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ORIGINAL ARTICLE

Left atrial strain predicts cardiovascular response to exercise in young adults with suboptimal blood pressure

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Abstract

Aims: To investigate the left ventricular response to exercise in young adults with hypertension, and identify whether this response can be predicted from changes in left atrial function at rest.

Methods: A total of 127 adults aged 18–40 years who completed clinical blood pressure assessment and echocardiography phenotyping at rest and during cardiopulmonary exercise testing, were included. Measurements were compared between participants with suboptimal blood pressure ≥120/80mm Hg (n = 68) and optimal blood pressure <120/80mm Hg (n = 59). Left ventricular systolic function during exercise was obtained from an apical four chamber view, while resting left atrial function was assessed from apical four and two chamber views.

Results: Participants with suboptimal blood pressure had higher left ventricular mass ($p = 0.031$) and reduced mitral E velocity ($p = 0.02$) at rest but no other cardiac differences. During exercise, their rise in left ventricular ejection fraction was reduced ($p = 0.001$) and they had higher left ventricular end diastolic and systolic volumes ($p = 0.001$ and $p = 0.001$, respectively). Resting cardiac size predicted left ventricular volumes during exercise but only left atrial booster pump function predicted the left ventricular ejection fraction response ($\beta = .29$, $p = 0.011$). This association persisted after adjustment for age, sex, body mass index, and mean arterial pressure.

Conclusion: Young adults with suboptimal blood pressure have a reduced left ventricular systolic response to exercise, which can be predicted by their left atrial booster pump function at rest. Echocardiographic measures of left atrial function may provide an early marker of functionally relevant, subclinical, cardiac remodelling in young adults with hypertension.

KEYWORDS
exercise echocardiography, exercise ejection fraction, hypertension, left atrial strain, speckle tracking echocardiography, Young adults

1 | INTRODUCTION

The prevalence of hypertension in young adults is increasing, with at least one in 17 adults below the age of 40 years being hypertensive.[1] Blood pressure levels in young adulthood are associated with risk of stroke and cardiovascular disease in later life.[2,3] Therefore, identification of those who may benefit from intervention early in life is important. Traditional biomarkers used to risk stratify patients for treatment, such as left ventricular hypertrophy, tend to be less sensitive for identification of those at risk at younger ages, due to relatively shorter durations of exposure.[4,5] Left ventricular hypertrophy develops because blood pressure elevation increases afterload and left ventricular wall stress. However, gross changes in left ventricular morphology sufficient to reach criteria for the diagnosis of left ventricular hypertrophy are not often observed until severe disease is established.[6–8]

One of the other reported functional impacts of increased left ventricular loading and myocardial fibrosis[9–11] is an abnormal left ventricular response to physical exercise.[12–14] This has been observed in older patients with hypertension and, although initially believed to be due to coexisting coronary artery disease,[15] was found in older asymptomatic, moderately-hypertensive patients without evidence of coronary disease.[14] Using speckle tracking echocardiography, changes in left atrial function have also been shown to be altered in older hypertensive patients before the presence of ventricular structural abnormalities.[16] Subclinical alterations of left ventricular mechanics could, in part, be explained by these changes in left atrial function[16,17] as the left atrial booster pump phase, in particular, is known to vary with left ventricular compliance and end diastolic pressure.[18]

We hypothesized abnormal left ventricular-atrial coupling should become evident early in the development of hypertension and, therefore, identifiable in young adults with advancing hypertensive disease.[19] To test this hypothesis, we studied whether a reduced left ventricular response to exercise is evident in young people with mild degrees of hypertension. In addition, to examine whether this exercise response could be detected at rest, we tested whether this response can be predicted by changes in left atrial function.

2 | METHODS

2.1 | Study population

We performed a retrospective, observational case control study, with frequency matching between groups for age, sex, and bodyweight. Young adults were identified from all participants aged between 18 and 40 years, who were not already on anti-hypertensive medication, and had undergone stress exercise echocardiography as part of clinical studies into young adult hypertension in the Cardiovascular Clinical Research Facility at the John Radcliffe Hospital in Oxford between January 2014 and September 2019. Participants were identified consecutively from clinical research records until the required sample size was achieved. All participants had undergone a similar detailed clinical assessment of blood pressure profiles, anthropometry, resting transthoracic echocardiography, and cardiopulmonary exercise testing with stress echocardiography imaging. All participants with adequate stress echocardiography image quality were included in this analysis. Ethical approval for these studies had been granted by the South Central Berkshire Research Ethics Committee (14/SC/0275) and Oxford B Research Ethics Committee (16/SC/0016) and study protocols and activities fully complied with the Declaration of Helsinki. All participants had provided signed informed consent when they originally participated.

