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Arterial stiffness in pregnancies complicated
by pre-eclampsia

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Abstract:

Aims of the study: Pre-eclampsia (PE) is characterized by an altered maternal cardiovascular adaptation to pregnancy and increased cardiovascular risk later on in life. The aim of the current study was to compare arterial stiffness in women with pre-eclampsia and those with normotensive pregnancies.

Methods This was a cross sectional study involving 69 normotensive, pregnant women and 54 women with preeclampsia. Maternal wave reflection (augmentation index; Alx) and pulse wave velocity (PWV) of the carotid-radial and carotid-femoral part of the arterial tree were assessed non-invasively using applanation tonometry.

Results Compared to normotensive pregnant controls, women with pre-eclampsia had significantly increased Alx ($4\pm 13.6\%$ vs $24.3\pm 10.3\%$, $p<0.0001$) and current PE was significantly ($p<0.0001$) and independently associated with increased wave reflection in a model that also included maternal age ($p=0.002$), heart rate ($p<0.0001$), gestational age at entry ($p=0.03$) and aortic Tr ($p<0.0001$). The PWV (carotid-femoral and carotid-radial) were significantly higher in women with pre-eclampsia ($7.2\pm 1.2\text{m/sec}$ vs $5.5\pm 0.7\text{m/sec}$, $p<0.0001$ and $9.4\pm 1\text{m/sec}$ vs $7.5\pm 1.2\text{m/sec}$, $p<0.0001$ respectively) and pre-eclampsia was significantly ($p<0.0001$) and independently associated with increased PWV (carotid-femoral) in a model that also included maternal age ($p<0.0001$), mean arterial pressure ($p<0.0001$) and black race ($p<0.0001$). The results were similar for PWV of the carotid-radial. There was no statistical significant difference in the above parameters between women with early (before 34 weeks of gestation) and late onset PE.

Conclusions Pre-eclampsia is characterized by increased maternal wave reflection and arterial stiffness.

INTRODUCTION:

The cardiovascular system undergoes important modifications in pregnancy with increased blood volume, cardiac output and heart rate as well as reduced blood pressure and vascular resistance.

All these modifications occur in order to ensure adequate uteroplacental supply.(1)

Plasma volume expansion and increased cardiac output are thought to be triggered or preceded by the decrease in systemic vascular resistance. Schrier et al (2,3) hypothesized that the primary event in normal pregnancy is peripheral arterial vasodilatation which leads to a state of relative underfilling of the arterial circulation with subsequent renal sodium and water retention and consequently expansion of the extracellular and plasma volume.

A decrease in vascular resistance and the generalised vasodilatation affect arterial stiffness. In normal pregnancy arterial stiffness decreases during the first trimester and remains low until the end of pregnancy due to either reduced smooth muscle tone or vessel wall remodelling. (4)

Pre-eclampsia is one of the leading causes of maternal and perinatal morbidity and mortality. It occurs in 3-10% of all pregnancies (5) and is associated with reduced plasma volume, increased vascular resistance and vasoconstriction.

It is defined as blood pressure of 140/90 mmHg on two consecutive occasions at least 4 hours apart associated with proteinuria of at least 300 mg per 24 h or 2+ on dipstick.(6)

Recent studies report increased arterial stiffness both with age and in patients with increased cardiovascular risk due to certain diseases such as hypertension, diabetes and hypercholesterolemia.(7,9).These are known to cause endothelial dysfunction hence reducing arterial compliance. Changes have also been observed prior to the appearance of a clinically apparent disease therefore this method is likely to be useful in risk assessment for myocardial infarction and stroke.

Non invasive evaluation of aortic stiffness is possible with a simple, validated and reproducible technique of applanation tonometry. (10,11) Pulse wave analysis (PWA) and pulse wave velocity (PWV) can be performed. The aortic waveform, peripheral and central pressures are derived using

a transfer function from the assessment of the radial artery waveform. (12,13) hence the augmentation index (AI) a marker of vascular compliance is obtained. On the other hand, PWV is the speed at which the pressure wave is transmitted from the aorta through the vascular tree and the stiffer the vessels the higher the velocity.

Since pre-eclampsia is related with increased peripheral vascular resistance as with these diseases the objective of our study was that of evaluating whether the patients with pre-eclampsia had stiffer arteries than control subjects and if this method would eventually be useful in detecting women with, or at increased risk of pre-eclampsia earlier.

