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Association Of Carotid Intima-Media Thickness With Common Carotid And Ophthalmic Artery Resistance Indices For Assessing Subclinical Atherosclerosis In Apparently Healthy Adult Nigerians

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ABSTRACT

Carotid intima-media thickness measured by B-mode Ultrasound can act as an effective tool and a non-invasive surrogate marker for the detection of subclinical atherosclerosis in apparently healthy individuals for aggressive and preventive intervention. Also, Color Doppler Ultrasound can be used as an excellent screening tool to detect subclinical atherosclerosis at an early stage in order to prevent its progression which can lead to stroke and myocardial infarction. A cross-sectional cohort study was performed to determine the association of carotid intima-media thickness with common carotid and ophthalmic artery resistance indices in apparently healthy adult Nigerians. A total of 221 consenting individuals among the staff and students of Jos University Teaching Hospital participated in this study. The carotid intima-media thickness, common carotid and ophthalmic artery resistance indices were measured by 7.5 MHz linear transducer attached to a Logiq 5 Expert Duplex ultrasound system. There was a significant positive relationship between the common carotid intima-media thickness with the resistance index of the ophthalmic artery, $R=0.237$, $p < 0.01$. Moreover, we found a hemodynamic relationship between extra-cranial (common carotid artery) and intra-cranial (ophthalmic artery) blood flow resistances. Our results indicate that OARI may be considered a new marker of subclinical atherosclerosis in apparently healthy adult Nigerians.

Keywords: Common Carotid Artery, Ophthalmic Artery, Intima-Media Thickness, Resistance Index, Pulsatility Index, Subclinical Atherosclerosis, Color Doppler Ultrasound.

INTRODUCTION

Carotid intima-media thickness (C-IMT) is widely used for risk stratification in individuals and as an end point in interventional studies because it can accurately predict future risk of clinical vascular events [1]. Therefore, it can act as an effective tool and a non-invasive surrogate marker for the detection of subclinical atherosclerosis in apparently healthy individuals for aggressive and preventive intervention [2, 3]. The C-IMT complex which is made up of various elements like the endothelial cells, connective tissue and smooth muscles is easily, safely, reliably and inexpensively measured with B-mode ultrasound but C-IMT is also found to be ethnicity dependent [3-5]. Therefore, the risk cut-off values currently in use for subclinical atherosclerosis in other parts of the world may not be suitable for the clinical use in sub-Saharan African populations. Increased C-IMT is considered as an early marker of atherosclerosis and it was reported that there is a positive association between C-IMT and the incidence of strokes of all types [6].

Carotid artery Doppler on the other hand, is also a non-invasive procedure and has no radiation hazards involved in its use. Therefore, it can be used as an excellent screening tool to detect subclinical atherosclerosis at an early stage in order to prevent its progression which can lead to stroke and myocardial infarction [7]. This is based on Doppler shift frequencies, where the ultrasound frequency of echoes from moving red blood cells is increased or decreased as the cells move toward or away from the transducer. In spectral mode, the blood flow in a specific vessel can be assessed by placing a sample gate cursor on the image of the lumen of the chosen vessel. Also an angle cursor can be used to represent the angle of intersection of the ultrasound beam with the direction of blood flow called the Doppler angle. Doppler shift frequency and the Doppler angle are used by the ultrasound system for computing the blood velocity [8]. The Doppler spectrum represents the changing velocities over time in association with the pulses of cardiac cycles and the Doppler ultrasound system displays the peak systolic, end diastolic and time-averaged maximum velocities for a selected cardiac cycle. The hemodynamic indices, Resistance Index (RI) and Pulsatility Index (PI) are ratios that are computed from various points of the spectrum using the following equations. RI = (PSV-EDV)/PSV and PI = (PSV-EDV)/TAMAX [9]. The RI and PI provide information about blood flow and resistance that cannot be obtained from the measurements of absolute velocity alone. Increased RI and PI values indicate increased resistance and decreased perfusion of the distal tissues of the artery [8]. The PI is a reflection of the vascular resistance distal to the examined artery and RI reflects the local wall extensibility and related vascular resistance [10]. Previous studies suggested that PI and the RI of Common Carotid Artery may also be used as surrogate markers of atherosclerosis in cerebral arteries [11-12].