2.2 | Baseline clinical cardiovascular characteristics

Demographic data including age, height, and weight were collected from all enrolled participants. Resting blood pressure measurements were obtained using a digital blood pressure monitor (GE Dinamap V100, GE Healthcare, Chalfont St. Giles, United Kingdom) to record three consecutive blood pressure readings on the left arm with a minute apart. The last two measurements were averaged and included in the analysis. Ambulatory blood pressure monitoring for 24 hours was performed for all participants using (TM-2430, A&D Instruments, Abingdon, United Kingdom). At the end of the study visit, participants were fitted with Axivity AX3 wrist-worn (Axivity Ltd, Newcastle, UK), tri-axial accelerometers which were worn for nine days then posted back to the study team. Physical activity information was extracted from raw sensor data using the same analysis pipeline used for UK Biobank participants.[20] The first seven days of wear data were analysed to quantify time spent in vigorous physical activity (VPA) (i.e., jogging, running, active sport).[21]

2.3 | Resting echocardiography

A comprehensive 2D and 3D echocardiography scan was performed for each participant using a Philips EPIC 7C, Philips iE33 echocardiography ultrasound machine (Philips Healthcare, Surrey, United Kingdom) and following the British Society of Echocardiography standards in image optimization and acquisition. Conventional image analysis was completed according to the latest published guidelines for chamber[22] and valvular[23] assessment using Philips IntelliSpace Cardiovascular (ISCV) 2.1 (Philips Healthcare Informatics, Belfast, Ireland), and TomTec Image Arena 4.6 (Chicago, IL, United States) software was used to perform advanced left ventricular speckle tracking analysis. Speckle tracking analysis of the left atrium was performed to assess left atrial phases, known as left atrial reservoir, conduit, and booster pump function. The left atrial endocardium was traced in apical four and two chamber views to allow for biplane assessment. Measurements from both views were then averaged. Peak atrial longitudinal strain (PALS), peak atrial contraction strain (PACS), and the difference between PALS and PACS were measured. These three parameters reflect the left atrial reservoir, booster pump, and conduit function, respectively. Left atrial analysis was performed using TomTec Image Arena 4.6 (Chicago, IL, United States) software with the QRS complex used as a reference point for the measurement in accordance with the latest EACVI recommendations.[24]

2.4 | Cardiopulmonary exercise test (CPET)

A peak Cardiopulmonary exercise test (CPET) was completed for all participants following a validated protocol on a seated stationary cycle ergometer (Ergoline GmbH, Bitz, Germany) with instructions to maintain a rate of 60 rotations per minutes throughout the test. Ventilation variables and respiratory gases were recorded using a computer-based system (Metalyzer 3B, Cortex Biophysik, Leipzig, Germany). Perceived exertion rate was collected every 2 minutes using the standard Borg scale. Every 3 minutes, a blood pressure measurement was taken by a manual mercury sphygmomanometer (Accoson Freestyle, Essex, United Kingdom). The test was continuously monitored by a trained investigator, and prior to the procedure participants were encouraged to reach their maximum exercise intensity.

2.5 | Stress echocardiography

Echocardiography imaging was obtained on the upright cycle position during a moderate exercise intensity for all participants. Moderate exercise intensity was identified by performing a CPET prior to the stress echocardiography imaging for the first 56 participants. For the remainder, a simplified protocol was used comprising of a single CPET with optimal timing of echocardiography planned before the procedure based on calculation of an exercise heart rate zone coinciding with an estimated 60% of heart rate reserve.[25] Precise workload at time of measurement was then assessed after completion of the CPET. Apical four chamber images were acquired during the estimated moderate exercise intensity using the same ultrasound machines used for resting echocardiography. Left ventricular ejection fraction was estimated using the method of discs (modified Simpson's method) and the global longitudinal strain was calculated using speckle tracking echocardiography analysis as an average of all left ventricular segments in apical four chamber view. All measurements were performed offline using ISCV 2.1 (Philips Healthcare Informatics, Belfast, Ireland), and TomTec Image Arena 4.6 (Chicago, IL, United States) software.