Indices of arterial stiffness

| Term | Definition | Methods of measurement |
|--------------------------------|---|--|
| Elastic modulus** | The pressure change required for theoretical 100% stretch from resting diameter $(\Delta P \times D) / \Delta D$ (mmHg) | Ultrasound* MRI |
| Young's modulus ** | Elastic modulus per unit area ($\Delta P \times D) / \Delta D \times h$) (mmHg/cm) | Ultrasound* MRI |
| Arterial distensibility ** | Relative change in diameter (or area) for a given pressure change; inverse of elastic modulus $\Delta D / (\Delta P \times D)$ (mmHg ⁻¹) | Ultrasound* MRI |
| Arterial compliance** | Absolute diameter (or area) change for a given pressure step $\Delta D / \Delta P$ (cm/mmHg) (or cm ² / mmHg) | Ultrasound* MRI |
| Pulse wave velocity | Velocity of travel of the pulse along a length of artery Distance/ Δt (cm/sec) | Pressure waveform* Volume waveform Ultrasound MRI |
| Augmentation index | The difference between the second and first systolic peaks as a % of pulse pressure | Pressure waveform* |
| Stiffness index (β) ** | Ratio of \ln (systolic/diastolic pressures) to (relative change in diameter) $\beta = \frac{\ln(P_s/P_d)}{(D_s - D_d) / D_d}$ | Ultrasound * |
| Capacitative compliance | Relationship between pressure change and volume change in the arteries during the exponential component of diastolic pressure decay $\Delta V / \Delta P$ (cm ³ /mmHg) | Pressure waveform* |
| Oscillatory compliance | Relationship between oscillating pressure change and oscillating volume change around the exponential pressure decay during diastole $\Delta V / \Delta P$ (cm ³ /mmHg) | Pressure waveform* |

P, pressure; D, diameter; V, volume; h, wall thickness; t, time; v, velocity; s, systolic; d, diastolic. * most common method of measurement, ** also requires pressure measurements

METHODS OF MEASURING ARTERIAL STIFFNESS

PULSE PRESSURE:

This is given by the difference between systolic and diastolic blood pressures and depends on the cardiac output, large artery stiffness and wave reflection. It was recognized already in the 1920s by Bramwell and coll (14) as a surrogate for arterial stiffness. Pulse pressure has however shown to be an unreliable method as it varies along the arterial tree. In-fact it gets amplified as it travels from the aorta to the periphery and therefore measurements of the latter do not accurately reflect the actual central pulse pressure. Moreover since the heart, brain and kidneys are affected by the aortic pressure, the cardiovascular risk is more accurately related to the central blood pressure. Central blood pressure can be measured invasively using intra-arterial catheters, however non-invasive validated methods which are simple, feasible and reproducible are now available.

ULTRASOUND- DERIVED INDICES

Ultrasound can be used to measure arterial stiffness (distensibility and compliance) . Its use however is limited to the larger and more accessible arteries. It has been used mainly on the brachial, femoral , carotid and abdominal aorta. Several images of the vessel wall are obtained per cardiac cycle and the maximum and minimum areas of the vessel are calculated. Distensibility and hence compliance (inverse of stiffness) can be calculated using the following formulae:

$$\text{Distensibility} = \frac{\Delta V}{\Delta P \cdot V}$$

$$\text{Compliance} = \frac{\Delta V}{\Delta P}$$

Where Δv = change in volume, Δp = change in pressure, and V = volume

Use of ultrasound however is not feasible as the resolution is limited making the detection of very small changes in the vessel diameter difficult to detect. It therefore requires an experienced operator and expensive equipment.

MAGNETIC RESONANCE IMAGING (MRI)

This technique has recently been used to measure vascular distensibility and compliance. Most of the studies have been on the aorta: MRI has been used to demonstrate the inverse relationship between aortic distensibility and age, reduced arterial compliance in hypertensive patients (15) and in those with coronary artery disease while its increased in athletes.(16)

MRI however remains expensive and therefore its use remains limited to research studies.

WAVEFORM ANALYSIS.

Arterial pressure waveform is a composite of the forward pressure produced by ventricular contraction and a reflected wave. Reflected waves come from the periphery principally from branch points or sites of impedance mismatch. The arterial waveform will therefore vary throughout the arterial tree. The velocity at which this waveform travels is influenced by the stiffness of the arteries and therefore the stiffer the arteries the higher the velocity.

In elastic vessels, the reflected wave arrives back to the aorta during diastole, serving to increase diastolic pressure and consequently improving coronary artery perfusion.