The ophthalmic artery (OA) is incidentally the first major branch of the internal carotid artery and therefore, changes in OA blood flow can easily provide insight into various vascular disorders including the carotid artery stenosis [13]. Also, the OA Doppler investigations have anatomical advantages over the Carotid Doppler due to the absence of ultrasonic obstacles associated with systemic atherosclerosis [14]. Moreover, the computation of both RI and PI is not influenced by the Doppler angle [15]. The RI of the ophthalmic artery (OARI) is considered to be more appropriate for evaluating waveforms with high systolic and diastolic flows and it has been reported that the OARI is better than the OAPI which is more appropriate in vascular beds with mild-to-moderate resistance [16].

The aim of this study is to investigate the association between the C-IMT with Right Common Carotid Resistance Index (RCCRI) and Right Ophthalmic Artery Resistance Index (ROARI) and also to determine whether there is any hemodynamic association between the Carotid artery (extra-cranial) and Ophthalmic artery (intra-cranial) for the subclinical atherosclerotic risk in apparently healthy adult Nigerians.

MATERIALS AND METHODS

A cross-sectional study was carried out at the Jos University Teaching Hospital, Jos, Nigeria. The approval of the study protocol was granted by the Ethical Clearance Committee of the hospital and informed and written consents were obtained from randomly selected 221 participants, mostly the staff and students of the hospital. Apparently healthy 139 females and 82 males who never received treatment for cardiovascular diseases or any other chronic disease conditions were included in this study. Pregnant women and those who are below 18 years were excluded. All the participants were duly registered with their contact information, age and gender and signed the consent forms.

Measurement of body weight and height

Body weight was measured to the nearest 0.1 kg and height to nearest 0.1 cm using a Hana bathroom scale and a stadiometer respectively. The body mass index (BMI) was computed using the formula BMI = Weight (kg) / Height^2 (m^2) and the obesity status of the participants were determined according to the World Health Organization classification [17].

Measurement of C-IMT and Doppler ultrasound parameters

The right Carotid IMT as well as the blood flow velocities of right common carotid and ophthalmic arteries were performed with a GE Logiq 5 Expert Duplex Ultrasound system (USA) with a 7.5 MHz linear transducer. All measurements were taken by a qualified and experienced Sonologist with participants lying in supine position. The main hemodynamic parameters of Doppler ultrasound imaging, peak systolic velocity (PSV), end-diastolic velocity (EDV), resistance index (RI), and pulsatility index (PI) were determined. PSV is the blood flow velocity during the systolic phase of the cardiac cycle and EDV is the blood flow velocity at the end of diastolic phase of the cardiac cycle [18]. Moreover, PSV reflects the extent of vascular filling and blood supply in the vessel while EDV reflects the blood perfusion situation of the distal blood vessel tissue [19]. A decreased value of RI shows low resistance in the distal vascular bed and greater blood flow in the vessel while a decreased PI value shows that the diastolic blood flow in the vessel has increased [19]. Figures 1 and 2 show the color Doppler flow images with associate Doppler spectral waveforms of common carotid and ophthalmic arteries which can be used to determine the PSV, EDV, TAMAXV values as well as the RI and PI values.

RESULTS

The age range of the participants was 20-75 years with mean age of 36.9 ± 11.4 years. The participants were classified into six groups of 10 year intervals for easy reference. The highest number of participants was found in 30-39 years age group (76) while the least number was in 60-69 years age group (2). Figure 3 shows the classification of the age groups of the 221 participants. The BMI of each participant was computed and the participants were grouped as underweight, normal, overweight and obese according to the BMI classification as shown in Figure 4. Out of the 221 participants 132 of them (59.7%) were found to be overweight or obese and 88 (39.8%) were normal. The mean BMI of the participants was 27.4 ± 5.6 kg/m^2. Descriptive statistics of all the study parameters are given in Table 1. The mean right common carotid intima-media thickness (RCCIMT) was found to be 0.053 ± 0.015 cm. The mean values of peak systolic velocity and end diastolic velocity of the right common carotid (RCCPSV and RCCEDV) were 99.5 ± 25.1 cm/s and 26.8 ± 7.1 cm/s respectively while that of the right ophthalmic artery (ROAPSV and ROAEDV) were 30.5 ± 7.3 cm/s and 8.6 ± 2.2 cm/s respectively. From the Pearson correlations given in Table 2, it can be seen that out of hemodynamic indices only ROARI had a significant positive correlation with RCCIMT ($R = 0.237$, $p < 0.01$). However, we did not find any significant correlation between RCCIMT and RCCRI. Moreover, RCCRI and ROARI had a significant positive correlation ($R = 0.279$, $p < 0.01$). This means that there is a significant association between right common carotid resistance index (extra cranial) and right ophthalmic artery resistance index (intra cranial). The linear regression graph between these two parameters is shown in Figure 5 with a linear relationship given by ROARI = 0.27 RCCRI + 0.53.