2.6 | Statistical analysis

To determine blood pressure-related differences, either systolic and/or diastolic blood pressure ≥120/80mm Hg were classified in the suboptimal blood pressure group and compared to an age, sex, and frequency-matched optimal blood pressure group (<120/80 mm Hg). Statistical analyses were performed using R software Version (4.0.2). Shapiro-Wilk test and visual assessment were used to assess for normality. Between-group comparisons were performed using independent samples Student t-tests for normally distributed data and Mann-Whitney and Kruskal-Wallis tests for non-normally distributed data. Multivariable linear regression modelling was performed to study the continuous association between resting echocardiographic features and left ventricular response to exercise adjusted for potential confounders (age, sex, body mass index, and mean arterial blood pressure). A *p*-value of ≤0.05 was used to indicate statistical significance.

The sample size calculation was based on a previously reported standard deviation of left ventricular ejection fraction (8.6%) during exercise in young adults.[26] A sample size of 100 participants, with 50 participants in each group, allowed a 5% difference in ejection fraction to be identified between groups with 85% power at $\alpha = .05$. As this was a retrospective study, we included all participants who met the inclusion criteria, which was greater than 100 participants.

TABLE 1 Baseline clinical characteristics

	Optimal BP *n* = 59	Suboptimal BP *n* = 68	*p* value
Age	25.61 ± 4.3	26.56 ± 4.6	0.241
Male *n* (%)	28 (47.5)	38 (55.9)	0.086
Height (cm)	173.04 ± 8.9	172.5 ± 9.4	0.776
Weight (kg)	69.9 ± 10.6	72.6 ± 10.2	0.152
Systolic blood pressure (mm Hg)	113.6 ± 8.8	130.6 ± 8.8	<**0.0001**
Diastolic blood pressure (mm Hg)	67.3 ± 5.8	79.3 ± 9.2	<**0.0001**
Mean arterial blood pressure (mm Hg)	82.7 ± 4.4	96.4 ± 8.2	<**0.0001**
VPA (h/wk)	.8 ± 1.1	.7 ± 1.1	0.417

Data are expressed as mean ± standard deviation, and percentages (%) were appropriate.
Abbreviations: BP, blood pressure; VPA, vigorous physical activity.

3 | RESULTS

3.1 | Baseline clinical characteristics

We identified 127 young adults (59 with optimal blood pressure and 68 with suboptimal blood pressure) who fulfilled the selection criteria and had images available for analysis. Resting brachial systolic and diastolic clinic blood pressure in the suboptimal blood pressure group were 130 ± 9 mm Hg and 79 ± 9 mm Hg and in the optimal blood pressure group 113 ± 9 mm Hg and 67 ± 6 mm Hg. The daily physical activity levels were similar in both groups. Group baseline clinical characteristics are provided in Table 1.

3.2 | Resting echocardiography

Echocardiography results at rest are presented in Table 2. Resting echocardiography demonstrated similar left ventricular dimensions, volumes and ejection fraction, but greater left ventricular mass (131.4 ± 32.2 g vs 118.5 ± 33.2 g, $p = 0.031$) in those with higher blood pressure. No participants exceeded clinical thresholds for left