On the contrary, with stiff arteries, the reflected wave arrives back to the central arteries earlier, increasing systolic pressure and a consequent decrease in diastolic pressure. High systolic pressures accelerate the development of left ventricular hypertrophy, whereas low diastolic pressures reduce coronary artery perfusion. The amplitude of the reflected wave increases as the arterial stiffness increases further augmenting central systolic pressure.

The O'Rourke Pulse wave Analysis (PWA) system is a simple, non invasive, validated method of measuring arterial stiffness.(17) Applanation tonometry is used to record pressures in the

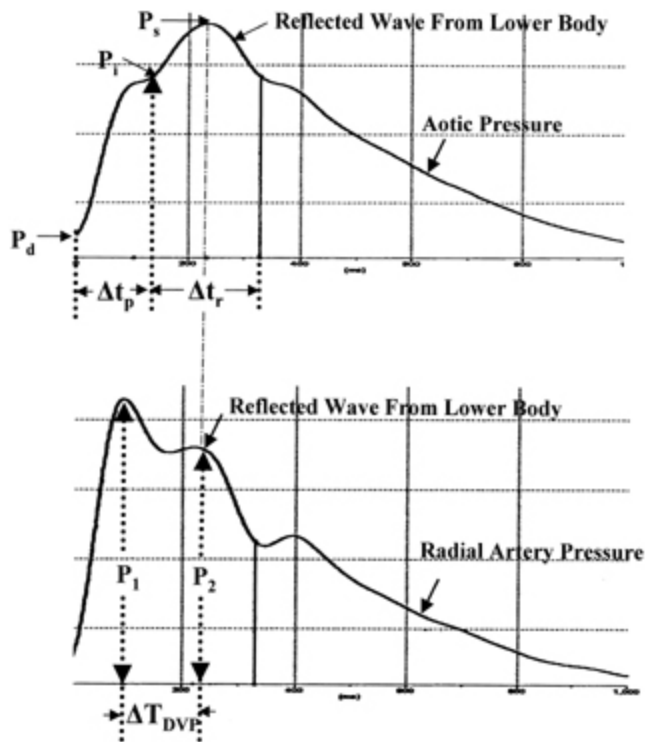
peripheral arteries and a validated generalised transfer factor is then applied to derive the corresponding central waveform. The principle behind this is that when a curved surface of a cylinder is flattened, the circumferential pressures are equalized and intraluminal pressures can be recorded accurately. In practise, a pencil-like probe, with a high fidelity micromanometer at its tip is applied to the skin above the artery and gentle downwards pressure is used to flatten the artery against the underlying tissues.



Augmentation index, which is the difference between the first and second systolic peaks, (the first systolic peak is the maximum pressure given by the forward going pressure wave while the second is the sum of the forward and backward going waveforms) expressed as a percentage of the pulse pressure, and a measure of systemic stiffness can then be derived .(18)

The inflection point on the upward part of the systolic part of the systolic curve is caused by the start of wave reflection. Since the main site of wave reflection is the aortic bifurcation, determination of the inflection point provides a measure of aortic pulse wave velocity. (19) By integrating the pressure-time signal, the mean arterial pressure can be calculated as can the tension time index (TTI) which is the area under the systolic portion of the pressure waveform per minute (the systolic pressure-time integral), and is an index of systolic stress. Likewise, the diastolic pressure-time (20) can be derived and from these variables the subendocardial viability index (SEVR) calculated as the ratio diastolic pressure time integral: tension time index. This provides a measure of the relationship between subepicardial and subendocardial blood flow and

therefore the potential for myocardial ischaemia.(21) Ejection duration is calculated as the time from the foot of the pressure wave to the incisura.



Top Aortic pressure wave synthesized from the measured radial artery pressure wave (applanation tonometry) using a generalized transfer function. The abbreviation P_s indicates peak systolic pressure; P_i is an inflection point that indicates the beginning upstroke of the reflected pressure wave; P_d is minimum diastolic pressure; Δt_p is the round trip travel time of the forward (or incident) wave from the ascending aorta to the major reflecting site and back; and Δt_r is the systolic duration of the reflected pressure wave. Pulse pressure is $(P_s - P_d) = (P_i - P_d) + (P_s - P_i)$. Augmentation index (AI_a) = $(P_s - P_i)/(P_s - P_d)$ and wasted LV pressure energy (E_w) = $2.09\Delta t_r (P_s - P_i)$. **(Bottom)** Noninvasive high-fidelity recording of the radial artery pressure wave. The wave has been shifted leftward to align with the aortic pressure wave. The variations in the pressure wave, like those of the aortic pressure wave, are due to wave reflections from the lower body superimposed on the wave. The abbreviation P_1 is the sum of the incident (ejected) wave and reflected wave (from hand); P_2 is the peak of the reflected wave from the lower body minus end-diastolic pressure; P_2/P_1 is the radial artery augmentation index (AI_r); and ΔT_{DVP} is the difference between the first two peaks of the pressure wave and has been used as a measure of arterial stiffness.

