Carotid-Femoral Pulse Wave Velocity Assessment amongst 10-Year Cardiovascular Disease Risk Groups of Hypertensive Patients in Primary Health Care

Norhayati MN 1*, Hanif I 2, Rasool AH 3

1 Department of Family Medicine, School of Medical Sciences, Universiti Sains Malaysia Health Campus, 16150 Kubang Kerian, Kelantan, Malaysia
2 Klinik Kesihatan Mahligai, 16400 Bachok, Malaysia
3 Department of Pharmacology, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, 16150 Kubang Kerian, Kelantan, Malaysia

* Corresponding Author: Dr Norhayati Mohd Noor
Department of Family Medicine, School of Medical Sciences, Health Campus
Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia
Email: hayatikk@usm.my, drnorhayati_mn@yahoo.com
Tel No: +609-7676605, +6013-9388416 | Fax No: +609-7642172

Abstract

Introduction: Carotid-femoral pulse wave velocity (cfPWV), a marker of central arterial stiffness is highly predictive of cardiovascular events and helps to discriminate between patients at low and high risk of adverse cardiovascular outcomes when added to the conventional risks.

Objectives: To describe the 10-year cardiovascular disease (CVD) risk and to determine the difference in cfPWV in 10-year CVD risk groups in hypertensive patients attending primary health care.

Methods: A cross-sectional study was conducted from January to December 2012 in Out-Patient Clinic, Universiti Sains Malaysia Hospital. The CVD risk and arterial stiffness were assessed by Framingham Coronary Disease Risk Prediction Score (FRS) and cfPWV respectively. ANOVA and ANCOVA analyses were done using SPSS version 19.0.

Results: A total of 197 hypertensive patients were involved with a response-rate of 92.4%. The proportion of 10-year CVD of low (<10%), intermediate (10-20%) and high (>20%) risk groups were 71.1%, 25.4% and 3.6% respectively. ANCOVA showed no difference in cfPWV in 10-year CVD risk categories after adjusting for body mass index, waist-hip ratio, duration of hypertension, education, family history of CVD and diabetes mellitus (P=0.562).

Conclusion: Although the cfPWV was not different among the 10-year CVD risk categories in hypertensive patients, there was a significant alterations of aortic function even in low 10-year CVD risk and the cfPWV index was increased in higher risk categories. The measured level of target organ damage in each CVD risk groups would hopefully motivate more treatment that is aggressive and presumably improved health outcomes in hypertensive patients.
Key words: pulse wave analysis, cardiovascular diseases, hypertension, primary health care, Malaysia

Introduction

Pulse Wave Velocity (PWV), an index of arterial stiffness, has been widely validated as providing additional risk prediction\(^1\) independent of conventional risk factors for cardiovascular diseases (CVD).\(^2,3\) It also helps to discriminate between patients at low and high risk of adverse cardiovascular (CV) outcomes when added to the conventional risks.\(^4\) Arterial stiffness is not only a measure of Target Organ Damage (TOD) itself, but may prove useful in identifying individuals at risk for subclinical cardiac TOD.\(^5\) The measurement of PWV is accepted as the most simple, non-invasive, robust and reproducible method to determine arterial stiffness. Carotid-femoral (cf) PWV is a direct measurement and it corresponds to the propagative model of the arterial system.\(^6\) However, the availability of techniques for measuring PWV is limited to research centers.

Preventing CVD efficiently and effectively is the primary goal of healthcare organizations. However, clinical decision for prevention of CVD has focus on reduction of individual risk factors such as hyperlipidemia and hypertension rather than the overall CV risk reduction.\(^7\) Cardiovascular risk factors are associated with each other and have a multiplicative rather than additive effect on health. A slight elevation in two or more risk factors has noticeably increased the risk for CVD.\(^8\) Considering CV risk in the overall clinical management could prevent an estimated 38% more cardiac events without increasing the number of treated patients. Overall CV risk assessment could be measured using various tools, one of the most commonly used and validated coronary heart diseases (CHD) risk assessment tool was the Framingham Coronary Disease Risk Prediction Score (FRS).\(^9\)

Original Framingham studies have brought attention to hypertension, which is now the leading cause of mortality globally.\(^10\) Hypertension confers an increase in CVD risks. However, decisions regarding initiation of therapy and treatment goal are normally based on a specific blood pressure cut-off point rather than the individual’s actual level of risk.\(^11\) Treatment strategies focusing on single risk factors while ignoring the fact that even people with identical blood pressures, lipid values or diabetes can vary tremendously in the cardiac risks.\(^7\)

This study uses the FRS for assessing CV risk as a framework. Risk factors used in Framingham scoring include age, total cholesterol, high-density lipoprotein cholesterol, blood pressure and cigarette smoking and divides persons with multiple risk factors into 10-year risk for CHD of >20%, 10-20%, and <10%.\(^9\) Determining the difference in cfPWV between the 10-year CVD risk categories may help in identifying the severity of organ damage. This enables the attending physicians or health care personnel to identify patients for optimal pharmacological treatment. This study aims to describe the 10-year CVD risk and to determine the difference in cfPWV in 10-year CVD risk groups in hypertensive patients attending primary health care.
A 10-year CVD risk is defined as the probability of an individual experiencing a CV event over a 10-year period\textsuperscript{12} based on FRS,\textsuperscript{9} meanwhile, cfPWV refers to the velocity of pulse wave travel along the carotid femoral segment measured using the Sphygmocor device.

