have previously reported extremely large changes in sBP [7] (reductions of >12mmHg) equivalent to an effect statistic of >2.2 with similar intervention. Using G*Power software [17], a more conservative (albeit still large) effect statistic of 1.2 was selected, and with power of 80% and $p<0.05$, the estimated sample size of 12 participants per group were recruited.

Statistical analysis

Continuous variables are expressed as mean±SD. Post-trial group differences for sBP, mBP, dBP and haemodynamic parameters were assessed using Analysis of Covariance (ANCOVA), with baseline scores for each parameter included as a covariate in the model. All data were analysed using the statistical package for social sciences (SPSS 26 release version for Windows; SPSS Inc., Chicago, Illinois, USA).

Results

All participants completed the intervention safely, with no adverse events following any IET session. There were no significant differences between the groups at baseline for any of the physiological variables or participant characteristics, including height (IET: 178.6±8cm; Con: 178.2±7.2) and mass (IET: 88.5±11.1; Con: 90.4±13.9).

Adherence to the IET sessions was 77% across all participants (3x IET sessions per week). None of the participants withdrew from the intervention. One participant re-performed the IET incremental wall squat test after 7-months to re-calculate a sufficient knee joint angle, as routine monitoring of HR data recorded during training sessions demonstrated the training did not elicit the appropriate intensity.

Resting blood pressure and haemodynamics

As seen in Table 1 and Figure 1, the IET group demonstrated significant reductions in resting clinic sBP (-8.5±5 mmHg, $p<0.001$) and dBP (-7.3±5.8 mmHg, $p<0.001$) compared to the control group. Figure 2 illustrates the individual changes pre and post IET and control period. There was also a significant reduction in resting HR (-4.2±3.7 $b \cdot min^{-1}$, p=0.009) with adjacent significant increases in SV (11.2±2.8 ml, p=0.012) and SV index (5.3±1.9 $ml \cdot m^2$, p=0.013), but no significant change in CO (0.12±2.8 $L \cdot min^{-1}$, p=0.7) or CO index (0.03±0.2 $L \cdot min^{-1} \cdot m^2$, p=0.82). Separately, there was a significant reduction in TPR (-246±88 $dyne \cdot s \cdot cm^{-5}$, p=0.011).

Discussion

This is the first study to investigate the longitudinal (one-year) efficacy of IET as an anti-hypertensive intervention. This novel research supports IET as an effective long-term strategy in the management of resting BP, capable of both producing and maintaining clinically important BP adaptations in patients with high normal BP. Additionally, the findings of this study support the function of IET in sustaining clinically relevant haemodynamic adaptations, with significant reductions in resting HR and TPR concurrent to a significant increase in SV. Importantly, this work also evidences substantially higher adherence to IET than that typically seen when following the current recommended exercise guidelines (44.6%) [18] or with clinical pharmacotherapy [19].

While the ability of IET to produce statistically significant reductions in resting BP is well-established [2], this study provides the first evidence that such adaptations can be sustained long-term. We observed reductions in sBP and dBP by 8.5 and 7.3 mmHg, respectively, following 1-year of IET, which is both greater than the average reduction seen from other modes of exercise [20,21] as well as that of standard dosage anti-hypertensive monotherapy [3]. In particular, Anderssen et al. [22] investigated the effects of a 1-year aerobic exercise intervention and reported reductions of 4.1 and 5.1 mmHg sBP and dBP, respectively. Despite having a lower baseline BP, the present study demonstrates more than twice the magnitude of reduction over the same intervention duration. In terms of their clinical importance, previous large-scale data suggest these IET reductions to be associated with a reduced risk of ischaemic heart disease, stroke, cardiovascular disease events and cardiovascular mortality by 16.8%, 27.3%, 21% and 10.5% respectively [24].

Of interest, the dBP reductions from the present study are particularly substantial, being of a far greater magnitude than generally achievable with any other form of anti-hypertensive intervention [21,23] and greater than that observed following short term IET [9,25]. While the underpinnings of this finding are unknown, acute data shows that wall squat IET produces large post-exercise hypotensive effects on dBP, with previous studies reporting reductions close to 20 mmHg from baseline to the recovery phase in both normotensive [26], and hypertensive participants [16]. This response is certainly much larger than seen following other modes of exercise [27–29]. Indeed, the consistent repetition of such acute hypotensive responses elicited from each IET session may translate into the chronic reductions reported from this 1-year intervention, and may be an important mechanism for the cardiovascular adaptations previously reported [7,30].

