Heart, Lung and Circulation (2018) **xx**, 1–10
1443-9506/04/$36.00
https://doi.org/10.1016/j.hlc.2018.04.279

ORIGINAL ARTICLE

Estimation of the Blood Pressure Response With Exercise Stress Testing

Benjamin T. Fitzgerald, MBBS [a,b,c*], Emma L. Ballard, BAppSc, PhD [d], Gregory M. Scalia, MBBS [a,b,c,e]

[a]HeartCare Partners, Brisbane, Qld, Australia
[b]The Wesley Hospital, Brisbane, Qld, Australia
[c]The Prince Charles Hospital, Brisbane, Qld, Australia
[d]Queensland Institute of Medical Research Berghofer Medical Research Institute, Brisbane, Qld, Australia
[e]University of Queensland, Brisbane, Qld, Australia

Received 12 September 2017; received in revised form 2 February 2018; accepted 6 April 2018; online published-ahead-of-print xxx

Background The blood pressure response to exercise has been described as a significant increase in systolic BP (sBP) with a smaller change in diastolic BP (dBP). This has been documented in small numbers, in healthy young men or in ethnic populations. This study examines these changes in low to intermediate risk of myocardial ischaemia in men and women over a wide age range.

Methods Consecutive patients having stress echocardiography were analysed. Ischaemic tests were excluded. Manual BP was estimated before and during standard Bruce protocol treadmill testing. Patient age, sex, body mass index (BMI), and resting and peak exercise BP were recorded.

Results 3200 patients (mean age 58 $\pm$ 12 years) were included with 1123 (35%) females, and 2077 males, age range 18 to 93 years. Systolic BP increased from 125 $\pm$ 17 mmHg to 176 $\pm$ 23 mmHg. The change in sBP (ΔsBP) was 51 mmHg (95% CI 51,52). The ΔdBP was 1 mmHg (95% CI 1, 1), from 77 to 78 mmHg, $p < 0.001$). The upper limit of normal peak exercise sBP (determined by the 90th percentile) was 210 mmHg in males and 200 mmHg in females. The upper limit of normal ΔsBP was 80 mmHg in males and 70 mmHg in females. The lower limit of normal ΔsBP was 30 mmHg in males and 20 mmHg in females.

Conclusions In this large cohort, sBP increased significantly with exercise. Males had on average higher values than females. Similar changes were seen with the ΔsBP. The upper limit of normal for peak exercise sBP and ΔsBP are reported by age and gender.

Keywords Blood pressure • Hypertension • Exercise • Stress testing • ΔsBP

Introduction

Stress testing is a well-documented non-invasive method for the assessment for myocardial ischaemia [1–4]. Exercise testing also permits measurement of the blood pressure (BP) and chronotropic response, as well estimating exercise capacity [1–4]. The definition of an exaggerated BP response with exercise testing has been described as a systolic BP (sBP) of greater than 210 mmHg in men and of greater than 190 mmHg for women. This has been based on generally small studies of predominantly fit, young males [5–10]. Limited data are available regarding the usual blood pressure response with exertion. Broad population statistics are even more limited.

Guidelines give recommendations for the normal increase in BP with exercise but acknowledge that the data determining the guidelines are limited. The recent European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) (ESH/ESC) guidelines state, "BP increases during dynamic and static exercise, whereby the increase is more pronounced for systolic than diastolic BP". They also note

*Corresponding author at: HeartCare Partners, Wesley Hospital, Brisbane, Australia. Tel.: +61 7 3648 2501., Email: BFitzgerald@heartcarepartners.com.au

that there is ''no consensus on the normal BP response during dynamic exercise testing''. A lack of a large database is also acknowledged [5]. This study was designed to address this. The aim of this project was to describe the blood pressure response to treadmill exertion in a population of men and women defined as having low to intermediate risk of myocardial ischaemia.

Materials and Methods

A prospective clinical audit was conducted on consecutive patients, age 18 years and older, undergoing stress echocardiography at the HeartCare Partners testing facility in Brisbane, Australia. Typically, the indication for the stress test was chest pain for investigation. Patients with elevated cardiac troponins or those with new or unexplained regional wall motion abnormalities were not exercised and excluded. Patients with a test suggestive of ischaemia (based on the stress echocardiogram result) were subsequently excluded from this analysis. Patients referred for dobutamine stress testing were not assessed. All remaining subjects were included and represented a general population of stress test patients with low to intermediate risk for myocardial ischaemia. Patient age, sex, body mass index (BMI), and resting and peak exercise BP and heart rates (HR) were recorded. The patient's medical history (including history of hypertension and of medications) was taken before the test began. A history of hypertension was not a reason for exclusion, as these patients are part of the population to be examined.

General Electric medical grade treadmills using Case systems were used to replicate and estimate exercise. Standard Bruce protocols were used to produce exercise stress in a controlled environment, and in a reproducible manner. Imaging was performed using high end echocardiography machines including the General Electric Vivid e9 and Vivid 7, Siemens SC2000 and SC2000 Prime and the Phillips ie33 scanners. All tests were supervised and read by cardiologists with subspecialty training in stress echocardiography, and an exercise physiologist. The echocardiogram was performed by cardiac sonographers with subspecialty training in stress echocardiography. Results were then over-read, standardised and recorded by a stress echocardiography specialty cardiologist.

Blood pressure was manually estimated standing, at rest (before exercise) and then at the 2 minute mark of each stage during standard Bruce protocol treadmill testing, and at 2:00 and 5:00 minutes during the recovery period [1]. The blood pressure was estimated using a manual sphygmomanometer and stethoscope by an exercise physiology technician trained in supervising treadmill stress and taking BPs in a standardised technique. Blood pressure measurement was performed, according to the recommended method of taking a manual blood pressure, as described in the guidelines [5]. Technicians were briefed on the technique, and a quality audit was conducted in an attempt to standardise measurements (see Results). The maximum exercise capacity in metabolic equivalents (METs) was also recorded. This was estimated based on the time and distance achieved on the standard Bruce protocol. The ejection fraction was estimated using the Simpson's biplane method.