METHODS:

We recruited 54 pre-eclamptic women admitted to the William Gilliatt Ward of the Kings College Hospital, London and compared them to a control group of 69 women recruited from the Antenatal clinic and from the Harris Birthright Research Centre.

Pre-eclampsia was defined as blood pressure over 140/90 on two consecutive readings atleast 4 hours apart, edema and proteinuria of atleast 2+ on dipstick or 300 mg/ 24 hr urine collection. Superimposed pre-eclampsia was diagnosed if a chronic hypertensive patient's systolic and/or diastolic levels rose ≥ 30 or ≥ 15 mmHg, respectively, and/or if proteinuria appeared de novo or increased substantially. Other Laboratory tests done included platelet count, uric acid, Creatinine and aspartate aminotransferase.

The control group comprised of healthy pregnant women with uncomplicated pregnancies that were not on treatment and did not have any family history of early heart disease.

Maternal age, ethnic group, smoking status, parity, pre-pregnancy weight, current weight, height, previous obstetric history, past medical history, drugs, and family history were recorded.

The study was approved by the Institutional Review Committee and all women gave written informed consent.

The patients were examined after 10 minutes of rest in the left lateral position to avoid compression of the Vena Cava from the uterus.

Peripheral BP was measured in the right arm using an ambulatory blood pressure monitor (Microlife Medical 90207, WA, US), which has been validated in pregnancy.²²

Two measurements were taken and averaged. The mean arterial BP (MAP) was then derived from the systolic and diastolic BP (SBP, DBP)

Pulse wave velocity:

The sygmoCor (PWV Medical, Sydney, Australia)^{23,24} system was used to assess Aortic (carotid-femoral) and brachial (carotid- radial) PWV by applanation tonometry. The PWV was determined by sequential acquisition of pressure waveforms from these arteries. The timing was compared

with that of the R wave on the simultaneously recorded electrocardiogram (25) The time delay was measured automatically by the computer software. The distance travelled by the pulse wave between the carotid and femoral arteries was measured in a straight line using a pair of compasses to reduce the influence of altered body contours induced by pregnancy. The proximal distance was measured from the sternal notch to the sampling site on the carotid artery and the distal distance was measured from the sternal notch to the sampling site on the femoral artery. The carotid- to-femoral path length was calculated by subtracting the proximal from the distal distance. In the case of brachial PWV the proximal distance was from the sternal notch to the sampling site on the carotid artery while the distal distance was the measurement from the sternal notch to the sampling site of the radial artery.

Pulse wave velocity was then calculated as the ratio of the distance travelled by the pulse wave and the foot-to-foot time delay between the pulse waves and expressed in meters per second.(25)

For each patient a two waveform recordings were obtained. The mean was then used for statistical analysis.

Pulse Wave Analysis:

The SphygmoCor system was used for the analysis of the radial pressure wave contour. The radial artery was pressed gently at the site of maximal pulsation with the tip of the tonometer containing a micromanometer that accurately records the pressure within the artery (SPC-301; Millar Instruments, Houston, Tex)

Aortic waveform, peripheral mean pressure and central pressures were obtained from the radial artery waveform by using a transfer function.

Augmentation index (AIx), is calculated from the difference between the first and second systolic peaks expressed as a percentage of the pulse pressure and is determined by the integrated software. Mean arterial blood pressure (MAP) and central systolic, diastolic and pulse pressure (CSBP, CDBP and CPP) were also determined. Information on first systolic peak and its time (P1,

T1), height of the first systolic peak (P1H), second systolic peak and its time (P2, T2), and aortic Tr (time between the start of the systolic curve and the inflection point) was also given.

All the measurements were obtained twice and the mean was used for the statistical analysis.

The measurements were done by the same operators (C.K, J.A) and were subjected to quality control by the software.

Statistical analysis

Normality of the distribution of the data was examined with the Kolmogorov-Smirnov test. For those parameters that were not normally distributed logarithmic transformation was performed. Data were expressed as mean \pm standard deviation or as median (interquartile range) for normally and non-normally distributed data respectively. Comparisons between groups were performed using unpaired Student t-test or chi-square (χ^2) for numerical and categorical data respectively. Univariate analyses were performed between AIx, PWV and maternal age, BMI, MAP, heart rate (HR), gestational age (GA) at entry, and Tr to look for potential confounders. Multiple regression analysis was performed when adjustment for potential confounders thought to be necessary. The statistical analyses were performed using the Statistical Package for Social Sciences (Version 12.0).