TABLE 2 Resting echocardiography parameters

	Optimal BP $n = 59$	Suboptimal BP $n = 68$	p value
RESTING LEFT VENTRICULAR STRUCTURE			
Interventricular septum (cm)	.86 ± .15	.82 ± .17	0.185
LV internal dimension diastole (cm)	4.76 ± .46	4.76 ± .4	0.979
Posterior wall thickness (cm)	.86 ± .16	.89 ± .14	0.236
LV internal dimension systole (cm)	3.16 ± .39	3.18 ± .38	0.721
Relative wall thickness	.36 ± .06	.38 ± .06	0.240
LV mass (g)	118.5 ± 33.2	131.4 ± 32.2	**0.031**
LV biplane end diastolic volume (ml)	99.3 ± 25.8	100.6 ± 23.7	0.767
LV biplane end systolic volume (ml)	53.9 ± 11.6	53.7 ± 10.3	0.898
RESTING LEFT VENTRICULAR FUNCTION			
LV biplane ejection fraction (%)	63.1 ± 4.9	63.1 ± 5.08	0.946
LV global longitudinal strain (%)	-21.4 ± 3.04	-21.25 ± 2.4	0.737
Mitral valve E velocity (cm/s)	85.1 ± 15.6	78.6 ± 14.09	**0.020**
Mitral valve A velocity (cm/s)	48.3 ± 12.2	48.6 ± 11.3	0.918
Mitral valve E/A ratio	1.8 ± .65	1.6 ± .46	0.069
Average E' velocity (cm/s)	14.6 ± 2.3	13.9 ± 2.5	0.092
Average E/E' ratio	6.05 ± 1.9	6.01 ± 1.4	0.883
RESTING LEFT ATRIAL STRUCTURE AND FUNCTION			
LA volume (ml)	36.6 ± 10.1	38.4 ± 11.5	0.342
LA Reservoir strain (%)	40.7 ± 6.9	38.9 ± 7.2	0.170
LA Conduit strain (%)	31.6 ± 6.6	29.9 ± 6.4	0.163
LA Pump strain (%)	9.1 ± 3.9	8.9 ± 4.4	0.827
RESTING RIGHT VENTRICULAR FUNCTION			
Tricuspid regurgitation max velocity (cm/s)	185.03 ± 24.1	184.8 ± 29.2	0.973
TAPSE (cm)	2.2 ± .36	2.1 ± .32	0.702
RV S' velocity (cm/s)	12.4 ± 2.06	12.7 ± 1.5	0.380

Data are expressed as mean ± standard deviation.
Abbreviations: BP, blood pressure; LA, left atrium; LV, left ventricle; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion.

ventricular hypertrophy (115 g/m^2 in males, 95 g/m^2 females).[22] Lower mitral valve E velocity was found in the suboptimal blood pressure group (78.6 ± 14.09 cm/s vs 85.1 ± 15.6 cm/s, $p = 0.02$). Left ventricular global longitudinal strain was similar between groups. There was no difference in the left atrial structure and function between groups at rest.

3.3 | Physical exercise blood pressure, echocardiography, and fitness

Table 3 demonstrates the blood pressure and echocardiographic characteristics during moderate exercise load. Mean ejection fraction was reduced in participants with suboptimal blood pressure (74.4 ± 5.2 % vs 77.6 ± 4.1 %, $p = 0.001$) during exercise. Differences in resting left ventricular ejection fraction and its response to moderate exercise intensity between groups are shown in Figure 1. Left ventricular end diastolic and systolic volumes were greater ($p = 0.001$ and $p = 0.001$, respectively) in those with higher blood pressure. There was no between-group difference in left ventricular deformation during physical exercise. Peak VO2 and ventilatory anaerobic threshold (VAT) were also similar between groups. There was no association between daily physical activity and exercise left ventricular ejection fraction ($p = 0.542$) even when adjusted for age, sex, and body mass index ($p = 0.722$).

3.4 | Prediction of cardiac response to physical exercise

Association between resting echocardiography parameters and left ventricular response to physical exercise adjusted for age, sex, body mass index, and mean arterial blood pressure is presented in Table 4. Resting left ventricular mass and left atrial biplane volume were associated with left ventricular volumes during exercise but not with the ejection fraction. Left atrial booster pump function at rest was the only parameter associated with left ventricular ejection fraction during physical exercise ($\beta = .29$, $p = 0.011$, DF = 98) and was also

TABLE 3 Clinical and echocardiography parameters during moderate exercise intensity

	Optimal BP $n = 59$	Suboptimal BP $n = 68$	p value
EXERCISE MEASURES			
Exercise intensity (%)	57.5 ± 10.2	57.9 ± 8.2	0.793
Heart rate (bpm)	144.3 ± 11.8	146.9 ± 9.3	0.209
Systolic blood pressure (mm Hg)	151.2 ± 16.9	166.7 ± 22.3	**<0.0001**
Diastolic blood pressure (mm Hg)	77.04 ± 9.5	79.1 ± 14.9	0.401
Mean arterial blood pressure (mm Hg)	101.8 ± 9.6	108.3 ± 12.05	**0.003**
EXERCISE LEFT VENTRICULAR STRUCTURE AND FUNCTION			
LV ejection fraction (%)	77.6 ± 4.1	74.4 ± 5.2	**0.001**
LV end diastolic volume (ml)	64.8 ± 26.07	80.8 ± 23.7	**0.001**
LV end systolic volume (ml)	16.5 ± 6.9	21.3 ± 7.2	**0.001**
LV global longitudinal strain (%)	-23.9 ± 1.9	-23.8 ± 2.6	0.867
EXERCISE RESPIRATORY FUNCTION			
Peak VO2 (ml/min/kg)	38.5 ± 8.6	37.4 ± 8.8	0.481
VAT (ml/min/kg)	22.1 ± 6.04	20.8 ± 6.6	0.235
RPE at VAT	10.9 ± 2.6	10.6 ± 2.6	0.563

