Central arterial stiffness in Zambian normotensive and hypertensive participants

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Abstract

Central arterial stiffness is a strong and independent predictor of cardiovascular events and mortality including hypertension in any given population. A few studies have found that being black could be associated with elevated arterial stiffness thereby accounting for the high prevalence of hypertension in them. The present study sought to determine and compare central arterial stiffness using Carotid femoral PWV (cfPWV) in a population of Zambian normotensive (NT) participants and hypertensive (HT) participants (both treated hypertensives (HTC) and untreated hypertensives (HTN)) between 30 – 65 years of age. CF PWV was measured in 146 participants. A Complior® Analyse device (Version 1.9 Beta 2013; ALAM-Medical, France) was used. Superficial pulses were accessed noninvasively over the carotid–femoral segment. The cfPWV values in HTN participants (N=23) were significantly higher than in NT (N=64) participants (11.4±4.2 vs 9.1±3.2, p=0.009). In HTC participants (N=59), their cfPWV values (10.4±5.6) tended to approach those in HTN participants, with no statistical differences between them (p > 0.500). Furthermore, the mean cfPWV found in NT participants was considerably higher than any found in previous studies. Carotid femoral PWV did not show significant age–related increase in all three blood pressure categories (r²< 0.03, p > 0.100). These findings show that central elastic arteries of HT participants are stiffer and thus less compliant than those in NT participants adding to their burden of hypertension. Regrettably, HTC participants showed poor BP control inferring from their considerably high cfPWV values.

Key words: Carotid femoral pulse wave velocity, central arterial stiffness, hypertension, Zambian.

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Introduction

Central arterial stiffness is described as the hardening of the large elastic arterial walls such as the aorta and common carotids due to endothelial wall dysfunction as well as loss of elastin [1]. Central arterial stiffness has been found to independently predict cardiovascular morbidity and mortality in the general population including normotensive and hypertensive participants [2, 3]. Noninvasively, it is best measured directly by carotid-femoral PWV (cfPWV) which is the speed at which pulse wave travels on an arterial segment from the carotid artery to the femoral artery when the heart contracts in systole. In elastic arteries such as the aorta, common carotids and other large elastic arteries, the pulse wave travels slowly, whilst in stiffer arteries, the pulse wave travels faster partly due to the increase in the number of reflection sites like it is in the muscular peripheral arteries [2, 3].

In a stiff vessel the volume change, and therefore compliance, is reduced for any given pressure change. Thus the loss of elastin in the large elastic fibers (due to elevated central arterial stiffness) results into decreased arterial compliance which is the reduced capability of an artery to expand or distend (during systole) and contract/recoil (during diastole) in response to arterial blood pressure changes. Thus elevated central arterial stiffness could account for sustained increases in blood pressure independent of other risk factors [1, 4].

The stiffening of arterial walls and thus elevated cfPWV has been shown to increase
physiologically with age as well as with cardiovascular related disorders such as hypertension, cardiac failure, diabetes mellitus and stroke [5] in Caucasian populations. However, this trend does not seem so in Black populations in which arterial stiffness could already be elevated from early years of life or even birth [6, 7]. It has been shown that if PWV is improved, cardiovascular risk decreases [8]. For these reasons, central arterial stiffness assessment with cfPWV is now a recommended procedure by several researchers and clinicians in developed countries in understanding the pathophysiology and management of hypertension [2, 9].

In Zambia, hypertension like in most African countries is managed by the traditional approach in which the main aim is to lower peripheral blood pressure only in the hypertensive patients without an attempt to select anti-hypertensive therapy that would decrease both arterial stiffness and blood pressure (BP). This is largely because little is known about central arterial stiffness inspite of the high prevalence of hypertension especially in urban areas [10]. Therefore, the present study sought to determine central arterial stiffness using cfPWV in a population of Zambian normotensive and hypertensive participants between 30–65 years of age. In addition, to compare the relationship of central arterial stiffness in normotensive and hypertensive participants with age and brachial mean arterial pressure (bMAP). It was hoped that the results of the study would become the basis for further research and reason to implement cfPWV measurements alongside the use of sphygmomanometre in the management of hypertension.