The cut-off value of ROARI for subclinical atherosclerotic risk was determined by Receiver Operating Characteristic (ROC) curve analysis to be 0.735 (Sensitivity = 80.0%, Specificity = 57.3% with an area under the curve (AUC) = 0.716 (95% Confidence interval between 0.604 -0.828). The ROC curve of ROARI is shown in Figure 6.

DISCUSSION

Diagnostic Ultrasound is the only non-invasive imaging modality recommended by the American Heart Association for inclusion in risk assessment for cardiovascular disease (CVD) [20]. Ultrasound Carotid-IMT values are found to correlate well with pathological measurements and are potent predictors of myocardial infarction and stroke. It was reported that for each 0.1mm increase in common carotid IMT, the risk of myocardial infraction increases by 11% [21]. Also, a previous study revealed that carotid artery stenosis can decrease the blood flow velocity in the ophthalmic artery when the stenosis is greater than 70% [22]. Grima et al. reported that ophthalmic artery resistance index (OARI) could be considered a surrogate of cardiovascular risk in HIV- 1- infected patients [23]. The results of this study indicate that OARI may have a potential as a new surrogate marker of subclinical atherosclerosis in apparently healthy populations. Moreover, we found a linear equation connecting RCCRI and ROARI which can be considered as a hemodynamic relationship between the extra- and intra-cranial blood flows in common carotid and ophthalmic arteries. The PSV and EDV mean values obtained in this study (30.5 ± 7.3 and 8.6

± 2.2) are comparable with some of the previous studies (31.0 ± 3.0 and 9.0 ± 1.0) [24], (31.4 ± 3.7 and 9.1 ± 2.3 [25] and (34.7 ± 6.4 and 8.0 ± 1.7) [26]. The mean resistance index of the ophthalmic artery in this study, ROARI = 0.73 ± 0.06 is also comparable with others 0.71 ± 0.03 [24], 0.71 ± 0.05 [25] and 0.77 ± 0.04 [26].

CONCLUSION

To our knowledge, this is the first study to compare ophthalmic artery resistance index (OARI) and common carotid intima-media thickness (C-IMT) in apparently healthy adult Nigerian population in order to establish that OARI could be considered a surrogate marker of subclinical atherosclerosis. In this study, we also found a linear relationship between the extra- and intra-cranial hemodynamic indices (common carotid and ophthalmic artery resistance indices).

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Table 1 Descriptive statistics of the study parameters

Descriptive Statistics					
	N	Minimum	Maximum	Mean	Std. Deviation
AGE	221	20	75	36.92	11.358
BMI	221	18.15	44.92	27.4126	5.58020
RCCIMT	221	.020	.100	.05329	.014718
RCCPSV	221	53.6	173.1	99.532	25.0711
RCCEDV	221	9.3	52.0	26.764	7.0615
RCCPI	221	1.00	4.88	1.7388	.60779
RCCRI	221	.60	.87	.7248	.05852
ROAPSV	221	19.5	58.1	30.502	7.2545
ROAEDV	221	4.5	18.3	8.566	2.1662
ROAPI	221	.81	3.95	1.5368	.52416
ROARI	221	.56	.87	.7265	.05702

Table 2 Pearson correlations of RCCIMT with hemodynamic indices

Correlations						
		RCCIMT	RCCPI	RCCRI	ROAPI	ROARI
RCCIMT	Pearson Correlation	1	.027	-.126	.066	.237**
	Sig. (2-tailed)		.691	.061	.328	.000
	N	221	221	221	221	221
RCCPI	Pearson Correlation	.027	1	.628**	.092	.256**
	Sig. (2-tailed)	.691		.000	.174	.000
	N	221	221	221	221	221
RCCRI	Pearson Correlation	-.126	.628**	1	.144*	.279**
	Sig. (2-tailed)	.061	.000		.032	.000
	N	221	221	221	221	221
ROAPI	Pearson Correlation	.066	.092	.144*	1	.475**
	Sig. (2-tailed)	.328	.174	.032		.000
	N	221	221	221	221	221
ROARI	Pearson Correlation	.237**	.256**	.279**	.475**	1
	Sig. (2-tailed)	.000	.000	.000	.000	
	N	221	221	221	221	221