The statistical analysis was performed using SPSS version 22 (IBM Corp., Armonk, NY, USA). The outcome variables of interest were the peak exercise systolic blood pressure (sBP), and the delta systolic blood pressure (ΔsBP, described as the peak exercise sBP minus the resting sBP). The data were screened for outliers, checked for normality and homogeneity of variances. Comparison of peak exercise to resting BP measurement was made using a paired t-test. The mean and 95% confidence intervals are reported for each age group (both outcomes), stratified by gender. A one-way ANOVA was used to examine difference between age groups for gender for each outcome. Where the p-value was significant ($p > 0.05$), pairwise comparisons were made using a LSD post hoc test. To adjust for multiple comparisons, a Bonferroni corrected p-value of 0.004 was considered significant. Correlation between resting and peak exercise sBP was examined using the Pearson correlation coefficient. Weighted percentiles stratified by gender and age are reported.

The effect of METs on predicted peak exercise sBP and ΔsBP was examined using a linear regression model containing METs, gender and their interaction, with the estimated marginal means reported for each gender. The effect of METs on predicted peak exercise sBP and ΔsBP was also examined using a linear regression model containing METs, gender, age categorised as (<50, 50 to 59, 60 to 69 and 70+ years) and the interaction between age and gender, with the estimated marginal means reported for each gender by age group. Linear regression models to examine the effect of hypertension on predicted peak exercise sBP and ΔsBP were examined in models containing hypertensive status, gender and their interaction, with the estimated marginal means reported for each gender. Age was not included in the hypertensive model due to low numbers of hypertensive females in the different age groups. Weighted percentiles of the observed values for each outcome stratified by hypertensive status and gender are reported.

Exaggerated systolic blood pressure values for each gender are shown as the 95th percentile of peak exercise sBP, which is the value commonly described in the literature [11]. Assuming a normal distribution, the tenth percentile represents the lower limit of normal and the 90th percentile represents the upper limit of normal [12–14].

Results

There were 3200 patients in the dataset, with a mean age of 58 ($\pm$12) years, with an age range of 18 to 93 years. There were 1123 (35%) females and 2077 (65%) males. The baseline characteristics are listed in Table 1.

The average estimated exercise capacity was 10.8 ± 3.3 METs, with a range of 1.6 to 23.6 METs. The peak heart rate achieved was $94.7 \pm 9.5\%$ of maximum predicted for age.

Please cite this article in press as: Fitzgerald BT, et al. Estimation of the Blood Pressure Response With Exercise Stress Testing. Heart, Lung and Circulation (2018), https://doi.org/10.1016/j.hlc.2018.04.279

Table 1 Characteristics of patient demographics.

Patient Characteristics (n = 3200)	
Sex (n (%))	
Male	2077 (64.9%)
Female	1123 (35.1%)
Age (n (%))	
<50	685 (21.4%)
50 to 59	899 (28.1%)
60 to 69	1063 (33.2%)
70+	553 (17.3%)
Body Mass Index (n = 2084, n (%))	28.0
Underweight/Normal range (<25)	492 (23.6%)
Overweight (25.00 to 29.99)	867 (41.6%)
Obese (30+)	725 (34.8%)
Body surface area (n = 3192) (mean (SD))	2.0 (0.3)
History of hypertension (n = 2824, n (%))	958 (33.9%)
High systolic blood pressure (BP) at rest (≥140 mmHg (n (%))	772 (24.1%)
Currently on hypertension medication (n = 2821, n (%))	1008 (35.7%)
Peak exercise heart rate achieved (n = 3193) (mean (SD))	94.7% (9.5)
Metabolic equivalents (mean (SD))	10.8 (3.3)
Ejection fraction (n = 2541) (mean (SD))	64.2 (4.9)

Abbreviation: SD, standard deviation; BMI, body mass index; SD, standard deviation; BP, blood pressure.

Body mass index was 28 ± 5 kg/m^2 and the BSA was 2.0 ± 0.3 m^2. The ejection fraction was 64 ± 5%.

On average, sBP increased from 125 ± 17 mmHg to 176 ± 23 mmHg, with a ΔsBP of 51 (95% CI 51, 52 mmHg, $p < 0.001$). The average, dBP increased with exercise (77 ± 9 to 78 ± 9 mmHg, mean difference of 1 mmHg [95% CI 1, 1, $p < 0.001$]), although this increase was unlikely to be of clinical significance. The mean resting dBP was 77 ± 9 mmHg for males and 77 8 mmHg for females (p = 0.088). There is a moderately strong positive correlation between resting and peak exercise sBP (p = 0.530, $p < 0.001$). See Figure 1.

The mean peak exercise sBP was 180 mmHg (95% CI 179, 181) for males and 169 mmHg (95% CI 168, 171) for females. The estimated marginal mean peak exercise sBP after adjusting for METs was significantly higher for males being 180 mmHg (95% CI 179, 181) compared to 168 mmHg (95% CI 166, 169) for females (interaction term $p < 0.001$ with METs value of 10.8266 used). In males, the 90th percentile for peak exercise sBP was 210 mmHg and 200 mmHg in females.

The mean ΔsBP was 55 mmHg (95% CI 54, 55) for males and 45 mmHg (95% CI 44, 47) for females compared to estimated marginal means of 54 mmHg (95% CI 53, 55) for males and 47 mmHg (95% CI 45, 48) for females after adjusting for METs. The interaction term was not significant (p = 0.77) indicating that as METs increase, ΔsBP is always higher for males compared to females. In males, the 90th percentile ΔsBP was 80 mmHg and for females, 70 mmHg.

A resting sBP of greater than or equal to 140 mmHg was used to define a hypertensive sub-group of patients. This identified 772 (24.1%) patients who had an elevated sBP at rest (greater than or equal to 140 mmHg), with 501 (24.1%) being male and 271 (24.1) being female. There were 686 patients who gave a history of a diagnosis of hypertension. Of these, 363 (53%) had elevated BP (≥140 mmHg) at rest. The estimated mean peak exercise sBP for a hypertensive male (resting sBP ≥140 mmHg) was 196 mmHg (95% CI 194, 198) and 187 mmHg (95% CI 184, 189) for females compared to 175 mmHg (95% CI 174, 176) for non-hypertensive males and 164 mmHg (95% CI 162, 165) for non-hypertensive females. The interaction term was not significant (p = 0.32) indicating that peak exercise sBP is higher in males than female regardless of hypertensive status at rest. The estimated marginal mean ΔsBP for a hypertensive male was 48 mmHg (95% CI 46, 49) and 39 mmHg (95% CI 37, 41) for females compared to 57 mmHg (95% CI 56, 58) for non-hypertensive males and 47 mmHg (95% CI 46, 49) for non-hypertensive females. The interaction term was not significant (p = 0.71) indicating that ΔsBP is higher in males than female regardless of hypertensive status at rest. Table 2 summarises the observed values for each outcome stratified by age and gender.