**Material and Methods**

**Study participants**

A cross-sectional study was conducted in the Out-Patient Clinic, Universiti Sains Malaysia (USM) Hospital, Kota Bharu, Kelantan. We included essential hypertensive patients based on WHO-ISH guidelines aged at or above 20 years old on pharmacological or non-pharmacological intervention. Individuals with established CHD and previous history of stroke were excluded, determine from the medical history and records.

This is part of a bigger study and thus, the sample size was determined based on other objectives that yielded the biggest sample size. It was calculated by means of sample, power and precision calculator for single sample correlation on risk factor total cholesterol. With correlation coefficient between PWV and total cholesterol of 0.20,\textsuperscript{13} precision of 0.05, power of 0.8 and 10\% non-response, the sample size calculated was 213. Systematic random sampling in the ratio of 1:2 based on attendance list in the Out-Patient Clinic was applied. The study was approved by Human Research Ethics Committee, USM and all participants gave written informed consent.

**Basic profile, physical and laboratory assessment**

The researcher obtained details by questionnaire, physical examination and laboratory assessment. Demographic, social, family and health-related data such as personal history of CVD, diabetes mellitus (DM), family history of CHD and smoking status within the previous one month\textsuperscript{9} were obtained. Physical examination included anthropometry and measurement of blood pressure. The body mass index (BMI) \[\text{[weight (kg) / height (m}^2\text{)]}\] and waist-to-hip ratio (WHR) were calculated. Blood pressure was measured while the patient was relaxed and seated with arm outstretched and supported. The measurement of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were taken using a calibrated desktop sphygmomanometer. Blood samples were taken from a peripheral vein during the morning following an 8-hour overnight fast. Fasting blood sugar and fasting lipid profile of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglyceride (TG) were collected in fluoride bottles and plain bottles, respectively and were sent to laboratory.

**Cardiovascular risk assessment**

Cardiovascular risk of each participant was assessed based on Framingham scoring system. Separate score sheets were used for men and women. Points associated with age, cholesterol and smoking status, which depend on age, HDL and SBP either treated or untreated were summed
and the 10-year coronary risk was determined. Using this score, the risk of 10-year CVD was categorized into low (<10%), intermediate (10-20%), and high (>20%).

**Carotid-femoral PWV measurement**

Participants underwent measurement of arterial stiffness in Pharmacology Laboratory in the morning following at least 3-hour fast from food, caffeine, cigarettes and alcohol. The participants were studied in a supine position after a 10-minute rest. The distance between carotid and femoral arteries was measured with a tape over the surface of the body. Arterial tonometry of the right carotid and femoral arteries was measured with a validated non-invasive SphygmoCor device (AtCor Medical, Sydney, Australia) and simultaneous electrocardiography (ECG) recording. The transit time between the onset of carotid and femoral waveforms was determined as the mean of 10 consecutive cardiac cycles against a simultaneously measured QRS complex from the ECG. Carotid-femoral PWV was calculated from the distance between measurement points and the measured time delay as follows: \( \text{cfPWV} = \frac{\text{distance (m)}}{\text{transit time (s)}} \).

**Analyses**

Data entry and analysis were done using Statistical Package for the Social Sciences, (SPSS Inc, Chicago, Illinois) version 19.0. Descriptive analysis was used to evaluate the 10-year CVD risk based on FRS. ANOVA and ANCOVA were used to determine the difference of cfPWV index in 10-year CVD risk of low, intermediate and high risk groups. Dependent variable is cfPWV index and fixed factor is 10-year CVD risk groups (low, intermediate and high) after adjusting for BMI, WHR, duration of HPT, education, family history of CHD and DM.

**Results**

A total of 213 hypertensive patients were recruited. However, only 197 responded giving a response rate of 92.4%. Non-responses were due to abnormal pulse wave and difficulty to detect pulse due to obesity. Table 1 shows the socio-demographic and medical characteristics of participants.

The mean (SD) of FRS among hypertensive subjects was 13.3 (3.66) and majority (71.1%) have low 10-year CVD risk (Table 2).

