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Myocardial performance index as a measure of global left ventricular function improves following isometric exercise training in hypertensive patients

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Abstract

As the leading cause of cardiovascular disease and mortality, hypertension remains a global health problem. Isometric exercise training (IET) is established as efficacious in reducing resting blood pressure (BP); however, no research to date has investigated its effects on myocardial performance index (MPI). 24 unmedicated hypertensive patients were randomised to 4-weeks of IET and a control period in a cross-over design. Tissue doppler imaging was used to acquire cardiac time intervals pre and post the IET and control periods. IET significantly improved all measures of cardiac time intervals, including isovolumic relaxation time (83.1±10.3 vs 76.1±11.2ms, p=0.006), isovolumic contraction time (84.8±10.3 vs 72.8±6.4ms, p<0.001), ejection time (304.6±30.2 vs 321.4±20.8ms, p=0.015) and MPI (0.56±0.09 vs 0.47±0.05, p<0.001). This is the first study to demonstrate that IET significantly improves cardiac time intervals. These findings may have important clinical implications, highlighting the potential utility of IET in the management of cardiac health in hypertensive patients.

Key Words: Cardiac time intervals, blood pressure, hypertension, isometric exercise training

Introduction

As the leading cause of cardiovascular disease and mortality [1], arterial hypertension remains a global health problem. Previous evidence has reported the risk of cardiovascular disease to double for every increase in systolic blood pressure (BP) by 20mmHg, with a more recent analysis reporting a 13% increase in risk of mortality for every 10mmHg [2,3]. As a primary contributor to such detrimental clinical prognosis, long-standing hypertension is commonly associated with the progressive deterioration in cardiac functional and structural health [4]. Therefore, hypertension management strategies which both reduce BP and improve cardiac performance are critical.

Our group have recently demonstrated that a programme of isometric exercise training (IET) can significantly reduce arterial BP by 12.4 and 6.2 mmHg in systolic and diastolic respectively [5], which has been associated with significant improvements in myocardial efficiency and left ventricular (LV) cardiac mechanics [6]. However, the analysis performed in this work is highly complex and requires specialist software for offline analysis. Conversely, tissue doppler-derived cardiac time intervals are sensitive markers of cardiac health and can be easily obtained during the acquisition of cardiac images [7]. Additionally, cardiac time intervals have been demonstrated to provide significant prognostic utility independent of conventional echocardiography, with myocardial performance index (MPI) identified as a strong predictor in the risk of developing congestive heart failure [8–10].

Therefore, the aim of this study was to assess whether there are significant changes in cardiac time intervals following 4-weeks of IET in a hypertensive population.

Methods

Study population and ethical approval

Twenty-four physically inactive participants (43.8±7.3 years), classified as stage 1 hypertensive in accordance with current guidelines [11] were recruited. None of the participants were under any acute or chronic pharmacotherapy, including antibiotics. All participants had no history of cardiac or metabolic disease, were non-smokers and presented with normal clinical cardiovascular examination and 12-lead ECG. This research study conformed to the Declaration of Helsinki principles and was approved by the local ethics committee (Ref:12/SAS/122). Written informed consent was obtained from all participants before testing.

Experimental Procedures

In a cross-over design, participants were randomized to a 4-week IET intervention or a 4-week control period, separated by a 3-week washout period (see Figure 1, study flow diagram). Participants were required to attend the Canterbury Christ Church University Laboratory on five separate occasions. The initial visit comprised of an incremental isometric wall-squat test to determine the appropriate individualised knee joint angle for effective IET intensity prescription, as previously described [5], with the remaining sessions dedicated to the acquisition of the relevant 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

Using a validated automated device (Dinamap Pro 200 Critikon; GE Medical Systems, Freiburg, Germany) and according to current guidelines [11], brachial artery BP was recorded in a temperature-controlled room pre and post the IET intervention and control period.

Cardiac time intervals

Cardiac time intervals were acquired using tissue Doppler imaging in the apical four-chamber view (See Figure 2). The sample volume was placed at the lateral and septal mitral annulus, with measures averaged. Isovolumetric relaxation time (IVRT) was acquired by measuring between the end of the S’ wave and the onset of the E’ wave and isovolumetric contraction time (IVCT) by measuring from the end of A’ wave to the onset of the S’ wave. Ejection time (ET) was measured from onset to the end of the S’ wave. Myocardial performance index (MPI) was calculated as (IVCT + IVRT) /ET. The images were stored in raw archive DICOM data for offline analysis and measurements were recorded by an experienced echocardiographer who was blinded to participant characteristics and group allocation.

Isometric exercise training intervention

The IET intervention consistent of 3 sessions per week for 4 weeks in an unsupervised home-based setting, performed as a wall-squat (12 sessions total). Each session comprised of 4 x 2-min bouts of isometric wall squat, separated with 2-min rest intervals. IET sessions were performed at an individualised knee joint angle acquired from an incremental lab test to ensure an effective intensity as previously described [5]. Each participant recorded their heart rate at the end of each IET bout (Polar RS400 Computer and a Polar WearLink V2 transmitter; Polar Electro Oy, Kempele, Finland) and uploaded their data to a personal online database, which was monitored in regards to the regulation of exercise intensity. Each training session was separated by 48-hours recovery. During the control period, participants were requested to maintain their usual routine and daily activities with adherence to this confirmed prior to laboratory assessment.

Sample size estimation

In accordance with previous evidence [12], we expected this IET intervention to elicit a clinically significant [13] minimum reduction of 5mmHg in resting systolic BP, with no significant change in the control group. Based on this predicted change and the coefficient of variation (4.6%) for systolic BP from Wiles et al [12], we estimated a sample size of 18 participants, with 80% power and P less than 0.05. Accounting for an estimated dropout rate of 20-30%, we determined an appropriate sample size of 24 participants. Our aim was to investigate changes in cardiac time intervals in a cohort powered for a reduction in arterial BP.

