Original Article

Central and peripheral blood pressure profile of young offspring with hypertensive and normotensive parents

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Objectives: In this cross-sectional study we compared the central aortic systolic pressure (CASP), peripheral brachial systolic pressure (PSP), peripheral brachial diastolic pressure (PDP) and augmentation index (AIx) between normotensive offspring of nonhypertensive parents (ONT) and normotensive offspring with at least one hypertensive parent (OHT).

Methodology: A total of 100 healthy ONT (mean age 20.95 ± 2.06) and 100 healthy OHT (mean age 20.89 ± 2.12) individuals were recruited. Parental history of hypertension was determined by detailed history taking. CASP, PSP, PDP and AIx were measured using the BPro device. All blood pressure (BP) measurements were calibrated using oscillometric BP readings.

Results: The OHT group had higher PSP (117.57 ± 10.06 versus 114.52 ± 8.94, $P < 0.05$), PDP (72.39 ± 7.28 versus 70.39 ± 6.50, $P < 0.05$) and CASP (103.72 ± 8.95 versus 101.37 ± 7.74, $P < 0.05$) compared to the ONT group. There was no significant difference in AIx in the ONT group (57.97 ± 11.02 versus 58.08 ± 12.16, $P = 0.95$) in comparison to the OHT group. However, following adjustments for certain cardiovascular risk factors, only PSP (117.33 versus 114.76, $P < 0.05$) remained significantly higher in the OHT group compared to the ONT group. Analysis of adjusted data within sex showed that CASP was higher in the female OHT group compared to the female ONT group, whereas PDP were higher in the male OHT group compared to the male ONT group.

Conclusion: Alterations in PSP, PDP and CASP are already present in early life in normotensive offspring of hypertensive parents, with possible differences in mechanism between different sexes.

Keywords: augmentation index, central aortic systolic pressure, hypertension, offspring

Abbreviations: AIx, augmentation index; CASP, central aortic systolic pressure; OHT, offspring of hypertensive parents; ONT, offspring of normotensive parents; PDP, peripheral diastolic systolic pressure; PSP, peripheral brachial systolic pressure

INTRODUCTION

Noninvasive measurements of central aortic systolic pressure (CASP) and other indicators of arterial stiffness such as augmentation index (AIx) are now considered a more robust predictor of cardiovascular outcome [1]. Studies had also claimed that AIx has a significant heritable component and is altered in people with a genetic predisposition to hypertension, which is largely independent of the influence of blood pressure (BP), heart rate, height and age [2]. Although there are already a few studies that have looked to compare indicators of arterial stiffness, that is central pulse pressure, AIx and pulse wave velocity, in populations that are genetically predisposed to developing hypertension [9–12], the participants in these studies often possess certain risk factors that may confound its findings. CASP, particularly in the young disease-free age group, has also not been studied intensively. In this cross-sectional study, we compared the CASP, peripheral brachial systolic pressure (PSP), peripheral brachial diastolic pressure (PDP) and radial AIx between young healthy normotensive offspring of nonhypertensive biological parents (ONT), and normotensive offspring with at least one hypertensive biological parent (OHT).

METHODOLOGY

The study was conducted primarily at the Clinical Research Laboratory in Cyberjaya University College of Medical Sciences, Selangor, Malaysia. A majority of the study participants were the student and young working population in the vicinity of Cyberjaya. The study obtained ethical approval from the Ethics Committee of the National Heart Institute and all participants gave informed written consent prior to their participation in this study. All the participants were consecutively enrolled after stringent screening, following voluntary response to advertisements around university campuses and workplaces in Cyberjaya.

Parental history of hypertension was thoroughly obtained by detailed history taking. Participants were asked

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TABLE 1. General characteristics of study participants

Characteristic	ONT	OHT	*P*
Number of recruits	100	100	
Age (years)	20.95 ± 2.06	20.89 ± 2.12	0.84
Female sex (%)	61 (61)	64 (64)	0.66
Body height (m)	1.62 ± 0.08	1.62 ± 0.08	0.65
Body weight (kg)	56.75 ± 11.93	58.25 ± 11.57	0.37
BMI (kg/m^2)	21.57 ± 3.49	22.06 ± 3.48	0.32
Heart rate (beats/min)	78.93 ± 11.16	79.86 ± 11.98	0.57
Total cholesterol (mmol/l)	4.68 ± 0.66	4.74 ± 0.56	0.51
HDL-cholesterol (mmol/l)	1.46 ± 0.31	1.46 ± 0.27	0.93
LDL-cholesterol (mmol/l)	2.84 ± 0.63	2.93 ± 0.55	0.31
Glucose (mmol/l)	4.43 ± 0.44	4.48 ± 0.34	0.38