The arterial stiffness as determined by cfPWF was skewed to the right with median (IQR) of 11.5 (2.3) m/s ranging from 7.9 to 33.0 m/s. cfPWF was not different among the low, intermediate and high 10-year CVD risk groups \((P=0.562)\) after adjusted for BMI, WHR, duration of HPT, education, family history of CHD and DM (Table 3).
Discussions

The proportion of low, intermediate and high 10-year CVD risk study in our hypertensive population were 71.1%, 25.4% and 3.6%, respectively. The major proportion of low 10-year CVD risk was slightly lower compared to a study done in essential hypertensive patients in Italy (76.9%). However, a 10-year Framingham global risk in 1,509 United State hypertensive patients aged ≥ 30 years from the National Health and Nutrition Examination Survey (NHANES) 2005-2006 showed that 27.6% of subjects were low risk, 30.1% intermediate risk and 42.4% high risk of CVD. Still, the mean (SD) of FRS among hypertensive patients in this study was higher than the general populations, which varies from 9.6 to 11.4.

A bigger proportion of low risk and smaller proportion of high risk was expected in general population. A nationally representative sample of Korean women without CVD or DM showed 98.5% had low, 1.4% had intermediate and 0.1% had high 10-year risk for CHD. The proportion of low risk were often represented by three-quarter of the population but the proportion of high risk may varies from 4.8% in Korea to 10.6% in India. The varying results may be explained by different sampling methods and demographic characteristics of the participants involved. Wong et al. have added that the greater extent of obesity and related cardiometabolic risk factors have contributed to greater proportion of high risk hypertensive patients in the United States.

Arterial stiffness is an independent predictor of CV after accounting for conventional CV risk factors. This shows that arterial stiffness has a better predictive value than each of the conventional risk factors. It may be because arterial stiffness integrates the damage of the CV risk factors on artery walls, while blood pressure, plasma glucose and lipid, changes depending on the time of risk assessment, thus do not reflect the extent of damage on the arterial wall.

The groups of <10%, 10-20% and >20% 10-year CVD risk in this hypertensive population failed to show significant difference although the cfPWV in the high risk group were 1.3 m/s higher than the low and intermediate groups. On the contrary, Giannarelli et al. were able to demonstrate significantly higher cfPWV in the group with FRS ≥ 10% than in the group with FRS <10% by 1.2m/s difference. Although cfPWV was not different in 10-year CVD risk groups, significant alteration of aortic function exist even in the low 10-year CVD risk group which accounts for more than two-third of this study population.

Observed alterations at the site of arteries have a real pathophysiological link with the clinical outcome. And endothelial dysfunction is believed to be a basic phenomenon of CVD. Various cut-off points indicating significant arterial stiffness ranging from 9.6 to 13.0 m/s have been suggested as a marker of the CV risk in hypertensive patients. The latest guidelines for hypertension of the European Society of Hypertension / European Society of Cardiology has considered cfPWV higher than 10 m/s as indicative of asymptomatic TOD. In fact, a recent meta-analysis reported that 1 m/s increase in aortic PWV was associated with a 7% increased risk of a CV events for a 60-year-old man who is non-smoker, not diabetic, not on any blood pressure medication, with SBP of 120 mmHg, TC of 5.5 mmol/l and HDL of 1.3 mmol/l. The presence of organ damage at vascular level indicates a high risk condition for cardiovascular events and prompt initiation of more aggressive therapy such as pharmacological treatment.
Conclusions

Although the cfPWV was not different among the 10-year CVD risk categories in hypertensive patients, there was a significant alteration of aortic function even in low 10-year CVD risk and the cfPWV index was increased in higher risk categories. The measured level of TOD in each CVD risk groups would hopefully motivate more treatment that is aggressive and presumably improved health outcomes in hypertensive patients.

Limitations

This study used self-reported data about diagnoses of CVD and smoking status, thus the findings may be subject to response bias. FRS was based on conventional CVD risk factors that include age, total cholesterol, high-density lipoprotein cholesterol, blood pressure and cigarette smoking. Other potential confounders such as socio-economic or life-style related factors were not adjusted for in analysis.

List of abbreviations

BMI: body mass index
CV: cardiovascular
CVD: cardiovascular disease
cfPWV: carotid-femoral pulse wave velocity
CHD: coronary heart diseases
DM: diabetes mellitus
DBP: diastolic blood pressure
ECG: electrocardiography
FRS: Framingham Coronary Disease Risk Prediction Score
HDL-C: high-density lipoprotein cholesterol
LDL-C: low-density lipoprotein cholesterol
NHANES: National Health and Nutrition Examination Survey
PWV: pulse wave velocity
SD: standard deviation
SBP: systolic blood pressure
TOD: target organ damage
TC: total cholesterol
TG: triglyceride
USM: Universiti Sains Malaysia
WHR: waist-to-hip ratio

Conflict of interest statement

The authors declare that there are no conflicts of interest.
Authors' contributions

NMN has contributed in the research concept and design; HI has collected and assembled the data; NMN did the data analysis and interpretation; NMN wrote the article; RAH critically revised the article; NMN, HI and RAH approved the final version of the article.