Materials and Methods

Study design, study setting, study population and inclusion/exclusion criteria.

This was a cross-sectional study involving 146 participants aged 30 to 65 years. Data was collected over a period of four weeks in June-July, 2014. Hypertensive participants (HTN subjects; brachial BP ≥ 140/90 mm Hg and HTC subjects; those on anti-hypertensive drugs) were volunteers visiting the cardiovascular clinic of the University Teaching Hospital (UTH) in Lusaka, a national referral facility. NT participants; brachial BP ≤ 139/89 mm Hg) included volunteers who escorted their relatives and friends to the hospital. Those with any known major cardiovascular disease including diabetes (other than hypertension) as well as pregnant women were excluded from the study. Written ethical clearance was sought from the ERES Converge Research Ethics Committee pertaining research in human participants.

Protocol

The protocol used conforms to the 2007 ESC/ESH hypertension guidelines for the non-invasive measurement of central arterial stiffness in humans [2]. Each participant was invited for a nonrecurring study to clinic 5 of the UTH, Lusaka. This was done in the morning. The participant was introduced to the set-up and after the organizational procedures had been explained to him/her, he/she was asked to sign informed consent forms and then interviewed using a standard questionnaire. Questions asked concerned habits like smoking, alcohol consumption, whether on anti-hypertensive medication or not, level of routine exercise and medical history.

Body height and weight of each participant were taken according to standard procedures. Maximum height was measured to the nearest 0.1 cm and Weight to the nearest 0.1 kg using the Invicta Stadiometer (IP 1465, Leicester, UK). After a 5 minutes rest in the sitting position, the participant was asked to lie in supine position on the examination bed. Using the OMRON HEM-757 (Omron, Kyoto, Japan) apparatus brachial systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate were measured. The BP cuff was placed on the right upper arm over the brachial artery. The participant lay comfortably during measurements but he/she was not allowed to sleep. Two measurements were taken, with a 5-minute rest interval and the mean of the two recorded. Room temperature was kept within 23 – 25 degrees Celsius.

Thereafter, cfPWV was measured using noninvasively accessible superficial pulses using the Complior Analyse device (V1.9 Beta Version 2013; ALAM-Medical, France) over the carotid - femoral segment. Using a measuring tape, the distance between carotid and femoral artery pulse sites was measured on the right side as the path length for the determination of cfPWV( in cm). Then carotid and femoral sensors, connected to the Complior (which in turn connected to a Computer (PC)), were placed over the carotid artery pulse site on the right side of the neck and over the femoral artery pulse site in the groin or mid inguinal area on right side respectively. The start button on the Complior software on the PC desktop was turned on and the screen displayed continuous shapes of both carotid and femoral pulses.
When the above were valid, the screen displayed VALID which was stopped after 5 - 10 valid pulses for every participant. The data was automatically recorded and stored on the PC for further analysis.

All measurements were taken by the Principal Investigator and a trained Research Assistant for all participants. The device was set to correct the carotid - femoral distance entered by multiplying it with 0.8 to avoid overestimation of PWV.

Each participant received a report concerning their basic health information including PWV results immediately. The entire procedure took about 15 – 20 minutes per participant. In the event of a participant being identified with any abnormalities, the participant was referred to the Physician on-call or indeed the respective clinic within the UTH.

Data analysis: All statistical analyses including some graphs were done using IBM SPSS software version 16 with the aid of Microsoft excel for some graphs. Results were reported as means (standard deviation) using a statistical significance of $P \leq 0.05$ unless stated otherwise. CfPWV values in each BP and age category were represented as means (standard deviation) as well as with graphs. One way Analysis of Variance (ANOVA) was used to compare statistical differences in cfPWV in the age and BP categories. Furthermore, partial correlations were conducted to check for association between cfPWV and age or bMAP after controlling for confounders. Linear regression was computed for the same variables to determine their relationship. In all analyses, equal variances were assumed.