RESULTS:

Recordings were successfully obtained from all women and they all tolerated the studies well. The group of women with PE included 20 women with early onset PE, who had to be delivered before or at 34 weeks due to the severity of the condition. In all tables, values are given for early and late PE, although the comparisons were done between normotensive women and women with PE overall.

The demographic characteristics of the study participants are given in Table 1. Women with PE were more likely to be black, with higher BMI and delivered smaller babies earlier, than expected.

The hemodynamic parameters are given in Table 2. Compared to normotensive women, women with PE had slower HR and longer heart cycle, which was mainly due to longer duration of the diastole rather than the ejection duration time. By definition, all blood pressure indices (peripheral and central, systolic and diastolic) were significantly higher in women with PE. Peripheral pulse pressure (peripheral PP), a valuable surrogate measurement of arterial stiffness, was higher in women with PE.

In women with PE, the height of P1 (the maximum pressure created by the forward-going pressure wave), P1H (an index of peak ventricular ejection velocity) and P2 were significantly elevated. The increased P2 could also be explained by the shorter aortic Tr, the timing of the reflected wave, which causes a shift of the reflected wave earlier into systole.

The Alx was significantly increased in women with established PE. In a multiple linear regression analysis with the Alx as a dependent variable, current PE ($p < 0.0001$) was independently associated with increased wave reflection in a model that also included maternal age ($p = 0.002$), HR ($p < 0.0001$), GA at entry ($p = 0.03$) and aortic Tr ($p < 0.0001$). Parity, smoking, ethnic group, BMI and MAP were not significant determinants of Alx. The above findings were confirmed with univariate analysis of variance, which showed that the difference of Alx between the two groups of women was significant even after adjusting for age, HR, GA at entry and aortic Tr.

The PWV (carotid-radial and carotid-femoral) were significantly higher in women with established PE. In a multiple linear backward regression analysis with the PWV (carotid-radial) as a dependent variable, current PE was independently associated with increased PWV ($p < 0.0001$) in a model that also included age ($p < 0.0001$), MAP ($p < 0.0001$) and black race ($p < 0.0001$). Parity, smoking, BMI, HR and GA at entry were not significant predictors of PWV (carotid-radial). The results were similar for PWV (carotid-femoral).

The Alx and PWV (carotid-radial and carotid-femoral) were not correlated with any of the haematological or biochemical markers measured in women with established PE (platelets, aspartate aminotransferase, creatinine and proteinuria/24h) (data not shown).

All the above changes, described above, between normotensive women and those with PE were more pronounced, but not necessarily significantly, in women with early onset disease. The statistical significance of the comparisons between women with early and late onset disease are given in parentheses in Tables 1 and 2.

DISCUSSION:

A previous study performed in our centre demonstrated that in an uncomplicated pregnancy there is a decrease in central systolic and diastolic BP and AIx. These changes appear already in the first trimester and reach their nadir in mid-pregnancy and thereafter rise to approximately pre-pregnancy levels by term. They also found that normal pregnancy is associated with a decline in wave reflections within the arterial tree.(26).

In this study, the pre-eclamptic women had higher central blood pressures than their normal controls and the pulse pressure an indicator of arterial stiffness was significantly different between the two groups. This confirms the generalised conception that pre-eclampsia is a state of vasoconstriction of the peripheral vessels. We also observed an increase in both the PWV in the aortic (carotid- femoral PWV) and brachial, (carotid- radial PWV) arteries. An increase in the PWV causes an earlier reflection of the pulse wave towards the heart in systole and this is expressed as augmentation index which appeared increased in the pre-eclamptic group compared to the control group even after having adjusted for the BP and heart rate. Women with pre-eclampsia also had smaller babies this is probably due to the reduced plasma volume expansion and placental circulation.

The most common factors that have been reported to be related with increased arterial stiffness in the normal population are age and hypertension where central elastic vessels become stiffer, diastolic pressure decreases and central systolic and pulse pressures are increased due to increased PWV and early return of reflected waves to the heart from the periphery . (27,28) This has been thought to be due to various causes occurring over a long period of time. These include

reduced elastin, increased collagen, increased calcium content in the arterial wall, increased creatinine and norepinephrine, reduced β -receptor tone of the smooth muscle cells, reduced release of nitric oxide (NO) and increased release of endothelin. (29,31)

The increased arterial stiffness in pre-eclampsia could be related to endothelial dysfunction.(30,31)

The endothelium has shown to play an important role in the regulation of arterial stiffness by releasing vasoactive substances like NO.(32,33) whose production is reduced in pre-eclampsia.