The sBP response to exercise was evaluated for differing age groups (< 50 years, 50–59 years, 60–69 years and 70 years and older) and stratified by gender. Categorisation of age groups was data lead but in keeping with previous research for comparison [5,6,11–13].

Please cite this article in press as: Fitzgerald BT, et al. Estimation of the Blood Pressure Response With Exercise Stress Testing. Heart, Lung and Circulation (2018), https://doi.org/10.1016/j.hlc.2018.04.279

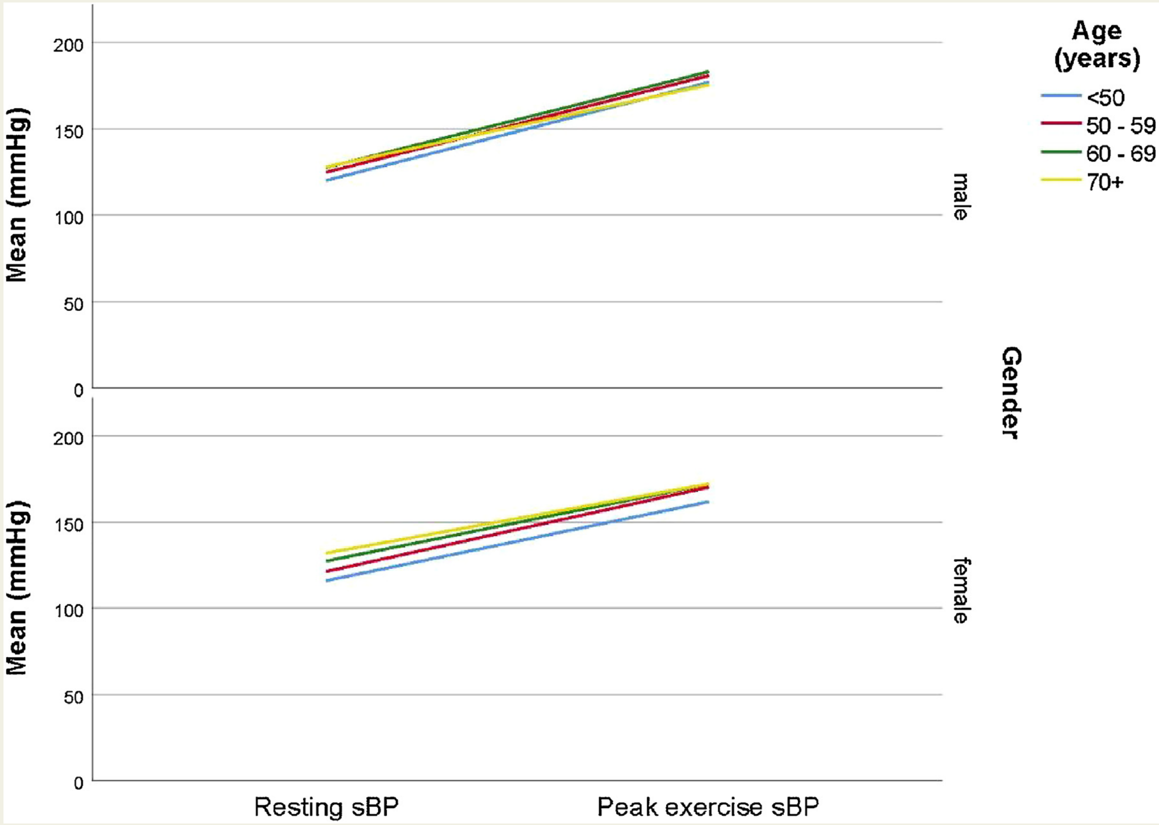

Figure 1 Mean change in systolic blood pressure with exercise for females and males by age.

Table 2 Percentiles of peak exercise systolic blood pressure (mmHg) for each age group and gender.

		Percentiles for peak exercise systolic blood pressure (mmHg)								
Gender		2.5	5	10	25	50	75	90	95	97.5
Male	All	140	145	150	165	180	190	210	220	230
	By age (years)									
	<50 = 436)	140	145	150	160	175	190	210	220	230
	50 to 59 (n = 589)	140	145	150	165	180	195	210	220	230
	60 to 69 (n = 687)	145	150	160	170	180	200	211	225	230
	70+ (n = 365)	131	140	150	160	175	190	200	214	224
Female	All	130	135	140	155	170	180	200	210	220
	By age (years)									
	<50 (n = 249)	125	130	135	148	160	170	190	210	220
	50 to 59 (n = 310)	124	135	140	160	170	180	200	210	220
	60 to 69 (n = 376)	130	140	145	160	170	180	200	205	220
	70+ (n = 188)	139	140	150	160	170	185	200	205	220

The mean peak exercise sBP for males less than 50 years was 177 mmHg (95% CI 175, 179), which was similar to that of males 70 years or older (176 mmHg, 95% CI 173, 178) (p = 0.36). Males aged 50 to 59 year and 60 to 69 years had similar mean peak exercise sBP [181 mmHg (95% CI 179, 183) compared to 183 mmHg (95% CI 182, 185) respectively, p = 0.072]. Both of these age groups had significantly higher sBP values than the youngest and oldest age groups. See Figures 1 and 2. The estimated marginal mean peak exercise sBP after adjusting for METs was 179 mmHg (95% CI 177, 181) for men <50 years of age, for 50 to 59 years 182 mmHg (95% CI 180, 184), 60 to 69 years 183 mmHg (182, 185) and 70+ years 174 (95% CI 172, 177), which is very similar to the unadjusted values. Males aged 70 years and older had

Please cite this article in press as: Fitzgerald BT, et al. Estimation of the Blood Pressure Response With Exercise Stress Testing. Heart, Lung and Circulation (2018), https://doi.org/10.1016/j.hlc.2018.04.279