Values represent mean ± SD, or percentage of participants. HDL, high-density lipoprotein; LDL, low-density lipoprotein; OHT, offspring of hypertensive parents; ONT, offspring of normotensive parents.

to verify with their parents regarding their hypertension status. Hypertension for this purpose was defined as SBP of 140 mmHg or more and DBP of 90 mmHg or more, and/or use of antihypertensive medications. Participants with a personal history of hypertension or heart disease, cigarette smokers, alcohol consumers and pregnant or lactating women were excluded. Further blood investigations to determine blood cholesterol and sugar levels were done during the study visit.

From the initial intake, 19 participants were excluded due to elevated BP during the visit ($n = 7$) or because of insufficient pulse wave quality ($n = 12$). Elevated BP was defined as a peripheral SBP reading of more than 140 mmHg or peripheral DBP more than 90 mmHg, whereas waveforms were considered to be of insufficient quality when the systolic or diastolic variability of consecutive waveforms was more than 10%.

Recruited participants were then divided into two groups, based on parental history of hypertension, and were matched for age and sex. All the study measurements were obtained using BPro, which is a noninvasive pulse wave acquisition device that derives CASP from the radial pressure waveform using an N-point moving average method (HealthStats International, Singapore) [3]. The device was calibrated using peripheral BP readings from a validated oscillometric BP monitor, on the nondominant arm in the supine position, following rest for at least 15 min. The BPro device was then positioned on the radial pulse of the same arm, from which real-time radial pulse waveforms were captured for at least 5 min. The waveforms were then analysed using the A-Pulse software version 2.6.1 (HealthStats International, Singapore) to obtain the values for CASP, PSP, PDP and AIx. The results shown in this study is the average of the values obtained during the 5-min pulse waveform-recording period.

Statistical analysis was carried out using IBM SPSS Statistics version 19 (IBM, New York, New York, USA). Means were compared using the independent-samples Student's *t*-test. The data were also scrutinized for potential covariates using analysis of covariance (ANCOVA). Sample sizes were calculated using a formula as published in the BMJ for the primary parameters of interest [4]. The study had a power of 80% with α set at 0.05. The calculation of the sample size was based on the following two variables: the difference in value (D) of the primary parameter which is of clinical interest, that is CASP, and the likely SD of the parameter in the study population. For this study the values for D and SD are set at 4 and 9 mmHg, respectively, giving a minimum required sample size of 79. Values for the calculation of the sample size were taken from a previous similar study [5].

RESULTS

A total of 200 young and healthy individuals were recruited into the ONT group ($n = 100$) and the OHT group ($n = 100$). Table 1 lists the characteristics of the participants according to their respective groups. There were no significant differences in baseline clinical characteristics between the two groups.

Following haemodynamic measurements, as shown in Table 2, the OHT group exhibited higher PSP (117.57 ± 10.06 versus 114.52 ± 8.94, $P < 0.05$), PDP (72.39 ± 7.28 versus 70.39 ± 6.50, $P < 0.05$) and CASP (103.72 ± 8.95 versus 101.37 ± 7.74, $P < 0.05$) compared to the ONT group. There was no significant difference in AIx in the ONT group (57.97 ± 11.02 versus 58.08 ± 12.16, $P = 0.95$) in comparison to the OHT group in unadjusted analysis.

Using ANCOVA, we adjusted all haemodynamic measurements for age, heart rate, height, weight, total

TABLE 2. Results of haemodynamic measurements

Characteristic	ONT	OHT	*P*
PSP (mmHg)	114.52 ± 8.94	117.57 ± 10.06	<0.05
PDP (mmHg)	70.39 ± 6.50	72.39 ± 7.28	<0.05
CASP (mmHg)	101.37 ± 7.74	103.72 ± 8.95	<0.05
AIx (%)	57.97 ± 11.02	58.08 ± 12.16	0.95

Values represent mean ± SD. AIx, augmentation index; CASP, central aortic systolic pressure; OHT, offspring of hypertensive parents; ONT, offspring of normotensive parents; PDP, peripheral diastolic systolic pressure; PSP, peripheral brachial systolic pressure.