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

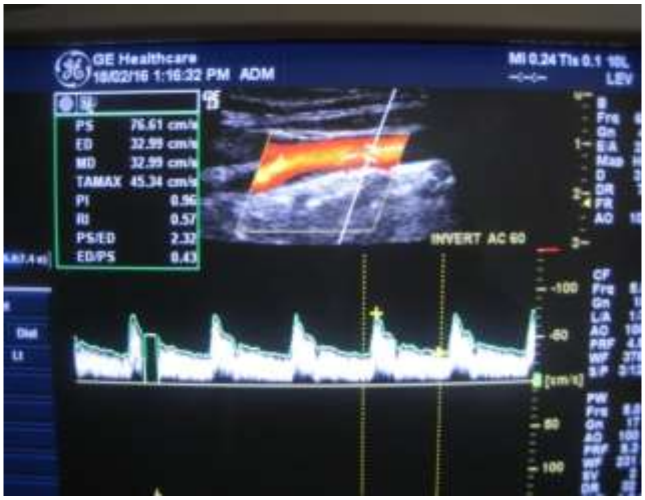

Figure 1 Doppler Color Image and Spectral Waveform of Common Carotid Artery

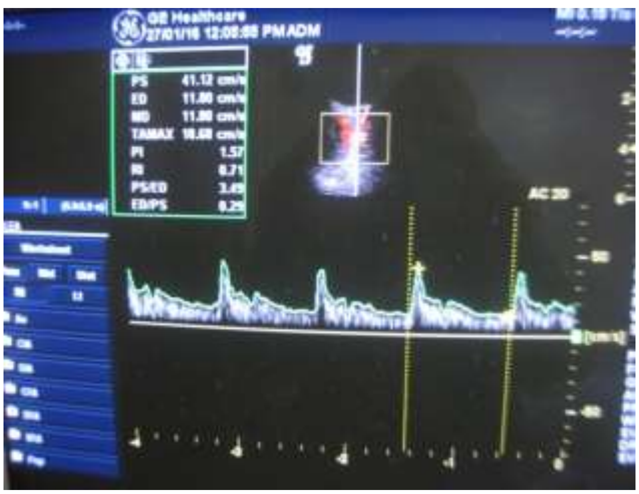

Figure 2 Doppler Color Image and Spectral Waveform of Ophthalmic Artery

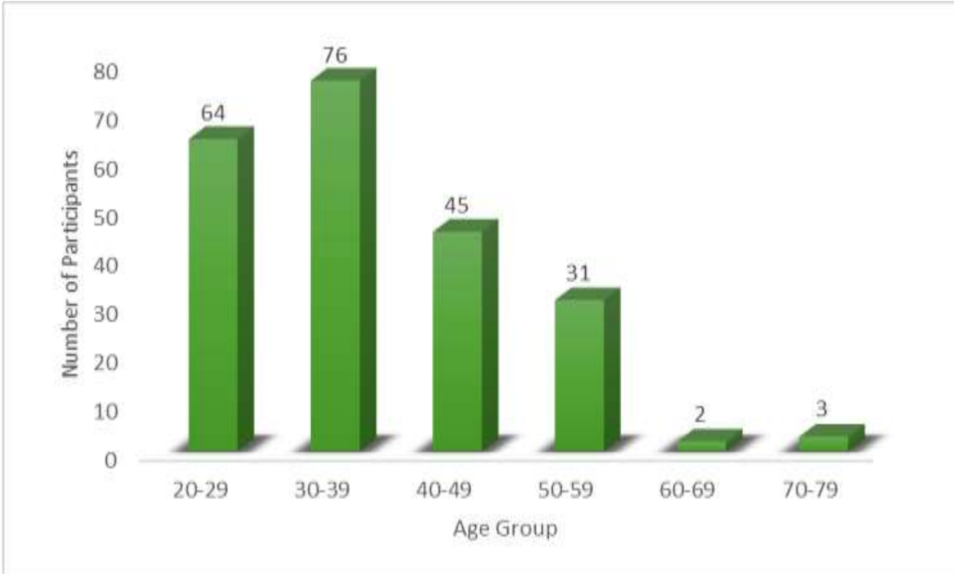

Figure 3 Classification of Age Groups of the 221 Participants.