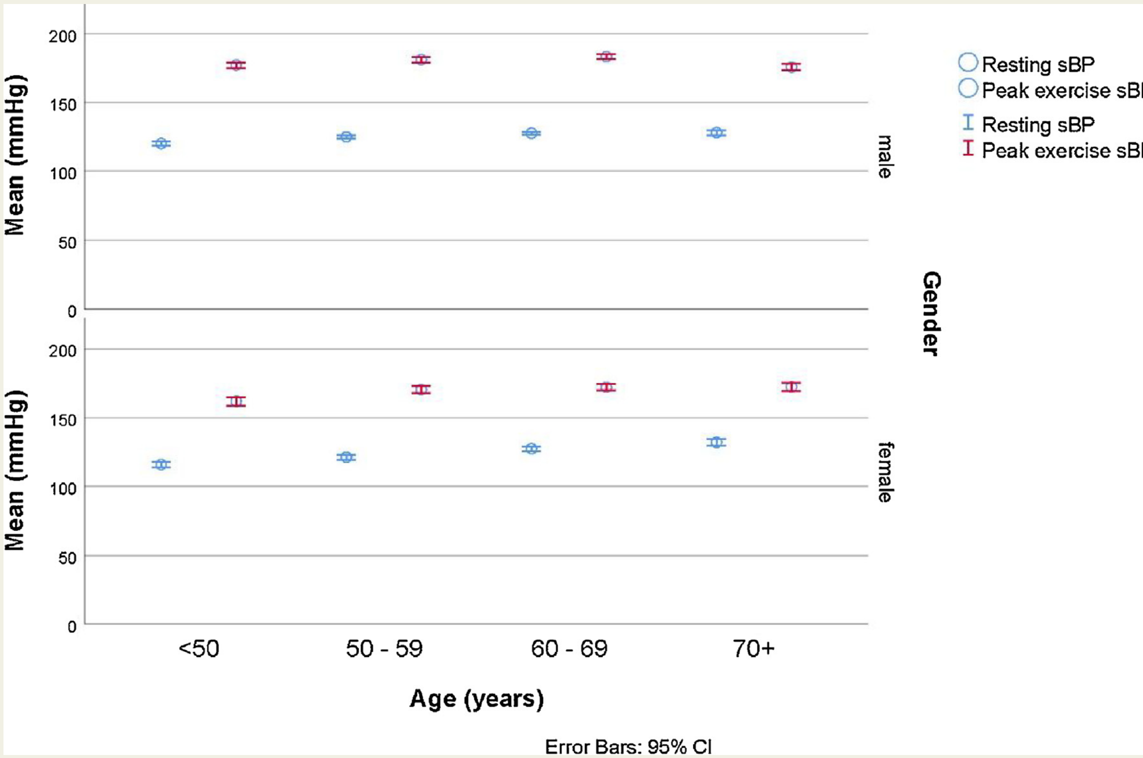

Figure 2 Mean systolic blood pressure (mmHg) for each age group and gender, at rest and at peak exercise.

smaller ΔsBP (48 mmHg, 95% CI 45, 50) than males ages less than 50 years (57 mmHg, 95% CI 55, 59), 50 to 59 years (56 mmHg, 95% CI 55, 58) and 60 to 69 years (56 mmHg, 95% CI 54, 57) (all $p < 0.001$). All other age groups were not statistically significantly different than each other. For males, the estimated marginal mean ΔsBP after adjusting for METs was 55 mmHg (95% CI 53, 57) for men <50 years of age, for 50 to 59 years 55 mmHg (95% CI 54, 57), 60 to 69 years 56 mmHg (95% CI 54, 57) and 70+ years 49 mmHg (95% CI 47, 51), which is very similar to the unadjusted values.

Figure 2 shows females aged less than 50 years had a lower mean sBP (162 mmHg, 95% CI 159, 165) than females aged 50 to 59 years (170 mmHg, 95% CI 168, 173), females aged 60 to 69 years (172 mmHg, 95% CI 170, 174) and those aged 70 years and older (172 mmHg, 95% CI 169, 175) (all $p < 0.001$). Mean peak exercise sBP for women above 50 are not statistically significantly different for any age group. For females, the estimated marginal mean peak exercise sBP after adjusting for METs was 163 mmHg (95% CI 160, 165) for women <50 years of age, for 50 to 59 years 170 mmHg (95% CI 168, 173), 60 to 69 years 171 mmHg (168, 173) and 70+ years 170 (95% CI 166, 173), which is very similar to the unadjusted values. Females aged 70 years and older had a smaller ΔsBP (40 mmHg, 95% CI 37, 43) than females aged less than 50 years (46 mmHg, 95% CI 44, 48, $p = 0.002$), females aged 50 to 59 years (49 mmHg, 95% CI 47, 51, $p < 0.001$) and those aged 60-69 years (45 mmHg, 95% CI 43, 47, $p = 0.009$). The ΔsBP for females aged less than 50 years was statistically significantly different than women aged 70 years and older ($p = 0.002$) but not different than women aged 50 to 59 years or 60 to 69 years. The ΔsBP for females age 50 to 59 years was statistically different to women aged 60 to 69 years ($p = 0.003$). For females, the estimated marginal mean ΔsBP after adjusting for METs was 45 mmHg (95% CI 43, 48) for women <50 years of age, for 50 to 59 years 49 mmHg (95% CI 47, 51), 60 to 69 years 46 mmHg (95% CI 44, 48) and 70+ years 43 (95% CI 40, 46), which is very similar to the unadjusted values. Figure 3 shows box plots of the ΔsBP by age and gender.

Table 3 shows a range of percentiles for the sBP by gender and age group. Table 4 shows a range of percentiles for the ΔsBP by gender and age group. Table 5 shows that in males, the upper limit of normal for resting sBP was 150 mmHg for those aged 70 years and older and 140 mmHg for men less than 50. In females, the upper limit of normal for resting sBP was 155 mmHg for women aged 70 or older and 140 mmHg for women under 50.

The lower limit of normal ΔsBP is shown in Table 5. This could be used to estimate the minimum normal ΔsBP with exertion. For males the lower limit of normal for ΔsBP was 30 mmHg. Age differences were detected, with a lower limit of normal ΔsBP of 20 mmHg for those aged 70 years and older and 35 mmHg for men under 50. In females, the lower limit of normal for ΔsBP was 20 mmHg. Again there were differences between age groups, with a lower limit of normal ΔsBP of 25 mmHg for women aged 70 or older and 20 mmHg for women under 50.