TABLE 3. Adjusted haemodynamic measurements

Characteristic	ONT	OHT	*P*
PSP (mmHg)	114.76 (113.11–116.40)	117.33 (115.69–118.98)	<0.05
PDP (mmHg)	70.45 (69.11–71.80)	72.33 (70.98, 73–7)	0.05
CASP (mmHg)	101.45 (99.91–103.00)	103.64 (102.09–105.18)	0.05
AIx (%)	57.71 (55.52–59.90)	58.34 (56.15–60.53)	0.69

Values are adjusted mean (95% confidence interval). All haemodynamic measurements were adjusted for age, height, weight, heart rate, fasting total cholesterol and fasting blood glucose. AIx, augmentation index; CASP, central aortic systolic pressure; OHT, offspring of hypertensive parents; ONT, offspring of normotensive parents; PDP, peripheral diastolic systolic pressure; PSP, peripheral brachial systolic pressure.

cholesterol and glucose [6,7]. Following adjustments, only PSP (117.33 versus 114.76, $P < 0.05$) remained significantly higher in the OHT group compared to the ONT group. Differences in PDP and CASP were no longer significant, whereas the difference in AIx between the two groups remained statistically insignificant (Table 3).

As the radial AIx has previously been shown to be higher in women [8], we also looked at the corrected results separately in both sexes (Tables 4 and 5). We found that there were no significant differences in AIx between the ONT and OHT group in either sex. Interestingly, both unadjusted and adjusted CASP of the OHT group was found to be higher in women but not men (101.73 versus 98.16, $P < 0.05$ and 101.51 versus 98.40, $P < 0.05$, respectively), whereas unadjusted and adjusted PDP (74.94 versus 71.18, $P < 0.05$ and 75.15 versus 70.99, $P < 0.05$, respectively) of the OHT group was found to be higher in men but not women, compared to the ONT group. PSP was also significantly higher in the female OHT group preadjustment (113.98 ± 9.06 versus 110.44 ± 7.60, $P < 0.05$), but the significance disappeared as the data were adjusted for age, heart rate, height, weight, total cholesterol and glucose.

DISCUSSION

This study has shown that PSP, PDP and CASP are significantly higher in young and healthy normotensive offspring of hypertensive parents, compared to their peers with normotensive parents. Correction for known cardiovascular risk factors removed most of its significance, but separate analysis of corrected haemodynamic measurements between male and female individuals suggested possible differences in mechanism in which elevated BP and increased arterial stiffness may manifest in this age group.

These findings are fairly consistent with results from earlier studies on comparable populations. In a previous study done by Kucerova *et al.* [9] in 2006, it was shown that peripheral systolic, diastolic and pulse pressure are higher in OHT parents, compared to offspring of normotensive parents. Similarly, the same study exhibited no significant differences between the two groups in corrected values for central and peripheral AIx and pulse wave velocity following complex adjustments for characteristics including age, heart rate, smoking prevalence, alcohol intake and serum cholesterol. Unlike our study, certain general characteristics compared between the two groups in this 2006 study such as age, body weight and BMI were significantly different at the onset.

AIx had been shown previously to be higher in young adults of families with essential hypertension [10]. In the aforementioned study, despite similar results in brachial pulse wave velocity, the difference in central AIx was evident in a regression model that corrected for known cardiovascular risk factors. This previous study had a higher mean age compared to our study and there were also differences in smoking prevalence, blood glucose levels, HDL-cholesterol and creatinine between the two groups.

Rajzer *et al.* [11] in 1999 showed that although participants with a family history of hypertension had higher systolic, diastolic, pulse and mean arterial pressures, aortic stiffness in terms of pulse wave velocity was not significantly different in comparison to the control group. Again, the same group of individuals also had higher baseline BMI and LDL-cholesterol levels.

Another study looking at arterial stiffness in young and nonobese children and adolescents aged 10–21 found that individuals with a parental history of hypertension had higher carotid, but not aortic stiffness [12]. However, the findings were not corrected for BP, which was higher in this age group.