Acknowledgement

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References

### Table 1: Socio-demographic and medical characteristics of 197 hypertensive respondents

<table>
<thead>
<tr>
<th>Variables</th>
<th>mean(SD&lt;sup&gt;a&lt;/sup&gt;)</th>
<th>n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Socio-demographic characteristics</strong></td>
<td></td>
<td></td>
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<tr>
<td>Age (year)</td>
<td>54.7(8.22)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>82(41.6)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>115(58.4)</td>
<td></td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nil</td>
<td>13 ( 6.6)</td>
<td></td>
</tr>
<tr>
<td>Primary and secondary school</td>
<td>121(61.4)</td>
<td></td>
</tr>
<tr>
<td>College and university</td>
<td>63(32.0)</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
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<tr>
<td>Non-smoker</td>
<td>154(78.2)</td>
<td></td>
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<tr>
<td>Ever smoker</td>
<td>29(14.7)</td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>14 ( 7.1)</td>
<td></td>
</tr>
<tr>
<td><strong>Medical characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of hypertension (year)</td>
<td>6.0(8.00)&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence</td>
<td>130(66.0)</td>
<td></td>
</tr>
<tr>
<td>Presence</td>
<td>67(34.0)</td>
<td></td>
</tr>
<tr>
<td>Family h/o ischemic heart disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence</td>
<td>139(70.6)</td>
<td></td>
</tr>
<tr>
<td>Presence</td>
<td>58(29.4)</td>
<td></td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence</td>
<td>73(37.1)</td>
<td></td>
</tr>
<tr>
<td>Presence</td>
<td>124(62.9)</td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg/m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>28.0( 3.66)</td>
<td></td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.9( 0.08)</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>132.7(13.12)</td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>82.0 (9.35)</td>
<td></td>
</tr>
<tr>
<td>Fasting blood sugar (mmol/L)</td>
<td>5.7( 1.50)&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Total-cholesterol (mmol/L)</td>
<td>5.4( 1.16)</td>
<td></td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol (mmol/L)</td>
<td>1.3( 0.30)</td>
<td></td>
</tr>
<tr>
<td>Low-density lipoprotein cholesterol (mmol/L)</td>
<td>3.3( 1.01)</td>
<td></td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>1.4( 1.02)&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Standard deviation  
<sup>b</sup> median (interquartile range)
Table 2: Framingham risk score and 10-year CVD risk of hypertensive respondents

<table>
<thead>
<tr>
<th>Variable</th>
<th>mean(SD&lt;sup&gt;a&lt;/sup&gt;)</th>
<th>n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Framingham point total</td>
<td>13.3 (3.66)</td>
<td></td>
</tr>
<tr>
<td>10-year CVD risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>low</td>
<td>140 (71.1)</td>
<td></td>
</tr>
<tr>
<td>intermediate</td>
<td>50 (25.4)</td>
<td></td>
</tr>
<tr>
<td>high</td>
<td>7 (3.6)</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Standard deviation

Table 3: Difference of pulse wave velocity in 10-year CVD risk groups

<table>
<thead>
<tr>
<th>10-year CVD risk</th>
<th>n</th>
<th>Desc mean&lt;sup&gt;a&lt;/sup&gt; (sd&lt;sup&gt;b&lt;/sup&gt;)</th>
<th>EMM&lt;sup&gt;c&lt;/sup&gt; (95 % CI&lt;sup&gt;d&lt;/sup&gt;)</th>
<th>F stat&lt;sup&gt;e&lt;/sup&gt; (df&lt;sup&gt;f&lt;/sup&gt;)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>140</td>
<td>12.0 (3.37)</td>
<td>12.5 (11.72, 13.23)</td>
<td>0.58 (2, 186)</td>
<td>0.562</td>
</tr>
<tr>
<td>intermediate</td>
<td>50</td>
<td>12.5 (2.80)</td>
<td>12.5 (11.50, 13.52)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>high</td>
<td>7</td>
<td>13.5 (1.56)</td>
<td>13.8 (11.40, 16.15)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Descriptive mean  
<sup>b</sup> Standard deviation  
<sup>c</sup> Estimated marginal mean  
<sup>d</sup> Confidence Interval  
<sup>e</sup> F statistic  
<sup>f</sup> degree of freedom  
<sup>g</sup> There was no interaction between fixed factor and the controlled variables; model assumptions met. Adjusted for BMI, WHR, duration of HPT, education, family history of CHD, DM