Results

Description of study participants

Table 1 summarises the description of basic parameters (using independent student t test) across the three BP categories. The study population was 146 participants. Participants were subdivided into one of the three BP categories such as NT, HTC and HTN participants as described under methodology. The number of females was 42, 36 and 17 in NT (n=64), HTC (n=59) and HTN (n=23) participants respectively. Their mean age was 42±8.7, 47±8.8 and 47±8.9 years respectively. Compared with normotensive subjects, both categories of hypertensive subjects were older, had a higher body mass index, and had the highest cfPWV and thus stiffer and less compliant central arteries. In addition, they had higher brachial BP values although were as equally likely to have a history of hypertension and diabetes as NT subjects.

Table 1: Summary of basic parameters of study population (N = 146)

<table>
<thead>
<tr>
<th>Blood Pressure Category</th>
<th>NT (n=64)</th>
<th>HTC (n=59)</th>
<th>HTN (n=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (no. females)</td>
<td>42</td>
<td>36</td>
<td>17</td>
</tr>
<tr>
<td>Age (years)</td>
<td>42±8.7</td>
<td>47±8.8</td>
<td>47±8.9</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161.6±11.4</td>
<td>162.7±7.6</td>
<td>156±34.8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>70.5±13.9</td>
<td>79.1±14.3</td>
<td>75±14.4</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>27.5±8.0</td>
<td>30.0±5.9</td>
<td>28.3±5.1</td>
</tr>
<tr>
<td># (%) of active smokers</td>
<td>2(3.1%)</td>
<td>2(3.4%)</td>
<td>0</td>
</tr>
<tr>
<td># (%) of alcohol drinkers</td>
<td>9(14.1%)</td>
<td>18(30.5%)</td>
<td>4(7.4%)</td>
</tr>
<tr>
<td># (%) history of Diabetes Mellitus</td>
<td>11(17.2%)</td>
<td>14(23.7%)</td>
<td>6(26.1%)</td>
</tr>
<tr>
<td># (%) history of Hypertension</td>
<td>36(56.2%)</td>
<td>34(57.6%)</td>
<td>13(56.5%)</td>
</tr>
<tr>
<td># (%) Vigorous work</td>
<td>10(15.6%)</td>
<td>10(16.9%)</td>
<td>3(13.0%)</td>
</tr>
<tr>
<td># (%) Moderate work</td>
<td>6(9.3%)</td>
<td>47(79.7%)</td>
<td>18(78.3%)</td>
</tr>
<tr>
<td>Walking/bicycle to work (days/week)</td>
<td>6±1.9</td>
<td>5±2.9</td>
<td>6±2.4</td>
</tr>
<tr>
<td>Brachial Systolic Blood Pressure</td>
<td>123±9.7</td>
<td>153±30.5</td>
<td>156±17.7</td>
</tr>
<tr>
<td>Brachial Diastolic Blood Pressure</td>
<td>79±7.1</td>
<td>98±19.4</td>
<td>98±11.3</td>
</tr>
<tr>
<td>Brachial Pulse Pressure</td>
<td>44±7.9</td>
<td>55±16.6</td>
<td>58±12.4</td>
</tr>
<tr>
<td>Brachial MAP¹</td>
<td>94±7.2</td>
<td>116±22.3</td>
<td>117±23.4</td>
</tr>
<tr>
<td>Carotid Femoral distance (cm)</td>
<td>48±4.25</td>
<td>49±3.5</td>
<td>49±3.15</td>
</tr>
<tr>
<td>Carotid Femoral transit time (ms)</td>
<td>60±28.5</td>
<td>55±18.8</td>
<td>49±19.4</td>
</tr>
<tr>
<td>Carotid Femoral PWV (m/s)</td>
<td>9.1±3.2</td>
<td>10.4±5.6</td>
<td>11.4±5.1</td>
</tr>
</tbody>
</table>

Figure 1: Comparison of Carotid femoral pulse wave velocity (cfPWV) across the blood pressure (BP) categories. Bar charts represent the mean values of cfPWV in each BP category (results of independent student t test). A p value ≤ 0.05 (results of one way ANOVA) indicates significant difference in cfPWV between the BP categories being compared (shown by colored dotted lines).
Table 2: Partial correlations between carotid femoral PWV and age or brachial blood pressure in each BP category.