The results of our study must be considered together with its limitations. Being a cross-sectional study in nature, we had to take into account intraday and interday variations in BP. The interoperator variability of the measurements

TABLE 4. Unadjusted and adjusted haemodynamic measurements in female participants

Characteristic	ONT	OHT	*P*
PSP (mmHg)	110.44 ± 7.60	113.98 ± 9.06	<0.05
PSP, adjusted (mmHg)	110.82 (108.73–112.90)	113.63 (111.60–115.66)	0.06
PDP (mmHg)	69.89 ± 6.53	70.95 ± 7.17	0.39
PDP, adjusted (mmHg)	70.00 (68.23–71.77)	70.84 (69.12–72.57)	0.51
CASP (mmHg)	98.16 ± 6.67	101.73 ± 8.78	<0.05
CASP, adjusted (mmHg)	98.40 (96.41–100.39)	101.51 (99.56–103.46)	<0.05
AIx (%)	59.02 ± 11.36	60.88 ± 12.31	0.38
AIx, adjusted (%)	58.84 (55.82–61.86)	61.04 (58.09–63.99)	0.31

Values represent mean ± SD or adjusted mean (95% confidence interval). Adjusted haemodynamic measurements were corrected for age, height, weight, heart rate, fasting total cholesterol and fasting blood glucose. AIx, augmentation index; CASP, central aortic systolic pressure; OHT, offspring of hypertensive parents; ONT, offspring of normotensive parents; PDP, peripheral diastolic systolic pressure; PSP, peripheral brachial systolic pressure.

TABLE 5. Unadjusted and adjusted haemodynamic measurements in male participants

Characteristic	ONT	OHT	*P*
PSP (mmHg)	120.90 ± 6.97	123.94 ± 8.56	0.09
PSP, adjusted (mmHg)	120.73 (118.29–123.18)	124.12 (121.57–126.67)	0.06
PDP (mmHg)	71.18 ± 6.47	74.94 ± 6.85	<0.05
PDP, adjusted (mmHg)	70.99 (68.82–73.15)	75.15 (72.90–77.41)	<0.05
CASP (mmHg)	106.38 ± 6.58	107.25 ± 8.21	0.62
CASP, adjusted (mmHg)	105.86 (103.53–108.18)	107.82 (105.40–110.25)	0.257
AIx (%)	56.33 ± 10.40	53.11 ± 10.29	0.18
AIx, adjusted (%)	55.67 (52.53–58.81)	53.83 (50.55–57.11)	0.43

Values represent mean ± SD or adjusted mean (95% confidence interval). Adjusted haemodynamic measurements were corrected for age, height, weight, heart rate, fasting total cholesterol and fasting blood glucose. AIx, augmentation index; CASP, central aortic systolic pressure; OHT, offspring of hypertensive parents; ONT, offspring of normotensive parents; PDP, peripheral diastolic systolic pressure; PSP, peripheral brachial systolic pressure.

taken with the BPro device must also be considered. Although the sample size of this study was considered statistically adequate, the fact that most of our volunteers came from a restricted geographical location may question the representativeness of the sample on the general population. Due to financial constraints, we only determined parental hypertensive status through detailed history taking of the offspring, and this was not verified by actual BP measurements of the parent.

In conclusion, this study has shown that despite adequate health status and the absence of major cardiovascular risk factors, alterations in PSP, PDP and CASP are already present in early life in normotensive offspring of hypertensive parents, with possible differences in mechanism between different sexes. This may indicate a future role for risk factor screening and early intervention in this particular cohort of the population.

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Conflicts of interest

There are no conflicts of interest.

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Reviewers' Summary Evaluations

Reviewer 1

In this study the mean values of central and peripheral blood pressure were measured in 100 individuals with and in 100 without parental hypertension, non-smoking, living in Malaysia, consecutively enrolled and matched for age and sex. In subjects from hypertensive families higher peripheral BP values were observed, while after adjustments for heart rate and height, aortic BP was similar, as well as augmentation index. This should be taken to suggest no influence of wave reflection on central BP in individuals without cardiovascular risk factors. Data on serum creatinine or albuminuria are lacking.

Reviewer 2

The authors studied haemodynamic parameters in the offspring from normotensive and from hypertensive families. The groups were well matched for all possible confounding factors. The study was done in a Malaysian population free of obesity and with low prevalence of cardiovascular risk factors; this is major advantage. In all similar studies the risk factors were clustered in hypertensive families, and this might influence results. The study suggests that there may be some different role of pressure wave reflection in males and females at risk of hypertension. The major study weakness is the rather small study sample.