In males, the upper limit of normal for ΔsBP was 80 mmHg for those aged 70 years and over, and 75 mmHg for men less 50. In females, the upper limit of normal for ΔsBP was

Please cite this article in press as: Fitzgerald BT, et al. Estimation of the Blood Pressure Response With Exercise Stress Testing. Heart, Lung and Circulation (2018), https://doi.org/10.1016/j.hlc.2018.04.279

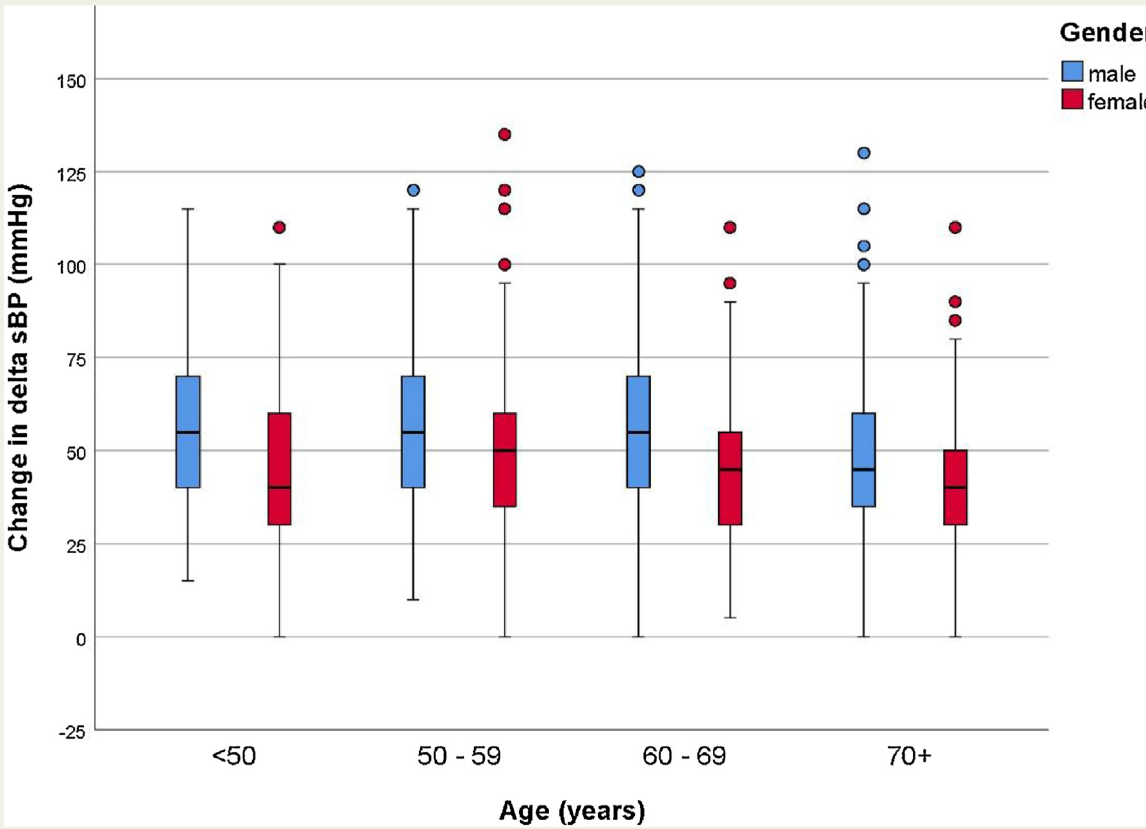

Figure 3 Box plot of delta systolic blood pressure for the overall cohort, for females and males and for the different age groups.

Table 3 Percentiles of delta systolic blood pressure (mmHg) for each age group and gender.

		Percentiles for delta systolic blood pressure (mmHg)								
Gender		2.5	5	10	25	50	75	90	95	97.5
Male	All	20	25	30	40	50	70	80	90	95
	By age (years)									
	<50 (n = 436)	25	30	35	40	55	70	80	95	100
	50 to 59 (n = 589)	25	30	35	40	55	70	80	90	95
	60 to 69 (n = 687)	20	20	30	40	55	70	80	90	100
	70+ (n = 365)	10	17	20	35	45	60	75	85	95
Female	All	10	15	20	30	45	60	70	80	85
	By age (years)									
	<50 (n = 249)	15	20	25	30	40	60	70	80	85
	50 to 59 (n = 310)	15	20	25	35	50	60	70	80	91
	60 to 69 (n = 376)	10	15	20	30	45	55	70	80	85
	70+ (n = 188)	5	10	20	30	40	50	65	70	86

65 mmHg for women aged 70 or older and 80 mmHg for women under 50. Figure 3A shows the distribution of ΔsBP by gender and age. Table 1 additionally describes these limits of normal by hypertensive status at rest.

It is also possible to calculate the exaggerated (or hypertensive) sBP response to treadmill exercise (the 95th percentile of sBP). From the data presented here, the exaggerated BP response would be 220 mmHg in males and 210 mmHg in

Please cite this article in press as: Fitzgerald BT, et al. Estimation of the Blood Pressure Response With Exercise Stress Testing. Heart, Lung and Circulation (2018), https://doi.org/10.1016/j.hlc.2018.04.279

Table 4 Percentiles of resting, peak exercise and delta systolic blood pressure (mmHg) for each gender by resting systolic blood pressure less than 140 mmHg and 140 mmHg or more.

Gender	Resting sBP less than 140 mmHg									Resting sBP 140 mmHg or more								
	Percentiles									Percentiles								
	2.5	5	10	25	50	75	90	95	97.5	2.5	5	10	25	50	75	90	95	97.5
	Resting sBP (mmHg)									Resting sBP (mmHg)								
Male	95	100	105	110	120	130	130	135	135	140	140	140	140	145	150	160	170	170
Female	92	100	100	110	120	125	130	132	135	140	140	140	140	145	150	160	165	170
	Peak exercise sBP (mmHg)									Peak exercise sBP (mmHg)								
Male	140	140	150	160	170	190	200	210	220	160	160	170	180	190	210	230	240	247
Female	125	130	140	150	160	180	190	200	205	155	160	160	170	180	200	210	220	236
	Delta sBP (mmHg)									Delta sBP (mmHg)								
Male	20	30	35	40	55	70	80	90	100	13	20	20	35	45	60	75	85	95
Female	15	20	25	35	48	60	70	80	90	9	10	20	25	40	50	65	72	80

Abbreviation: sBP, systolic blood pressure.

Table 5 Simplified table summarising the upper limit of normal for resting sBP, ΔsBP and peak exercise sBP, the lower limit of normal for ΔsBP and exaggerated sBP.