<table>
<thead>
<tr>
<th>Carotid Femoral PWV (m/s)</th>
<th>NT (n=64)</th>
<th>HTC (n=59)</th>
<th>HTN (n=23)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>r</td>
<td>r</td>
<td>r</td>
<td>R</td>
</tr>
<tr>
<td>Pvalue</td>
<td>Pvalue</td>
<td>Pvalue</td>
<td></td>
</tr>
<tr>
<td>Age(years)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>.077</td>
<td>.571</td>
<td>.084</td>
</tr>
<tr>
<td>Brachial MAP(mmHg)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.201</td>
<td>.138</td>
<td>.176</td>
</tr>
</tbody>
</table>

NB. r – Pearson’s linear correlation coefficient, all correlations (r) with α ≤ 0.05 were significant (strongly related).

<sup>a</sup> Adjusted for gender, smoking, alcohol consumption, history of diabetes & hypertension, days/week one does moderate exercise, body mass index, brachial systolic BP, brachial MAP.

<sup>b</sup> Adjusted for gender, age, smoking, alcohol consumption, history of diabetes & hypertension, days/week one does moderate exercise, body mass index, brachial systolic BP.

<sup>*</sup>Partial correlations (linear) were insignificant for all variables under HTN patients after adjusting for confounders. Thus the results shown (for HTN participants) are unadjusted correlations.

**Cf PWV according to BP category**

Comparison of cfPWV across BP categories is shown in figure 1. Compared to NT participants, both categories of hypertensive participants had higher cfPWV (figure 1). However, only the cfPWV of HTN participants was significantly higher than that of NT (9.1±3.2 versus 11.4±4.2, p = 0.009), indicating that central arteries of HTN were even stiffer and thus noncompliant. On the contrary, values of cfPWV [figure 1] and brachial BP [table 1] of HTC and HTN participants were not significantly different from each other (p > 0.100).

The summary of cfPWV values according to age category is shown in figure 2. Even though cfPWV values did not reach significant differences across the three age categories for each of the BP category (p > 0.100), the observed values showed an increase with increasing age category [figure 2]. Hence the 30 – 39 age category had the least mean values, followed by the 40 – 49 age category and highest measurements were observed in the 50 – 65 age category in all BP categories. Furthermore, HTN subjects showed the highest cfPWV values in all age categories than any of the two BP categories. On the contrary, NT subjects showed the lowest cfPWV values with increasing age, with HTC values being only slightly lower than those in HTN subjects. Thus for any given age group, both treated and untreated hypertensive participants showed stiffer and less compliant central arteries when compared to normotensive subjects [figure 2].

**Figure 2:** Carotid femoral pulse wave velocity (cfPWV) according to age category in all three BP categories. A p-value ≤ 0.05 indicates significant differences in cfPWV among the age categories in each blood pressure (BP) category. Points signify mean values

**Cf PWV according to age category**

![Figure 2](image-url)

**Figure 3:** Cf PWV vs age. Regression lines denote the results of linear regression of cfPWV on age for each blood pressure (BP) category. R sq. linear – R² (coefficient of determination).

![Figure 3](image-url)

**Figure 4:** Cf PWV vs brachial MAP. Regression lines denote the results of linear regression cfPWV on mean blood pressure for each blood pressure category. R sq. linear – R² (coefficient of determination).

![Figure 4](image-url)
Correlations and regressions of central arterial stiffness with age and brachial MAP
Partial Pearson’s correlation and linear regression analyses’ were conducted to examine the relationship between cfPWV (and thus central arterial stiffness) with age as well as brachial mean arterial pressure (bMAP) values [table 2 and figures 3 - 4]. The cfPWV of both NT and HTC subjects was positive and weakly though insignificantly correlated with age after adjusting for confounders (r = 0.077, p = 0.571 and r = 0.084, p= 0.556 respectively). However, there were stronger positive associations observed between cfPWV and bMAP in both NT and HTC participants after controlling for confounding than that observed for age above [table 2]. Infact, this is confirmed by the weak coefficients of determination in regression lines between cfPWV and age in figure 3 for all BP categories (r² < 0.03). After adjusting for confounders, all correlations of above parameters were insignificant for HTN subjects. On the contrary, there was significant association between cfPWV and bMAP in HTN subjects after adjusting for confounding (r=0.475, p < 0.02) with 22.6% increase in cfPWV being explained by increasing bMAP (r² = 0.226, figure 4).