Data are expressed as mean ± standard deviation.
Abbreviations: BP, blood pressure; LV, left ventricle; RPE, rate of perceived exertion; VAT, ventilatory anaerobic threshold.

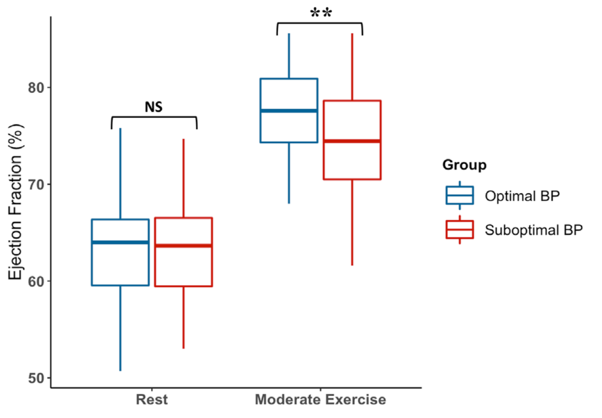

Figure 1 Differences in left ventricular ejection fraction during physical exercise between participants with optimal and suboptimal blood pressure. During moderate exercise intensity, participants with suboptimal blood pressure (red) had lower ejection fraction response than the optimal blood pressure group (blue) (p=0.001). ** Denotes p<0.01. NS Denotes p>0.05

associated with left ventricular end systolic volume (β = -.49, p = 0.002, DF = 98). Figure 2 demonstrates the association between exercise ejection fraction and resting left atrial pump function. In those with suboptimal blood pressure, the sensitivity and specificity for identification of those likely to have lower ejection fraction value during exercise (≤75%) when left atrial contraction strain is measured equal to or below 9% was calculated at 64.5% and 71.4%, respectively.

4 | DISCUSSION

In this study, we investigated the differences in left ventricular response to physical exercise between young adults with optimal and suboptimal blood pressure, and whether this response is associated with subclinical resting left atrial remodelling. Young adults with suboptimal blood pressure (≥120/80 mm Hg) had lower left ventricular ejection fraction during moderate exercise intensity when compared to those with optimal blood pressure (<120/80 mm Hg). Although resting left ventricular mass was relatively increased in the suboptimal blood pressure group, this was independent of the left ventricular functional variation in response to exercise. Left atrial booster pump function estimated from left atrial peak contraction strain was the only independent variable associated with the reduction in left ventricular ejection fraction during exercise.

Previous studies reported an abnormal left ventricular response to physical exercise in symptomatic older patients with hypertension.[13,14,27] Reduced left ventricular ejection fraction during exercise was believed to be due to coexisting coronary artery disease or left ventricular hypertrophy.[13,15] However, this abnormal left ventricular response was also found in asymptomatic, older hypertensive populations with mild to moderate hypertension and no evidence of cardiac disease or hypertrophy.[14,28] Hypertensive patients had lower left ventricular ejection fraction and greater end systolic volume and stroke volume during exercise compared to normotensives.[14] Our study extends these findings to much younger groups, with lower average levels of blood pressure suggesting this change in exercise response of the left ventricle may be a very early sign of remodelling, likely to be present in a large proportion of the population. Although left ventricular ejection fraction during exercise in the suboptimal group (74 ± 5%) is relatively high compared with exercise ejection fractions reported in some previous studies, these prior studies have tended to be in older populations. Younis et al., studied the influence of age on left ventricular ejection fraction during upright exercise, and reported ejection fraction during exercise reduces with age.[29] In the

TABLE 4 The association between resting echocardiography parameters and left ventricular response to physical exercise adjusted for age, sex, BMI, and mean arterial blood pressure