The association of arterial stiffness and endothelial dysfunction has been demonstrated in a previous study that reports reduced pulse wave reflection induced by the administration of glyceryl trinitrate. (34,35)

In addition, other characteristics of pre-eclampsia such as increased levels of homocysteine (36) and insulin resistance (37) could also be contributing factors to the observed increased maternal arterial stiffness, as all these factors have been associated with increased arterial stiffness in non-pregnant populations (38,39).

We have also demonstrated that women with established pre-eclampsia have increased PWV both in the carotid-radial and carotid-femoral pathways, even after adjustment for possible confounders. Previous studies assessing the arterial stiffness of other vascular pathways such as base of the aorta to popliteal artery (40) and abdominal aorta (41) have confirmed increased arterial stiffness in women with established PE. These findings suggest that large conduit arteries, together with the peripheral vasculature, are also involved in the aberrant hemodynamic adaptation of pre-eclampsia.

Moreover, studies in former pre-eclamptic women have demonstrated increased PWV (carotid-femoral) four months following delivery (42) and persistence of maternal endothelial dysfunction (43) years after the index pregnancy. The increased arterial stiffness and endothelial dysfunction during PE and probably following a pregnancy complicated by pre-eclampsia (42,43) could provide a plausible link between this condition and the increased risk of cardiovascular events that these women experience later on in life (44).

In summary, we have shown that PE is associated with increased maternal *systemic* arterial stiffness, as assessed by the method of applanation tonometry. Although arterial stiffening characterizes women with established pre-eclampsia, it is uncertain whether this is the cause or the consequence of the disease. To what extent this method can be used to identify women at risk prior to the development of the condition remains to be determined.

TABLES:

Table 1. Demographic characteristics of the study populations. Values are given for late and early pre-eclampsia (PE). Comparisons were performed between normotensive women and women with PE overall and also between women with early and later onset PE (last P Value column). Data are presented as mean±SD or as median (interquartile range) for normally and non-normally distributed data respectively.

| Parameter | Controls | | PE (N=54) | | P Value (PE overall) |
|---------------------------------------|-------------------|--|------------------|-----------------|-------------------------|
| | (N=69) | | Late PE (N=34) | Early PE (N=20) | |
| Maternal age (yrs) | 30.7±6 | | 30.5±7 | 30.7±6.6 | 0.9 |
| Ethnic group | | | | | 0.02 |
| White, n (%) | 35 (50.7) | | 13 (38.2) | 1 (5) | |
| Black, n (%) | 28 (40.6) | | 16 (47.1) | 17 (85) | |
| Others, n (%) | 6 (8.7) | | 5 (14.7) | 2 (10) | |
| Smoking, n (%) | 15 (21.7) | | 7 (20.6) | 2 (10) | 0.4 |
| Nulliparity, n (%) | 43 (62.3) | | 21 (61.8) | 9 (45) | 0.4 |
| Maternal height (m) | 1.6±0.05 | | 1.6±0.06 | 1.6±0.05 | 0.98 |
| Maternal weight (kg) | 75±12.6 | | 81.8±14.4 | 83.6±14.5 | 0.003 |
| Body mass index (kg/m ²) | 28±4.4 | | 30.5±4.8 | 31±5.4 | 0.002 |
| Gestational age at entry (days) | 221±36 | | 255±12 | 200±23 | 0.02 |
| Gestational age at delivery (days) | 281 (273-286) | | 262 (256-270) | 210 (196-227) | <0.0001 |
| Birthweight (centiles) | 59.6 (31.8-76) | | 20.4 (6.2-57.3) | 1.5 (0.1-7.8) | <0.0001 |