Discussion
The main result of this study is the measurement and establishment of carotid femoral PWV and hence central arterial stiffness values in a population of Zambian normotensive and hypertensive participants. This is the first study in Zambia (a predominantly black population) that attempts to understand the pathophysiology of hypertension by using an already widely accepted non invasive method to measure cfPWV in an individual. These results represent a critical step in the implementation of PWV as a clinical tool for detecting subclinical organ damage in routine patient workup.

Carotid femoral pulse wave velocity and central arterial stiffness
In this cross sectional study, we demonstrate that being hypertensive (both treated and untreated subjects) is associated with elevated cfPWV values compared with being normotensive as supported in other studies [11]. In this context, a significant finding is the notable difference of cfPWV values between NT control participants and HTN participants (9.1±3.2 versus 11.4±4.2, p=0.009). In addition, HTN participants had consistently elevated cfPWV values for any given age or age category compared to NT participants. On the contrary, this increase in cfPWV with age was not significant for any of the three BP categories. Most notably, the mean cfPWV found in Zambian normotensive participants was very high; about 1.0 m/s higher than that found in previous studies involving similar populations of normotensive but white control participants (9.1m/s versus 8.1m/s respectively [6, 7, 9]. Thus Zambian normotensive subjects were more likely to develop a CVD disease including hypertension than their Caucasian subjects.

These findings show that the aorta, common carotids and other central elastic arteries of hypertensive participants are stiffer and thus less compliant than those for NT participants at any given age below 65 years. In addition, the findings that increase in cfPWV in both hypertensive and normotensive subjects was not significantly associated with advancing age even after adjusting for confounders strongly supports a few studies that have found that arteries in black populations could already be stiff from birth or early years of life when compared to white populations [6, 7]. Regrettably, even normotensive and treated hypertensive participants, although both had similar and lower cfPWV values than the untreated hypertensive group, were still likely to develop a major cardiovascular disorder considering their high cfPWV when compared to reference values of same age in previous studies [6, 7, 9]. In individuals with stiff, noncompliant arteries, the bulk of the reflected pulse wave returns to central circulation sooner, during late systole (instead of early diastole), thereby increasing cardiac after load and decreasing the pressure support for coronary perfusion [3, 11, 12]. Eventually, if anti – hypertensive therapy that is able to lower both central arterial stiffness and blood pressure is not started soon; irreversible arterial wall damage ensues including left or bilateral ventricular hypertrophy. The result is obviously poor CVD prognosis with possible death [6, 7].

Conclusion and Recommendations
To the knowledge of the authors, this is the first study in Zambia and among the few in Africa to have evaluated cfPWV in the given populations. The findings of this study show that central arteries of both categories of hypertensive participants were stiffer and thus less compliant than those in normotensive participants. Furthermore, cfPWV values found in both NT and HT subjects were higher than those found in previous studies of similar age-controlled white populations. This could partly be
explained by existing evidence that arteries in black populations could already be stiff from birth or early years of life when compared to similar white populations in addition to physiological endothelial wall degeneration. In addition, brachial blood pressure values of both treated and untreated hypertensive participants were elevated and not significantly different from each other. This means a poor BP control in the patients on treatment; a finding that implies that even treated hypertensive participants still had substantial risk of developing a major cardiovascular disorder like stroke considering their high cfPWV and peripheral blood pressures.

Therefore, these findings challenge Scientists and Clinicians alike to improve and carryout more research in the overall pathophysiology and management of hypertension. In this regard, it is hoped that Cardiologists use this information in their choice of antihypertensive therapy to choose therapies which do not only lower peripheral (brachial) pressures but also reduce central arterial stiffness which is a significant and independent predictor of cardiovascular outcome and death.

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Authors’ Contributions: FM and FMG conceived and initiated the research with FM and LL conducting data collection, data analyses and manuscript preparation of which FM supervised and edited throughout. NJS and SS helped with data analyses, interpretation and manuscript editing.

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Conflict of interest: None declared.

References