This study echoes the wider mechanistic literature in that IET predominantly induces reductions in resting BP independent of changes in CO [1,7,8]. While significant reductions are seen in resting HR, CO remains unchanged as the consequence of a significant increase in SV, which is likely mediated through the significant left ventricular functional and mechanical adaptations recently evidenced following IET [30]. As such, IET-induced BP reductions appear to be primarily modulated through TPR, such as altered autonomic and baroreflex vasomotor control [7,31], local endothelial-dependant mechanisms [7,32] and systematic structural vascular remodelling [33]. However, the exact contribution of each of these potential processes is not yet known.

While the study sample size of this research is limited, the overall adherence to this 1-year intervention was impressive. Poor adherence rates have been deemed a primary contributor to the current ineffectiveness of both the present exercise guidelines and medical therapy [34,35]. Current physical inactivity rates in accordance with recommended exercise guidelines have been cited at 27.5% [35], or even as low as 5% via objective accelerometer measures [36], while the average adherence to anti-hypertensive medical therapy is typically reported at less than 50% 1-year following prescription [19]. As the first study to provide long-term adherence data in IET, these findings support the hypothesis that adherence to IET is likely to be greater than other anti-hypertensive means, especially given the well-cited report that 50% of people who start an exercise programme will abstain within 6 months [37]. At 77% adherence from a 1-year intervention, this work strengthens IET as a successful intervention in clinical practice. However, comparative large-scale randomised controlled data is needed to truly discern the differing adherence rates between IET and the current physical activity guidelines.

Limitations

This research was single centre with a limited sample size and only included males. Therefore, future multi-centre work in a large-scale population including female and different ethnic groups is warranted. In addition, this work was not statistically powered to detect haemodynamic changes, and thus only limited inferences can be made from this data. Finally, the exclusion of smokers from this work limits the relative applicability of these findings to such individuals who tend to derive an even greater benefit from effective anti-hypertensive interventions.

Conclusion

This is the first study to investigate the long-term efficacy of IET in the management of resting BP. 1-year of IET produces and maintains statistically and clinically significant reductions in resting BP, superior to that of the current exercise guidelines as well as anti-hypertensive pharmacotherapy. These reductions are likely mediated through peripheral vascular adaptations, while also producing significant improvements in resting HR and SV. Importantly, this work also demonstrates impressive long-term adherence rates, further supporting the clinical implementation of IET as a means of BP management.

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Table 1: Resting office blood pressure and haemodynamic adaptations pre and post isometric exercise training and control period.

	Control (n=12)		Isometric Exercise Training (n=12)	
	Pre	Post	Pre	Post
Resting Office BP				
sBP (mmHg)	132.4 ± 5.7	130.4 ± 6.5	132.3 ± 5.8	121.8 ± 3.9**
mBP (mmHg)	98.5 ± 6.1	96.5 ± 5.8	98.6 ± 5.4	88.7 ± 3.2**
dBP (mmHg)	81.5 ± 6.7	81.3 ± 6.4	81.7 ± 6.9	73.7 ± 5.1**
Resting Haemodynamic Variables				
Heart Rate ($b \cdot min^{-1}$)	58.5 ± 6.6	59.5 ± 6.8	61.8 ± 10.0	57.9 ± 8.8*
Stroke Volume (ml)	85.8 ± 13.2	85.2 ± 11.3	82.5 ± 12	94.3 ± 13.7*
Stroke Index ($ml \cdot m^2$)	40.8 ± 5.7	40.6 ± 6.3	39.7 ± 6.7	45.2 ± 6.6*
Cardiac Output ($L \cdot min^{-1}$)	4.8 ± 1	5.1 ± 0.9	5.3 ± 0.8	5.5 ± 1.3
Cardiac Index ($L \cdot min^{-1} \cdot m^2$)	2.3 ± 0.4	2.4 ± 0.5	2.5 ± 0.4	2.6 ± 0.6
TPR ($dyne \cdot s \cdot cm^{-5}$)	1622 ± 328	1565 ± 312	1650 ± 288	1355 ± 314*

Note: Values are mean ± SD. * $p<0.05$, ** $p<0.001$ differences between change scores from control and IET condition. BP = blood pressure; sBP = systolic blood pressure; mBP = mean blood pressure; dBP = diastolic blood pressure; TPR = total peripheral resistance; TPRI = total peripheral resistance index.

Figure Legend:

Figure 1: Mean sBP (A), mBP (B), and dBP (C) change values following control (closed circles) and IET (open circles) conditions. Note: *Significant ($P < 0.05$) difference in the control and IET change value.

Figure 2: Individual changes in sBP, mBP and dBP following control and IET conditions. Grey lines represent individual participants and black lines represent the mean changes at baseline and following 1-year of IET.