	Exercise LV EF		Exercise LV EDV		Exercise LV ESV	
	β	p value	β	p value	β	p value
RESTING LEFT VENTRICULAR STRUCTURE						
Relative wall thickness	12.05	0.141	-24.4	0.533	-13.5	0.241
LV mass (g)	-.01	0.481	**.27**	**0.001**	**.08**	**0.001**
LV biplane end diastolic volume (ml)	-.01	0.448	**.48**	**<0.0001**	**.14**	**<0.0001**
LV biplane end systolic volume (ml)	-.05	0.281	**.99**	**<0.0001**	**.3**	**<0.0001**
RESTING LEFT VENTRICULAR FUNCTION						
LV biplane ejection fraction (%)	.05	0.564	.04	0.923	-.09	0.484
LV global longitudinal strain (%)	-.2	0.310	-1.001	0.278	.009	0.974
Mitral valve E velocity (cm/s)	-.01	0.771	-.27	0.091	-.03	0.470
Mitral valve A velocity (cm/s)	-.02	0.713	-.48	0.045	-.1	0.111
Average E' velocity (cm/s)	.18	0.393	-.94	0.350	-.25	0.401
RESTING LEFT ATRIAL STRUCTURE AND FUNCTION						
LA volume (ml)	.01	0.748	**.83**	**<0.0001**	**.19**	**0.004**
LA Reservoir strain (%)	.03	0.634	-.1	0.729	-.07	0.405
LA Conduit strain (%)	-.06	0.364	.09	0.788	.08	0.387
LA Pump strain (%)	**.29**	**0.011**	-.6	0.273	**-.49**	**0.002**
RESTING RIGHT VENTRICULAR FUNCTION						
TAPSE (cm)	1.53	0.335	12.75	0.096	1.3	0.544
RV S' velocity (cm/s)	.08	0.777	.79	0.562	-.03	0.937

Abbreviations: EDV, end diastolic volume; EF, ejection fraction; ESV, end systolic volume; LA, left atrium; LV, left ventricle; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion; *β*, Regression coefficient.

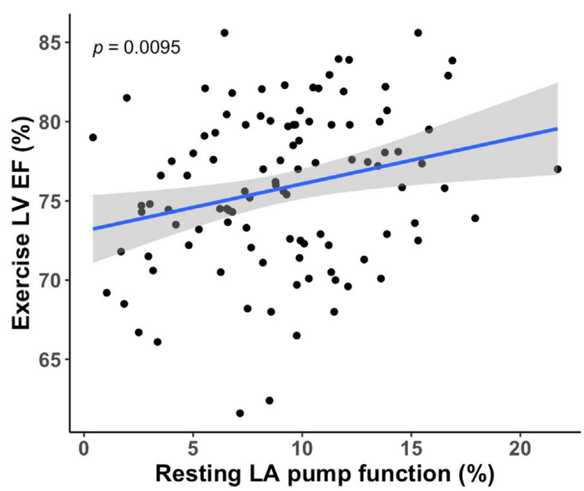

Figure 2 The relationship between resting left atrial pump function and left ventricular ejection fraction during moderate exercise for the study cohort. The reduction in left atrial pump function at rest is associated with lower ejection fraction response during exercise (p=0.009)

subgroup of younger men in their cohort they report a mean of 80 ± 4% ejection fraction during exercise[29] consistent with our findings.