Gender		Upper limit of normal resting sBP[a]	Lower limit of normal ΔsBP[b]	Upper limit of normal ΔsBP[a]	Upper limit of normal peak exercise sBP[a]	Exaggerated sBP[c]
Male	All (n = 2077)	150	30	80	210	220
	By age (years)					
	<50 (n = 436)	140	35	80	210	220
	50 to 59 (n = 589)	150	35	80	210	220
	60 to 69 (n = 687)	150	30	80	211	225
	70+ (n = 365)	150	20	75	200	214
	By resting sBP					
	<140 mmHg (n = 1576)	130	35	80	200	210
	≥140 mmHg (n = 501)	160	20	75	230	240
Female	All (n = 1123)	150	20	70	200	210
	By age (years)					
	<50 (n = 249)	140	25	70	190	210
	50 to 59 (n = 310)	140	25	70	200	210
	60 to 69 (n = 376)	150	20	70	200	205
	70+ (n = 188)	155	20	65	200	205
	By resting sBP					
	<140 mmHg (n = 852)	130	25	70	190	200
	≥140 mmHg (n = 271)	160	20	65	210	220

Abbreviations: sBP, systolic blood pressure; ΔsBP, delta systolic blood pressure.
[a]90th percentile.
[b]10th percentile.
[c]95th percentile.

females. See Table 2. For males aged less than 50 years the exaggerated sBP value was 220 mmHg and 214 mmHg men 70 years and older. In females, the exaggerated sBP value was 210 mmHg in those aged less than 50 years and 205 mmHg for females 70 years and older.

In males, the upper limit of normal for peak exercise sBP was 200 mmHg for those aged 70 years and older and 210 mmHg for men less 50. In females, the upper limit of normal for peak exercise sBP was 200 mmHg for those aged 70 years and older and 190 mmHg for those aged less than 50.

Please cite this article in press as: Fitzgerald BT, et al. Estimation of the Blood Pressure Response With Exercise Stress Testing. Heart, Lung and Circulation (2018), https://doi.org/10.1016/j.hlc.2018.04.279

One of the weaknesses of the methodology was the manual assessment of BP, involving different technicians. The technicians used a laboratory benchmark technique to attempt to replicate measurements, according to the standard method of taking a manual BP, as per the guidelines [5]. A quality audit of sBP measurement variability was performed as part of the study. A subset of 50 consecutive patients had multiple measurements taken by two separate technicians at each exercise stage, using the same equipment; 152 comparison sBP estimations were evaluated. Technicians were blinded to the measurements that were taken by other technicians, and the data only compiled separately after all the measurements had been recorded. The mean difference between exercise sBP measurements was 6.14 ± 4.6 mmHg, or an average variation of $4.1 \pm 3.2\%$. These findings would suggest that the measurement variation between technicians was small and acceptable.

Discussion

Blood pressure is a physiological parameter that is readily measurable. Abnormal levels are correlated with pathology and persistently elevated BP results in adverse events and outcomes for patients [5,15,16].

Blood pressure can be measured during exertion. It changes in a predictable manner. This has previously been described as significant increase in systolic BP and a smaller increase, no change or a small decrease in the diastolic BP [5,16]. A number of studies have recorded these changes, but have been performed with small numbers, in males, or in young, fit, healthy volunteers (e.g. armed forces personnel) [5–9]. One group reported changes in a larger Asian population [10].

Some studies have suggested that an excessive rise in sBP with exercise predicts the development of hypertension in an individual. An exaggerated sBP increase with exertion may also suggest an increase in cardiovascular risk and events [17–21].

Guidelines have attempted to provide recommendations for the normal increase in BP with exercise, despite the limitations in the data [5]. The data presented here attempt to bridge that gap and assess the response during dynamic exercise testing.

From the data presented, population values can be calculated for the rise in BP with exercise testing. These values can be broken down by sex and stratified by age. Rest and peak exercise values appear to be different for patients with defined hypertension, or with an elevated BP at rest. Hypertensive patients were included, as they are part of the overall stress testing population. In general, the data presented here are consistent with the current guidelines [5]. Males and females appear to have similar changes in BP with exercise, with males from a higher base and to a higher peak value. Patients with high BP measurements at rest showed the same type of response, but to higher overall BPs. Resting blood pressures increased as expected with increasing age, but with peak exercise BPs to a similar mean value as younger patients. The exaggerated BP response to exercise stress testing can also be determined, with the potential of identifying individuals who are at increased risk of cardiovascular events [20–24]. Adjusting for exercise capacity did not show appreciable differences from the unadjusted values. The patients in this cohort were all exercised to the maximum tolerated workload, not to a set heart rate or exercise level. This may be the explanation as to why exercise capacity had little effect on the unadjusted measurements.

Assessment of the change in sBP from rest to peak (ΔsBP) provided interesting results. Females have slightly, but significantly lower ΔsBP than males. The ΔsBP appears to decrease with age, meaning that the peak exercise estimated sBP remains relatively similar (due to the rising resting sBP with ageing). Patients with an elevated BP at rest (equal to or greater than 140 mmHg), had a significantly blunted ΔsBP with exertion. This change may reflect a subset of patients who had an elevated resting blood pressure due to anxiety regarding the test itself. The subsequent rise with exertion may have simply been to their ''true'' expected elevation, resulting in the ''blunted'' response. Older patients showed a similar blunted response. Reduced exercise capacity did not explain this finding (see Figure 4)

Blood pressure has been documented to increase with age [5,15,16]. In this study, BP at rest and with exertion was evaluated for differing age groups. Some studies have suggested that BP responses may be different at age over 60 years [5,16,22,23]. A number of differing age stratifications have been used in the hypertension literature [24–26]. The raw data presented here showed a progressive increase in the resting sBP with increased age (Tables 2 and 5, Figures 1 and 2). Somewhat surprisingly, there were similar peak BPs in each of the age groups. While there was a statistical difference in the peak exercise predicted SBP with exercise between groups, the numerical difference was relatively small (6 mmHg).

As expected (and by definition), the patients with high BP at rest had higher BPs than the general population. What was surprising was that these patients had a blunted ΔsBP, compared to the normal cohort. The mean ΔsBP was 45 mmHg compared with 51 mmHg in age and sex matched controls ($p = 0.001$ for the difference). This is likely to be a heterogeneous group. Some of these patients may be undiagnosed hypertensives, while a proportion of this group may have had an elevated resting sBP due to the anxiety of having the test. As such, their resting sBP may have been falsely elevated, with a subsequent overall rise more in keeping with the ''normal'' population. It would have been interesting to document the BP changes in the patients with a history of hypertension, but the numbers were too small making the data analysis incomplete. The blunted ΔsBP may be a result of patients with ''falsely'' elevated resting sBP (due to anxiety) having a rise to a ''normal'' sBP. Stress testing could be used to differentiate between ''real'' hypertension, and patients with elevated blood pressure due to concerns about the test (and possibly ''white coat'' hypertension). Reproduction of these data in other populations would assist in establishing these hypotheses (Table 5).