Table 2: Vascular parameters of early and late PET

| Parameter | Pregnant controls (N=69) | PE (N=54) | | P Value |
|---|-----------------------------|---------------------|---------------------|-----------------|
| | | Late PE (N=34) | Early PE (N=20) | |
| Heart rate (bpm) | 81 ± 11.1 | 75.7 ± 11.1 | 71.9±13.1 | 0.002 (NS) |
| Heart cycle (ms) | 749.9±116.2 | 810.1±123 | 859.1±152.7 | 0.001 (NS) |
| Ejection duration (msec) | 312.6 ± 29.7 | 311 ± 25.7 | 324.7±21.8 | 0.48 (NS) |
| Diastole time (msec) | 437.3 ± 97.4 | 499 ± 105.7 | 534.4±138.1 | <0.0001 (NS) |
| PSBP (mmHg) | 114.8±10.3 | 138±13.3 | 144±16.5 | <0.0001(NS) |
| PDBP (mmHg) | 69.4±7.9 | 88.4±7.2 | 91.3±10.5 | <0.0001(NS) |
| Mean arterial pressure (mmHg) | 84.5±8.1 | 104.9±8.5 | 108.9±11.8 | <0.0001(NS) |
| PP (mmHg) | 45.4±7.3 | 49.6±9.9 | 52.7±10.4 | 0.001 (NS) |
| CSBP (mmHg) | 96.5 (89-102.2) | 125.2 (120-134) | 133.7 (128.6-138.3) | <0.0001 (0.004) |
| CDBP (mmHg) | 68 (64-71) | 89.2 (82-93) | 91 (84.1-102) | <0.0001 (0.06) |
| CPP (mmHg) | 27 (24.2-31.5) | 36.2 (30.2-44.1) | 43.5 (37.7-47.8) | <0.0001 (0.19) |
| P1H (mmHg) | 25 (23.5-28.7) | 27.7 (24-30.5) | 32 (25.7-34.3) | 0.002 (0.03) |
| P1 (mmHg) | 95±9.4 | 116.2±7.7 | 125.6±11.7 | <0.0001 (0.001) |
| P2 (mmHg) | 96.4±11.6 | 126±12.5 | 136.8±13.5 | <0.0001 (0.005) |
| Aortic T1 (msec) | 115.3±17.3 | 110.2±9.9 | 105.3±11.7 | 0.01(NS) |
| Aortic T2 (msec) | 195.4±23.9 | 215.1±22.5 | 219.4±25.7 | <0.0001(NS) |
| Aortic Tr (msec) | 152.5(144.7-166) | 141.5 (134.2-146.5) | 136.5 (132.5-145.3) | <0.0001(NS) |
| SEVR (ratio) | 119.4±19.4 | 137.5±22.8 | 138.6±31.6 | <0.0001 (NS) |
| Augmentation Index (AIX) % | 4±13.6 | 23.8 ± 9.9 | 25.1±11.2 | <0.0001(NS) |
| Amplification ratio (PPP/PP) | 1.6±0.1 | 1.3±0.1 | 1.3±0.1 | <0.0001 (NS) |
| Non-augmented amplification ratio (P1-CDBP) | 1.7 (1.6-1.8) | 1.7 (1.7-1.7) | 1.7 (1.7-1.8) | 0.17 (NS) |
| PWV (carotid-radial)(m/sec) | 7.5±1.2 | 9.5 ±1.1 | 9.3±0.7 | <0.0001 (NS) |
| PWV (carotid-femoral)(m/sec) | 5.5±0.7 | 7.2± 1.4 | 7.3±0.9 | <0.0001 (NS) |

DBP: diastolic blood pressure; CDBP: central diastolic blood pressure; PDBP: peripheral diastolic blood pressure

SBP: systolic blood pressure; CSBP: central systolic blood pressure; PSBP: peripheral systolic blood pressure

PP: pulse pressure; CPP: central pulse pressure

Figure 1:

Box and whisker plot comparing the maternal augmentation index between normotensive controls and women with established pre-eclampsia (* $p < 0.0001$). Boxes represent inter-quartile range, where the line represents the median. Whiskers at top and bottom of the box represent the highest and lowest values.