Cuocolo *et al.*, showed that the decline in left ventricular ejection fraction during exercise is related to abnormal diastolic filling measured by radionuclide angiography at rest.[27] Radionuclide angiography is not easily translatable into clinical practice, but early diastolic alterations can be identified from left atrial deformation analysis using speckle tracking echocardiography.[30] Several studies reported that all left atrial phases (reservoir, conduit, and booster pump) are impaired in patients with hypertension. Mondello et al., demonstrated that asymptomatic hypertensive patients have impaired left atrial reservoir and conduit function despite normal left atrial volume.[31] Impairment of left atrial phasic function was also found in a cohort of hypertensive patients with preserved left ventricular ejection fraction and no evidence of left atrial enlargement and left ventricular hypertrophy.[16] These findings suggest that left atrial deformation indices using speckle tracking echocardiography can identify subclinical remodelling in patients with hypertension.[18] In our group of young adults, we have now shown left atrial booster pump function at rest is also a predictor of functionally relevant changes in myocardial response to exercise. If left atrial contraction strain falls below the mean, less than around 9%, then in those with suboptimal blood pressure, there is a reasonable likelihood based on sensitivity and specificity, that these individuals will have a lower ejection fraction on exercise. Left atrial booster pump function is influenced by left ventricular end diastolic pressure, left ventricular compliance and intrinsic left atrial properties.[17] This may explain the association between the left atrial pump function at rest and left ventricular performance during exercise. Mitral A-wave velocity has been used as an indicator of the left atrial pump function. The A-wave velocity reflects the amount of blood flow between the left ventricle and left atrium due to the atrioventricular pressure gradient, rather than intrinsic left atrial myocardial function.[32] Interestingly, the mitral valve A-wave velocity measured at rest was not correlated to left ventricular ejection fraction during exercise ($r = .05$, $p = 0.602$), even when adjusted for age, sex, BMI, and mean arterial blood pressure. Although left ventricular global longitudinal strain has been reported as an early marker of systolic dysfunction in older patients with hypertension,[33,34] there was no difference in left ventricular strain between groups in this cohort. This could reflect the young age of participants with relatively early changes in blood pressure and short duration of hypertension.

According to recent US and European guidelines for hypertension prevention and management, there is a gap in the evidence for whether to start anti-hypertensive medication in young adults with stage I hypertension.[9,10] Although lifestyle modifications, such as performing regular aerobic exercise, have shown a beneficial impact on controlling blood pressure, exercise interventions to manage blood pressure in young patients have varying degrees of success[8] and a heterogeneous blood pressure response to exercise has been observed in young adults with hypertension.[35] This has been explained by a variety of factors including the intensity of exercise, the level of adherence to exercise sessions, or subclinical cardiovascular remodelling.[35] The results of this study could explain some of this variation in response as the reduced left ventricular ejection fraction response would also be expected to influence workload perception during exercise, which could adversely influence training adherence. Whether either the ventricular response, or left atrial remodelling, is reversible with lifestyle, pharmaceuticals or blood pressure control requires further study. In clinical practice, young adults who are presenting with suboptimal blood pressure and, in addition, are found to have evidence of altered left atrial function on their resting echocardiography may warrant more detailed evaluation and potentially more targeted intervention. However, we accept this needs further evaluation in follow on studies and trials. Early identification of the reduced left ventricular response to exercise is complicated because of the requirement for exercise stress echocardiography. However, as resting left atrial deformation appears to predict this response, resting left atrial measures may be a relatively simple way for clinicians to risk-stratify hypertensive young adults.

5 | STUDY LIMITATIONS

Firstly, our study is a case-control study using retrospective data to understand pathophysiological mechanisms. Although participant selection was not dependent on the echocardiographic parameters, repeated studies in clinical populations are required to replicate the results. Secondly, a relatively large number of participants were excluded from the analysis because the frame rates required for assessment of left ventricular ejection fraction and global longitudinal strain could not always be acquired due to the increase in heart and breathing rate during moderate exercise. This potentially could bias the study population to those with higher levels of fitness (with relatively lower heart rate and breathing rate during moderate exercise workload), which might lead to an underestimation in differences between groups. Thirdly, resting echocardiography was performed in the lateral decubitus position, while the exercise images were obtained on the upright cycle position. The upright cycle ergometry was selected for CPET and stress echocardiography to minimize torso movement during image acquisition. However, this means we cannot directly compare ejection fraction at baseline with those acquired during moderate exercise due to the effect of change in posture.[36] Finally, left atrial strain assessment was performed at rest only using left ventricular speckle tracking software due to lack of validated specific left atrial speckle tracking software. However, for the left atrial assessment endocardial tracking was selected, and the QRS complex was used as a reference point, following the latest EACVI recommendations for left atrial strain measurements.[24] Left atrial assessment during exercise was not considered as the aim of this work was to predict left ventricular response during exercise from resting echocardiography parameters. Therefore, echocardiography imaging during exercise was focused on the left ventricle. This ensured optimal left ventricular image quality during exercise.

6 | CONCLUSION

This study shows that young adults with suboptimal blood pressure have physiological differences in their submaximal left ventricular ejection fraction response to physical exercise. This response was independently associated with left atrial booster pump function at rest. Subclinical left atrial remodelling appears to be an independent early marker of cardiac alterations secondary to elevated blood pressure in young adults.

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CONFLICT OF INTEREST

None declared.

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