Please cite this article in press as: Fitzgerald BT, et al. Estimation of the Blood Pressure Response With Exercise Stress Testing. Heart, Lung and Circulation (2018), https://doi.org/10.1016/j.hlc.2018.04.279

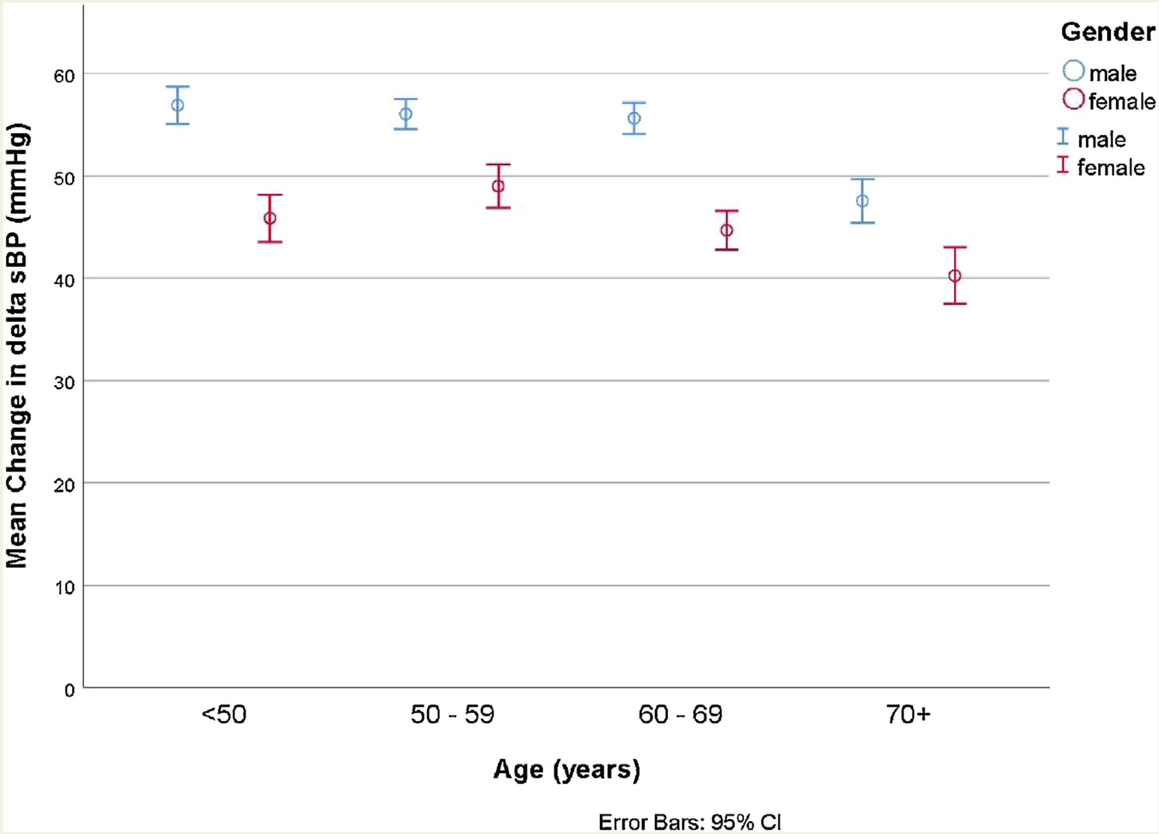

Figure 4 Mean delta systolic blood pressure (mmHg) for each age group and gender.

From a statistical viewpoint, the outcome variables of interest were the sBP and change in systolic BP (ΔsBP). Multivariable modelling to adjust for the important predictors of systolic blood pressure should be considered in future studies.

The estimated minimum ΔsBP can also be estimated. Males and younger patients tended to have higher tenth percentile ΔsBPs than females and older patients. This ''minimal'' expected ΔsBP was 20 to 25 mmHg in females and 20 to 35 mmHg in males.

There are a number of limitations with this study. It was a single centre experience. The population was predominantly Caucasian, limiting extrapolation to other racial groups. It can be argued that stress echocardiography does not maximally stress patients, due to the need for the patient to be able to breath hold to maximise image quality for the peak image acquisition. The practice in this laboratory is to stress patients to peak or near peak exertion, not just to a predetermined heart rate or exercise level. Analysis of this cohort of patients revealed exercise to very near peak capacity (the mean MPHR for the cohort was approximately 95%), minimising this concern. Manual estimation of blood pressure is fraught with difficulties, especially measurement of diastolic BP [5]. These concerns are magnified in the stress test environment. Blood pressures in this study were taken manually by different technicians. The technicians involved were all trained in a similar manner, in order to minimise measurement variation. The BP measurement quality assessment detailed above also suggests only a small variation in the exercise estimation between different observers. Nonetheless, questions remain regarding the accuracy of measurements and reproducibility of the BP, with rounding errors particularly a concern. An accurate baseline of BP measurement was not performed. The results presented here do reflect real world conditions, making it more applicable to the manner in which many centres would perform stress testing. Automated measurement may have provided a more uniform method of data acquisition, but these authors have found these devices to be more prone to incomplete or delayed measurements during stress testing. Women made up 35% of the total number of patients studied. This does reflect a bias in cardiac testing that results in lower numbers of women being referred and analysed. It does reflect ''real world'' practice. More than 1000 females were tested, however. This does represent a significant number of women from whom to obtain blood pressure estimates. This is the largest cohort of women tested in this manner.

Conclusions

This is a large prospective cohort documenting the estimated blood pressure response with exercise. It examined a wide range of patients undergoing stress echocardiography, with a significant and large number of women. It compared older

Please cite this article in press as: Fitzgerald BT, et al. Estimation of the Blood Pressure Response With Exercise Stress Testing. Heart, Lung and Circulation (2018), https://doi.org/10.1016/j.hlc.2018.04.279

and younger patients. It examined the changes in patients with hypertension, and with differing starting BPs, and adjusted for exercise capacity. Current guidelines for the expected and exaggerated response of BP with exercise are based on limited data. This research adds significantly to the accumulated database. In this study, the systolic BP increased significantly, and diastolic BP essentially remained the same. There were significant differences in the response to exercise between men and women. From the data presented here, the normal upper limit for peak exercise systolic blood pressure can be described as 210 mmHg in males, and 200 mmHg in females. The lower limit of normal ΔsBP was 30 mmHg in males and 20 mmHg in females. The upper limit of normal ΔsBP was 80 mmHg for men and 70 mmHg in women. These data can be used to practically assist clinicians in assessing the expected blood pressure response during stress testing and exercise.