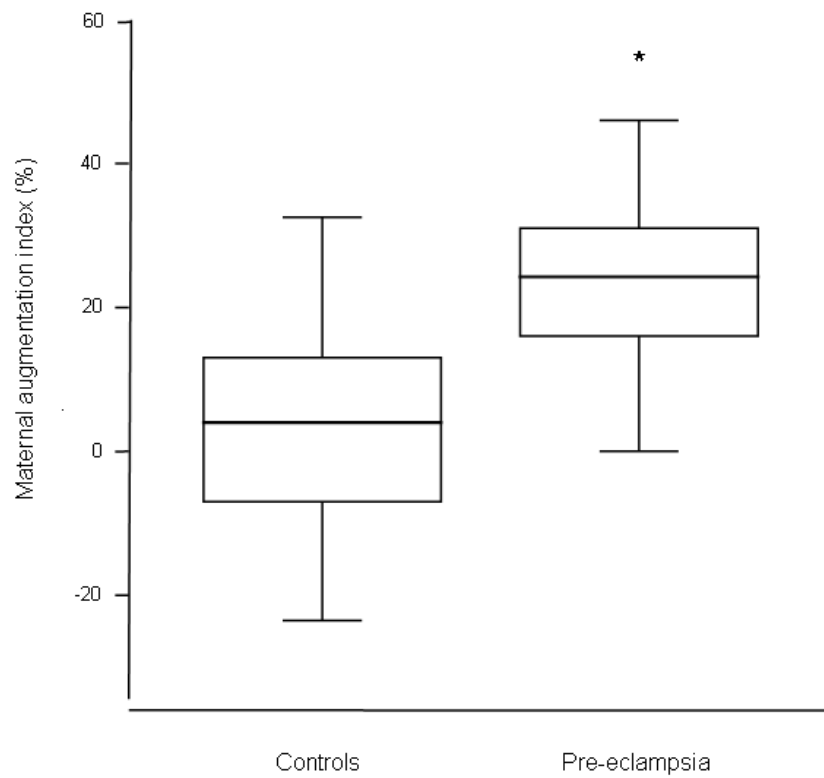
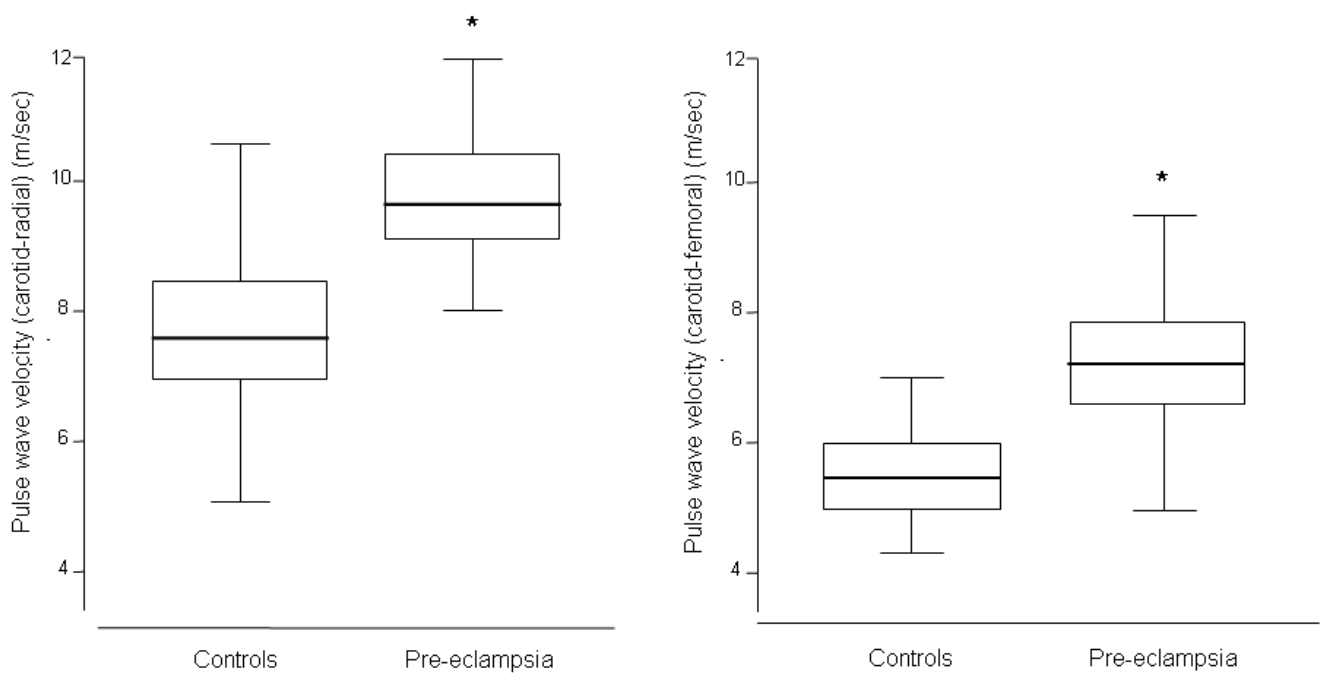


Figure 2:

Box and whisker plots comparing the maternal pulse wave velocity of the carotid-radial and carotid-femoral part of the arterial tree between normotensive controls and women with established pre-eclampsia (* $p < 0.0001$). Boxes represent inter-quartile range, where the line represents the median. Whiskers at top and bottom of the box represent the highest and lowest values.



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