Statistical analysis

Analysed using the statistical package for social sciences (SPSS 26 release version for Windows; SPSS Inc., Chicago IL, USA), a two-way repeated measures ANOVA was performed with a Bonferroni post hoc test, for comparison of outcome measures between (IET vs control condition) and within groups (pre vs post intervention). Continuous variables are expressed as mean±standard deviation.

Results

All participants completed the IET sessions (100% adherence) with successful image acquisition in 100% of the participants. There were no adverse events following any IET session.

Resting clinic systolic and diastolic BP significantly decreased following IET (132.4±5.6mmHg to 120.1±5.7mmHg and 81.4±6.9mmHg to 75.2±6.2mmHg, respectively) compared to control (132.2±5.4mmHg to 132.5±4.9mmHg and 81.9±6.25mmHg to 81.7±6.5mmHg, respectively) (both p<0.001) and these results have been reported previously[6].

Cardiac time intervals

As detailed in Table 1, there were significant differences (Bonferoni post hoc p values presented) between IET and control in all measures of cardiac time intervals, including isovolumic relaxation time (83.1±10.3 vs 76.1±11.2ms, p=0.006), isovolumic contraction time (84.8±10.3 vs 72.8±6.4ms, p<0.001), ejection time (304.6±30.2 vs 321.4±20.8ms, p=0.015) and myocardial performance index (0.56±0.09 vs 0.47±0.05, p<0.001).

Discussion

To our knowledge this is the first study to investigate the effects of a short-term IET intervention on cardiac time intervals. Concurrent to previously reported significant decreases in resting clinic BP [5], IET produced significant improvements in IVRT, IVCT, ET, and MPI. Of clinical importance, these measures of the cardiac cycle have been shown to change relative to disease progression and identify cardiac dysfunction in hypertensive patients, independent of conventional echocardiography examination [9]. While our previous work has demonstrated the efficacy of IET on traditional echocardiographic indices of cardiac function and 2D speckle tracking measures of myocardial mechanics and efficiency [6], such measures are often complex, requiring specific techniques and analysis as well as appropriate image quality. However, cardiac time intervals provide sensitive information, which is more accessible and reproduceable, and can be performed in patients with poor image quality.

IVRT is known to be lengthened with impaired LV relaxation and thus is indicative of diastolic dysfunction [14,15]. With this, our findings of a significant decrease in IVRT highlights the efficacy of IET in improving indices of diastolic function in hypertensive patients. Indeed, these findings are similar to that previously observed following aerobic exercise training of substantially longer (mean of 18 weeks) interventional durations [16,17]. As a combined index with ET, IVRT is significantly predictive of future ischaemic cardiovascular diseases, even after adjustment for hypertension status, left-ventricular hypertrophy and BP [9,18]. Given that we also report a significant increase in ET, our findings may have important clinical implications regarding cardiovascular risk, even in those who display no standard echocardiographic abnormalities [9].

MPI, which provides a global measure of cardiac function, significantly decreased following IET, suggesting an improvement in cardiac contractility and relaxation [19,20]. Importantly, MPI is a robust independent predictor of adverse outcomes, with previous research highlighting its prognostic utility in various populations, including hypertensive patients [9] and cohorts representative of the general population [21]. Specifically, MPI has been demonstrated to predict cardiovascular disease [9], congestive heart failure [8] and all-cause mortality, with an increased risk of death by 31% per 0.1 increase in MPI [21]. Therefore, the findings of this study exhibit the potentially important role of IET in the long-term clinical management of hypertensive patients.

Mechanistically, cardiac time intervals are understood to be load-dependant parameters [22], with these cardiac changes observed in the context of a significant decrease in resting BP. As such, the observed anti-hypertensive effects of IET may contribute to improved cardiac time intervals through favourable LV and aortic pressure-volume changes. Specifically, decreasing aortic pressure reduces the time required for LV pressure to overcome that of the aorta, consequently reducing IVCT and IVRT. These time periods of the cardiac cycle are subsequently replaced by an increase in ET which enhances myocardial efficiency, while maintaining an unchanged cycle duration. Accordingly, these changes improve cardiac function over a single cycle, as represented through the decrease in MPI. Therefore, the mechanistic underpinnings of such cardiac responses may be explained via the same pathway in which BP is reduced following IET, which has been previously linked to enhancements in autonomic and peripheral vascular function and health [5,23].

Limitations

This study only included male Caucasian participants, limiting the relative applicability of these findings to female participants and different ethnic populations. In particular, sex and ethnicity are understood to be key moderators of resting BP with differing baseline values between populations [13]. Given that the efficacy of any anti-hypertensive intervention is dependant on baseline BP, group-specific data is required before the present findings can be extrapolated to differing populations [5]. Additionally, this study was single-centre and only 4-weeks in duration, thus longer-term prospective multi-centre research is needed. Finally, whether these findings are reproducible in medicated hypertensives is unknown.

Conclusion

This novel study demonstrated the efficacy of a short-term IET intervention on cardiac time intervals. IET significantly improved IVRT, IVCT, ET and MPI, which may have clinical implications regarding long-term cardiac health and risk of adverse outcomes. Future longitudinal research investigating the efficacy of IET in females and different ethnic populations is needed.

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Conflicts of Interest: None

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Figure Legends

Figure 1: Study flow diagram

Figure 2: Tissue doppler imaging acquisition of cardiac time intervals: isovolumetric contraction time (IVCT), ejection time (ET) and isovolumetric relaxation time (IVRT)