Acknowledgements

Wesley Medical Research for providing assistance with the statistical analysis.

References

[1] Doan AE, Peterson DR, Blackmon JR, Bruce RA. Myocardial ischemia after in healthy men. A method for detecting potential coronary heart disease? Am Heart J 1965;69:11–21.
[2] Bruce RA, McDonoagh JR. Stress testing in screening for cardiovascular disease. Bull N Y Acad Med 1969;45(12):1288–305.
[3] Armstrong WF, O'Donnell DJ, Dillon JC, McHenry PL, Morris SN, Feigenbaum H. Complementary value of two-dimensional exercise echocardiography to routine treadmill exercise testing. Ann Intern Med 1986;105(6):829–35.
[4] Marwick TH, Nemec JJ, Pashkow FJ, Stewart WJ, Salcedo EE. Accuracy and limitations of exercise echocardiography in a routine clinical setting. J Am Coll Cardiol 1992;19(1):74–81.
[5] Mancia G, Faggard R, Narkiewicz K, Redón J, Zanchetti A, Böhm M, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens 2013;31(7):1281–357.
[6] Sue DY, Hanson J. Normal values in adults during exercise testing. Clin Chest Med 1984;5:89–98.
[7] Robinson TE, Sue DY, Huszczuk A, Weiler-Ravell D, Hansen JE. Intra-arterial and cuff blood pressure responses during incremental cycle ergometry. Med Sci Sports Exerc 1988;20(2):142–9.
[8] Tabakin BS, Hansen JE, Merriam Jr TW, Caldwell EJ. Hemodynamic response of normal men to graded treadmill exercise. J Appl Physiol 1964;19:457–64.
[9] Wolthuis RA, Froelicher VJ, Fischer J, Triebwasser JH. The response of healthy men to treadmill exercise. Circulation 1977;55:153–7.
[10] Itoh H, Ajisaka R, Koike A, Makita S, Omiya K, Kato Y, et al. Heart rate and blood pressure response to ramp exercise and exercise capacity in relation to age, gender, and mode of exercise in a healthy population. J Cardiol 2013;61(1):71–8.
[11] Le VV Mitiku T, Sungar G, Myers J, Froelicher V. The blood pressure response to dynamic exercise testing: a systematic review. Prog Cardiovasc Dis 2008;51(2):135–60.
[12] Herrera L. The precision of percentiles in establishing normal limits in medicine. Transl Res 1958;52(1):34–42.
[13] Falkner B, Daniels SR, Flynn JT, Gidding S, Green LA, Ingelfinger JR, et al. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 2004;114(Suppl. 2):555–76.
[14] Dubowitz T, Ghosh-Dastidar M, Eibner C, Slaughter ME, Fernandes M, Whitsel EA, et al. The women's health initiative: the food environment, neighborhood socioeconomic status, BMI, and blood pressure. Obesity (Silver Spring) 2012;20(4):862–71.
[15] Kiowski W, Bühler F, Fadayomi MO, Erne P, Müller FB, Hulthén UL, et al. Age, race, blood pressure and renin: predictors for antihypertensive treatment with calcium antagonists. Am J Cardiol 1985;56(16):81H–5H.
[16] Zanchetti AHL, Dahlöf B, Elmfeldt D, Kjeldsen S, Kolloch R, Larochelle P, et al. Effects of individual risk factors on the incidence of cardiovascular events in the treated hypertensive patients of the Hypertension Optimal Treatment Study. HOT Study Group. J Hypertens 2001;19(6):1149–59.
[17] Verdecchia P, Gentile G, Angeli F, Reboldi G. Should we prefer different drugs to treat hypertension in older and younger adults? Practical implications of clinical trials: European perspective. Pol Arch Med Wewn 2008;11(8):513–6.
[18] Kaplan NM. Hypertensive and atherosclerotic cardiovascular disease. In: Mann D, Zipes D, Libby P, Bonow R, editors. Braunwald's heart disease. 10th ed. Philadelphia, USA: Saunders; 2004.
[19] Mancia G, Grassi G, Redon J. Manual of hypertension of the European society of hypertension. London: Informa; 2008.
[20] Gupta MP, Polena S, Coplan N, Panagopoulos G, Dhingra C, Myers J, et al. Prognostic significance of systolic blood pressure increases in men during exercise stress testing. Am J Cardiol 2007;100.
[21] Mahoney LT, Scheiken R, Clarke WR, Lauer RM. Left ventricular mass and exercise responses predict future blood pressure. The Muscatine Study. Hypertension 1988;12(2):206–13.
[22] Lewis GD, Gona P, Larson MG, Plehn JF, Benjamin EJ, O'Donnell CJ, et al. Exercise blood pressure and the risk of incident cardiovascular disease (from the Framingham Heart Study). Am J Cardiol 2008;101(11):1614–20.
[23] Kjeldsen SE, Mundal R, Sandvik L, Erikssen G, Thaulow E, Erikssen J. Supine and exercise systolic blood pressure predict cardiovascular death in middle-aged men. J Hypertens 2001;19(8):1343–8.
[24] Lauer MS, Levy D, Anderson KM, Plehn JF. Is there a relationship between exercise systolic blood pressure response and left ventricular mass? The Framingham Heart Study. Ann Intern Med 1992;116:203–10.
[25] Aronow WS. Blood pressure goals and targets in the elderly. Curr Treat Options Cardiovasc Med 2015;17(7):394.
[26] Tuomilehto J, Rastenyte D, Birkenhäger WH, Thijs L, Antikainen R, Bulpitt CJ, et al. Effects of calcium-channel blockade in older patients with diabetes and systolic hypertension. Systolic Hypertension in Europe Trial Investigators. N Engl J Med 1999;340(9):677–84.

Please cite this article in press as: Fitzgerald BT, et al. Estimation of the Blood Pressure Response With Exercise Stress Testing. Heart, Lung and Circulation (2018), https://doi.org/10.1016/j.hlc.2018.04.279