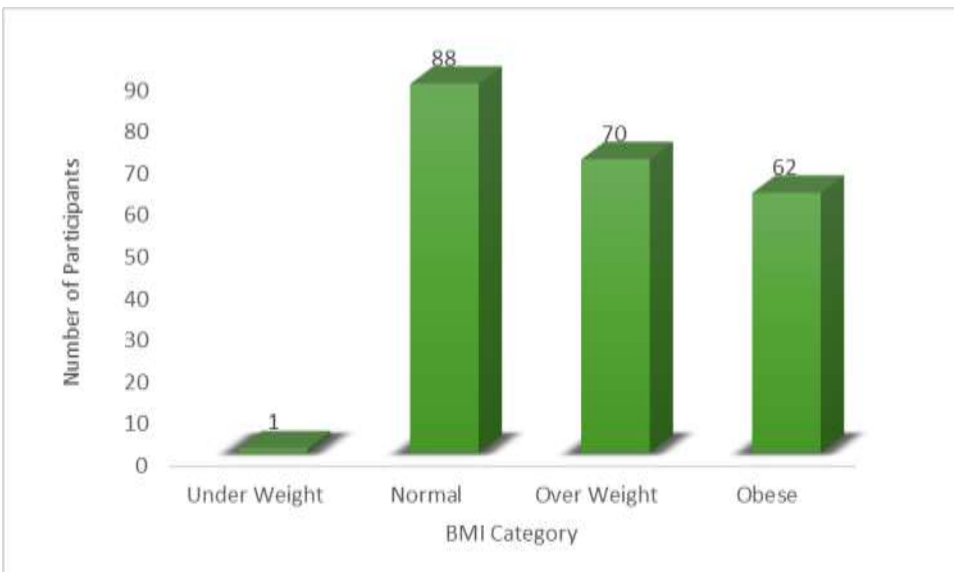

Figure 4 Classification of Obesity Status of the 221 Participants According to BMI

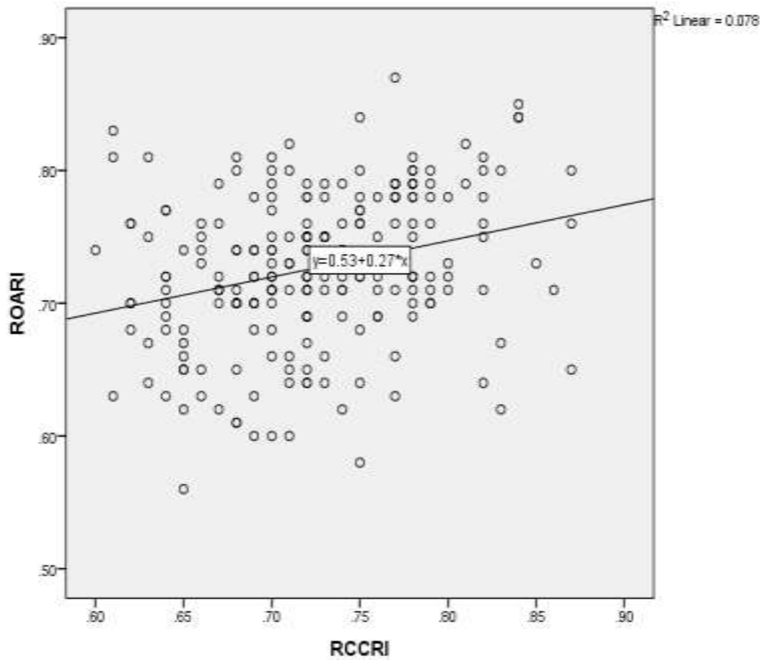

Figure 5 Linear Regression graph between ROARI and RCCRI

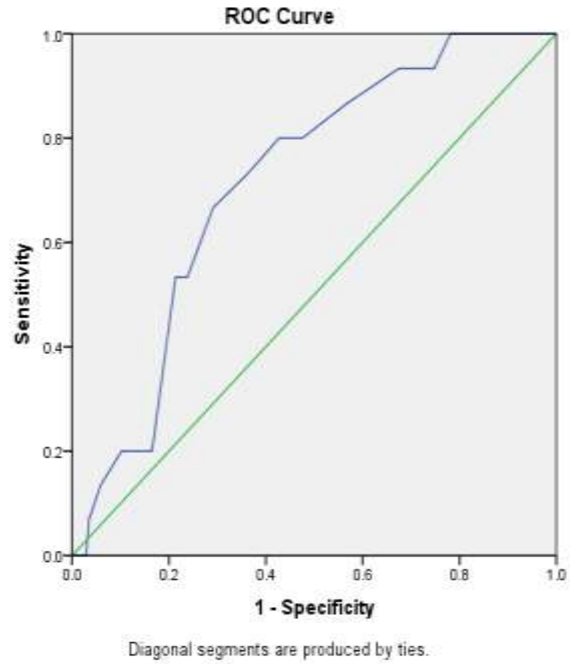

Figure 6 ROC Curve of ROARI